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APASL 2022 SEOUL

LEAP Together to the Future of Hepatology

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Abstract S1

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ABSTRACTS

Abstract

Plenary Session

Plenary Session 1

[L-OP-1287]

Multiplexed digital spatial protein profiling reveals distinct phenotypes of portal mononuclear phagocytes in livers with advanced fibrosis

Pil Soo Sung[1], Chang Min Kim[2], Jaejun Lee[1], Jung Hoon Cha[1], Jin Young Park[2], Yun Suk Yu[2], Eun Sun Jung[1], Si Hyun Bae[1]

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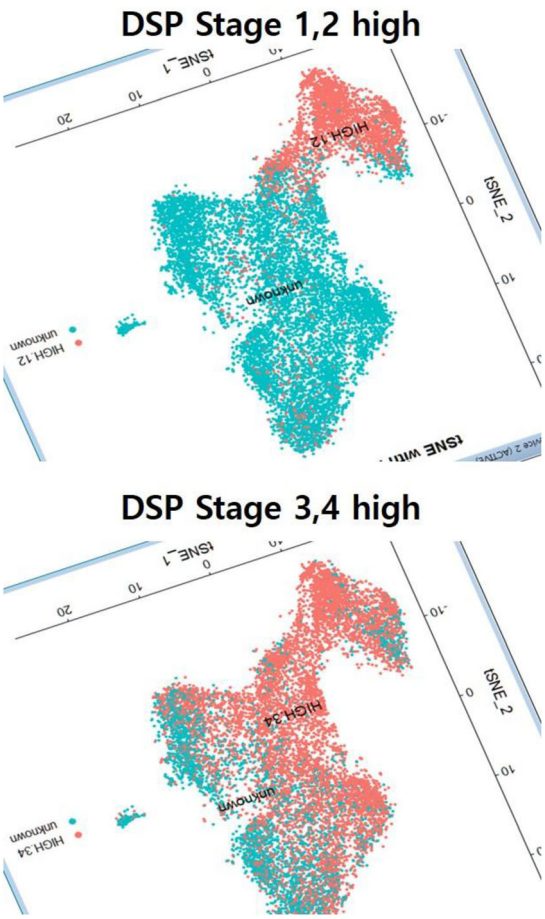
Objectives: In this study, using multiplexed digital spatial profiling, we aimed to identify distinct phenotypes of portal mononuclear phagocytes in livers with advanced fibrosis.
Materials and Methods: Snap-frozen liver tissues with various chronic liver diseases at different fibrosis stages were subjected to spatially-defined protein-based multiplexed profiling (Nanostring GeoMX^{TM}). CD3, CD68, and α-SMA markers were used to identify specific cell types. Single-cell RNA-Seq analysis was performed using GEO datasets from normal livers and cirrhotic livers.
Results: Eighty-eight portal ROIs were selected for the spatial profiling, with 41 ROIs classified into "inflammatory" (high T cell number) and 47 ROIs classified into "non-inflammatory" (low T cell number). In "non-inflammatory" ROIs, which were used for the further analyses, there were liver tissues with various fibrosis grade as F0 (n = 7), F1 (n = 12), F2 (n = 3), F3 (n = 12), and F4 (n = 13). In CD68^{+} cells, protein markers for activation of mononuclear phagocytes (CD66b, STING, OX40L, VISTA, CD80) were detected significantly stronger in early stage fibrosis (F1 and F2) than advanced fibrosis (F3 and F4). Conversely, CD68 and HLA-DR, which are known to be upregulated in scar-associated macrophages (SAMacs) rather than Kupffer cells, were detected stronger in advanced fibrosis. Combined analysis of single cell RNA-Seq data from GEO datasets (GSE136103) and spatially-defined protein-based multiplexed profiling revealed that most proteins upregulated in F1 and F2 livers in portal CD68^{+} cells were specifically marked in Kupffer cell clusters, whereas proteins upregulated in F3 and F4 livers were marked in SAMacs, Kupffer cells, and tissue monocytes, highlighting the different phenotypes of portal CD68^{+} cells according to the fibrosis stages.
Conclusion: This is the first study that used spatially-defined protein-based multiplexed profiling demonstrating the critical difference in the phenotypes of mononuclear phagocytes between livers of early stage fibrosis and those of late stage fibrosis.



[OP-1010]

Spectrum of Wnt/β-catenin oncogenic "drivers" in serially occurring HCC nodules; Needs of tumorized therapy

Masao Omata[1,3], Kenji Amemiya[2], Yosuke Hirotsu[2], Shuntaro Obi[4], Hitoshi Mochizuki[1,2], Atsushi Takano[5], Yuji Iimuro[5]

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Objectives: Tumor nodules carrying Wnt/β-catenin signaling pathway abnormalities were shown to have unique features of pathology (rich bile production/pseudo tubular formation), of imaging findings (EOB-MRI high) and of poor ICI response. However, HCC occurrence is multi-centric and metachronous in many occasions. In this communication, we disclosed the spectrum of dynamic changes among nodules with Wnt/β-catenin abnormalities.
Materials and Methods: Surgically resected 135 tumor nodules from 61 patients were laser micro-dissected and NG-sequenced by in-house panel (72 genes, spanning 177,048 nt) including 5 (CTNNBI, AXIN, APC, NCORI, F6F19) genes of Wnt/β-catenin signaling pathways.
Results: We first revealed the involvement of Wnt/β-catenin signaling pathways abnormalities in 16 patients with solitary nodules. In 6 of 16 (38%), abnormality of the pathway was detected. We then studied 45 cases with multiple recurrence of HCC (119 nodules). Of these 119 nodules, only 22 (18%) had Wnt/β-catenin abnormalities. Of the 45 cases, 15 cases (33%) had at least one nodule having Wnt/βabnormality, but only 3 cases (20%) constantly had Wnt/β-catenin signaling pathway abnormality thereafter and the remaining 80% (12 cases) had other types of "drivers" in recurrent nodules.
Conclusion: In real life, serial occurrence of HCC is so common. This study indicates the change or switching of the drivers to promote carcinogenesis occurs from nodules to nodules. Only in 20% of cases they are constantly showing Wnt/β-catenin abnormality and others had different drivers. For the future, appropriate tumorized therapy is needed.

[OP-1086]

Sensitive and accurate viral integration detection in HBV-associated hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) is prevalent worldwide and with high cancer-related mortality. Hepatitis B virus (HBV) infection is one of the key etiological risk factors for HCC. The virus can integrate into human genome and lead to hepatocarcinogenesis through different underlying mechanisms by activating oncogenes or disrupting tumor suppressors. Sensitive and accurate detection of HBV integration is crucial to the investigation of molecular pathogenesis of HCC.
Materials and Methods: In our original algorithm of Virus-Clip, there are several limitations regarding the issues of single-read consideration, PCR duplicates, false positives, and low sensitivity towards short chimeric fragments. Pinpointing to these shortcomings, we adopted specific measures, e.g. read realignment, clustering and procedural streamlining, to develop an enhanced version of Virus-Clip (we denote as Virus-Clip2 thereafter). We have generated simulated datasets that focused specifically on the complexity of sequencing coverage, number of integration sites, insert size and intra-tumoral heterogeneity. Performance comparison was performed by testing Virus-Clip2 against other tools. We also tested Virus-Clip2 in different public and in-house HCC datasets.
Results: We demonstrated that Virus-Clip2 is of high sensitivity, specificity and runtime efficiency for detecting HBV integration. In particular, Virus-Clip2 outperformed BATVI and SurVirus in terms of precision, F1-score, recall and AUC value. Virus-Clip2 is a strand-specific virus integration detection tool, which can identify the viral integration direction. Notably, regarding the landscape of HBV integration in HCC, we were able to sensitively and accurately identify recurrent HBV integration events related to TERT, KMT2B and CCNE1.
Conclusion: Virus-Clip2 has outstanding and all-rounded performance in detecting HBV integration. It facilitates the genome-wide investigation of viral integration in different HBV-associated diseases. Moreover, our findings on HBV integration landscape using different HCC datasets enables better understanding of the mechanism of HBV-associated hepatocarcinogenesis.

[OP-0463]

Validation of a new HBV cure strategy in HBV infected uPA/SCID chimeric mice

Yong-Yuan Zhang[1], Bai-Hua Zhang[1], Yuanping Zhou[2], Steve Horrigan[3], Fabien Zoulim[4], David Baltimore[5]

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Objectives: Clinical evidence shows frequent serum viral population turnover in chronic HBV infection, which reflects frequent cccDNA turnover in the livers and highlights frequent new rounds of infection in CHB patients. To cure HBV infection, new rounds of infection must be blocked. This study aimed to validate a new HBV cure strategy that constantly blocks new rounds of infection in an HBV infected animal model.
Materials and Methods: An optimized AAV vector that carries human anti-HBs genes was used to express sustained high level of anti-HBs antibody. HBV infected uPA/SCID mice were treated with AAV vector expressing malaria antibody or anti-HBs antibody at day 49 post infection. Serum HBV DNA and HBsAg level were monitored until day 183 and liver HBV DNA was determined through 20 random samplings of each autopsied liver.
Results: $>$ 100 ug/mL expressed antibodies were sustained for at least 200-day after a single injection. Blocking new rounds of infection retarded HBV infection and lowered HBV infection level by up to $>$ 100-fold in anti-HBs antibody treated group compared to malaria antibody-treated group. HBV functional cure was achieved in one animal with viremia of 4.6E8 HBV DNA copies/ml. Average cccDNA level $\leq$ 1 copy/cell was detected in 260 (46%) of 566 cccDNA samplings, suggesting cccDNA was already lost in a fraction of infected cells in HBV infected human livers of chimeric mice. Blocking new rounds of infection significantly expands a net cccDNA loss including nearly complete cccDNA loss in one animal and lowers Intrahepatic rcDNA level by 4,000 to 10,000 copies/cell across all 9

livers with anti-HBs treatment compared to malaria antibody treated animal.

Conclusion: Blocking new rounds of infection profoundly impacts HBV infection at both cccDNA and rcDNA level and is required for durable HBV cure. This engineered immunology-based HBV cure drug is adaptive immunity independent and may remedy anti-HBs deficiency in CHB patients.

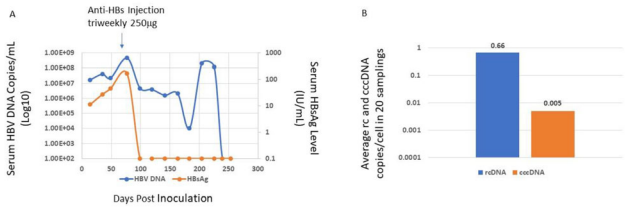

Figure 1. HBV functional cure in animal 970. A. Showing both viremia and serum HBsAg became undetectable after starting anti-HBs treatment. The lower limit of detection for serum HBV DNA is 100 copies/ml and 0.1IU/ml for HBsAg. **B.** Average intrahepatic rcDNA and cccDNA copies/cell from 20 randomly liver samplings.

Plenary Session 2

[OP-0935]

Discovering the potential mortality-associated gut microbial biomarker in liver cirrhosis condition

Satya Priya Sharma[1], Eunju Park[1], Haripriya Gupta[1], Sung- Min Won[1], Jin-Ju Jeong[1], Raja Ganesan[1], Yoseph Asmelash Gebru[1], Dong Joon Kim[1], Ki Tae Suk[1]

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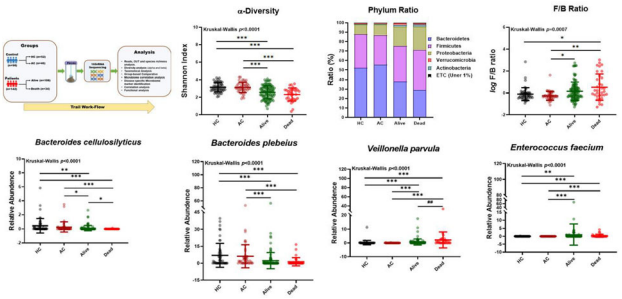
Objectives: Liver Cirrhosis is the one of leading cause of liver-related death, globally and shift in gut microbiome composition is linked with liver cirrhosis diseases severity. Here, we compared the gut microbiome in alive and died patients with liver cirrhosis to pin down the mortality-associated gut microbial biomarkers in cirrhosis condition.

Materials and Methods: 240 Stool samples (control + cirrhosis patients) were subjected to variable region based (V3-V4) 16S rRNA sequencing by using the MiSeq sequencer on the illumina platform and Microbiome Taxonomic Profiling was performed till species level to discover the mortality-associated gut microbial biomarkers.

Results: Out of total 240 individual's 142 were cirrhotic patients, 52 were healthy control (HC) and 46 were alcoholic healthy control (AC). In cirrhotic patients, 33% were females (n = 47, age 61 ± 13.42 years) and mortality rate was 24% (n = 34, age 60.88 ± 9.12 years), whereas higher mortality rate was observed in male (74%) comparative to female (26%) cirrhotic patients. All 142 patients were classified in two groups: Dead (n = 34), and alive (n = 108, age 57.42 ± 11.24 years). Gut microbial composition in dead group showed significant reduction in Operational Taxonomic Units (OUT's) abundance, phylogenetic diversity, and α-diversity without suppressing the total bacterial number compared with both control groups. Relative abundance of Bacteroidetes phylum was significantly decreased consequently increased the F/B ratio significantly. Furthermore, the Proteobacteria and Actinobacteria were also significantly increase in dead patients, Whereas Firmicutes was non-significantly increased in dead patients. At species level, Bacteroides cellulosilyticus, Bacteroides plebeius, Faecalibacterium prausnitzii, exhibited a significant decline and Veillonella parvula, Enterococcus faecium showed significant upsurge in dead patients compared to control.

Conclusion: In this comparative analysis, we have identified mortality-associated gut microbial biomarkers which can be targeted for further research to produce robust diagnostic and therapeutic tool for early detection and management of the Liver cirrhosis condition.



[OP-0027]

Tenofovir alafenamide for Chinese pregnant women with active chronic hepatitis B: A multicenter prospective study

Qing-Lei Zeng[1], Hong-Xu Zhang[2], Ji-Yuan Zhang[3], Guang-Ming Li[4], Ying-Hua Feng[5], Guo-Fan Zhang[6], Jiang-Hai Xu[7], Wan-Bao Lin[8], Guang-Hua Xu[9], Guo-Qiang Zhang[10], Wei Li[11], Ning Song[12], Meng Wang[13], Zhi-Min Chen[14], Guang-Lin Cui[15], Yi-Hua Zhou[16], Zu-Jiang Yu[1], Fu-Sheng Wang[3]

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Objectives: Data on long-term tenofovir alafenamide (TAF) therapy for pregnant women with active chronic hepatitis B (CHB, immune clearance and reactivation phases) are lacking. The aim of this study was to investigate the safety and effectiveness of TAF in pregnant women with active CHB and their infants.

Materials and Methods: Pregnant women with active CHB treated with TAF and tenofovir disoproxil fumarate (TDF) were enrolled in

this multicenter prospective study, and infants received standard immunoprophylaxis. The primary outcomes were rates of adverse (safety) events in pregnant women and defects in infants and fetuses. The secondary outcomes were virological responses in pregnant women, infants' safety, hepatitis B surface antigen (HBsAg) status, and growth conditions. The pregnant women and their infants were followed until at least 6 months after delivery and 7 months of age, respectively.

Results: One hundred three and 104 pregnant women were enrolled, and 102 and 104 infants were born in the TAF and TDF groups, respectively. In the TAF group, the mean age, gestational age, alanine aminotransferase level, and viral loads at treatment initiation were 29.3 years, 1.3 weeks, 122.2 U/L, and 5.1 $\log_{10}$ IU/ml, respectively. TAF was well tolerated, and the most common adverse event was nausea (29.1%) during a mean of two years of treatment. Notably, 1 (1.0%) TAF-treated pregnant woman underwent induced abortion due to noncausal fetal cleft lip and palate. No infants in either group had birth defects. In the TAF group, the hepatitis B e antigen seroconversion rate was 20.7% at postpartum month 6, infants had normal growth parameters, and no infants were positive for HBsAg at 7 months of age. The TDF group had comparable safety and effectiveness profiles.

Conclusion: TAF administered throughout or beginning in early pregnancy is generally safe and effective for pregnant women with active CHB and their infants.

Characteristics of pregnant women at baseline	TAF (n=103)	TDF (n=104)	P value
Age, years	29.3 ± 4.7	29.4 ± 4.4	0.935
Gestational age, weeks	1.3 ± 14.6	1.0 ± 12.1	0.913
HBeAg positivity	82 (79.6)	88 (84.6)	0.347
HBV DNA, $\log_{10}$ IU/ml	5.1 ± 3.4	4.6 ± 3.4	0.138
ALT, U/L	122.2 ± 97.5	94.6 ± 78.3	0.051
Treatment durations, weeks	96.1 ± 24.4	98.7 ± 21.9	0.285
Most common maternal adverse events during treatment-Nausea	30 (29.1)	33 (31.7)	0.684
Most common maternal complications during treatment-Premature rupture of membranes	13 (12.6)	14 (13.5)	0.858
Characteristics of infants at birth	n=102†	n=104	
Gestational age, weeks	39.3 ± 1.1	39.3 ± 1.2	0.982
Apgar score at 1 minute	9.7 ± 0.5	9.5 ± 0.5	0.031
Congenital defects or malformations	1/103 (1.0)	0/104 (0)	0.498
Anthropometric indices‡	Normal	Normal	All>0.05
At postpartum month 6 for pregnant women	n=102	n=104	
HBV DNA undetectable	101 (99.0)	103 (99.0)	1.000
ALT normalization	93 (91.2)	97 (92.3)	0.575
HBeAg seroconversion	17/82 (20.7)	15/88 (17.0)	0.539
At 7 months of age for infants	n=102	n=104	
Anthropometric indices‡	Normal	Normal	All>0.05
HBsAg positive infants	0 (0)	0 (0)	-
At postpartum month 18 for pregnant women	n=30	n=32	
Cumulative HBeAg seroconversion	20/82 (24.4)	21/88 (23.9)	0.936
At 18 months of age for infants	n=30	n=32	
Anthropometric indices‡	Normal	Normal	All>0.05

Data are presented as the means ± standard deviations, n (%), or n/N (%). †One pregnant woman exposed to agricultural chemicals during early pregnancy who initiated TAF from 12 weeks plus 2 days of gestation underwent induced abortion at 23 weeks plus 4 days of pregnancy due to the diagnosis of cleft lip and palate for the fetus at 22 weeks of gestation, this fetus was regarded as a congenital defect (most likely not related to TAF, because the developmental processes of the lip and palate are completed by 6-10 weeks of embryogenesis) but did not have other parameters to be included in this table. ‡Including the parameters of weight, height, and head circumference.

[OP-0262]

Prognostic factors for patients with primary biliary cholangitis treated with a combination of ursodeoxycholic acid and bezafibrate

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Objectives: Ursodeoxycholic acid (UDCA) is a first-line treatment for primary biliary cholangitis (PBC), while approximately 20–30% of patients do not respond well to UDCA. In Japan, bezafibrate (BZF) has been used as a de-facto second-line treatment, and we demonstrated that a combination therapy of UDCA and BZF was significantly associated with an improved liver-transplantation (LT) free survival compared to UDCA monotherapy, taking advantage of a large-scale retrospective cohort comprising 9,919 patients in the PBC registry (J Hepatol, 2021). Nevertheless, some patients resulted in death or LT even with UDCA and BZF treatment. In this study, we investigated prognostic factors contributing to poor outcome in patients treated with a combination of UDCA and BZF.

Materials and Methods: Among 9,919 patients with PBC, we enrolled those treated with UDCA and BZF and without any missing variable in terms of sex, age, diagnosis year, symptoms at presentation, bilirubin and albumin at presentation, and outcome. Then we analyzed the association of these variables with liver-related death or LT using Cox proportional hazard model.

Results: We enrolled 889 patients treated with UDCA and BZF (male 139, mean age 54.8 ± 10.7) in this study. Mean observation period was 9.9 ± years, and liver-related death or LT occurred in 16 patients (1.8%; death in 15 and LT in 1). Lower albumin, higher bilirubin, and more symptomatic were noted in these 16 patients compared to other 873 patients. By Cox proportional hazard model, serum albumin < 3.5 g/dL (adjusted HR 5.24, 95%CI 1.62–16.9, $p = 0.006$) and bilirubin ≥ 1.5 mg/dL (aHR 18.236, 95%CI 6.48–51.3, $p = 0.001$) at presentation were significantly associated with liver-related death or LT.

Conclusion: Lower albumin and higher bilirubin were significantly associated with poor outcome in PBC patients treated with a combination of UDCA and BZF, suggesting that patients at advanced, cirrhotic stage were at higher risk of mortality even with UDCA and BZF treatment.

[OP-0145]

Outcomes of living liver donors are worse than those of matched healthy controls: Nationwide cohort study

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Objectives: Donor death is the most serious complication of living liver donation, but is reported rarely. We investigated the actual

mortality of living liver donors (LLDs) compared with matched control groups based on analysis of the Korean National Health Insurance Services (NHIS) database.

Materials and Methods: This cohort study included 12,372 LLDs who donated a liver graft between 2002 and 2018, and were registered in the Korean Network for Organ Sharing. They were compared to three matched control groups selected from the Korean NHIS and comprising a total of 123,710 subjects: healthy population (Group I); general population without comorbidities (Group II); and general population with comorbidities (Group III).

Results: In this population, 78.5% of living liver donors were 20–39 years old, and 64.7% of all donors were male. Eighty-nine donors (0.7%) in the LLD group died (68 males and 21 females), a mortality rate (1000 person/year) of 0.91 (0.74–1.12). Mortality rate ratio and the adjusted hazard ratio of the LLD group was 2.03 (1.61–2.55) and 1.71 (1.31–2.25) compared to Control Group I, 0.75 (0.60–0.93) and 0.63 (0.49–0.82) compared to Control Group II, and 0.58 (0.46–0.71) and 0.49 (0.39–0.60) compared to Control Group III. LLD group, depression, and lower income were risk factors for adjusted mortality. The incidence of liver failure, depression, cancer, diabetes, hypertension, brain infarction, brain hemorrhage, and end-stage renal disease in the LLD group was significantly higher than in Control Group I.

Conclusion: Outcomes of the LLD group were worse than those of the matched healthy control group despite the small number of death and medical morbidities in this group. LLDs should receive careful medical attention for an extended period after donation.

Plenary Session 3

[OP-0161]

Among simple non-invasive scores, Pro-C3 and ADAPT best exclude advanced fibrosis in Asian patients with MAFLD

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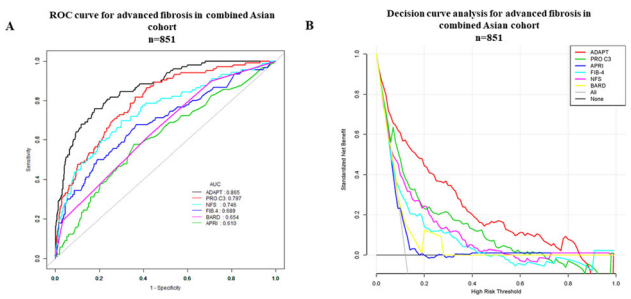
Objectives: With metabolic dysfunction-associated fatty liver disease (MAFLD) incidence and prevalence increasing, it is necessary to identify patients with advanced fibrosis (F3-F4). We evaluated the performance of new biomarkers and algorithms for diagnosing advanced liver fibrosis in an Asian population.

Materials and Methods: Data from two prospective Asian cohorts (851 biopsy-confirmed MAFLD [578 from Wenzhou, 273 from Hong Kong]) were studied. The association between N-terminal propeptide of type 3 collagen (PRO-C3) and the histologic severity of liver fibrosis was analyzed by multivariable linear regression. The area under the receiver operating characteristic curve was used to test the diagnostic performance of serum PRO-C3 and the ADAPT score for advanced fibrosis and compared to other established tests.

Results: Serum PRO-C3 increased progressively across stages of liver fibrosis (all $P < 0.01$) and correlated with advanced fibrosis ($P < 0.001$). The ADAPT score had an area under the receiver operating characteristics curve (AUROC) of 0.865 (95% confidence interval (CI) 0.829–0.901) for advanced fibrosis; the accuracy, sensitivity and negative predictive values (NPV) were 81.4%, 82.2% and 96.1%, respectively. This was better than PRO-C3 alone or other non-invasive biomarkers of advanced fibrosis (aspartate aminotransferase-to-platelet ratio index, Fibrosis-4, BARD, and NAFLD fibrosis score). In all subgroup analyses (including gender, age, diabetes, NAS, BMI and ALT), ADAPT has good diagnostic performance.

Conclusion: PRO-C3 and the ADAPT score reliably exclude advanced fibrosis in MAFLD patients and reduce the need for liver biopsy.



[OP-1119]

The dynamics of hepato-cardiac axis: A case–control study of left ventricular diastolic dysfunction in liver cirrhosis

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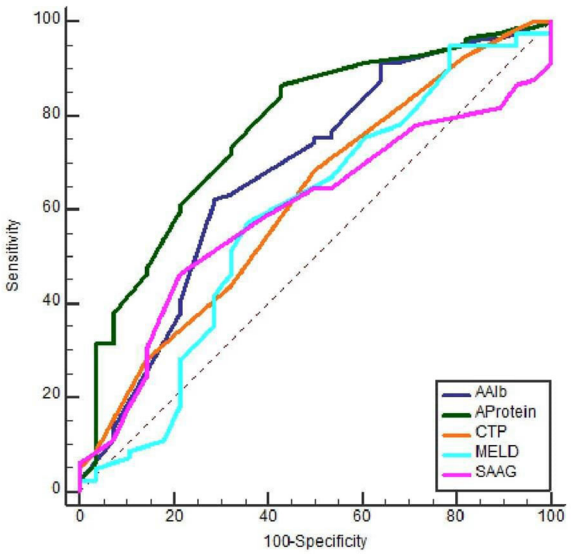
Objectives: Left Ventricular Diastolic Dysfunction(LVDD) is a formè frusté of Cirrhotic Cardiomyopathy. Our study aimed to evaluate the relationship of LVDD with the etiology of liver cirrhosis(LC), Severity, Sarcopenia and Short-term survival.
Materials and Methods: We prospectively screened 250 patients with LC. All patients underwent 2D-echocardiography with tissue Doppler imaging. LVDD was diagnosed based on the American Society of Echocardiography guidelines 2016.
Results: 203 patients were included. The mean age was 52.76 ± 10 years. 84.7% were males. 139(68.5%) had LVDD and 64(31.5%) did not have LVDD. 78(38.4%) had grade 1 LVDD and 61 (30%) had grade 2 LVDD. Alcohol in 63.9% and Non alcoholic steatohepatitis(NASH) in 18.2% were the main etiologies. LVDD was present in 65.9% of alcoholic cirrhosis and 86.5% of NASH cirrhosis. NASH had a greater predilection to develop LVDD($p < 0.001$). Child–Pugh class, Model for end stage liver disease(MELD) ($p = 0.001$), Ascites ($p < 0.001$), multiple large volume paracentesis ($p < 0.001$), history of Hepatic encephalopathy (HE) ($p < 0.002$) and Acute kidney injury (AKI) ($p < 0.001$) had significant correlation with LVDD. 76.23% patients with confirmed Sarcopenia had LVDD. Sarcopenia was similar between the grades of LVDD. 80.9% of the 68 patients with a history of obesity had LVDD. 1/3rd patients died during the study period. Mortality was 72%, 25% and 11% in patients with grade 2, grade 1 and grade 0 LVDD respectively. LVDD significantly correlated with survival ($p < 0.01$). Carotid intima-media thickness (CIMT) had a significant correlation with LVDD with a cut-off of 0.55. AUROC was maximum for Ascitic fluid Protein (0.78) and also independent predictor of LVDD (Youden index cut-off > 0.8 g/dl).
Conclusion: NASH related cirrhosis is at higher risk of developing LVDD. Child–Pugh score, MELD, Sarcopenia, Ascites, AKI, prior history of HE, history of obesity and CIMT are significantly associated with LVDD. Patients with Ascitic fluid protein > 0.8gm/dl should be evaluated for LVDD. Survival has a linear relationship with the grades of LVDD.

Figure: ROC curve of Ascitic albumin, Ascitic Protein, CTP , MELD and SAAG to predict LVDD



[OP-0349]

Association between statin use and risk of hepatocellular carcinoma recurrence following liver resection: A nationwide cohort study

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Objectives: The majority of patients with hepatocellular carcinoma (HCC) following curative liver resection experience tumor recurrence. Statin use is associated with a reduced risk of HCC development; however, the association between statin use and HCC recurrence remains unclear. This study aimed to investigate the effect of statin use on HCC recurrence after liver resection.
Materials and Methods: A nationwide cohort study was performed with data from the National Health Insurance Service Database in Korea. Among 65,101 HCC patients who underwent liver resection between January 2002 and December 2017, we finally included 21,834 patients. The risk of recurrence, liver transplantation (LT), or death was compared between statin users (n = 2,224) and non-users (n = 19,610).
Results: During the median follow-up of 44.0 months, 11,909 (54.5%) patients experienced recurrence, LT, or death. The cumulative incidence of recurrence, LT, or death was significantly lower in statin users (8.72 per 100 person-years) than non-users (11.53 per 100 person-years). In multivariable analysis, statin use (hazard ratio [HR], 0.63; 95% confidence interval [CI], 0.58–0.67), age (HR, 1.02; 95% CI, 1.01–1.02), male sex (HR, 1.34; 95% CI, 1.28–1.40), cirrhosis (HR, 1.22; 95% CI, 1.17–1.27), diabetes mellitus (HR, 1.10; 95% CI, 1.06–1.14), and Charlson comorbidity index (HR, 1.07; 95% CI, 1.01–1.14 for 1 and HR, 1.30; 95% CI, 1.23–1.38 for ≥ 2) were independent risk factors for recurrence, LT, or death, whereas aspirin use (HR, 1.03; 95% CI, 0.98–1.08) was not. The finding of a lower risk in statin users (HR, 0.67; 95% CI, 0.62–0.72) was still observed after one-to-four propensity score matching.

Conclusion: Statin use was associated with a lower risk of HCC recurrence, LT, or death among patients with HCC after liver resection. Further studies including clinical trials are needed to implement evidence-based practices.

[ABST-0310]

The outcomes of hepatic resection for HCC with portal vein tumor thrombosis: A multicenter study In South Korea

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Background: The presence of portal vein tumor thrombosis (PVTT) in patients with hepatocellular carcinoma (HCC) has been regarded as an advanced stage and associated with extremely poor prognosis. Most of guidelines for the treatment of HCC have recommended non-surgical treatment such as systemic therapy or transarterial chemoembolization (TACE) rather than surgical resection in these cases. The aim of this multicenter study was to evaluate the outcomes of hepatic resection (HR) for HCC patients with portal vein tumor thrombosis.
Methods: Two hundred seventy-six HCC patients with PVTT who underwent hepatic resection between 2005 and 2019 from 17 tertiary hospitals in South Korea were included in this study. We analyzed the outcomes of hepatic resection in these patients.
Results: The extent of PVTT was as follows; Vp1 in 71 patients (25.7%), Vp2 in 72 patients (26.1%), Vp3 in 99 patients (35.9%) and Vp4 in 33 patients (12.0%). The median survival time was 30.7 months and median recurrence-free survival time was 6.7 months. The 1-, 3-, and 5-year overall survival (OS) rates were 73%, 47% and 38%. The 1-, 3-, and 5-year recurrence-free survival (RFS) rates were 41%, 31%, and 26%. HR showed better outcomes compared with published outcomes of other treatment modality such as TACE or systemic treatment. The median survival time according to the extent of PVTT were 56.0 months in Vp1/Vp2 and 23.7 months Vp3/Vp4 ($p = 0.007$). The median recurrence-free survival time according to the extent of PVTT were 11.2 months in Vp1/Vp2 and 4.9 months in Vp3/Vp4 ($p = 0.009$). Perioperative mortality rate was 2.9% and postoperative complications with Clavien-Dindo classification grade III or above were seen in 44 patients (15.9%).
Conclusions: HR may lead to better survival outcomes compared with other treatment in HCC patients with PVTT. HR should be considered in selected patients with resectable HCC associated with PVTT.

Young Investigators Award (YIA) Session

[OP-0300]

Alcohol-induced glutamate vesicles trigger inflammatory liver injury through Kupffer cell activation

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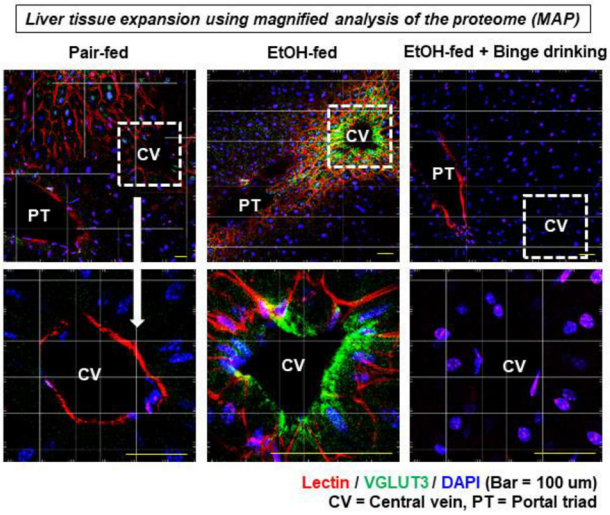
Objectives: Recently, lines of evidence have emerged that the intercellular crosstalk via glutamate signaling is involved in the development of alcoholic liver disease (ALD). However, the detailed role of hepatic glutamate in the pathogenesis of ALD is still unexplored. Here, we investigated the accumulative process of alcohol-induced glutamate vesicles in hepatocytes. Furthermore, we demonstrated the impact of glutamates in the aspect of inflammatory liver injury through the activation of Kupffer cells (KCs).
Materials and Methods: Alcoholic liver injury was achieved by chronic ethanol feeding plus a single binge (NIAAA model) mimicking alcoholic steatohepatitis in humans. Kupffer cell-specific NOX2 and metabotropic glutamate receptor 5 (mGluR5) knock-out ($NOX2^{\Delta KC}$ & $GRM5^{\Delta KC}$) mice were made to suppress reactive oxygen species (ROS) generation and mGluR5 activation in KCs, respectively. Data analyses were performed using RNA-sequencing in ethanol-fed hepatocytes and KCs.
Results: Glutamate is accumulated around central veins of hepatocytes through vesicle formation after the chronic ethanol consumption. Glutamate vesicle formation is regulated with NRF2 signaling pathway in the ethanol-fed mice. Alcohol binge drinking triggers glutamate release from hepatocytes to generate ROS in KCs through mGluR5. Correspondingly, the pharmacological inhibition of glutamate vesicle formation reduced alcoholic liver injury. In the alcohol-feeding model, $NOX2^{\Delta KC}$ and $GRM5^{\Delta KC}$ mice significantly attenuated inflammatory liver injury compared to the wild-type mice. Protein kinase (PKC) plays a pivotal role to active NOX2 complex after mGluR5 activation in KCs. Furthermore, pharmacological inhibition of PKC mitigates alcoholic liver injury through inactivation of mGluR5 of KCs. In human samples, we consistently demonstrated that glutamates released from vesicles have a positive correlation with the inflammatory response in alcoholic patients without liver cirrhosis.
Conclusion: Our results firstly proposed chronic alcohol consumption leads to accumulate glutamates with the vesicle formation in hepatocytes. Ethanol binge drinking consecutively triggers glutamate release prompting mGluR5-PKC-NOX2 activation of KCs to induce alcoholic liver injury.



[OP-0715]

In vivo RNA-interference (RNAi) screen identifies potential regulators of liver regeneration and disease

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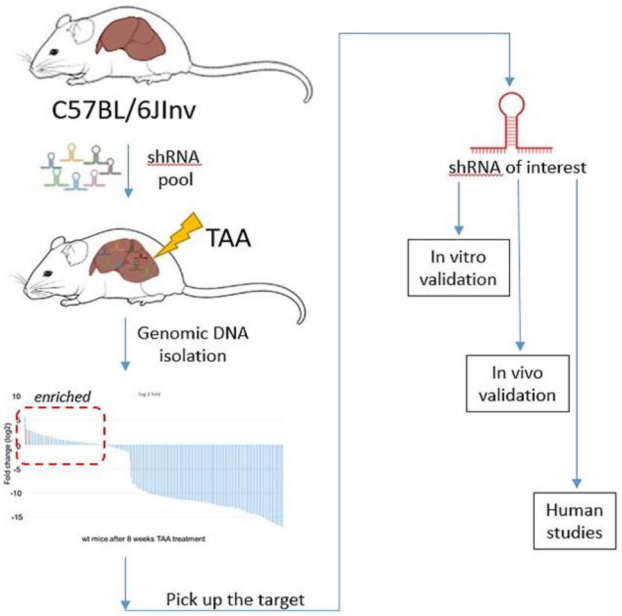
Objectives: End-stage liver disease leads to more than 2 million deaths per year worldwide. Currently, liver transplantation is the only curative method to treat such conditions; however, there is a global shortage of donor organs. New therapeutic approaches are needed, therefore we conducted an in vivo functional genetic screen in a mouse model of chronic liver disease for the identification of new therapeutic targets.
Materials and Methods: We delivered a pool of shRNAs by hydrodynamic tail vein injections (HDTV) into C57BL/6JInv mice and then, applied thioacetamide (TAA) treatment to induce chronic liver damage. After 8 weeks TAA, the abundance of each shRNA compared to starting pool was calculated, and enriched shRNAs were selected for further in vitro and in vivo validation.
Results: Under the top-enriched shRNAs were surprisingly two independent shRNAs targeting Glyoxylate Reductase/Hydroxypyruvate Reductase (GRHPR). GRHPR dysfunction in humans causes primary hyperoxaluria type 2. Excess oxalate leads to kidney stone formation and kidney damage. We went on to investigate the effect of hepatocyte-specific GRHPR knockdown on cell proliferation and liver regeneration. In vitro assays using immortalized mouse hepatocyte lines, showed a significantly faster proliferation rate in case of GRHPR knockdown compared to non-targeting control. For in vivo repopulation assays, we delivered our constructs into the fumarylacetoacetate hydrolase (FAH-/-) knockout mouse livers by HDTV and observed faster clonal expansion in case of GRHPR knockdown compared to control. In the case of full liver repopulation, when every hepatocyte expressed the shRNA of interest, mice with shGrhpr showed faster liver regeneration upon partial hepatectomy and reduced fibrosis upon chronic TAA treatment.
Conclusion: An in vivo functional genetic screen identified GRHPR as a target for enhancing liver regeneration attenuating chronic liver disease. As GRHPR dysfunction in humans causes primary hyperoxaluria type 2, the potential for hepatocyte-specific transient Grhpr siRNA therapy to improve liver function has to be further evaluated.



[OP-0358]

Risk of hepatocellular carcinoma, but not hepatic decompensation, persists beyond 7 years after hepatitis B surface antigen seroclearance: A territory-wide cohort of 9,769 patients

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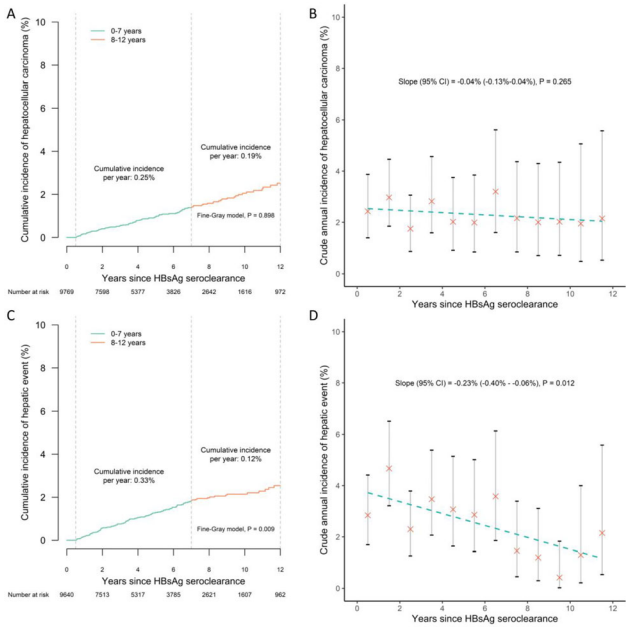
Objectives: To examine the long-term trend of incident hepatocellular carcinoma (HCC) and hepatic decompensation among chronic hepatitis B (CHB) patients who have achieved hepatitis B surface antigen (HBsAg) seroclearance.
Materials and Methods: All adult CHB monoinfected patients who cleared HBsAg between January 2000 and June 2021 were identified using a territory-wide database in Hong Kong. Patients with liver transplantation and/or HCC before HBsAg seroclearance or follow-up less than 6 months were excluded. Hepatic decompensation included ascites, variceal bleeding, hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, liver transplantation, and

liver-related death. Comparison of patients before and after year 7 of HBsAg loss was handled as clustered data in Fine-Gray model.
Results: We identified 9,769 CHB patients with HBsAg seroclearance (mean age 57 years, 60.0% male, 3.7% cirrhosis); most had compensated liver function at HBsAg loss. At a mean follow-up of 5.7 ± 4.4 years, 107 (1.1%) patients developed HCC. Patients who developed HCC were older, more likely to be male and cirrhotic, and had higher alanine aminotransferase and lower platelets than patients without HCC. The cumulative incidence of HCC remained steady in 0–7 and 8–12 years after HBsAg loss (P = 0.898) (crude annual incidence drop: -0.04%, 95% CI -0.13%–0.04%, P = 0.265) (Figs. 1A-1B). Moreover, 129/9,640 (1.3%) patients without prior hepatic decompensation developed hepatic decompensation. The growth in cumulative incidence of hepatic decompensation decelerated in 8–12 years after the first 7 years of HBsAg loss (P = 0.009) (crude annual incidence drop: -0.23%, 95% CI -0.40% – -0.06%, P = 0.012) (Figs. 1C-1D). HBsAg loss for over 7 years was found to be associated with a reduced risk of hepatic decompensation (adjusted subdistribution hazard ratio [aSHR] 0.53, 95% CI 0.30–0.94, P = 0.030) but not HCC (aSHR 1.31, 95% CI 0.81–2.11, P = 0.264) after adjusting for age, gender, and cirrhosis.
Conclusion: HCC risk persists in patients after HBsAg loss, whereas the risk of hepatic decompensation reduces over time.



[OP-0899]

Progress towards hepatitis C elimination: The feasibility and success of a nurse and harm reduction practitioner led model of care utilising rapid point of care HCV RNA testing at a medically supervis

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Objectives: To achieve HCV elimination, efforts must focus on models of care engaging people who inject drugs (PWID). The XpertÒ HCV VL FS point of care (POC) test provides an HCV RNA level within 1 h, allowing rapid diagnosis and treatment. We report the 12-month outcomes of a novel program incorporating HCV RNA POC testing at a medically supervised injecting room (MSIR).
Materials and Methods: Prospective cohort study recruiting PWID attending a high-volume MSIR in Melbourne, Australia between 9/11/20–9/11/21. All clients were offered HCV screening using the XpertÒ HCV VL FS POC test, venepuncture for HBV/HIV screening, and fibrosis assessment (APRI/FibroScan). HCV RNA results were returned same day where possible. Testing/treatment was led by a full-time hepatology fellow during the initial nine-week pilot program, and a nurse or harm reduction practitioner (HRP) for the remainder of the study period. DAA treatment was prescribed immediately upon return of a positive HCV test if the hepatology fellow was on-site, or by a GP/hepatologist after remote consultation for nurse/HRP assessments. Primary endpoints were number of clients screened for HCV and number commencing DAAs. Testing rates were compared to a historical control period (9/11/18–9/11/19) of standard HCV venepuncture testing at the MSIR.
Results: 573 PWID consented to HCV RNA POC testing. By comparison, 180 clients underwent HCV testing during the control period, representing a 218% increase with POC testing. 161 (28%) were HCV RNA + . 90% (n = 145/161) of HCV RNA + clients were prescribed DAA therapy. Median time to treatment start was 8 days (IQR, 2–22); 13 clients (9%) initiated treatment same day as diagnosis. Among those with complete follow up data (n = 43), SVR was 74%. Causes of non-SVR were re-infection (n = 3), relapse (n = 4), and non-response from medication non-adherence (n = 4).
Conclusion: Rapid HCV POC testing in a MSIR rapidly upscales testing and was associated with high rates of treatment initiation.

[OP-0234]

LEARN algorithm: A novel option for predicting non-alcoholic steatohepatitis

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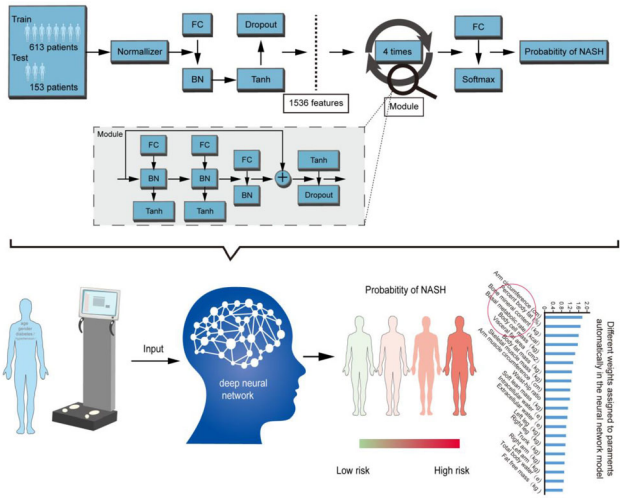
Objectives: There is an unmet need for accurate non-invasive methods to diagnose non-alcoholic steatohepatitis (NASH). Since impedance-based measurements of body composition are simple, repeatable and have a strong association with non-alcoholic fatty liver disease (NAFLD) severity, we aimed to develop a novel and fully automatic machine learning algorithm, consisting of a deep neural network based on impedance-based measurements of body composition to identify NASH (the LEARN algorithm, bioeLectrical impEdance Analysis foR Nash).
Materials and Methods: 1,259 consecutive subjects with suspected NAFLD aged 12–75 years were screened from six medical centers across China from 2016 to 2021. 766 patients with biopsy-proven NAFLD were included in the final analysis. Patients were randomly divided into the training and validation groups, in a ratio of 4:1. The LEARN algorithm (utilizing impedance-based measurements of body composition along with age, sex, history of hypertension and diabetes) was developed in the training group to identify NASH, and subsequently, tested in the validation group.
Results: The LEARN algorithm showed good discriminatory ability for identifying NASH in both the training and validation groups (AUROC: 0.81, 95%CI 0.77–0.84 and 0.80, 0.73–0.87, respectively). This algorithm performed better than serum cytokeratin-18 neoepitope M30 level or other non-invasive NASH scores (including HAIR, ION, NICE) for identifying NASH (p-value < 0.001). Additionally, even in a condition of partial missing the data of body composition, LEARN algorithm performed well in identifying NASH (AUROC: 0.82, 95%CI 0.72–0.92). Subgroup analysis showed that the LEARN algorithm performed well in different subgroups.
Conclusion: The LEARN algorithm, utilizing simple easily obtained measures, provides a fully automated, simple, non-invasive method for identifying NASH.



[OP-0304]

L-ornithine L-aspartate in acute treatment of severe Hepatic encephalopathy: A double-blind randomized controlled trial

Arpan Jain[1], Barjesh Chander Sharma[1], Bhawna Mahajan[2], Siddharth Srivastava[1], Ajay Kumar[1], Sanjeev Sachdeva[1], Ujjwal Sonika[1], Ashok Dalal[1]

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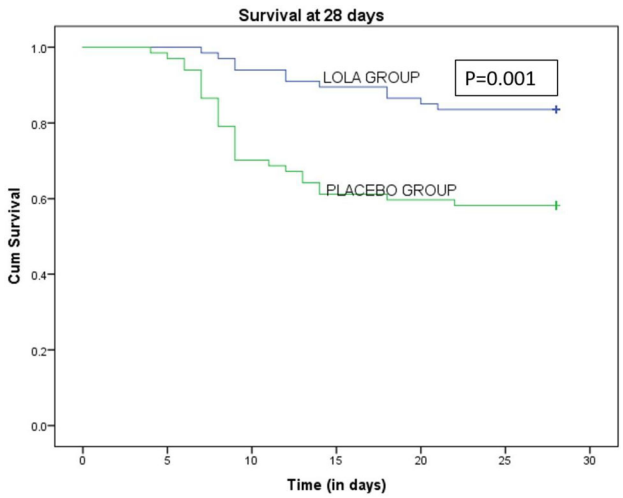
Objectives: Data on the use of intravenous L ornithine L aspartate (LOLA) in the treatment of overt hepatic encephalopathy (OHE) is limited. We evaluated the role of intravenous LOLA in cirrhotics with OHE grade III-IV.
Materials and Methods: In a double-blind randomized placebo-controlled trial, 140 patients were randomized to a combination of LOLA, lactulose, and rifaximin (n = 70) or placebo, lactulose, and rifaximin (n = 70). LOLA was given as continuous intravenous infusion at a dose of 30 g over 24 h for 5 days. Ammonia levels, serum tumor necrosis factor α, interleukins, and endotoxins were measured on days 0 and 5. The primary outcome was the improvement in the grade of HE at day 5.
Results: Higher rates of improvement in grade of HE (92.5% vs 66%, $p < 0.001$), lower time to recovery (2.70 ± 0.46 vs 3.00 ± 0.87 days, $p = 0.03$) and lower 28 day mortality (16.4% vs 41.8%, $p = 0.001$) were seen in LOLA group as compared to placebo. Levels of inflammatory markers were reduced in both groups. Significantly higher reductions in levels of blood ammonia, IL-6, and TNF-α were seen in the LOLA group.
Conclusion: Combination of LOLA with lactulose and rifaximin was more effective than only lactulose and rifaximin in improving grades of HE, recovery time from encephalopathy with lower 28-day mortality.



Day	0	5	10	15	20	25
LOLA	67	67	63	60	57	56
Placebo	67	65	47	41	40	39

[OP-0764]

The accuracy of microvascular invasion prediction based on radiomics methods in hepatocellular carcinoma: A systematic review and meta-analysis of diagnostic study

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Objectives: Hepatocellular carcinoma (HCC) is one of the most lethal malignancies in the world. The high mortality rate of HCC was associated with high recurrence in postoperative stage. Microvascular invasion has become the prognostic factor of lower survival rate and high-recurrence incidence. The preoperative evaluation by imaging methods as well as the using of machine learning algorithm potentially predicts the presence of microvascular invasion. The aim of this study was to perform meta-analysis about the accuracy of radiomic prediction to microvascular invasion in HCC.
Materials and Methods: Comprehensive literature searched of PubMed, Science Direct, and Google Scholar for between 2016–2021. The articles were diagnostic studies that using imaging methods and logistic regression algorithm to predict the microvascular invasion incidence in patients with hepatocellular carcinoma. The data extraction including true positive, false positive, true negative, and false negative proportion. The meta-analysis was performed by using R Studio with Mada packages. The pooled results that synthesized were log positive likelihood ratio, log negative likelihood ratio, and log diagnostic odds ratio. Those data were analysed by DerSimonian-Laird method.
Results: Eight studies were included with total 863 number of datasets. The imaging modality were using computed tomography, magnetic resonance imaging, and ultrasound. The meta-analysis showed that log negative likelihood ratio was 0.303 (95% CI 0.204–0.450, p = 0.325, I2 = 13.405%), log positive likelihood ratio was 3.481 (95% CI 2.790–4.344, p = 0.445, I2 = 0%), and log diagnostic odds ratio was 13.115 (95% CI 7.010–24.534, p = 0.439, I2 = 0%). Those data indicates that radiomics method by logistic regression algorithm has fair-very good prediction tools for microvascular invasion in hepatocellular carcinoma patient.
Conclusion: The radiomics method were feasible to predict macrovascular invasion in hepatocellular carcinoma cases. It has promising application in clinical settings so that physicians have more complete consideration regarding the risk of postoperative recurrency.

[OP-0659]

Surgical outcomes of pure laparoscopic versus open liver resection for intrahepatic cholangiocarcinoma

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Objectives: Surgical resection is the only curative treatment for intrahepatic cholangiocarcinoma (iCCA). Although laparoscopic liver resection (LLR) is associated with improved clinical and oncological outcomes in hepatocellular carcinoma and metastatic liver cancer compared to open liver resection (OLR), LLR remains controversial in the treatment of intrahepatic cholangiocarcinoma.
Materials and Methods: We retrospectively reviewed patients who underwent surgery for iCCA between January 2013 and February 2020. OLR and LLR were compared after propensity score matching. Overall and disease-free survival were compared between the matched groups.
Results: During the study period, 219 patients met the inclusion criteria (OLR = 170 patients, 77.6%; LLR = 49 patients, 22.4%). Two groups of 48 patients each were analyzed after propensity score matching. The 3-year disease-free survival was 37.0% in the OLR group and 50.7% in the LLR group (p = 0.192). The 3-year patient survival was 42.8% in the OLR group and 79.2% in the LLR group (p = 0.023). However, LLR was not a risk factor for recurrence and death in multivariate analysis (p = 0.257 and p = 0.230). The mean operation time for the OLR group was 216.0 ± 70.2 min and the LLR group was 225.8 ± 115.5 min (p = 0.615). Hospital stay was significantly shorter in the LLR group (7.9 ± 2.7 days) than in the OLR group (11.4 ± 5.1, $p < 0.001$). Total postoperative complications and complication rates for those Clavien–Dindo grade 3 or higher were similar between the OLR group and the LLR group (p = 0.286 and p = 0.715).
Conclusion: LLR provides short-term advantages without increasing complications or affecting oncologic outcomes compared to OLR for the treatment of iCCA.

[OP-0938]

Long term post-transplant survival outcome following the bridging locoregional therapy in hepatocellular carcinoma patients: A systematic review and meta-analysis study

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Objectives: For the past few decades, liver transplantation (LT) has attracted considerable interest due to its curative efficacy. However, liver donor grafts availability was insufficient, in contrast to the long line of waiting-list recipients. Pretransplant neoadjuvant locoregional therapy (LRT) or bridging therapy has emerged to help prevent tumor progression. A recent review in 2018 found that bridging LRT was associated with a nonsignificant trend towards better survival outcomes after transplantation. Since then, several new debatable comparative studies have been available. This meta-analysis aimed to compare the survival and recurrence outcomes between those HCC patients with and without bridging LRT.
Materials and Methods: We identified relevant studies by searching on databases, including Medline, Scopus, and Cochrane Library from inception to January 31st, 2021. We screened titles and abstracts for eligible studies. Data were extracted and analyzed by parametric survival regression (Weibull distribution).
Results: A total of seventeen cohorts were eligible for analyses. The 1-,3-,5- and 10-year overall survival (OS) rates were 93.3%,85.2%,79.3% and 67.3% for those in bridging LRT group, compared to 91.9%,82.7%,76.4% and 59.6%, respectively for those without preceding LRT. Our results share several similarities with the previous meta-analysis. There is a modest improvement in OS (HR 0.90; 0.78–1.05, P = 0.19) with a slightly longer median survival time (17.8 to 16.0 years) in the bridging group compared to no LRT group, however not statistically significant. (Fig. 1A) Interestingly, we discovered a remarkable result proving that bridging therapy help prolong survival significantly in a high-risk population with a long waiting time (HR 0.76; 0.60–0.96, P = 0.02). (Fig. 1D) Unfortunately, bridging LRT failed to improve disease-free survival (HR 0.98; 0.86–1.11, P = 0.70) and not-dropping out rates (HR 0.86; 0.46–1.59, P = 0.63). (Fig. 1B).
Conclusion: Our work has led us to conclude that bridging LRT does not change post-LT outcomes in general. Remarkably, we have obtained satisfactory results proving that bridging LRT can significantly improve survival in those waiting for LT with a long waiting time.

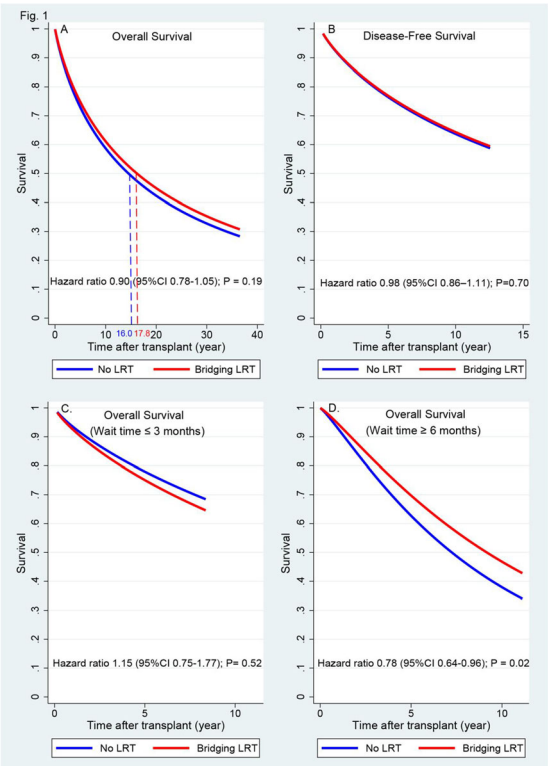

Fig.1 - Survival function of Overall Survival(A.), Disease-Free Survival(B.), Overall survival of short waiting time population(C.) Overall survival of long waiting time population(D.) estimated by Weibull model.

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[OP-0790]

Liver sinusoidal CD56hiCD8 + T cells are NK-like T cells activated by NKG2C

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Objectives: The liver acts as an immune sentinel against gut-derived microbes and provides a unique niche of lymphocytes enriched with a large proportion of innate-like T cells. However, the heterogeneity and functional characteristics of the hepatic T-cell population remain to be fully elucidated.
Materials and Methods: We obtained liver sinusoidal mononuclear cells from the liver perfusate of healthy donors and recipients with hepatitis B virus (HBV)-associated chronic liver disease (CLD) during liver transplantation. We performed a comprehensive single-cell multi-omics analysis of liver sinusoidal $CD45^+$ cells including transcriptome, surface proteome, and TCR repertoire anlaysis. Then we examined the phenotype and functions of the liver sinusoidal $CD8^+$ T cell clusters identified in the single-cell multi-omics anlaysis by performing flow cytometry analysis.
Results: We identified a distinct liver enriched $CD56^{hi}CD161^-CD8^+$ T-cell population characterized by NK-related gene expression and uniquely restricted TCR repertoire, and their frequency among the liver sinusoidal $CD8^+$ T-cell population was significantly increased in patients with HBV-CLD. Although $CD56^{hi}CD161^-CD8^+$ T cells exhibit weak responsiveness to TCR stimulation, $CD56^{hi}CD161^-CD8^+$ T cells highly expressed various NK receptors, including CD94, KIRs, and NKG2C, and exerted NKG2C-mediated NK-like effector functions, including IFN-γ secretion and cytotoxic degranulation, even in the absence of TCR stimulation. In addition, $CD56^{hi}CD161^-CD8^+$ T cells highly expressed receptors for innate cytokines, such as IL-12/18 and IL-15, and showed high levels of responsiveness to these innate cytokines in the absence of TCR stimulation.
Conclusion: In summary, the current study found a distinct liver enriched $CD56^{hi}CD161^-CD8^+$ T-cell population characterized by NK-like activation by TCR-independent NKG2C ligation. Further studies are required to elucidate the roles of liver sinusoidal $CD56^{hi}CD161^-CD8^+$ T cells in immune responses to microbial pathogens or liver immunopathology.

[OP-0922]

Integrated proteomics and metabolomics analysis reveals canonical and novel regulatory pathways linked to liver regeneration in living donor liver transplant (LDLT) donors

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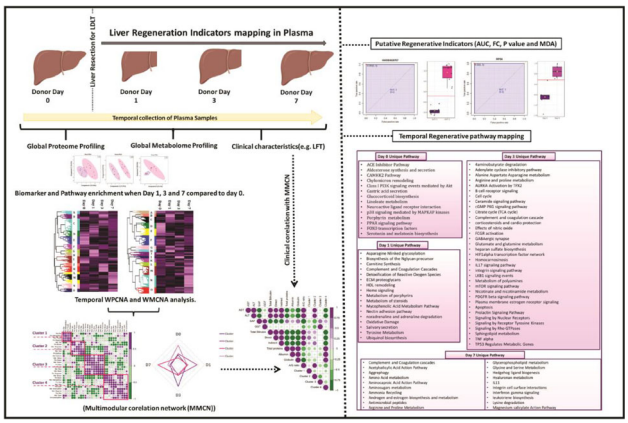
Objectives: Living donor liver transplant (LDLT) in Donor's provides a unique opportunity to unravel novel biological networks associated to regenerative response. To explore, plasma proteomic, metabolomic and the clinical characteristic of LDLT Donors were integrated using network-based modelling with the final aim of uncovering novel biological processes associated to regeneration.
Materials and Methods: Plasma proteomics/metabolomics were performed on (n = 10) healthy donors at baseline (pre-operative) and post-operative at Day1, Day3 and Day7. Multi-omics analysis using weighted protein/metabolite correlation network analysis W[P/M]CNA led to identify clusters of highly correlated proteins/metabolites modules differently expressed in donors at different days. Proteins/metabolites modules were cross correlated to form Multi-Modular Correlation Network (MMCN). Pathway associated to MMCN correlated with post-operative flare in liver enzymes (AST and ALT; $p < 0.05$).
Results: In comparison to baseline donor sample; post-operative day1 sample showed 232 differentially expressed proteins (DEP; Up-113, Down-119; $p < 0.05$) and 177 differentially expressed metabolites (DEM; Up-105, Down-72; $p < 0.05$). At day 1 VEGF, Hedgehog signaling, Cell cycle, Tryptophan, Sphingolipid metabolism, Primary bile acid metabolism were increased and Arachidonic acid metabolism were decreased ($p < 0.05$). At Day3; 264 DEP (Up-157,Down-107; $p < 0.05$) and 267 DEM (Up-136,Down-131; $p < 0.05$) associated to ILGF signaling, IL-12, NFK-B, MAP-K, JAK-STAT signaling, alanine aspartate metabolism and butanoate metabolism were increased whereas Rho-GTPases, interferon-gamma, cytokine signaling were decreased ($p < 0.05$). Day7; 232 DEP (Up-97,Down-135; $p < 0.05$) and 299 DEM (Up-133,Down-166;) associated to autophagy, RHO-GTPases and primary bile acid biosynthesis increased and Folate metabolism, N-glycan biosynthesis, Arachidonic acid metabolism were decreased. Temporal integration performed using W[P/M]CNA identified MMCN clusters ($r2 > 0.5$). Correlation of these MMCN clusters with the clinical indicator of liver regeneration led to identification of day wise specificity of MMCN cluster; (Day1 specific MMCN-direct correlates with AST and ALT levels ($r2 > 0.5$, $p < 0.05$)). Pathway enrichment of MMCN cluster identified canonical pathways involving haemostasis and regeneration but also enriched novel pathways linked to regeneration.
Conclusion: Conclusion: Multi-modular network analysis not only validates canonical pathways involving haemostasis and regeneration but also highlight novel pathways linked to liver regeneration.



[OP-0255]

Anti-fibrotic effects of metabotropic glutamate receptor 5 in NK cells through augmented cytotoxicity against hepatic stellate cells

Tom Ryu[1], Young-Ri Shim[1], Hee-Hoon Kim[1], Keungmo Yang[1], Kyurae Kim[1], Sung Eun Choi[1], Minjeong Kim[1], Chaerin Woo[1], Katherine Po Sin Chung[1], Hyuk Soo Eun[2], Won-Il Jeong[1]

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Objectives: We reported that metabotropic glutamate receptor 5 (mGluR5) of hepatic stellate cells (HSCs) plays important roles in alcoholic steatosis previously. However, it is unclear how mGluR5 is related with glutamate metabolism in liver fibrosis. Consequently, we report that liver fibrosis is attenuated with the activation of mGluR5 of natural killer (NK) cells and it is induced by interferon-γ (IFN-γ) related cytotoxicity augmentation in mice and human.
Materials and Methods: Carbon tetrachloride (CCl_4) was injected intraperitoneally for 2 weeks to wild type (WT) mice, mGluR5 knockout (KO) mice and mice with mGluR5 conditional KO (cKO) in NK cell. NK cells were isolated from the liver of mice and humans using magnetic cell sorting, and HSCs were freshly isolated from the liver of mice utilizing hepatic perfusion. Chlorohydroxyphenylglycine (CHPG) was used for the pharmacologic mGluR5 activation. Cytotoxicity was measured by Calcein AM release assay.
Results: Compared to WT mice, mGluR5 KO mice had significantly aggravated CCl_4-induced liver fibrosis, with decrease of NK cell frequency in the liver. Furthermore, accelerated liver fibrosis with decreased IFN-γ production of hepatic NK cells via MEK/ERK pathway were observed in mGluR5 cKO mice. mRNA expression level of genes related with anti-fibrotic function, such as Ifng and Prf1, increased remarkably with in vitro treatment of CHPG to isolated NK cells from mice liver. In vivo, CHPG treatment to mice attenuated liver fibrosis with augmentation of NK cell cytotoxicity and adoptive transfer of NK cells to mice also alleviated liver fibrosis. In humans, CHPG treatment to isolated NK cells from the normal liver significantly increased cytotoxicity to human HSC cell line, but not from the cirrhotic liver.
Conclusion: Activation of mGluR5 of NK cells is crucial to the liver fibrosis alleviation by killing HSCs and it would be one of the therapeutic targets in liver fibrosis.

[OP-0753]

ZNF469 as a novel pro-fibrotic regulator in liver fibrosis

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Objectives: Activation of hepatic stellate cells (HSCs) plays vital roles in the progression of liver fibrosis; however, transcriptional network that promotes activated features of HSCs remains elusive. We identified a putative zinc-finger transcription factor, ZNF469, to be upregulated upon HSC activation and in human cirrhotic livers. Thus, we aim to investigate the roles of ZNF469 as a potential pro-fibrotic factor.
Materials and Methods: We performed gain- and loss-of-function of ZNF469 in primary human HSCs and examined phenotypes of activated HSCs. We also investigated regulation of ZNF469 expression by TGF-beta. Finally, we cloned a full-length open reading frame (ORF) of ZNF469 with an epitope tag for transcriptional studies.
Results: Short hairpin RNA- (shRNA) knockdown and CRISPR-knockout expression of ZNF469 in primary human HSCs reduced production of collagen and deposition of collagen in HSC spheroids. Conversely, CRISPR activation of ZNF469 in primary HSCs promoted collagen production. Continued suppression of ZNF469 inhibited TGFbeta-induced HSC activation, and expression of ZNF469 was controlled by TGF-beta in a Smad3-dependent manner. We have successfully cloned a full-length ORF of ZNF469 ($\sim$ 12 kb) with an epitope tag and identified a nuclear localization of the protein, supporting its function as a transcription factor.
Conclusion: ZNF469 is necessary and sufficient to promote collagen production during HSC activation. Current experiments include chromatin immunoprecipitation (ChIP) to elucidate a transcriptional network governed by ZNF469 and development of adeno-associated virus (AAV) to manipulate expression of ZNF469 in fibrotic livers. Together, these studies will advance our understanding in transcriptional regulation of activated HSCs and may lead to a new treatment for liver fibrosis by modifying ZNF469 expression.

[OP-0683]

Identification of shuttle protein hnRNPA1 as a modulating factor of circulating hepatitis B virus RNAs release in chronic hepatitis B patients

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Objectives: Circulating HBV RNA (CirB-RNA) reflects the transcriptional activity of the intrahepatic cccDNA, thus representing a promising non-invasive serum biomarker for the reduction or inactivation of cccDNA pool. Although several studies have suggested that cellular releasing pathways may determine the fate of these RNAs, the specific regulators of the shuttle machinery involved remain largely unknown.
Materials and Methods: Expression of candidate shuttle proteins were analyzed by Western Blotting and RT-qPCR in cell lysate and supernatant from HBV-infected HepG2-NTCP cells and Primary human hepatocytes (PHHs). Shuttle protein interaction with CirB-RNAs was investigated by RNP-IP (Ribonucleoprotein-Immunoprecipitation) and Biotin pull down assay. Adapted Iodixanol/Sucrose density ultracentrifugation allowed to isolate exosome-enriched fractions from sera of 5 untreated [2 HBeAg (+) and 3 HBeAg (-)], 2 HBeAg (-) chronic infection and 2 NUC-treated chronic hepatitis B (CHB) patients.
Results: Among the RNA-binding proteins analyzed, heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1) expression was increased in both cell lysates and supernatants of HepG2-NTCP cells and PHHs upon HBV infection. hnRNPA1 was also detected in the serum of CHB patients and, after density ultracentrifugation of serum samples, hnRNAP1 was mostly detected in the exosome-enriched fractions. Loss-of-function studies in HepG2-NTCP cells indicated that hnRNAP1 downregulation was associated to reduced expression of exosome markers CD9 and CD81 in cell supernatant, as well as a decreased secretion of CirB-RNA in exosome fractions. Anti-CD81 IP confirmed the association between hnRNAP1 and exosomes. RNP-IP experiments revealed that hnRNPA1 was able to bind to 5' region of 3.5 Kb RNA and to the 3' region common to all HBV transcripts. Specific binding sites for hnRNAP1 on HBV RNAs were mapped by Biotin pull-down assays.
Conclusion: Altogether, our data suggest that hnRNPA1 directly binds to HBV RNAs and can function as a novel shuttling mechanism for the export of HBV RNAs in vivo.

[OP-0685]

Preclinical immunogenicity and efficacy of VRON-0200: A novel therapeutic vaccine for potential functional cure therapies in patients with chronic HBV

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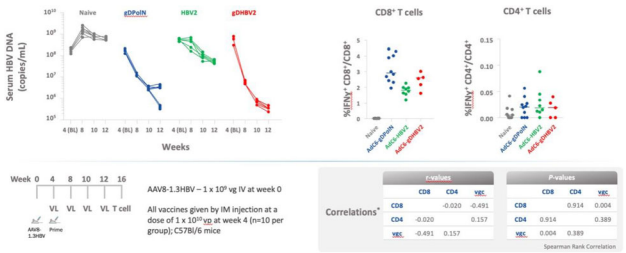
Objectives: Background: A functional cure for chronic HBV infection is needed. VRON-0200 (gD-HBV2) is a novel therapeutic HBV vaccine based on chimpanzee adenovirus (AdC) vectors that express conserved and highly immunogenic regions of the viral polymerase (pol) and core antigens fused genetically into herpes simplex virus glycoprotein D (gD), a checkpoint modifier of $CD8^+$ T cell activation. Preclinical data from the VRON-0200 program are presented.
Materials and Methods: Methods: Immunogenicity was evaluated in blood and splenocytes of C57Bl/6 and BALB/c mice. Efficacy was tested in C57Bl/6 mice that were first injected i.v. with increasing

doses of an AAV8-1.3HBV vector and then vaccinated 4 wks later with vaccines expressing sequences of the N-terminus of pol within gD (gDPolN), pol and core with or without gD (gD-HBV2, HBV2). Unvaccinated mice served as controls. Lymphocytes were tested after immunization for frequencies and epitope specificities of IFN-g producing vaccine-insert-specific $CD8^+$ T cells, sera were tested for levels of HBV DNA.

Results: Results: Vaccination induced $CD8^+$ T cells to the vaccine inserts in blood and spleen and gD enhanced responses. In mice injected with 10^9 viral genome copies (vg) of AAV8-1.3HBV, vaccination with gD-HBV2 achieved sustained 3 $\log_{10}$ declines in HBV DNA, while naïve mice showed $\sim$ 0.5 $\log_{10}$ increases (Figure); increasing the AAV dose to 10^{10} and 10^{11} vg decreased HBV DNA levels by 2 and 1 $\log_{10}$, respectively accompanied by reductions in circulating HBsAg. Frequencies of circulating vaccine-insert-specific $CD8^+$ T cells were inversely correlated with HBV viral loads.

Conclusion: Conclusions: These preclinical studies demonstrate that VRON-0200 induces a potent and broad $CD8^+$ T cell response in mice with sustained antiviral activity. An international Phase 1b study of VRON-0200 is in development.



[OP-0850]

Targeted HBeAg seroclearance in a chronic-like HBV mouse model using chimeric bio-nanoparticles

Yianni Droungas[1], Hugh Mason[1], Chee Leng Lee[1], Joan Ho[1], Rachel Hammond[1], Stephen Locarnini[1], Renae Walsh[1], Hans J Netter[1,3], Peter A Revill[1,2]

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Objectives: Chronic hepatitis B (CHB) contributes to more than 820,000 deaths each year, and despite an existing prophylactic vaccine and therapeutic advances, there is currently no cure. The hepatitis B e antigen (HBeAg) plays a role in CHB infection by modulating host immune responses. The presence of HBeAg is generally associated with ongoing HBV replication and liver disease, hence, HBeAg seroconversion is a current treatment endpoint and a preceding step to functional cure. This project utilises HBeAg-epitope expressing bio-nanoparticles (eAg-BNP) to promote HBeAg clearance as a novel therapeutic strategy.

Materials and Methods: In this project, eAg-BNP candidates were bioengineered using a panel of HBeAg-specific epitopes, followed by immunogenicity studies in BALB/c mice. The 2 most immunogenic eAg-BNP candidates (BNP3 and BNP6) were then assessed using a hepatitis B mouse model, based on the hydrodynamic injection (HDI) of replication-competent HBV DNA and persistent replication of HBV in the liver. HBV markers of replication, protein expression and antibody production were assessed.

Results: eAg-BNPs induced HBeAg-specific immune responses against the inserted HBeAg epitopes, whilst also maintaining some immunogenicity against the HBsAg backbone. Mice after HDI and persistent HBV replication showed that immunisations with eAg-BNPs resulted in seroclearance of HBeAg in 43% of eAg-BNP3 group (3/7) and 67% of eAg-BNP6 group (8/12). In addition, 17% of eAg-BNP6 group (2/12) also seroclearred HBsAg, achieving functional cure. None of the wild-type BNP control group (0/7) showed HBeAg seroclearance.

Conclusion: The immune factors contributing to HBeAg seroconversion in CHB patients remain unclear. This project is the first to use eAg-BNPs capable to selectively triggering immune responses against the native HBeAg and inducing its seroclearance. In turn, BNP6 also triggered immune responses that led to HBsAg seroclearance (functional cure) in some mice. These findings suggest that targeting HBeAg and the induction of anti-HBe antibodies may be a promising therapeutic approach in immune competent settings.

[OP-0775]

Regulation and mechanism of NPM1 on HBV cccDNA level and transcriptional activity

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Objectives: To explore NPM1 how to affect HBV replication cycle and HBVcccDNA level.

Materials and Methods: HBV1.3 plasmid and NPM1 overexpression/interference were co-transfected in Huh7 and HepG2 cells, and the expression levels of HBV RNA and HBV DNA in each group were detected by Southern blot. HepAD38 and HepG2-NTCP cell with over-expression and knock-down of NPM1 were constructed. HBV cccDNA was extracted from all cells by Hirt DNA method. The levels of HBV cccDNA and preCore RNA were detected by Southern blot and Q-PCR respectively. HepG2 cells were transfected with HBV 1.3-mer WT replicon plasmid and HBc overexpression vector, and the cell localization and expression changes of NPM1 and HBc were detected by Co-IP, immunofluorescence and Western Blot.

Results: In Huh7 and HepG2 cell, overexpression of NPM1 could significantly increase the expression level of HBV pgRNA and rcDNA, meanwhile, the opposite effect was observed after knocking down NPM1 ($P < 0.001$). Southern blot results showed that overexpression of NPM1 in HepAD38 cells could significantly increase the level of HBV cccDNA, the expression level of preCore RNA and the transcription activity of HBV cccDNA, but this promotion disappeared after downregulating NPM1. Overexpression of NPM1 in HepG2-NTCP cells can significantly increase the level of HBV cccDNA ($P < 0.001$), the expression level of total RNA and the transcription activity of HBV cccDNA ($P < 0.01$). NPM1 and HBc proteins are mainly located in the nucleus of HepG2 cells and have co-localization signals. Further analysis of cytoplasmic and nuclear protein levels showed that NPM1 could promote the protein expression of HBc in cells with active HBV virus. At the same time, the

results of Co-IP experiment showed that NPM1 and HBc protein interacted with each other.
Conclusion: NPM1 can promote HBV replication and enhance transcriptional activity.The mechanism is related to the interaction with HBV core protein.

[OP-0104]

Intrahepatic inflammatory IgA + PD-L1high monocytes in hepatocellular carcinoma development and immunotherapy

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Objectives: To investigate the roles of inflammation-induced intrahepatic inflammatory $IgA^{+}PD\text{-}L1^{high}$ monocytes in the development and immune-based therapy of HCC.
Materials and Methods: Surgical and biopsy specimens from patients with chronic liver diseases or HCC were analyzed using multi-color flow cytometry and immunohistochemistry. Single-cell RNA-Seq analysis was performed using GEO datasets. We performed in vitro differentiation of macrophages, stimulation with coated IgA, and RNA sequencing.
Results: Serum IgA levels predicted fibrosis progression and HCC development in patients with chronic liver diseases ($P < 0.001$). Immunohistochemical staining of inflamed livers or HCC revealed IgA positivity in macrophages, with the frequency of IgA^{+} cells reflecting the IgA serum levels. Compared to IgA^{-} monocytes, intrahepatic IgA^{+} monocytes expressed higher levels of programmed death-ligand 1 (PD-L1) in inflamed livers or in tumor microenvironment of HCC. Single-cell RNA sequencing using NCBI Gene Expression Omnibus database identified that inflammation-associated genes were upregulated in monocytes of patients whose plasma cell IGHA1 expression was greater than or equal to the median value. Bulk RNA sequencing demonstrated that in vitro stimulation of M2-polarized macrophages with the coated IgA complex causes activation and PD-L1 upregulation via YAP-mediated signaling. In vivo blockade of IgA signaling decreased the number of tumor-infiltrating $IgA^{+}PD\text{-}L1^{high}$ macrophages and increased the number of $CD69^{+}CD8^{+}$ T cells, to enhance anti-tumor effects from anti-PD-L1 in an orthotopic HCC model.
Conclusion: Serum IgA levels reflected the intrahepatic and intratumoral infiltration of inflammatory $IgA^{+}PD\text{-}L1^{high}$ monocytes in chronic liver diseases and HCC. In HCC, these cells may be targeted by IgA neutralization/anti-PD-L1 to enhance the efficacy of immune-based therapy.

Free Papers 02 (NAFLD 1)

[OP-0319]

Alcohol-induced hepatic monocytes migration is regulated by leptin receptor + bone marrow stromal cells

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Objectives: About 80% of patients with alcoholic steatosis rarely progress into alcoholic steatohepatitis, suggesting the existence of unknown protective mechanisms. Here, we demonstrated that a subset of bone marrow (BM)-derived macrophages has an anti-inflammatory role for alcoholic liver disease (ALD) through the mesenchymal stromal cell (MSC)-mediated glutamate release in BM.
Materials and Methods: C57BL/6 J WT and NK cell-specific Grm5 KO mice were fed with liquid ethanol for 8 weeks. Single-cell RNA-seq analysis was performed using hepatic macrophages. In vitro, diverse doses of ethanol, glutamate, or interferon-γ (IFN-γ) were used to treat MSCs, natural killer (NK) cells, or monocytes. Human cells and plasma were collected from alcoholic patients. Flow cytometry, glutamate measurement, Western blotting, immunostaining, and qRT-PCR analysis were performed.
Results: In scRNA-seq and flow cytometry analyses, a specific subtype of $Ly6C^{low}$ macrophages with higher expression of interleukin-1 type II receptor (IL-1R2), a decoy receptor of IL-1β, and lower expression of CX_3C chemokine receptor 1 (CX_3CR1) in EtOH-fed WT. Besides, BM leptin receptor $(LepR)^{+}$ MSCs expressing CX_3CL1 could metabolize alcohol by alcohol dehydrogenase and expressed cystine-glutamate antiporter xCT and chemokines (CXCL9 and 10) after alcohol consumption. Furthermore, $CXCR3^{+}$ NK cells were recruited around $LepR^{+}$ MSCs, where excreted glutamate through xCT in LepR + MSCs stimulated metabotropic glutamate receptor 5 (mGluR5) in NK cells, leading to IFN-γ production, whereas IFN-γ production of NK cells and $Ly6C^{low}$ BM monocytes egress were significantly decreased in EtOH-fed mGluR5 cKO compared to WT mice. In turn, IFN-γ down-regulated CX_3CR1 expression in $Ly6C^{low}$ monocytes bound to CX_3CL1^{+} MSCs, consequently inducing egress of $Ly6C^{low}$ monocytes into the blood. In humans, plasma levels of soluble IL-1R2 and frequency of $IL\text{-}1R2^{+}CD14^{+}CD16^{+}$ blood monocytes were elevated in alcoholic patients compared to healthy control.
Conclusion: $LepR^{+}$ MSCs granted egress license on anti-inflammatory $IL\text{-}1R2^{+}Ly6C^{low}$ monocytes through CX_3CR1 suppression by NK cell-derived IFN-γ, produced via glutamate-mGluR5 signaling.

[OP-0975]

Baseline plasma metabolic phenotype of patients with severe alcoholic hepatitis and its association with outcome

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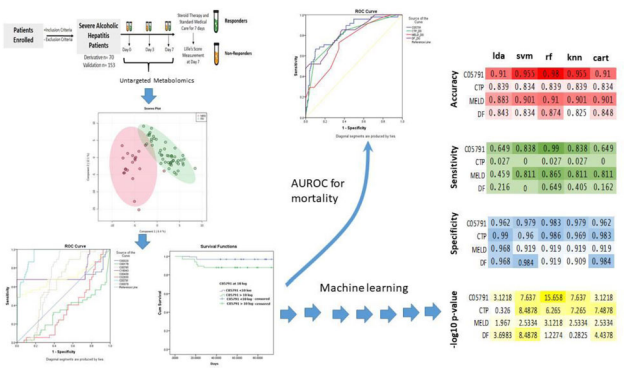
Objectives: Severe alcoholic hepatitis (SAH) has a high mortality and corticosteroid therapy is effective in reducing 28-day mortality in only about 60% of patients. There are reliable clinical indicators predicting steroid non-response after 7 days of therapy (Lille score > 0.45).
Materials and Methods: Plasma metabolic phenotype was studied using ultra-high-performance liquid chromatography and high-

resolution mass spectrometry to identify corticosteroid non-responders at baseline. Altogether, 223 SAH patients were included, 70 in derivative [50 responders (R) and 20 non-responders (NR)] and 153 in validation cohort [136 R, 17 NR]. Temporal change in the metabolic profile and Weighted Metabolome Correlation Network Analysis (WMCNA) were performed and correlated to disease severity.
Results: Of the 713 annotated features (metabolomic/biochemical/spectral databases), 8 plasma metabolites significantly discriminated non-responders; most importantly high urobilinogen (13-fold), cholesterol sulfate (6.9-fold), AMP (4.7-fold), N-Formimino-L-glutamate (4.3-fold), tryptophan (4.7 folds), and low 4-imidazoleacetate (tenfold), urocanic acid (2.2 fold) and thymine (2.4 fold) levels. Additionally, plasma urobilinogen, AMP, and cholesterol sulfate discriminated non-survivors ($P < 0.01$). Temporal change in metabolite expression was higher in responders ($p < 0.05$). WMCNA identified metabolite modules and linked pathways specific to NR and mortality with disease severity ($r > 0.7$; $P < 0.01$). In validation cohort, baseline plasma urobilinogen (C05791) showed high reliability [AUC = 0.94, 0.91–0.97] for predicting non-response with hazard-ratio of 1.5 (1.2–1.6) for mortality prediction. C05791 at 10 log (arbitrary units) cut-off reliably segregated non-survivors (p-value < 0.01, log-rank test) and showed 98% accuracy, 99% sensitivity and 98% specificity using Random Forest-based Machine-Learning model.
Conclusion: Plasma metabolome signatures can predict pre-therapy steroid response and disease outcome in patients with SAH. Baseline plasma urobilinogen levels should be used for determining corticosteroid response.



[OP-0218]

Intestinal sympathetic neurotransmitters drive hepatic growth differentiation factor 15 production to facilitate inflammatory Kupffer cell apoptosis

Hee-Hoon Kim[1], Young-Ri Shim[1], Keungmo Yang[1], Tom Ryu[1], Kyurae Kim[1], Sung Eun Choi[1], Minjeong Kim[1], Chaerin Woo[1], Katherine Po Sin Chung[1], Won Kim[2], Won-Il Jeong[1]

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Objectives: Hepatic sympathetic innervation suppresses inflammatory macrophages by producing norepinephrine to maintain the hepatic homeostasis in alcoholic liver disease (ALD). Although chronic alcohol consumption induces sympathetic neuropathy, alcoholic inflammation only develops in a small subset (10 ~ 35%) of patients with steatosis, indicating the presence of unknown mechanisms. Here, we unveiled how intestine-derived catecholamines limit inflammatory Kupffer cells (KCs) in response to chronic alcohol intake by hepatic growth differentiation factor 15 (GDF15).
Materials and Methods: C57BL/6 J wild type, hepatocyte-specific GDF15 or cytochrome P450 2E1 (CYP2E1) knock-out and β-adrenergic receptor (ADRB) 1/2 double knock-out (DKO) mice were fed with isocaloric (Pair) or 4.5% ethanol diet (EtOH) for 8 weeks. Different doses of ethanol, GDF15, and β2-agonist were used in vitro and in situ experiments. Serum and liver tissues of healthy donors and patients with ALD were analyzed. Single-cell RNA-sequencing, flow cytometry, qRT-PCR, western blot and immunostaining were performed.
Results: Single-cell RNA sequencing and immunostaining revealed a profound apoptosis of perivenous KCs in EtOH-fed mice, which had elevated catecholamine levels in the liver tissues, portal blood, and cecum. In ADRB2-expressing perivenous hepatocytes, intestinal catecholamines induced translocation of CYP2E1 into mitochondria, which enhanced GDF15 production. Interestingly, ADRB2 expression levels of the neighboring inflammatory KCs were strikingly increased by hepatic GDF15, which facilitated catecholamine-mediated apoptosis. In genetic ablation of Adrb2 or hepatic Gdf15 or Cyp2e1, a robust reduction of apoptosis in inflammatory KCs exacerbated alcoholic injury. Consistently, notable increases of the serum catecholamine and GDF15 levels and the perivenous expression of ADRB2/CYP2E1/GDF15 axis were observed in patients with the early phase of ALD. Finally, GDF15 and β2-agonist treatments similarly induced apoptosis of the human inflammatory KCs.
Conclusion: Our findings reveal unique catecholamine-sensitive KCs by hepatic GDF15 and identify a novel neuro-metabo-immune communication in the gut-liver axis that induces precise hepatoprotective processes to the alcoholic microbiome perturbation.

[OP-0217]

Clinical outcomes and gut microbiota analysis of severe alcohol-associated hepatitis patients undergoing healthy donor fecal transplant or pentoxifylline therapy—single center experience from Kerala

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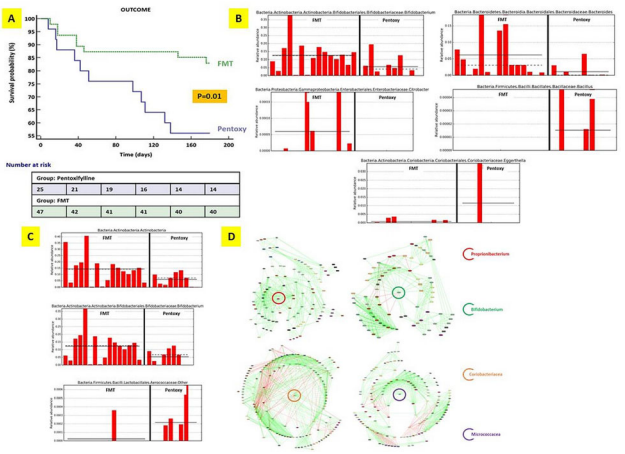
Objectives: Severe alcohol-associated hepatitis (SAH) patients with infections have high short-term mortality. Gut microbiota (GM) dysbiosis play a central role in the pathogenesis of SAH. Preliminary studies have demonstrated long term benefits with healthy donor fecal microbiota transplantation. Data on FMT compared with pentoxifylline (PTX) for SAH and relevant gut microbial changes is lacking in literature.
Materials and Methods: From January 2019 to February 2021, retrospective analysis of hospital records revealed 47 SAH patients

undergoing FMT (freshly processed, 100 mL daily via nasoduodenal tube x 7d) and 25 on PTX (400 mg Q8H for 28d). Primary end-point was survival at 6 mo. Secondary end-points included incidence of ascites, hepatic encephalopathy (HE), infections, acute kidney injury (AKI) and GM changes between groups post therapy. Prospective GM evaluation to identify significant taxa post treatment, using biomarker discovery method and network analysis, on retrospectively stored stool samples were performed at 3- and 6-mo.

Results: All were males, matched for portal hypertension events, HE, liver disease severity and infections at baseline. At 6mo, higher proportion of patients undergoing FMT survived, compared with PTX (83% vs 56%, P = 0.01; Fig.A). Significantly higher PTX treated patients experienced clinically significant ascites (56 vs 34.2%), HE (40 vs 10.6%), critical infections (52 vs 17%) [$P < 0.05$]. Multivariable biomarker discovery method revealed significant abundance of Bifidobacterium post-FMT compared to Eggerthella in PTX group at 3mo (Fig.B). Persistence of Bifidobacterium in FMT group and pathogenic Aerococcaceae in PTX group at 6mo notable (Fig.C). Network analysis showed beneficial taxa (Propionibacterium, Bifidobacterium) as central influencers post-FMT (Fig.D).

Conclusion: Healthy donor FMT compared to PTX in SAH, improves 6 mo survival with greater improvement in severity scores and liver-related complications, associated with beneficial modulation of pathogenic bacterial communities. Difficult to treat SAH patients may be safely bridged to transplantation using FMT. Controlled trials evaluating long term outcomes are an unmet need.



[OP-0966]

Diagnostic performance of procalcitonin for diagnosis of bacterial infection in severe alcoholic hepatitis compared with C-reactive protein

Nae-Yun Heo[1], Seung Ha Park[1], Eunju Kim[1], Jun Sik Yoon[2], Yang Hyun Paek[3], Young Mi Hong[4], Kwang Il Seo[5], Sang Su Lee[6], Yu Rim Lee[7], Soo Young Park[8], Jung-Gil Park[9], Min-Kyu Kang[9], Byung Seok Kim[10], Jeong Eun Song[10]

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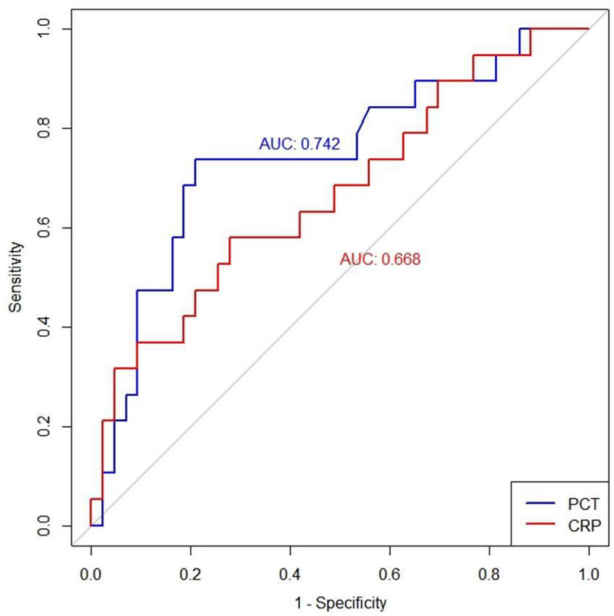
Objectives: Severe alcoholic hepatitis is a catastrophic disease in which the mortality at 30 day is up to 30–50%. Although bacterial infection is one of important prognostic factor among the patients with severe alcoholic hepatitis, it is still difficult to know the presence of bacterial infection immediately. Procalcitonin (PCT) is a well-known inflammatory marker which could detect early bacterial and fungal infection in various disease. Therefore, we are intended to evaluate the diagnostic accuracy of PCT for bacterial infection among severe alcoholic hepatitis.

Materials and Methods: The patients with severe alcoholic hepatitis based on Maddrey's Discriminant Function ≥ 32 were prospectively enrolled in multiple medical centers. At admission, initial evaluation including physical exam, radiology, and blood and urine culture, PCT, and C-reactive protein (CRP) was performed. Then, ROC curves for bacterial infection, systemic inflammatory response reaction (SIRS), and sepsis were compared between PCT and CRP.

Results: Interim analysis was performed after enrollment of 62 patients. The number of bacterial infection, SIRS, and sepsis was 19 (31%), 24 (39%), 10 (16%), respectively. MELD score (20.9 vs. 15.2), PCT (1.1 vs. 0.4 ng/mL), and CRP (5.2 vs. 3.1 mg/dL) was significantly higher in the patients with bacterial infection compared with those without it. AUROC of PCT vs. CRP for bacterial infection was 0.742, and 0.668, respectively (P = 0.444). AUROC of PCT vs. CRP for SIRS was 0.642, and 0.680, respectively (P = 0.660). AUROC of PCT vs. CRP for sepsis was 0730, and 0.602, respectively (P = 0.259).

Conclusion:: Among the patients with severe alcoholic hepatitis, PCT showed the trend of superior diagnostic performance in the early detection of bacterial infection compared with CRP. However, both inflammatory markers did not show the different diagnostic performance for SIRS. Further study is expected to confirm the superiority of PCT for early detection of bacterial infection.

Figure 1. ROC curve of the diagnosis for bacterial infection according to inflammatory marker



[OP-0285]

Rifaximin treatment in patients with severe alcoholic hepatitis; A multicenter, open-label, pilot randomized controlled trial

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Objectives: The short-term mortality of severe alcoholic hepatitis (SAH) is very high, but there are no effective treatments to improve short-term mortality other than corticosteroid. This study investigated the effects of rifaximin treatment in patients with SAH.
Materials and Methods: In an open-label trial, patients with SAH (Maddrey's discriminant function $\geq$ 32) were randomized to rifaximin or control group, each added to corticosteroid or pentoxifylline for 4 weeks. Randomization was stratified by SAH treatment. Transplantation free survival was evaluated.
Results: Total 49 patients were enrolled in this study (29 in control and 20 in rifaximin group). The mean Model for End-stage Liver Disease (MELD) score were 24.4 and 27.8 in control and rifaximin group (P = 0.083). Rifaximin treatment was tolerable and only 1 patients stopped due to adverse event. There were no differences in 3-month and 6-month mortality between two groups (P = 0.576 and P = 0.239, respectively). Corticosteroid group had higher 3-month and 6-month survival than pentoxifylline group (P = 0.03 and P = 0.016, respectively). When stratified by SAH treatment, there were no significant 3-month and 6-month survival between control and rifaximin treatment (P = 0.516 and P = 0.937 in corticosteroid group and P = 0.948 and P = 0.620 in pentoxifylline group, respectively). Cox Proportional hazard model showed that MELD score, white blood cell count, C-reactive protein were significant factors for 6-month survival, and MELD score was only independent factor for 6-month survival (Hazard ratio 1.188, P = 0.001).
Conclusion: In patients with SAH, adding rifaximin to corticosteroid or pentoxifylline was tolerable but had no survival benefit. MELD score was only significant factor for short-term mortality.

[OP-0212]

Intrahepatic infiltration of activated CD8 + T cells and macrophages is associated with the severity of liver injury in drug-induced liver injury: Implications in steroid therapy

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Objectives: Drug-induced liver injury (DILI) is caused by the interplay between drugs, their metabolites and host immune response. The aim of this study is to investigate the phenotypes of the infiltrating immune cells in DILI and the role of steroid treatment in DILI.
Materials and Methods: From January 2017 to June 2021, 53 patients with DILI who underwent liver biopsy were enrolled prospectively in this study. Liver biopsy was performed, and immunohistochemical stain and FACS analysis were done with the biopsy specimen. EILSA for serum CXCL10 and soluble CD163 were done.
Results: The number of intrahepatic T cells and macrophage showed positive correlation with serum levels of total bilirubin, AST, and MELD score (r = 0.326, 0.345, and 0.312, respectively, $p < 0.05$). The frequency of activated CD8 + T cells among the liver-infiltrating CD8 + T cells in DILI livers, was higher than that in healthy livers ($p < 0.05$). Importantly, the percentage of activated intrahepatic CD8 + T cells and macrophage in DILI livers showed positive correlation with ALT (r = 0.593 and 0.855, respectively, $p < 0.05$). Also, the serum CXCL10 levels were positive correlated with intrahepatic T cells infiltration and ALT (r = 0.366 and 0.640, respectively, $p < 0.05$). And the serum soluble CD163 levels were positive correlated with intrahepatic macrophage infiltration and ALT (r = 0.463 and 0.689, respectively, $p < 0.05$). Thirty six patients (70.6%) were treated with steroid. Among them, 22 patients (70.6%) showed more than 50% of reduction of ALT level after 1 week of steroid treatment.
Conclusion: In conclusion, we found the positive correlation between the number of intrahepatic macrophages, T cells, serum cytokine levels (CXCL10 and soluble CD163), activated CD8 + T cells and macrophage infiltrations, and the degree of liver injury in patients with DILI. We suggest that T cells and macrophage play critical roles in DILI. Therefore, steroid can be a treatment option for patient with DILI.

[OP-0609]

Thrap3 regulates non-alcoholic fatty liver disease (NAFLD) by determining AMPK translocation

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Objectives: Nonalcoholic fatty liver disease is a chronic metabolic disorder involving steatosis, steatohepatitis and fibrosis. Although many studies have been conducted, the progression mechanism and treatment of NAFLD remain unclear. In previous report, we suggested adipose Thrap3 as therapeutic target for metabolic diseases such as obesity and diabetes.

Materials and Methods: Here, we found that hepatic Thrap3 was increased by FFA and HFD. In NAFLD patients, hepatic Thrap3 increased with progression of fatty change of liver. We investigated the contribution of Thrap3 to NAFLD using liver specific KO mice.
Results: In both HFD and MCD fed mice, deprivation of Thrap3 significantly reduced hepatic lipid accumulation, triglyceride levels, and fibrosis. This improved glucose and insulin sensitivity and decreased NAFLD progression. mRNA-seq GSEA analysis showed an association of Thrap3 with AMPK and Autophagy pathway. AMPK/Autophagy signals, including phosphorylation of AMPK and ULK1, were elevated in Thrap3 KO, resulting in increased autophagic vesicles and energy expenditure. Deficient in Thrap3 enhanced the nuclear export and activation of AMPK. Thrap3 regulated AMPK translocation and activation by direct interaction through C-terminal domain.
Conclusion: Taken together, these results demonstrate that Thrap3 is involved in NAFLD progression and may be a promising therapeutic-targets for treating NAFLD.

[OP-1003]

Non-alcoholic fatty liver disease in adolescent children in relation to parental non-alcoholic fatty liver disease

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Objectives: Though genetic variants related with the incidence and development of non-alcoholic fatty liver disease (NAFLD) were identified, the heritability of NAFLD in ecological studies are inconsistent, and large-scale epidemiologic data are lacking. The aim of this study is to assess association between NAFLD in adolescent children and NAFLD in parents.
Materials and Methods: A total of 1,843 families with both parents (n = 3,686) and adolescent children aged 12 to 18 (n = 2,335) who participated in a Korean National Health and Nutrition Examination Surveys (KNHANES) were analyzed for the association between adolescent children and parental NAFLD. NAFLD was defined by body mass index and elevated alanine aminotransferase levels for adolescent and was defined by hepatic steatosis index ($\geq$ 36) for parents.
Results: The prevalence of NAFLD was higher for adolescents with parental NAFLD (10.2%) than adolescents with neither parental NAFLD (3.1%, $p < 0.001$). A fully adjusted odds ratio (OR), adjusting for age, sex, body mass index, central obesity, triglyceride, HDL cholesterol, fasting serum glucose, blood pressure, total caloric intake, physical activity and household income, was 1.75 (95% confidence interval (CI), 1.02–3.00), comparing adolescent with parental NAFLD to adolescent without parental NAFLD. The fully adjusted OR of adolescent NAFLD was 1.80 (1.01–3.20) who has paternal NAFLD, 2.21 (1.11–4.42) who has maternal NAFLD, and 2.60 (1.03–6.54) who has both parental NAFLD. In subgroup analysis, association between adolescent NAFLD and parental NAFLD was observed in all predefined subgroups without interaction.
Conclusion: NAFLD in adolescent children was associated with NAFLD in their parents. This suggests heritability contribute to NAFLD risk in adolescent, and that adolescent with parental NAFLD, particularly when both parents are NAFLD, might be a candidate for earlier screening.

Table 2. Risk of non-alcoholic fatty liver disease among adolescents according to parental NAFLD status

	No. of subjects	No. of NAFLD	NAFLD (%)	Unadjusted	Model 1	Model 2	Model 3
Without parental NAFLD	1,336	42	3.1	Reference	Reference	Reference	Reference
Either parental NAFLD	999	102	10.2	3.49 (2.41-5.08)	3.52 (2.42-5.10)	2.00 (1.22-3.27)	1.75 (1.02-3.00)
Paternal NAFLD	739	80	10.8	3.72 (2.53-5.49)	3.74 (2.53-5.52)	2.08 (1.23-3.50)	1.80 (1.01-3.20)
Maternal NAFLD	402	46	11.4	3.98 (2.57-6.17)	4.06 (2.61-6.31)	2.04 (1.07-3.90)	2.21 (1.11-4.42)
Both parental NAFLD	142	24	16.9	6.27 (3.63-10.8)	6.32 (3.61-11.1)	2.36 (1.03-5.42)	2.60 (1.03-6.54)

Model 1 was adjusted for age (per year) and sex, Model 2 was further adjusted for body mass index (per kg/m^2), central obesity (yes vs. no), triglyceride (< 150 mg/dL vs. ≥ 150 mg/dL), HDL-C (< 40 mg/dL vs. ≥ 40 mg/dL for boys, < 50 mg/dL vs. ≥ 50 mg/dL for girls), fasting serum glucose (< 100mg/dL vs. ≥ 100mg/dL), systolic blood pressure (< 130 mm Hg vs. ≥ 130 mm Hg), Model3 was further adjusted for total caloric intake (kcal), physical activity and household income (Q1, Q2, Q3, and Q4).

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[OP-0783]

Discovering prognosis-related potential biomarkers using patient-derived hepatocellular carcinoma organoid models

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Objectives: Recent development of organoid models using patient-derived cancer tissues has allowed a better understanding of human cancer as well as development of personalized therapeutic strategies. A better understanding between genetic background and drug response could facilitate precision treatment for HCC. In this study, we evaluate whether HCC organoids (HCO) exhibit different sensitivity to anti-cancer drugs and analyze the relationship between anti-cancer drug response and gene expression patterns in HCC for improving the drug sensitivity.
Materials and Methods: Patient-derived tumor tissue from fine needle biopsy was digested at 37 °C in the digestion solution and mixed with Matrigel. After polymerization of Matrigel, medium was added and changed twice a week. To evaluate sensitivity to drugs, we tested its sensitivity to anti-cancer drugs and analyzed the sensitivity in HCO lines with the difference in gene expression.
Results: We obtained tumor biopsies from 16 HCC patients among which 10 HCOs were established. HCOs exhibited heterogeneous morphological features, forming compact structures with or without thick-layered cyst-like structures. Expression levels of key HCC biomarkers were similar between tumor tissues and HCOs. Also, HCOs shared somatic mutations and showed high concordance of somatic mutation between primary tumor and organoids. Through the different gross morphology of HCO showed the differential gene expression of HCC. Using the differential gene expression, Wnt pathway was significantly enriched in the densely packed spherical shape of HCO compared to combined shape ($P < 0.05$). Also, packed spherical shape of HCO lines was resistant to treatment with Lenvatinib in vitro.

Conclusion: Our results demonstrated that HCOs retained characteristic gene expression patterns of the original tumors. Identification of HCOs with specific structural features provide platform to identify the relationship between drug response and Wnt activity in HCC.

[OP-0582]

Cytotoxic function of adoptive T cell immunotherapy against HBV-associated HCC circulating tumour cells

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Objectives: Circulating tumour cells (CTCs) is a major risk factor for recurrence in Hepatitis B virus-related hepatocellular carcinoma (HBV-HCC) patients after liver transplant (LT). It is currently unclear whether HBV-targeting T cell therapy can effectively eliminate HBV-HCC CTCs under the immunosuppressive post-transplant condition of these patients. Previously, we engineered HBV-TCR T cells capable of lysing HBV-HCC cells in the presence of clinically relevant quantities of immunosuppressive drugs (IDRA HBV-TCR T cells). Here we developed a microscopy-based assay to quantify CTCs in whole blood and used it to evaluate the ability of IDRA HBV-TCR cells to lyse HBV-HCC CTCs in conditions mimicking the peripheral blood of LT patients.
Materials and Methods: Using six HCC cell lines (HepG2.2.15, Hep3B, SNU354, SNU368, SNU387 and SNU475), we optimised an immunofluorescence panel using seven markers: pan-Cytokeratin and vimentin; glypican-3 and alpha-fetoprotein; CD34; CD45 and; DRAQ5 to identify HCC cells. To evaluate the cytolytic function of the HBV-TCR T cells, 100,000 HepG2.2.15 was spiked into 5 ml of healthy whole blood and incubated for 16 h with autologous IDRA HBV-TCR T-cells in presence of tacrolimus and MMF. Remaining HepG2.2.15 were isolated using RosetteSep^{TM} human CD45 depletion cocktail and Ficoll-Paque^{TM} density centrifugation; fixed and stained with the panel, using X-Zell Cryoimmunostaining^{TM} Suite.
Results: Using the assay, we consistently detected the small numbers of spiked HCC cells from peripheral blood cells ($\sim$ 30 million CD45 + in 5 ml of whole blood). In the presence of immunosuppressants, IDRA HBV-TCR T cells are better able to lyse CTCs compared to conventional ones. Through a dose titration, we demonstrated that 20,000 IDRA HBV-TCR T cells/ml of blood is sufficient to reduce CTCs numbers by $\sim$ 80%.
Conclusion: IDRA HBV-TCR T cells can effectively lyse HBV-HCC CTCs in whole blood with immunosuppressants. This is a proof-of-concept demonstration for the use of our therapy as a prophylaxis against recurrence after LT.

[OP-1014]

TIP47 accelerates fatty and dysplastic change of liver during alcohol ingestion in HBx transgenic mice

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Objectives: In chronic hepatitis B (CHB), alcohol is known to accelerate the progression of liver fibrosis and increase the incidence of hepatocellular carcinoma (HCC). However, little is known about the exact mechanism of progression. This study aimed to investigate the direct effect of alcohol on hepatitis B.
Materials and Methods: We performed using HBx transgenic and control C57BL/6[B6] mice (control-liquid diet [LD], control-ethanol, HBx-LD, HBx-ethanol). Real-time PCR, histologic and serologic exam were performed for analysis. Also, TIP 47 value was analyzed by ELISA using a patient sample.
Results: As for liver histology, there was no difference in degree of steatosis and ballooning between the control-ethanol group and the HBx-ethanol group, but PMNL infiltration showed a significant increase in the HBx-control group ($p < 0.005$). Also, the macrovesicular fatty change was predominant in the control?ethanol group whereas the microvesicular fatty change was observed in the HBx-ethanol group. When RT-PCR was performed to identify factors affecting the fatty change, mRNA results for mitochondrial beta oxidation enzymes (CPT1A, CPT1B, MCAD) showed a significant decrease in the HBx-ethanol group ($p < 0.05$). In the results of analyzing the mRNA expression level of the factors related to the fat vacuole size (perilipin, TIP47, Fsp27, Seipin), TIP47 was significantly increased in the HBx-ethanol group ($p < 0.001$) When suppressing the expression of TIP47 using TIP47-siRNA, it was showed significantly reduced in HBV-genome containing Hep3B cell ($p < 0.001$). To check the association between hepatic dysplastic change observed in the HBx-ethanol group and TIP 47 expression, ELISA was performed in CHB group 30 and HCC group 30. HCC group showed a significantly higher TIP 47 value (CHB group 5.22 vs HCC 9.08, $p = 0.000$) compared to CHB group.
Conclusion: This study showed that alcohol exacervated microvesicular fatty change and dysplastic change in liver of HBx transgenic mice and TIP47 can contribute to this process.

[OP-0667]

Multifocal HCCs genetically classified as multicentric occurrence (MO) possess better prognosis after surgery comparing to intrahepatic metastasis (IM)

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Objectives: Genetic differentiation of MO or IM in multifocal HCCs is possibly critical for decision-making in treatment. The AIM of present study was to analyze prognosis of multifocal HCCs after surgical resection on the basis of genetic differentiation; MO or IM.
Materials and Methods: We have genetically analyzed 163 HCC nodules from 90 patients who underwent surgical resection in our hospital. HCC samples obtained through Laser Microdissection were analyzed employing a next generation sequencer (NGS). We used an in-house targeted sequencing panel covering 72 SMGs associated with HCC reported in TCGC and ICGC. Among 90, we focused on 29 patients with multifocal nodules (2–4) at surgery analyzing post-surgical prognosis.
Results: Out of 29 patients with multifocal HCCs, 20 were MO harboring no common genetic mutation between the nodules. Meanwhile, 9 patients were IM possessing at least one common mutation. Recurrence-free survival (RFS) in MO/IM at 1, 2, 3 year was 84%/56%, 55%/37%, and 33%/37%, respectively ($p = 0.050$). Overall survival (OS) in MO/IM at 1, 2, 3 year was 100%/89%, 94%/59%, 81%/59%, respectively ($p = 0.074$). Intriguingly, recurrence was detected in 10 out of 20 MOs, while 6 out of 10 recurrences are HCC-free after second treatment (5, re-resection, 1, RFA), and 4 out of 5 patients who underwent re-resection were genetically MO recurrence. Exceptionally, one MO patient harboring oncogenic mutations (TP53, CTNNB1) had aggressive recurrence after surgery. Meanwhile, 6 out of 9 IMs experienced recurrence, and none of 6 were tumor-free after recurrence.
Conclusion: Multifocal HCCs genetically classified as MO had better prognosis after surgery. In these patients, relatively long tumor-free survival can be expected even after recurrence by appropriate second treatments. Genetic differentiation in multifocal HCCs using our in-house panel has important clinical significance, and possibly help decision-making in treatment.

[OP-0066]

Consensus subtypes of hepatocellular carcinoma associated with clinical outcomes

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Objectives: While many studies revealed transcriptomic subtypes of hepatocellular carcinoma (HCC), they are not translated to the clinic yet due to lack of consensus. We aim to examine consensus of transcriptomic subtypes and uncover their clinical significance.
Materials and Methods: We integrated 15 previously established transcriptomic signatures for HCC to uncover consensus subtypes. We also developed and validated a robust predictor of consensus subtype with 100 genes (PICS100). Informatics and statistics approaches were applied to find clinical relevant association of genomic features. Patient derived xenograft (PDX) models were used for testing hypothesis from analysis of transcriptomic data.
Results: We identified 5 clinically and molecularly distinct consensus subtypes. STM (STeM) is characterized by high stem cell features, vascular invasion, and poor prognosis. CIN (Chromosomal INstability) has moderate stem cell features but high genomic instability and low immune activity. IMH (IMmune High) is characterized by high immune activity. BCM (Beta-Catenin with high Male predominance) is characterized by prominent b-catenin activation, low miRNA expression, hypomethylation, and high sensitivity to sorafenib. DLP (Differentiated and Low Proliferation) is differentiated with high HNF4A activity. We also identified potential serum biomarkers that can stratify patients into 5 subtypes.
Conclusion: Five HCC subtypes are associated with potential response to treatments and highly conserved in pre-clinical models, providing a framework for selecting the most appropriate models for preclinical studies of new drugs and potentially for future clinical trials.

[OP-0155]

Prediction of microvascular invasion via gadoxetic acid-enhanced MRI in hepatocellular carcinoma: The implication of planning extent of the hepatectomy

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Objectives: The purpose of this study was to identify predictive factors for microvascular invasion (MVI) in hepatocellular carcinoma (HCC) using clinical factors and imaging findings of magnetic resonance imaging (MRI), to divide the patients into a subgroup with similar prognosis and finally to evaluate whether the extent of hepatectomy can affect long-term outcomes in the subgroup.
Materials and Methods: A total of 410 patients with surgically resected single HCC (≤ 5 cm) who underwent preoperative gadoxetic acid-enhanced MRI were included. Significant predictive factors for MVI were identified via univariate and multivariate analysis and used to divide the patients into low and high-risk groups. In the subgroup, long-term outcomes were analyzed after the minor versus major hepatectomy.
Results: Four variables were independently associated with MVI: alpha-fetoprotein ≥ 400 ng/ml ($p = 0.021$), tumor size ≥ 3 cm ($p < 0.001$), non-smooth tumor margin ($p < 0.001$) and arterial peritumoral enhancement ($p = 0.001$). Patients with a combination of three or more factors were classified as the high-risk group ($n = 103$), which showed a worse prognosis than the low-risk group ($n = 307$) ($p < 0.001$). While the extent of hepatectomy was not associated with prognosis in the low-risk group, major hepatectomy significantly improved disease-free survival ($p < 0.011$) and decreased early intrahepatic recurrence (< 2 years) ($p = 0.005$) than minor hepatectomy in the high-risk patients.
Conclusion: The patients who had a combination of three or more predictive factors for MVI showed a worse prognosis after hepatectomy for HCC and major hepatectomy improved long-term outcomes in these high-risk patients.

[OP-0176]

Development and validation of a safety and efficacy-associated risk calculator for hepatocellular carcinoma in the elderly after resection (SEARCHER): An international multicenter study

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Objectives: Increased life expectancy and improved perioperative management have synchronized a surge in the number of hepatic resections among elderly patients with hepatocellular carcinoma (HCC). However, individualized model for predicting the surgical safety and efficacy is lacking. The aim of this study is to establish a Safety and Efficacy-Associated Risk Calculator for HCC in the Elderly after Resection (SEARCHER).

Materials and Methods: From an international multicenter database, elderly patients (≥ 65 years) who underwent curative-intent hepatectomy for HCC were divided into 4 groups (65–69 years, 70–74 years, 75–79 years, and ≥ 80 years). The short- and long-term outcomes among these 4 groups were compared. Univariate and multivariate analyses of risk factors of postoperative 30-day major morbidity, cancer specific survival (CSS) and overall survival (OS) were performed in 2/3 of the patients randomly selected from the whole cohort. Dynamic online calculators were constructed and further validated in the remaining 1/3 of the whole cohort.

Results: With the increase of age stratification among the 4 groups of 699 patients in the training cohort, there was a significantly deteriorative tendency for postoperative major morbidity and OS (P = 0.001 and 0.020), but not for postoperative mortality and CSS (P = 0.577 and 0.890). On the basis of the results of multivariate analyses, three nomogram-based calculators were constructed for postoperative major morbidity, CSS, and OS (https://elderlyhcc.shinyapps.io/SEARCHER/). They demonstrated excellent calibration and optimal performance in both training and validation cohorts, and also performed better than several commonly-used staging system of HCC.

Conclusion: Considering higher postoperative major morbidity and poorer OS with aging, hepatectomy needs to be performed in selected elderly patients with HCC. The proposed prediction model named SEARCHER showed satisfactory performance of individualized prediction of the safety and efficacy of hepatectomy for elderly patients with HCC.

[OP-0468]

Novel liver stiffness-based nomogram for predicting the hepatocellular carcinoma risk in patients with chronic hepatitis B receiving antiviral therapy

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Objectives: Hepatocellular carcinoma (HCC) risk prediction among patients with chronic hepatitis B (CHB) is important to allow individualized surveillance approaches. We developed a novel HCC prediction model using liver stiffness (LS) for patients with receiving potent antiviral therapy (AVT).
Materials and Methods: We recruited 2,037 treatment-naïve patients with CHB who started to receiving entecavir or tenofovir, and used the Cox regression analysis to determine the key variables for model construction.
Results: Within 58.1 months (median), HCC developed in 182 (8.9%) patients. The patients with HCC showed higher cirrhosis prevalence (90.7% vs. 45.9%) and LS values (median 13.9 vs. 7.2 kPa) than did those without. A novel nomogram (score 0–304) was established using age, platelet count, cirrhosis development, and LS values, which were independently associated with increased HCC risks, along with hepatitis B e antigen positivity and serum albumin and total bilirubin levels. The cumulative HCC probabilities were 0.7%, 5.0%, and 22.7% in the low- (score $\leq$ 87), intermediate- (88–222), and high-risk ($\geq$ 223) groups, respectively. The c-index was 0.799 (internal validity: 0.805), higher than that of the PAGE-B (0.726), modified PAGE-B (0.756) and modified REACH-B (0.761) models (all $P < 0.05$).
Conclusion: Our nomogram showed acceptable performance in predicting HCC in Asian patients with CHB receiving potent AVT.

[OP-0194]

Decision tree-based algorithm predicts de novo hepatocellular carcinoma among chronic hepatitis C patients following viral eradication

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Objectives: Successful hepatitis C virus (HCV) eradication cannot eliminate the occurrence of hepatocellular carcinoma (HCC). Next-generation RNA sequencing provides a comprehensive genomic insight into the pathogenesis of HCC. Artificial intelligence opens a new era in precision medicine. This study aimed to integrate the clinical features and genetic biomarkers to establish a machine learning-based model for personalized surveillance of HCC following HCV cure.
Materials and Methods: A prospective cohort of HCV patients with advanced fibrosis who achieved a sustained virologic response after antiviral therapy were followed from 2004 to 2021. The primary endpoint was the occurrence of de novo HCC. Genomic signatures of peripheral mononuclear cells (PBMC) were determined by RNA sequencing at baseline and 24 weeks after end-of-treatment. Machine learning algorithms were implemented to extract important predictors of HCC.
Results: HCC was developed in 8 of the 55 HCV patients over 298.7 person-years of follow-up. Pre-treatment DEFA1B, HBG2, ADCY4, and post-treatment TAS1R3, ABCA3, FOSL1 gene expression were significantly downregulated in the HCC group compared to those without HCC occurrence. Overexpression of the pretreatment ANGPTL6 gene was significantly associated with HCC occurrence. The decision tree algorithm established an HCC predictive model: gene score = TAS1R3 (> = 0.63 FPKM, yes = 0, no = 1) + FOSL1 (> = 0.27 FPKM, yes = 0, no = 1) + ABCA3 (> = 2.40 FPKM, yes = 0, no = 1). The performance of this model achieved an accuracy of 95.7% and an area under the receiver operating characteristic curve of 0.913 (95%CI = 0.794–1.000, $p = 2.6 \times 10^{-4}$). The multivariate Cox regression showed this gene score was the most important predictor of HCC (HR = 2.54, 95%CI = 1.02–6.30, p = 0.045). The Kaplan–Meier survival analysis revealed significant differences in HCC risk among high- (score = 3), intermediate- (score = 1–2), and low-risk groups (score = 0) (log-rank p-value = 0.012).
Conclusion: Down-regulated post-treatment TAS1R3, ABCA3, and FOSL1 PBMC gene expression were significantly correlated with HCC development after HCV eradication. Decision tree-based algorithms can refine the assessment of HCC risk for personalized HCC surveillance.

Free Papers 04 (NAFLD 2)

[OP-0029]

acNASH index to accurately diagnosing nonalcoholic steatohepatitis: A prospective derivation and global validation study

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Objectives: There is an unmet need for non-invasive biomarkers for the diagnosis of nonalcoholic steatohepatitis (NASH) in non-specialized settings. We aimed to develop and validate a non-invasive test for diagnosing NASH in individuals with biopsy-proven nonalcoholic fatty liver disease (NAFLD).

Materials and Methods: We developed a non-invasive test named the acNASH index that combines serum creatinine and aspartate aminotransferase levels in a derivation cohort of 390 Chinese NAFLD patients and subsequently validated in five external cohorts of different ethnicities of patients with biopsy-confirmed NAFLD (pooled n = 1,089).

Results: The performance of the acNASH index for identifying NASH (defined as NAFLD activity score ≥ 5 with score of ≥ 1 for each steatosis, lobular inflammation and ballooning) was good in the derivation cohort with an area under receiver operating characteristics (AUROC) of 0·818 (95%CI 0·777–0·860). A cutoff of acNASH > 7 73 (i.e., the optimum threshold) gave a specificity (Sp) of 91%, sensitivity (Se) of 53% and a positive predictive value (PPV) of 85% for ruling-in NASH; conversely, a cutoff of acNASH index $< 4{\cdot}15$ gave a Se of 91%, a Se of 48% and a negative predictive value (NPV) of 83% for ruling-out NASH. In the pooled validation cohort (n = 1,089), the diagnostic performance of the index was also good with AUROC = 0·805 (95%CI 0·780–0·830), PPV of 73% and NPV of 93%. Subgroup analyses showed similar performance in patients with diabetes or subjects with normal serum transaminase levels.

Conclusion: The acNASH index shows promising utility as a simple non-invasive biomarker for diagnosing NASH among adults with biopsy-proven NAFLD of different ethnicities from different countries.

Table 2. Performance of the acNASH for the diagnosis of definite NASH on histology in the derivation cohort and external validation cohorts.

Cohort(s)	AUROC (95% CI)	N	Prevalence of definite NASH	Diagnostic performance using dual cut-offs (cut-offs from derivation cohort)		
				rule-out zone	*grey zone*	*rule-in zone*
Derivation cohort	0·818 (0·777-0·860)	390	190 (48·7%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=115 (29%)	n=158 (40%)	n=119 (30%)
				Se=0·91		Sp=0·91
				Sp=0·48		Se=0·53
				NPV=0·83		PPV=0·85
French cohort	0·807 (0·767-0·848)	448	148 (33·0%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=126 (28%)	n=224 (50%)	n=98 (22%)
				Se=0·97		Sp=0·90
				Sp=0·40		Se=0·46
				NPV=0·96		PPV=0·69
Turkish cohort	0·810 (0·738-0·883)	172	124 (72·1%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=28 (16%)	n=92 (53%)	n=52 (30%)
				Se=0·94		Sp=0·92
				Sp=0·44		Se=0·39
				NPV=0·75		PPV=0·92
Malaysian cohort	0·852 (0·805-0·898)	270	105 (38·9%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=88 (33%)	n=110 (41%)	n=72 (27%)
				Se=0·93		Sp=0·91
				Sp=0·49		Se=0·54
				NPV=0·92		PPV=0·79
Egyptian cohort	0·809 (0·701-0·918)	61	34 (55·7%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=9 (15%)	n=35 (57%)	n=17 (28%)
				Se=1·00		Sp=0·89
				Sp=0·33		Se=0·41
				NPV=1·00		PPV=0·82
Spanish cohort	0·785 (0·704-0·866)	138	35 (25·4%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=31 (22%)	n=58 (42%)	n=49 (36%)
				Se=1·00		Sp=0·74
				Sp=0·30		Se=0·63
				NPV=1·00		PPV=0·45
Pooled patient cohorts	0·805 (0·780-0·830)	1089	446 (41·0%)	**acNASH<4·15**	**acNASH: 4·15-7·73**	**acNASH >7·73**
				n=282 (26%)	n=519 (48%)	n=288 (26%)
				Se=0·96		Sp=0·86
				Sp=0·41		Se=0·47
				NPV=0·93		PPV=0·73

Performance associated with a dual cut-off approach is evaluated using the acNASH index when the cut-offs are calculated in the derivation cohort and applied in external validation cohorts. The lower cut-off constitutes a rule-out cut-off and is based on a sensitivity ≥0·91 in the derivation cohort. The higher cut-off constitutes a rule-in cut-off and is based on a specificity ≥0·91 in the derivation cohort. Individuals with an acNASH score between the rule-out and rule-in cut-offs are in the grey zone. In the rule-out group, the sensitivity is provided together with the specificity and negative predictive value to appraise the rule-out performance of the score. In the rule-in group, the specificity is provided together with the sensitivity and positive predictive value to appraise the rule-in performance of the score.

Abbreviations: AUROC: area under the receiver operating curve, NASH: non-alcoholic fatty liver disease, NPV: negative predictive value, PPV: positive predictive value, Se: sensitivity, Sp: specificity.

[OP-0321]

Two or more metabolic risks and/or diabetes are target population for screening significant hepatic fibrosis in primary care centers

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Objectives: Screening strategies for hepatic fibrosis are heavily focused on patients with sonographic fatty liver in primary care centers. However, metabolic risk factors are known to be independent risk factors for hepatic fibrosis. We aimed to investigate the target population for screening of significant hepatic fibrosis in primary care centers.

Materials and Methods: This was a retrospective cross-sectional cohort study using data from 13 nationwide centres. A total of 5,111 subjects who underwent both magnetic resonance elastography and abdominal ultrasound as part of their health check-up were included. Subjects with viral hepatitis and/or a history of significant alcohol consumption were excluded.

Results: The prevalence of significant hepatic fibrosis was 7.3%. Among subjects with significant hepatic fibrosis, 41.3% did not have fatty liver. Hepatic fibrosis burden increased according to the number of metabolic abnormalities. Nearly 70% of subjects with significant hepatic fibrosis also had two or more metabolic risks and/or diabetes. However, significant fibrosis prevalence did not differ between the groups with and without fatty liver among those with healthy metabolic conditions. The presence of two or more metabolic

abnormalities was an independent risk factor for significant hepatic fibrosis, even when the presence of fatty liver was corrected.
Conclusion: Presence of two or more metabolic risks and/or diabetes were risk factors for hepatic fibrosis, regardless of fatty liver status. Thus, active screening for hepatic fibrosis would better be extended to subjects with two or more metabolic risks and/or diabetes, beyond those with fatty liver in primary care centers.

[OP-0192]

Performance comparisons of two biomarker-based panels (ASAP Model and GALAD Score) for early diagnosis of hepatocellular carcinoma in nonalcoholic fatty liver disease: A multi-institutional study

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Objectives: The strategy of a combination of several serological biomarkers can enhance diagnostic accuracy of cancer diagnosis. Based on the combinations of sex, age, alpha-fetoprotein (AFP), and protein induced by vitamin K absence or Antagonist-II (PIVKA-II) with/without lens culinaris agglutinin-reactive alpha-fetoprotein (AFP-L3), ASAP model and GALAD score have been proposed as commonly-used diagnostic panels for hepatocellular carcinoma (HCC). We aimed to compare the diagnostic performance between ASAP model and GALAD model for early diagnosis of HCC in nonalcoholic fatty liver disease (NAFLD).
Materials and Methods: Participants with NAFLD or NAFLD-HCC were recruited at 6 Chinese hospitals. Serum AFP, PIVKA-II, and AFP-L3 level were measured. By using receiver operating characteristic curves (ROC) and corresponding area under the curve (AUC) analyses, the diagnostic performances of each biomarker alone, as well as ASAP model and GALAD score for the diagnosis of any-stage and early-stage NAFLD-HCC (defined by BCLC stage 0/A and 8th TNM stage I) were compared.
Results: In total, 147 patients with NAFLD-HCC and 460 control patients with NAFLD were enrolled. Both ASAP model and GALAD score had significantly higher AUCs than each biomarker alone (AFP, PIVKA-II, and AFP-L3) for the diagnosis of any-stage or early-stage NAFLD-HCC. Meanwhile, ASAP model yielded a significantly higher AUC than GALAD score for the diagnosis of any-stage NAFLD-HCC (0.910 vs. 0.879, P = 0.008), with a sensitivity of 80.3% and specificity of 92.8% at optimal cut-off of 0.156. In subgroup analyses of early-stage NAFLD-HCC, the AUC of ASAP model was higher than those of GALAD score (BCLC stage 0/A: 0.898 vs. 0.874, and TNM stage I: 0.887 vs. 0.625), with a closely significant difference (P = 0.070 and 0.052).
Conclusion: Although lacking one biomarker variable (AFP-L3), ASAP model has more diagnostic accuracy than GALAD score for the diagnosis of any-stage or early-stage HCC in patients with NAFLD.

Table. The diagnostic abilities and comparisons of the models and the individual HCC biomarkers at any-stage and early-stage.

	AUC (95%CI)	*P* value	Optimal Cut-off value	Sensitivity, %	Specificity, %	PPV	NPV	+LR	-LR
Any-stage HCC *vs.* NAFLD control									
ASAP model	0.910 (0.884-0.931)	reference	0.156	80.3	92.8	78.1	93.6	11.2	0.2
GALAD score	0.879 (0.850-0.904)	0.008	1.142	71.4	92.0	73.9	91.0	8.9	0.3
AFP, ng/ml	0.716 (0.679-0.752)	< 0.001	15.3	59.9	79.6	48.4	86.1	2.9	0.5
PIVKA-II, mAU/ml	0.849 (0.818-0.877)	< 0.001	54.0	74.8	92.4	75.9	92.0	9.8	0.3
AFP-L3, %	0.717 (0.680-0.753)	< 0.001	6.4	51.0	91.1	64.7	85.3	5.7	0.5
Early-stage HCC (BCLC stage 0+A) *vs.* NAFLD control									
ASAP model	0.898 (0.869-0.922)	reference	-0.0697	82.7	87.2	53.2	96.6	6.5	0.2
GALAD score	0.874 (0.843-0.901)	0.070	0.5434	77.8	81.1	42.0	95.4	4.1	0.3
AFP, ng/ml	0.631 (0.589-0.672)	< 0.0001	10.8	34.6	90.4	38.9	88.7	3.6	0.7
PIVKA-II, mAU/ml	0.815 (0.779-0.847)	< 0.0001	39	72.8	87.8	51.3	94.8	6.0	0.3
AFP-L3, %	0.629 (0.587-0.670)	< 0.001	0.9	34.6	91.1	40.6	88.8	3.9	0.7
Early-stage HCC (8th TNM staging I) *vs.* NAFLD control									
ASAP model	0.884 (0.854-0.910)	reference	-0.0697	81.1	87.1	55.3	95.9	6.3	0.2
GALAD score	0.858 (0.826-0.886)	0.052	0.9671	66.7	90.0	56.6	93.2	6.7	0.4
AFP, ng/ml	0.625 (0.583-0.665)	< 0.001	10.8	35.6	90.4	42.1	87.8	3.7	0.7
PIVKA-II, mAU/ml	0.803 (0.767-0.835)	0.001	54	65.6	92.4	62.8	93.2	8.6	0.4
AFP-L3, %	0.633 (0.591-0.673)	< 0.001	0.9	35.6	91.1	43.8	87.8	4.0	0.7

* ASAP: age, sex, AFP and PIVKA-II; GALAD: gender, age, AFP-L3%, AFP and PIVKA-II; AFP, α-fetoprotein; PIVKA-II, Protein induced by vitamin K absence or Antagonist-II; AFP-L3%, lens culinaris agglutinin a-reactive fraction of α-fetoprotein; AUC, area under curve; CI, confidence intervals; PPV, positive prediction value; NPV, negative prediction value; LR, likelihood ratio; NAFLD-HCC, non-alcoholic fatty liver disease related hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease.

[OP-0105]

The importance of metabolic syndrome status for the risk of non-viral hepatocellular carcinoma: A nationwide population-based study

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Objectives: The positive association between metabolic syndrome (MetS) and hepatocellular carcinoma (HCC) has been suggested. However, no studies have yet looked at how the risk of developing HCC varies with changes in MetS status. Therefore, we aimed to investigate the association between changes in MetS and subsequent HCC development.
Materials and Methods: Data were obtained from the Korean National Health Insurance Service. 5,975,308 individuals who participated in health screenings both in 2009–2010 and 2011–2012 were included. Subjects were divided into four groups according to change in MetS status during the two-year interval screening (from 2009 to 2011): sustained non-MetS, transition to MetS, transition to non-MetS, and sustained MetS. Cox regression analysis was used to examine the hazard ratios of HCC.
Results: During a median of 7.3 years follow-up, 25,880 incident HCCs were identified. Compared to the sustained non-MetS group, age, sex, smoking, alcohol, regular exercise, and body mass index-adjusted hazard ratios (95% confidence interval) for HCC development were 1.01 (0.97–1.05) for the transition to MetS group; 1.05 (1.003–1.09) for the transition to non-Met group; and 1.07 (1.03–1.10) for the sustained MetS group. Stratified analyses according to age, sex, smoking, alcohol intake, exercise, diabetes

mellitus, hypertension, dyslipidemia, and chronic kidney disease showed similar results.
Conclusion: A significantly increased HCC risk was observed in the sustained MetS and transition to non-MetS groups. The baseline status of MetS was associated with the risk of HCC development. Strategies to improve MetS, especially targeting insulin resistance might prevent HCC development.

[OP-0089]

Exercise Reduces the risk of chronic kidney disease in individuals with nonalcoholic fatty liver disease: A nationwide cohort study

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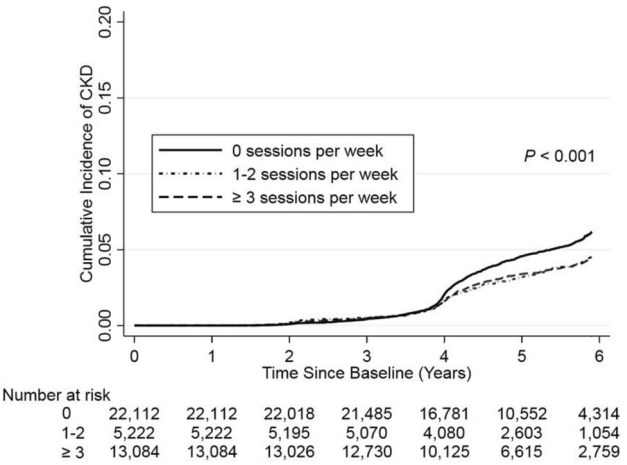
Objectives: Recent studies of individuals with nonalcoholic fatty liver disease (NAFLD) have indicated benefits of exercise in improving outcomes. We investigated whether exercise reduces the risk of chronic kidney disease (CKD) in individuals with NAFLD.
Materials and Methods: A total of 7,275 participants from the Korea National Health and Nutrition Examination Survey (KNHANES) cohort, and 40,418 participants with NAFLD from the National Health Insurance Service (NHIS) cohort were included for the cross-sectional and longitudinal analyses, respectively. For the cross-sectional analysis, the primary outcome was prevalent CKD, defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. For the longitudinal analysis, the primary outcome was incident CKD, defined as the occurrence of eGFR < 60 mL/min/1.73m^2 or proteinuria ($\geq$ trace on dipstick test) on two consecutive measurements during follow-up.
Results: In the KNHANES cohort, prevalent CKD was observed in 229 (6.1%), 48 (2.6%), and 36 (2.1%) participants in the 0, 1–2, and $\geq$ 3 exercise sessions/week groups, respectively. The likelihood of prevalent CKD was lowest in participants allocated to the $\geq$ 3 sessions/week group (adjusted OR 0.49; 95% CI, 0.33–0.71; $P < 0.001$). During a median follow-up of 5.0 years in the NHIS cohort, incident CKD occurred in 1,047 (9.7/1,000 person-years), 188 (7.3/1,000 person-years), and 478 (7.4/1,000 person-years) participants in the 0, 1–2, and $\geq$ 3 sessions/week groups, respectively. The risk of incident CKD was lowest in participants allocated to the $\geq$ 3 sessions/week group (adjusted HR 0.85; 95% CI, 0.76–0.95; $P = 0.004$).
Conclusion: Exercise was significantly associated with a reduced risk of both prevalent and incident CKD in individuals with NAFLD.



[OP-0122]

Association of physical activity with mutual exacerbation of liver fibrosis, sarcopenia, and cardiovascular risk in nonalcoholic fatty liver disease

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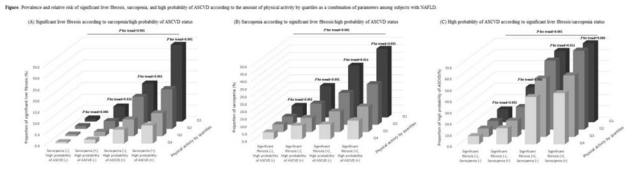
Objectives: International guidelines recommend physical activity for subjects with nonalcoholic fatty liver disease (NAFLD). This study investigated the association of physical activity with mutual risk exacerbation of liver fibrosis, sarcopenia, and cardiovascular disease (CVD) in NAFLD.
Materials and Methods: In this multicenter, cross-sectional study, 11,690 NAFLD subjects who underwent a health screening program and were assessed for physical activity (metabolic equivalent task [MET]-min/week) between 2014 and 2020 were recruited. Liver fibrosis was assessed using the fibrosis-4 index, NAFLD fibrosis score, and FibroScan-AST score. Sarcopenia using multi-frequency bioelectric impedance analysis and CVD risk using atherosclerotic CVD (ASCVD) risk score and coronary artery calcium (CAC) score were calculated.
Results: The prevalence of significant liver fibrosis, sarcopenia, high probability of ASCVD, and high CAC score significantly decreased with increasing quartiles of physical activity (all P for trend < 0.001). In a fully-adjusted model, physical activity above 600 MET-min/week ($\geq$ 3rd quartile) was independently associated with a reduced risk of significant liver fibrosis (adjusted odds ratio [aOR] = 0.59; 95% CI = 0.40–0.86), sarcopenia (aOR = 0.72; 95% CI = 0.58–0.88), high probability of ASCVD (aOR = 0.58; 95% CI = 0.46–0.73), and high CAC score (aOR = 0.32; 95% CI = 0.13–0.83;

all $P < 0.05$). Additionally, increasing amounts of physical activity was significantly associated with the mutual risk decrease between significant liver fibrosis, sarcopenia, and high probability of ASCVD (all P for trend < 0.001). In subjects with sarcopenic obesity or lean NAFLD, physical activity was also independently associated with a reduced risk of significant liver fibrosis and high probability of ASCVD (all $P < 0.05$).

Conclusion: Physical activity showed a protective effect against significant liver fibrosis, sarcopenia, and CVD in NAFLD.



[OP-0693]

Difference in impact of Diabetes mellitus and obesity on Liver-related events by age in a large-scale cohort study of Japanese patients with non-alcoholic fatty liver disease

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Objectives: Age, Diabetes Mellitus (DM), and obesity are well known to be risk factors of Liver-related events including Hepatocellular carcinoma (HCC). We estimated the impact of these factors on Liver-related events development according to age in Japanese patients with NAFLD.

Materials and Methods: We performed multi-center retrospective trial to analyzed the risk factors of Liver-related events in 1395 patients with biopsy-proven NAFLD in Japan. The median follow-up was 4.5 years.

Results: Among 1395 patients, 505 (36.2%) patients complicated DM. The median age was 57 years old. The median body mass index (BMI) was 27.4 kg/m^2 and the prevalence of obesity (BMI > 30) patients was 28.5%. During the follow-up period, 38 patients developed HCC and 59 patients developed Liver-related events. In total cohort, multivariate analysis identified advanced fibrosis (F3/4) (Hazard ratio (HR) 5.76, $p < 0.01$), age (> 65, HR 3.16, $p = 0.002$), and DM (HR 2.11, $p = 0.033$) as risk factors of development of HCC, and advanced fibrosis (HR 6.52, $p < 0.01$), age (> 65, HR 2.69, $p = 0.001$), and DM (HR 2.08, $p = 0.010$) as risk factors of development of Liver-related events. In 1005 patients under 65 years old, advanced fibrosis (HR 7.69, $p < 0.01$), and DM (HR 3.37, $p = 0.017$) as risk factors of development of HCC, and advanced fibrosis (HR 9.40, $p < 0.01$), and DM (HR 2.51, $p = 0.016$) as risk factors of development of Liver-related events. In 390 patients over 65 years old, advanced fibrosis (HR 4.80, $p = 0.003$), and BMI (> 30 kg/m^2, HR 4.24, $p = 0.008$) as risk factors of development of HCC, and advanced fibrosis (HR 4.61, $p < 0.01$), and BMI (> 30 kg/m^2, HR 3.98, $p = 0.003$) as risk factors of development of Liver-related events.

Conclusion: The presence of DM, add to advanced fibrosis, effect the development of Liver-related events in patients under 65 years old. In older patients, obesity, instead of DM contributes Liver-related events.

[OP-0028]

Prebiotics plus probiotics effect on the patients with nonalcoholic fatty liver disease

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is a very common disorder caused by a build-up of fat in the liver, often affecting overweight or obese people. Intestinal microbiota has been proved to play a role in the pathogenesis and development of obesity and NAFLD. The aim of the study was to explore the impact of probiotics' plus prebiotics' (synbiotics) on the patients with NAFLD.

Materials and Methods: We studied 79 patients in total. Control group with placebo was included. A mixture of 6 probiotic agents (Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus acidophilus, E-Coli M-17) and an auxiliary prebiotic component: fructoligosaccharide 50 mg. was prescribed to 41 patients (I group) with elevated aminotransferase and serum triglyceride (TGs) levels for 16 weeks versus 38 patients (II group) who were given placebo. Overall, the patient's alcohol consumption accounted for less than 30 g/day. Lifestyle modification was advised for both groups. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), TGs, Body Mass Index (BMI), ultrasonographic grades of fatty liver were assessed in the end of the trial.

Results: Totally, 73 patients completed the study (6 dropped out in the I group). In the first group there was a significant reduction in the serum aminotransferase levels ($p = 0.001$) and TGs levels ($p = 1.0$) comparing the placebo group. ($p = 0.998$ and $p = 0.993$, respectively). BMI reduction and improvement in ultrasonographic grading was more remarkable in synbiotics' group.

Conclusion: Synbiotics showed good results in 16 weeks in the treatment of NAFLD along with lifestyle modificitanion.

[OP-0228]

Nonalcoholic fatty liver disease accelerates loss of skeletal muscle mass: A longitudinal cohort study

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Objectives: Sarcopenia has grave physiological and clinical consequences. Early identification of at-risk population is needed for timely intervention. Whether non-alcoholic fatty liver disease (NAFLD) individuals are at increased risk of sarcopenia is not well-known.

Materials and Methods: A cohort of 52,815 men and women of 20 years of age or older who underwent at least 2 comprehensive health check-up examination with bioelectrical impedance analysis and abdominal ultrasound exam at Samsung Medical Center Health Screening Center were analyzed. NAFLD was defined with ultrasonography and excluding secondary causes. NAFLD severity was assessed using NAFLD fibrosis score. Bioelectrical impedance analysis was used to calculate appendicular skeletal muscle mass (ASM). The change of ASM during follow-up were compared for participants with and without NAFLD at baseline using linear mixed models for longitudinal data with random intercepts and random slopes.
Results: Participants with NAFLD showed faster decline in the ASM during a median of 5-years of follow-up [-0.23 kg per 5 years (95% confidence interval (CI) = -0.23, -0.22) and -0.28 kg per 5 years (95% CI = -0.29, -0.27) for participants without and with NAFLD ($P < 0.001$). In the multivariable adjusted analysis, participants with NAFLD had faster ASM loss than participants without NAFLD (-0.05 (95% CI = -0.07, -0.04) for 5 years change (kg)). When participants with NAFLD were further divided by NAFLD fibrosis score, ASM loss was much faster for NAFLD with high to intermediate NAFLD fibrosis score. In subgroup analysis, the positive association between NAFLD and change of ASM was consistently observed for all subgroups analyzed, and the association was stronger in women than men (p for interaction < 0.01).
Conclusion: NAFLD, especially those with fibrosis, was associated with faster loss of skeletal muscle mass. NALFD people need active screening and early intervention to halt skeletal muscle mass loss.

Free Papers 05 (HCC 2)

[OP-0530]

Favorable overall and recurrence-free survival following narrow-margin hepatectomy for hepatocellular carcinoma: A multicenter propensity-matched study from China

Tian Yang[1], Xiao-Xue Gou[2,3], Hong-Yun Shi[2,3], Lan-Qing Yao[1], Zheng-Liang Chen[4], Wei Ouyang[5], Jing Li[6], Yong-Kang Diao[7], Zi-Xiang Chen[8], Ting-Hao Chen[9], Wei-Min Gu[10], Jia-Le Pu[11], Ming-Da Wang[1], Chao Li[1], Cheng-Wu Zhang[7], Timothy M. Pawlik[12], Wan Yee Lau[13], Feng Shen[1], Jun Xue[14]

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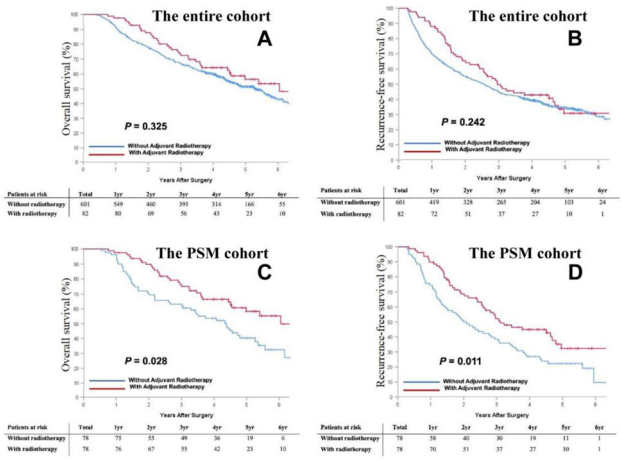
Objectives: R0 resection with wide margin is optimal for hepatocellular carcinoma (HCC), but in clinical real-world, R0 resection with narrow margin even or R1 resection is not uncommon and sometimes inescapable. This propensity-matched study aimed to identify the safety and efficacy of adjuvant radiotherapy on long-term prognosis following narrow-margin hepatectomy for HCC.
Materials and Methods: Using a multi-institutional Chinese database, the data of patients with HCC who underwent curative-intent but narrow-margin hepatectomy (resection margin ≤ 1.0 cm or pathologically positive margin) were retrospectively analyzed. The effect of adjuvant radiotherapy on long-term overall survival (OS) and recurrence-free survival (RFS) was evaluated before and after propensity score matching (PSM).
Results: Among 683 patients who met the inclusion criteria, 82 patients received adjuvant radiotherapy within 8 weeks after surgery. Radiation-induced liver disease was not reported in all these 82 patients with adjuvant radiotherapy. PSM analysis created 78 matched pairs of patients. In the PSM cohort, the median OS and RFS in patients who received adjuvant radiotherapy were more favorable than those who did not (72.5 vs. 52.5 months, P = 0.028; and 37.3 vs. 24.0 months, P = 0.011). After adjustment for other confounding factors on multivariable analyses, adjuvant radiotherapy remained independently associated with a favorable OS and RFS following narrow-margin hepatectomy for HCC (HR: 0.471; 95%, CI: 0.293–0.756, P = 0.002 and HR: 0.427, 95% CI: 0.281–0.647, $P < 0.001$, respectively).
Conclusion: Postoperative radiotherapy may be an effective, well-tolerated, and promising adjuvant strategy to improve long-term oncological prognosis for patients undergoing curative-intent but narrow-margin hepatectomy for HCC. Future randomized controlled trials are needed to further define the survival benefit of adjuvant radiotherapy in subset patients.



[OP-0710]

Long-term outcomes of transarterial radioembolization for large single hepatocellular carcinoma: A comparison to resection

Jihye Kim[1,2], Ju Yeon Kim[1], Jeong-Hoon Lee[1], Dong Hyun Sinn[2], Moon Haeng Hur[1], Ji Hoon Hong[1], Min Kyung Park[1], Hee Jin Cho[1], Na Ryung Choi[1], Yun Bin Lee[1], Eun Ju Cho[1], Su Jong Yu[1], Yoon Jun Kim[1], Jin Chul Paeng[3], Hyo Cheol Kim[4], Nam-Joon Yi[5], Kwang-Woong Lee[5], Kyung-Suk Suh[5], Dongho Hyun[6], Jong Man Kim[7], Jung-Hwan Yoon[1]

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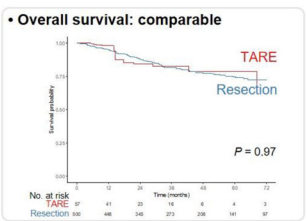
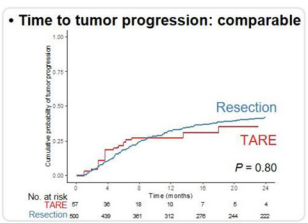
Objectives: The surgical treatment for large hepatocellular carcinoma (HCC) remains controversial due to a high risk of recurrence after resection. This study aimed to compare long-term outcomes of transarterial radioembolization (TARE) with resection for patients with large HCC.
Materials and Methods: This retrospective cohort study included a total of 557 patients who were initially treated with either resection (the resection group, n = 500) or TARE (the TARE group, n = 57) for large (≥ 5 cm) single nodular HCC at two tertiary centers in Korea. Patients with major portal vein tumor thrombosis or extrahepatic metastasis were excluded. The primary endpoint was overall survival (OS), and secondary endpoints were time to progression (TTP), time to intrahepatic progression (TTIP), and safety.
Results: The resection group were younger (median, 60 years vs. 69 years) with smaller tumor size (median, 7.0 cm vs. 10.0 cm) (all $P < 0.05$). After baseline characteristics were balanced using inverse probability of treatment weighting (IPTW), the TARE group showed comparable OS (hazard ratio [HR], 0.98; 95% confidence interval [CI], 0.40–2.43; P = 0.97), TTP (HR, 1.10; 95% CI, 0.55–2.20; P = 0.80), and TTIP (HR, 1.45; 95% CI, 0.72–2.93; P = 0.30) to the resection group. TARE was not an independent risk for OS (adjusted-HR, 1.04; 95% CI, 0.42–2.59; P = 0.93), TTP (adjusted-HR, 0.98; 95% CI, 0.50–1.95; P = 0.96), or TTIP (adjusted-HR, 1.30; 95% CI, 0.65–2.58; P = 0.46). The TARE group showed shorter hospital stay and fewer adverse events than the resection group.
Conclusion: TARE showed comparable OS, TTP, and TTIP with better safety profile compared to surgical resection for large single nodular HCC.





[OP-0470]

Atezolizumab/bevacizumab vs. lenvatinib as a first-line therapy for unresectable hepatocellular carcinoma: A real world, multi-center study

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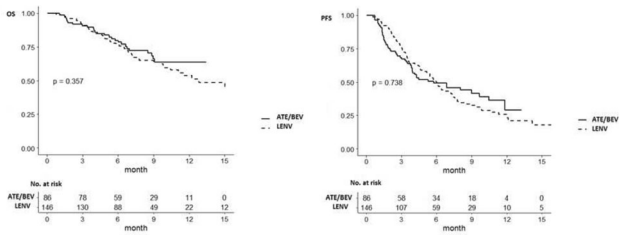
Objectives: Both lenvatinib and atezolizumab/bevacizumab have been approved as a first-line regimen to treat unresectable hepatocellular carcinoma (HCC). We aimed to compare their clinical efficacy and safety.
Materials and Methods: Patients receiving atezolizumab/bevacizumab (ATE/BEV group, n = 86) vs. lenvatinib (LENV group, n = 146) as a first-line treatment were recruited in three academic teaching hospitals. Overall survival (OS), progression-free survival (PFS), and radiological response by Response Evaluation Criteria in Solid Tumors criteria were assessed. Clinical features of two groups were balanced through propensity score (PS)-matching with 1:1 ratio and inverse probability of treatment weighting (IPTW) analyses.
Results: The median age was 62 years, with male predominance (83.6%). There was no significant difference in objective response rate between ATE/BEV and LENV groups (32.6% vs. 31.5%; p = 0.868). Neither median OS (not reached vs. 12.8 months; p = 0.357) nor PFS (5.7 vs. 6.0 months; p = 0.738) was also different between ATE/BEV and LENV groups, respectively. PS-matched and IPTW analyses yielded comparable results, in terms of OS and PFS (all $p > 0.05$). Grade ≥ 3 adverse events occurred in 5.8% and 8.2% among ATE/BEV and LENV groups, respectively (p = 0.486).
Conclusion: Both regimens as a first-line therapy against unresectable HCC provided comparable clinical efficacy and safety in the real world practice setting. Further studies with the larger sample size and longer follow-up are needed to validate these results.



[OP-0151]

Bevacizumab and atezolizumab as first-line therapy for unresectable hepatocellular carcinoma: A Taiwanese subgroup analysis

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Objectives: Two large clinical trials, IMbrave150 and GO30140, have established the combination of bevacizumab and atezolizumab as a standard first-line systemic treatment option for unresectable hepatocellular carcinoma (HCC). We examined the treatment outcomes of participants from Taiwan who received the combination in these two studies.
Materials and Methods: All patients who resided in Taiwan, enrolled in the aforementioned studies, and received bevacizumab and atezolizumab as the first-line systemic therapy were included. We extracted raw data from study records for analyses.
Results: In total, 40 patients were included; 36 (90%) had Barcelona Clinic Liver Cancer stage C disease. Macrovascular invasion was found in 20 (50%) patients. Hepatitis etiology was chronic hepatitis B and C in 62.5% and 27.5% of patients, respectively. According to RECIST 1.1, the response rate was 37.5%, and the disease control rate was 85% (Table 1). The median duration of response was 21.4 months. The median progression-free survival and overall survival was 8.6 (95% confidence interval [CI], 5.6–18.6) and 24.9 (95% CI, 14.2-not estimable) months, respectively. With a median duration of bevacizumab treatment of 8.7 months and that of atezolizumab treatment of 9.6 months, all-cause and treatment-related grade 3 or 4 adverse events developed in 27 (67.5%) and 20 (50%) patients, respectively. The most common adverse events were proteinuria (50%) and hypertension (37.5%), the median onset of which were 157 and 127 days, respectively.
Conclusion: In Taiwanese patients, the efficacy and safety outcomes of bevacizumab and atezolizumab treatment were consistent with the intent-to-treat populations of the two prospective clinical trials.

Table 1. Best overall response per RECIST 1.1

	N	%
Complete response	3	7.5
Partial response	12	30
Stable disease	19	47.5
Progressive disease	5	12.5
Response rate	37.5%	
Disease control rate	85%	

[OP-0546]

Hyperprogressive disease (HPD) and the importance of early radiological assessment in the treatment with atezolizumab plus bevacizumab for advanced hepatocellular carcinoma patients

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Objectives: Hyperprogressive disease (HPD) triggered by immune checkpoint blockade has already been reported in other types of malignancies, and is known to occur immediately after the administration. Sor far, little knowledge regarding to HPD in advanced hepatocellular carcinoma (HCC) treated with atezolizumab plus bevacizumab (Atezo/Bev) is available at this time. In this study, we conducted a detailed analysis of radiological response of patients treated with Atezo/Bev in a real-world clinical practice, and attempted to investigate the incidence of early PD and HPD as well as the factor associated with HPD.
Materials and Methods: We retrospectively collected data of advanced HCC patients who introduced Atezo/Bev from October 2020 to May 2021 at six institutions in Japan. The observation period was until August 2021. Early PD was defined as PD within 2 months after administration, and HPD was defined as previously reported: tumor growth of more than 50% of PD within 2 months, appearance of two or more new lesions, or appearance of new metastases in other organs. We performed a multivariate analysis in occurrence of HPD, including the neutrophil/lymphocyte ratio (NLR), which has been reported to be associated with HPD.
Results: In this study, 117 patients were collected. The median age of the patients was 73 years (48–89), and 35 patients (29.9%) had HCV and 22 patients (18.8%) had HBV. The median observation period was 6.4 months. Early PD and HPD were observed in 21 patients (17.9%) and 14 patients (66.7% of early PD). Logistic regression analysis showed higher baseline NLR was an independent factor of occurrence of HPD ($p = 0.031$).
Conclusion: The frequency of early PD was comparable to the results of the IMbave 150 trial. The majority of patients with early PD within 2 months classified as HPD in this study. High baseline NLR might be a predictor of HPD in patients with advanced HCC received.

[OP-0796]

The value of PD-L1 expression in predicting the response to PD-1 or PD-L1 inhibitors in patients with hepatocellular carcinoma: A systematic review and meta-analysis

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Objectives: The introduction of programmed death 1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitors into clinical practice has had a revolutionary effect on treatment of HCC, but consistent responses are only observed in a fraction of patients. A biomarker-driven clinical decision-making strategy is desirable. The aim of this systemic review and meta-analysis is to determine if PD-L1 expression is a prognostic factor for objective response rate (ORR) and disease control rate (DCR) in patients with HCC being treated with PD-1 or PD-L1 inhibitors.
Materials and Methods: A comprehensive search of PubMed, Embase, Web of Science, and the Cochrane Library was conducted. Studies comparing ORR and/or DCR based on tumor PD-L1 status in HCC patients were eligible. Only studies reporting results of clinical trials in English were included.
Results: Eleven studies with 1330 HCC patients treated with PD-1 or PD-L1 inhibitors were included. The pooled odds ratio (OR) revealed a significantly improved ORR in patients with PD-L1 positive HCC than that in patients with PD-L1 negative HCC (OR, 1.86, 95% CI, 1.35–2.55 $p < 0.001$; $I^2 = 0.0\%$). The pooled ORR in the PD-L1 positive and PD-L1 negative group were 26% (95% CI, 20%-32%) and 18% (95% CI, 13%-22%), respectively. For DCR, the pooled OR showed no significant difference between the PD-L1 positive patients and PD-L1 negative patients (OR, 0.92; 95% CI, 0.59–1.44, $p = 0.723$; $I^2 = 0.0\%$). The pooled DCR in PD-L1 positive and PD-L1 negative patients were 66% (95% CI, 55%-76%) and 69% (95% CI, 62%-76%), respectively.
Conclusion: For HCC patients receiving PD-1 or PD-L1 inhibitors treatment, PD-L1 positivity of the tumor is a prognostic factor for ORR but not for DCR. Additional studies with larger sample sizes are needed for further validation.

[OP-0724]

Comparable effectiveness of sorafenib and lenvatinib for unresectable hepatocellular carcinoma in patients with hepatic decompensation

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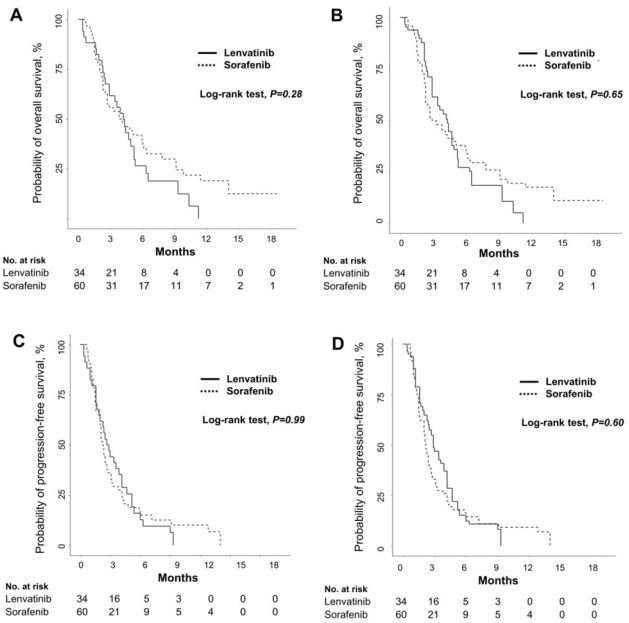
Objectives: Lenvatinib and sorafenib are currently available to treat patients with advanced hepatocellular carcinoma (HCC). However, since the clinical trials evaluating the efficacy of lenvatinib and sorafenib included only patients with Child–Pugh class A, little is known about the effectiveness of the treatments in patients with hepatic decompensation. We compared the effectiveness of lenvatinib and sorafenib in decompensated patients with unresectable HCC.
Materials and Methods: Consecutive patients who were classified as Child–Pugh class B or C and received lenvatinib or sorafenib as first-line systemic therapy for unresectable HCC between November 2018 and April 2020 at a tertiary referral center were included in this retrospective study. The primary outcome was overall survival (OS), and the secondary outcomes were progression-free survival (PFS), time-to-progression, best overall tumor response and safety profiles.
Results: Among 94 patients, 34 received lenvatinib and 60 received sorafenib. The median OS was 4.1 months (95% confidence interval [CI], 2.9–5.2): 4.2 months (95% CI, 2.9–5.3) for lenvatinib and 4.1 months (95% CI, 2.7–6.4) for sorafenib. The treatment regimen was not associated with significant improvement in OS after adjusting for covariables (adjusted hazard ratio [aHR], 0.92; 95% CI, 0.54–1.54; P = 0.74). The treatment regimen was not an independent predictor for PFS (lenvatinib vs. sorafenib; aHR, 0.77; 95% CI, 0.48–1.24; P = 0.28). HRs were maintained even after balancing with the inverse probability treatment weighting method. Objective response rates were 11.8% and 6.7% in patients receiving lenvatinib and sorafenib, respectively (P = 0.45). Ten patients in the both groups (5 in the lenvatinib group and 5 in the sorafenib group) underwent dose modification due to adverse events and there was no significant difference between the treatment groups (P = 0.49).
Conclusion: The effectiveness of lenvatinib and sorafenib was comparable for the treatment of unresectable HCC in decompensated patients.



[OP-0960]

Effectiveness and tolerability of carrelizumab combined therapy for advanced hepatocellular carcinomain in patients with Child–Pugh B: A retrospective, multicenter, observational study

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Objectives: Programmed cell death protein1 (PD-1) targeted immunotherapy has shown promising results in phase II studies of advanced hepatocellular carcinoma (aHCC). However, the effectiveness and tolerability of carrelizumab combined therapy in patients with aHCC and Child–Pugh B remains lack. Our study aimed to assess the antitumour activity and tolerability of carrelizumab combined therapy in a multicenter, real?world cohort in this population in China.

Materials and Methods: Patients received intravenous carrelizumab 200 mg every 3 weeks until unacceptable toxicity or disease progression. Primary endpoints were tolerability and 12-month overall survival (OS). The secondary endpoints were objective response rate (ORR) and Disease control rate (DCR) by investigator assessment (using Response Evaluation Criteria in Solid Tumors v1.1).

Results: Between 2019-1-10 and 2021-3-31, 127 patients were screened for eligibility, of whom 99 eligible aHCC patients with Child–Pugh B (n = 41) or Child–Pugh A (n = 58) were included. Median follow-up was 12.1 months. The OS probability at 12-months were 49.7% and 69.4% in Child–Pugh B and A, respectively. Grade 3/4 immune-related adverse events occurred in 26.8% patients with Child–Pugh B including one potentially treatment-related deaths (multiple organ failure). The most common were immune thrombocytopenia and **hepatotoxicity**, which similar with patients with Child–Pugh A. The ORR and DCR were 31.7% and 65.9% in patients with Child–Pugh B, were comparable with patients with Child–Pugh A. Median progression-free survival (PFS) were 5.1 months (95% CI 3.0–7.1) and 7.2 months (95% CI 4.7–8.3), respectively. The 6-month and 12-month PFS were 43.4% and 18.0% in Child–Pugh B patients, similar to Child–Pugh A patients. However, median OS was shorter in Child?Pugh B patients (11.3 vs 7.6 months; P = 0.12) (table 1).

Conclusion: Camrelizumab combined therapy showed clinical activity and favourable safety with manageable toxicities in Chinese patients with Child–Pugh B aHCC, suggesting it could be suitable for these population.

Table 1. Assessable radiological response, survival and tolerability

Variable	Overall response mRECIST (n,%)		
	Overall (n=99)	CHILD A (n=58)	CHILD B (n=41)
Complete response	7(7.1)	3 (5.2)	4(9.8)
Partial response	29(29.3)	20(34.5)	9(22.0)
Stable disease	31(31.3)	17(29.3)	14(34.1)
Progressive disease	32(32.3)	18(31.0)	14(34.1)
Objective response rate	36(36.4)	23(39.7)	13(31.7)
Disease control rate	67(67.7)	40(69.0)	24(65.9)
PFS, median (95% CI)	5.3 (4.3-6.9)	7.2 (4.7-8.3)	5.1 (3.0-7.1)
6-months PFS	45.5%	48.3%	43.4%
12-month PFS	20.7%	21.9%	18.0%
OS, median (95% CI)	8.9 (7.5-10.4)	11.3 (8.5-12.9)	7.6 (6.5-9.3)
6-months survival	71.7%	74.1%	66.0%
12-months survival	61.3 %	69.4%	49.7%
Any irAEs	52(52.5)	27(46.6)	25(61.0)
Grade 3 or 4	17(17.2)	10(17.2)	11(26.8)
Thrombocytopenia	10(10.1)	3(5.2)	7(17.1)
Hepatotoxicity	13(13.1)	7(12.1)	6(14.6)
Diarrhea	1(1.0)	0	1(2.4)
Cardiotoxicity	1(1.0)	0	1(2.4)
Hyperthyroidism	1(1.0)	0	1(2.4)
Pulmonary toxicity	1(1.0)	1(1.7)	0

[OP-0424]

Ranking of transarterial and targeted therapies for advanced hepatocellular carcinoma in the era of immuno-oncology: A network meta-analysis of randomized sorafenib-controlled trials

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Objectives: There have been no studies comparing the new first-line atezolizumab + bevacizumab with transarterial therapies combined with the prior standard-of-care, sorafenib, in patients with advanced hepatocellular carcinoma (HCC). We compared and ranked all relevant transarterial and targeted treatments competing with atezolizumab + bevacizumab in dealing with such disease, based on direct and indirect evidence.

Materials and Methods: The network meta-analysis was conducted in the context of a systematic review of phase 2 and 3 randomized sorafenib-controlled trials investigating systemic treatment strategies for metastatic and/or locally advanced HCC as first-line option published between 2008 and 2021. We ranked the treatments based on overall survival (OS) as the primary outcome, together with progression-free survival (PFS) and grade 3–4 adverse events. Subgroup

analyses were also implemented to estimate the efficacies of the interventions in particular groups.
Results: We identified 3,451 publications, and 15 trials comprising 7,158 patients were finally included in the analysis: they involved 14 different therapies including combinations of sorafenib with transarterial chemoembolization (TACE), hepatic arterial chemoinfusion, and radioembolization. Regarding OS, atezolizumab + bevacizumab was the only regimen significantly superior to sorafenib (hazard ratio 0.42; 95% confidence interval [CI] 0.25–0.70), and it ranked first. This combination was also the best in the PFS analysis (0.59; 0.47–0.74), followed by lenvatinib (0.66; 0.57–0.76) and TACE + sorafenib (0.73; 0.59–0.91), which all had significantly better outcomes than sorafenib alone. TACE + sorafenib (0.52; 0.27–1.00) was ranked first based on OS in a subset with portal invasion, but not in the metastatic series, with atezolizumab + bevacizumab second (0.58; 0.38–0.89). Lenvatinib (odds ratio 1.76; 95% CI 1.35–2.30) and TACE + sorafenib (2.02; 1.23–3.32), but not atezolizumab + bevacizumab (1.38; 0.93–2.05), were significantly less safe than sorafenib monotherapy.
Conclusion: Our results indicate that atezolizumab + bevacizumab is the best first-line clinically relevant systemic modality in patients with advanced HCC. TACE + sorafenib may also be considered for the disease with portal invasion. (PROSPERO No. CRD42021250701).

Free Papers 06 (Late-Breaking Abstracts)

[L-OP-1322]

Oncolytic activity of a chimeric influenza A virus carrying human CTLA4 antibody in hepatocellular carcinoma

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Objectives: Oncolytic virotherapy belongs to a kind of active immunotherapy, which could trigger potent anti-tumor immune response, showing a great potential in clinical application. Ovs could induce immune responses through the dual mechanisms of selective tumor-killing without destroying normal tissues and induction of systemic anti-tumor immunity.
Materials and Methods: In this study, we successfully rescued a chimeric oncolytic influenza virus carrying human CTLA4 antibody in the background of the A/PR/8/34 (PR8) virus. The chimeric virus, called rFlu-huCTLA4, contained the heavy and light chains of human CTLA4 antibody in the PB1 and PA segments of the PR8 virus, respectively.
Results: The first-generation hemagglutination (HA) titers of the rFlu-huCTLA4 virus ranged from 2^7 to 2^8, which could be passaged stably in specific pathogen-free (SPF) chicken embryos from P1 to P5. The morphology and size distribution of the chimeric virus was consistent with that of the wt influenza virus. rFlu-huCTLA4 virus could effectively replicate in various cells in time- and dose-dependent manners. ELISA assay revealed that the secreted huCTLA4 antibody levels in chicken embryos increased gradually over time. Furthermore, MTS and crystal violet analysis showed that the selective cytotoxicity of the virus was higher in hepatocellular carcinoma cells (HepG2 and Huh7) than in normal liver cells (MIHA). In vivo experiments displayed that intratumoral injection with rFlu-huCTLA4 reduced the tumor growth and increased the survival of mice compared with PR8 group. More importantly, in rFlu-huCTLA4 group, we founded that CD4 + and CD8 + T cells were significantly increased in tumor-bearing BALB/c mice.
Conclusion: Taken together, these results demonstrated that the chimeric oncolytic virus rFlu-huCTLA4 could selectively destroy hepatoma cells in vitro and in vivo, and may provide a promising clinical strategy for targeted immunotherapy of HCC with oncolytic flu virus.

[L-OP-1324]

Safety and antiviral activity of two monthly administrations of BRII-835 (VIR-2218), an X-targeting RNAi therapeutic, in Chinese patients with chronic HBV infection

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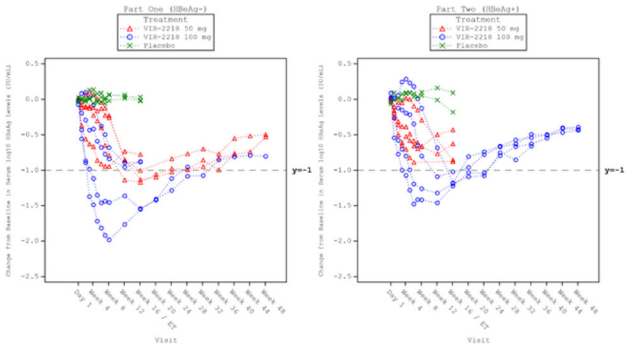
Objectives: BRII-835 (VIR-2218) is an investigational GalNAc-conjugated small interference RNA therapeutic in development for functional cure of chronic hepatitis B infection. A previous study showed that two doses of BRII-835 at 20–200 mg given monthly were well tolerated in CHB participants with substantial reductions in HBsAg observed in both HBeAg- and HBeAg + participants across all dose levels (EASL 2021). We present the safety and antiviral activity data from a phase 2 randomized, double-blind, placebo-controlled trial of BRII-835 in Chinese participants with CHB.
Materials and Methods: Non-cirrhotic, virally suppressed participants received 2 subcutaneous doses of BRII-835 or placebo 4 weeks apart. HBeAg-negative or HBeAg-positive participants were randomized (4:1) to receive 50 mg or 100 mg BRII-835. Assessments included safety and HBsAg level through Week 16 for all participants post 2nd dose and an additional 32 weeks of follow-up for participants achieving HBsAg reduction ≥ 1 $\log_{10}$.
Results: A total of 16 participants received BRII-835 (8 HBeAg-; 8 HBeAg +). 6/16 (37.5%) subjects receiving BRII-835 experienced at least one treatment emergent adverse event (TEAE). No participants discontinued due to AE, and all the TEAEs were either Grade 1 or 2 in severity. No clinically significant ALT elevations were observed. Mean maximum $\log_{10}$ HBsAg declines by Week 16 in HBeAg- participants receiving 50 and 100 mg BRII-835 were 1.06 and 1.35 IU/ml, respectively. For HBeAg + participants receiving 50 and 100 mg BRII-835, the mean maximum $\log_{10}$ HBsAg declines were 0.79 and 1.27 IU/ml, respectively.
Conclusion: Two monthly doses of BRII-835 at 50 or 100 mg were well tolerated in Chinese CHB patients. Notable reduction in serum HBsAg levels were observed in both HBeAg- and HBeAg + participants. Consistent with previous findings, these data suggest that BRII-835 may silence transcripts from both cccDNA and integrated DNA, supporting further development of BRII-835 as a key component of combination regimens to achieve functional cure.



[L-OP-1214]

Liver inflammation in Asian chronic hepatitis B patients with detectable HBV-DNA and normal alanine aminotransferase according to diverse upper limits of normal

Rui Huang[1], Jiacheng Liu[2], Jian Wang[1], Li Zhu[3], Yiguang Li[4], Ming Li[5], Zhonghua Lu[4], Yuanwang Qiu[4], Chuanwu Zhu[3], Weimao Ding[6], Jie Li[1], Chao Wu[1]

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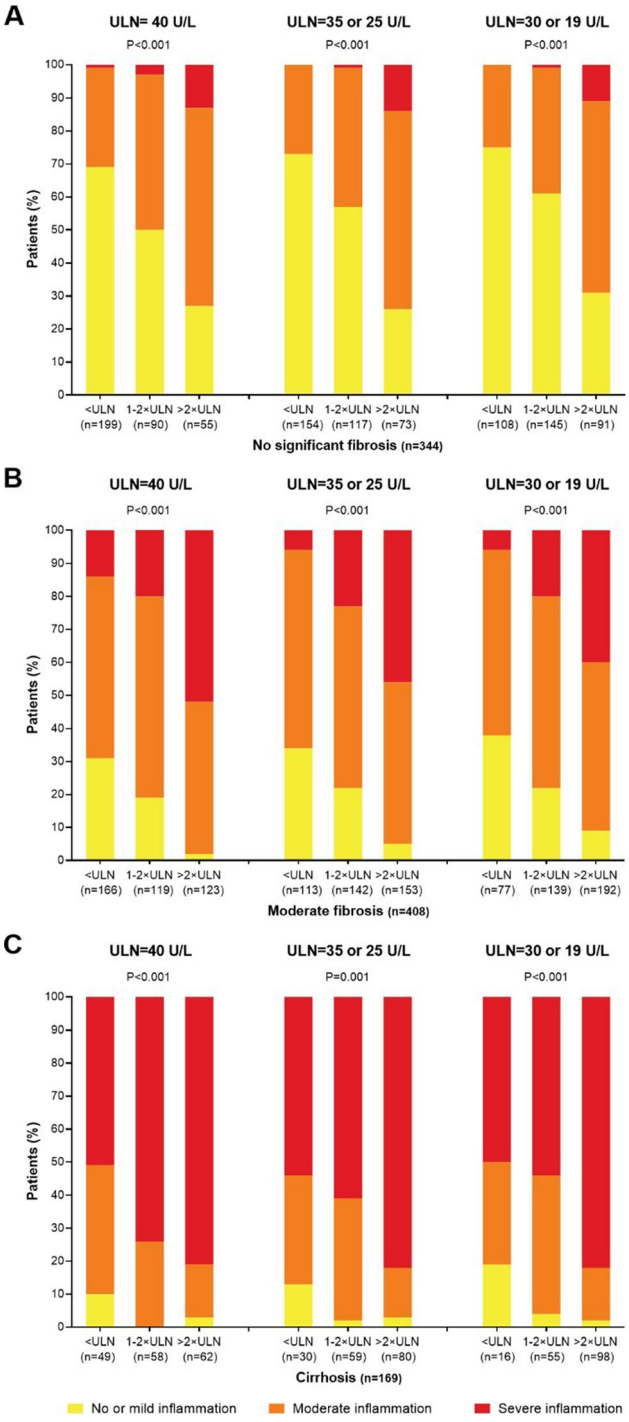
Objectives: Upper limits of normal (ULN) for alanine aminotransferase (ALT) are different among international guidelines or recommendations for chronic hepatitis B (CHB). We investigated the proportion of significant inflammation in Asian CHB patients with detectable HBV-DNA under diverse ALT ULNs.

Materials and Methods: CHB patients with detectable HBV-DNA underwent liver biopsy were included from four hospitals. Liver inflammation and fibrosis were assessed by Scheuer's classification. ULN was defined as 40 U/L in EASL 2017 and APASL 2015, 35/25 U/L (male/female) in AASLD 2018, and 30/19 U/L (male/female) in East Asia recommendations 2020. The definitions of significant inflammation and fibrosis were G $\geq$ 2 and S $\geq$ 2, respectively.

Results: Of 921 patients included, 640 (69.5%) patients had significant inflammation, while 577 (62.6%) had significant fibrosis. 85.6% of patients with significant fibrosis and 42.4% of patients without significant fibrosis had significant inflammation. Among CHB patients with detectable HBV-DNA and normal ALT, the proportions of those with significant inflammation was 43.8% according to the ALT ULN of 30/19 U/L (male/female), while the corresponding proportions were 53.1% and 48.1% according to the ULNs of 40U/L and 35/25 U/L (male/female), respectively. In patients with detectable HBV-DNA and normal ALT levels in absence of significant fibrosis, the proportions of significant inflammation were comparable among different ULNs of ALT by 40 U/L (30.7%), 35/25U/L (27.3%) and 30/19 U/L (25.0%).

Conclusion: A quarter of CHB patients with detectable HBV-DNA and normal ALT without significant fibrosis had significant inflammation irrespective of the ALT ULNs. The optimal ULNs of ALT for CHB patients deserve further investigation and novel biomarkers for liver inflammation are urgently needed.



[L-OP-1215]

Outcomes of interferon free direct acting antiviral therapy in patients with hcv-related decompensated cirrhosis: A systematic review and meta-analysis

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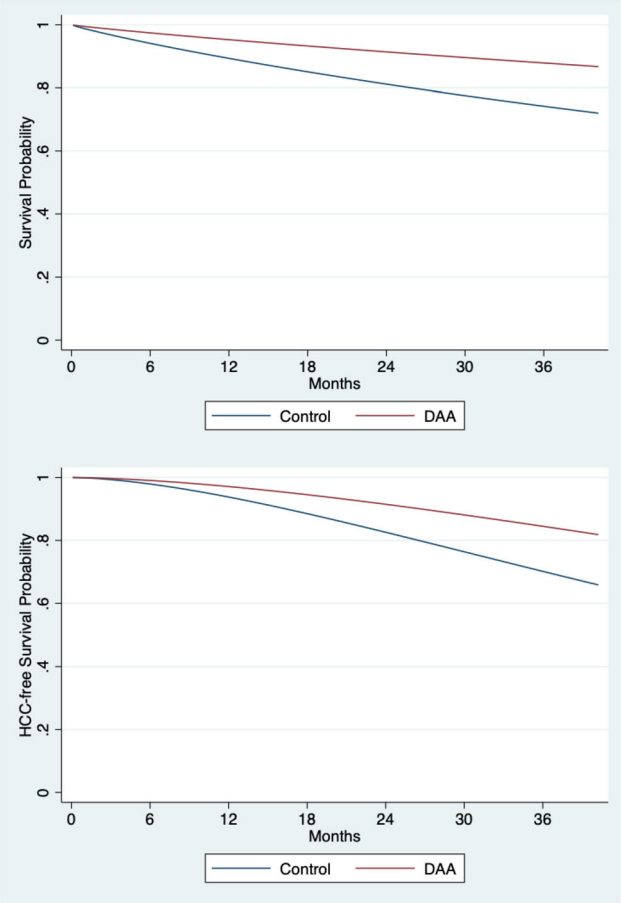
Objectives: Direct-acting antiviral (DAAs) is an effective treatment for chronic hepatitis C virus (HCV) infection. Even though, Interferon free DAAs show to be safe and high sustained virologic response (SVR) rate in decompensated HCV cirrhosis, but improvement of liver function test and mortality in this population after DAAs treatment remain questionable. This meta-analysis was performed to confirm the benefits of DAAs in decompensated HCV cirrhosis patients, including overall survival (OS), hepatocellular carcinoma (HCC) free survival and model for end-stage liver disease (MELD) score.

Materials and Methods: Relevant studies were identified by searching MEDLINE, SCOPUS and CENTRAL from inception to September 30th, 2021. Two independent reviewers screened titles and abstracts to ensure eligibility. Relevant data were extracted. One-stage meta-analysis using parametric survival regression with Weibull distribution was performed for overall survival and HCC free survival analyses. In addition, hazard ratios (HRs) and mean difference of the MELD score were also pooled in a two-stage random-effect meta-analysis.

Results: Of 4561 studies, seven cohorts with 3430 participants were included into meta-analysis (with DAAs vs. Control, 1568 vs. 1862 participants). The 12- and 24-month OS rates were 98% and 93% for those in DAAs group, compared with 94% and 87% for those in control group. The OS HR was 0.43 (95% CI: 0.32, 0.56; $p < 0.001$). The 12- and 24- month HCC free survival was higher in the DAAs group than those in control group: 97% versus 95% and 95% versus 90%, respectively. The HR was 0.69 (95% CI: 0.47, 1.02; $p = 0.060$). The MELD score was significantly improved in the DAAs group with the mean difference of -7.75 (95% CI: -14.52, -0.98; $p = 0.020$).

Conclusion: DAAs were effective treatments even in decompensated HCV cirrhosis patient to prolong survival and decrease HCC occurrence. Interestingly, DAAs treatment was significantly associated with improvement of MELD score within 6 months after treatment.



[L-OP-1217]

Natural history, response to corticosteroids and outcomes of acute on chronic liver failure in patients with alcohol associated hepatitis- a multicentric study from AARC

Rakhi Maiwall[1], Shiv Kumar Sarin[1], Ashok Choudhary[1], Dong Joon Kim[2], Ajit Sood[3], Harshad Devarbhavi[4], Anil Arora[5], Manoj Kumar Sahu[6], Sudhir Maharshi[7], Ajay Kumar Duseja[8], Y K Chawla[8], P N Rao[9], Hashmik Ghaznian[10], Saeed Hamid[11], C E E[12], Ananta Shreshtha[13], Samir Shah[14], Jinhua Hu[15], V G Mohan Prasad[16], Nan Yuemin[17], Xin Shaojie[18], R K Dhiman[19], Han Tao[20], Qin Ning[21], Charles Panackel[22], Madunil A Niriella[23], Soek-Siam Tan[24], A Kadir Dokmeci[25], Amna Subham[26], Akash Shukla[27]

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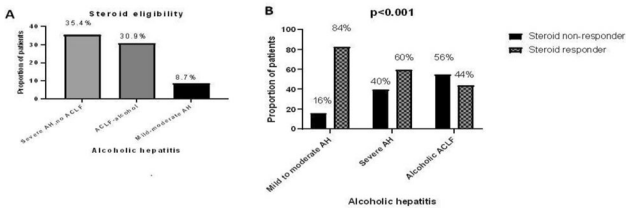
Objectives: Acute-on-chronic liver failure (ACLF) is reported to be a severe form of severe alcoholic hepatitis (SAH) We aimed to study the natural course, response to corticosteroids and outcomes of ACLF in AH patients.
Materials and Methods: Prospectively collected data from the Asia–Pacific-association of study of liver (APASL) research consortium (AARC) database was analyzed.
Results: Of the 1249 AH patients, (aged 43.8 ± 10.6 years, 96.9% male, AARC score 9.2 ± 1.9), 38.8% died on a 90-day follow-up. Of these, 150 (12.0%) had moderate AH (Gr.I), 65 (5.2%) had SAH without ACLF (Gr.II) and 1034 (82.8%) had SAH with ACLF [Gr.III] at enrolment. Two-hundred and eleven (16.9%) patients received corticosteroids (CS), of which, 101 (47.87%) were steroid responders by day 7 Lille's model, which was associated with improved survival [Hazard ratio (HR) 0.15, 95% CI 0.12–0.19]. Absence of AARC-ACLF grade 3 [OR 0.28, 0.14–0.55] was an independent predictor of steroid response and mortality [HR 3.29, 2.63–4.11]. Complications increased with degree of liver failure [AARC grade III vs. II vs 1, bacterial infections [48.6% vs. 37% vs.34.7%; $p < 0.001$); extra-hepatic organ failure [66.9% vs. 41.8% vs. 1 35.4%; $p < 0.001$] respectively. The AARC score better discriminated 90-day mortality (Harrell's Concordance index) (0.72) compared to other scores.
Conclusion: Nearly 4 of 5 patients with AH present with ACLF. Such patients have a higher risk of infections, organ failures, lower response to corticosteroids and higher mortality. Patients with AH and ACLF with AARC grade 3 should be considered for an early liver transplant.



[L-OP-1286]

Clinical significance of systemic inflammation in cirrhotic patients with acute decompensation

Baek Gyu Jun[1], Eileen Yoon[2], Young Kul Jung[3], Ki Tae Suk[4], Do Seon Song[5], Hee Yeon Kim[5], Sung Won Lee[5], Hyung Joon Yim[3], Sung Eun Kim[6], Seong Hee Kang[7], Moon Young Kim[7], Seung Won Jeong[8], Jae Young Jang[8], Sang Gyune Kim[9], Jeong-Ju Yoo[9], Jin Mo Yang[5], Jung Gil Park[10], Won Kim[11], Hyun Chin Cho[12], Dong Joon Kim[4]

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Objectives: Some evidence suggests that the systemic inflammatory response syndrome (SIRS) contributes to the poor outcome of Acute decompensation (AD) of cirrhosis. The aim of this study is to assess prevalence of SIRS and its relationship with in-hospital outcome and acute-on-chronic liver failure (ACLF).
Materials and Methods: A total of 1,071 alcoholic LC (liver cirrhosis) patients with AD were enrolled. ACLF was defined in the CANONIC study as an AD resulting in liver failure. Presence of SIRS was assessed on admission and during hospital stay. Main clinical outcomes were death and secondary clinical outcome is to evaluate association with SIRS and ACLF.
Results: SIRS was present on admission in 308 of 1162 patients (26.5%). Presence of SIRS and ACLF at admission was not associated with 28-day mortality ($p = 0.925$). On univariate analysis, presence of SIRS and ACLF during hospital day ($p < 0.001$), model for end-stage liver disease (MELD) score ($p < 0.001$), lactate ($p < 0.001$) was associated with 28-day mortality ($p = 0.001$). On multivariate analysis, presence of SIRS and ACLF during hospital day were associated with 28-day mortality ($p < 0.001$). ACLF was not associated with SIRS ($p = 0.858$) and was associated with MELD score ($p < 0.001$).
Conclusion: SIRS frequently occurs in patients with cirrhosis. The presence of SIRS with ACLF during the hospital is a major independent prognostic factor in patients with cirrhosis. SIRS and ACLF affect independently 28-day mortality in LC.

[L-OP-1255]

Unresectable locally advanced HCC downstaged to surgical resection by selective internal radiation Therapy with Yttrium-90 have overall survival superior to surgically resected locally advanced HCC

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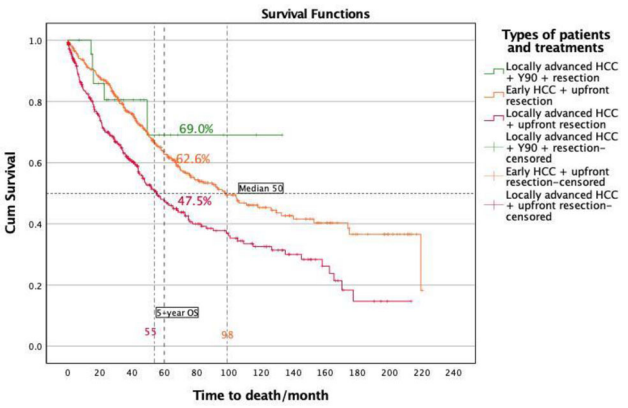
Objectives: Locally advanced HCC (beyond BCLC A, including PVT but without extra-hepatic metastases) that are unresectable because of inadequate future liver remnant may be downstaged by selective internal radiation therapy (SIRT) with Yttrium-90 (now FDA-approved standalone treatment for HCC), to subsequently receive surgical resection. We hypothesized that HCC downstaged to resection will have overall survival (OS) and recurrence-free survival (RFS) superior to locally advanced HCCs that were resected up front and at least similar outcome to surgically resected early staged HCC.
Materials and Methods: We reviewed all patients who underwent surgical resection for HCC between 1st January 2000 and 31st December 2019 and identified those that had locally advanced HCC, were downstaged with Y90-SIRT and were referred for consideration of surgical resection. OS and RFS of patients resected upfront for early and locally advanced HCC and those resected after downstaging were obtained using the Kaplan Meier method and compared using Log-rank (Mantel-Cox) test.
Results: 1141 patients had surgical resection for HCC within the study period. 875 were resected upfront (473 early, 402 locally advanced) and 23 locally advanced HCC were downstaged with SIRT before resection. These 23 patients had disease states not amenable to upfront surgical resection. Locally advanced HCC patients downstaged with Y90 before resection have significantly better OS and RFS than locally advanced HCC with upfront resection (5-year OS of 69.0% versus 47.5% p = 0.048; 5-year RFS of 53.5% vs 27.0%, p = 0.047) and similar OS and RFS with resected early HCC (5-year OS of 69.0% versus 62.6% p = 0.475; 5-year RFS of 53.5% vs 39.0%, p = 0.736).
Conclusion: In addition to downstaging HCC to resection, Y90-SIRT also produces a change in tumour biology that favours a better prognosis. A randomised controlled trial to the role of SIRT as neoadjuvant therapy in locally advanced HCC can potentially change the current practice.



[L-OP-1271]

Safety of tacrolimus monotherapy versus tacrolimus/mycophenolate mofetil therapy within 12 months after liver transplantation: Analysis with KOTRY registry data

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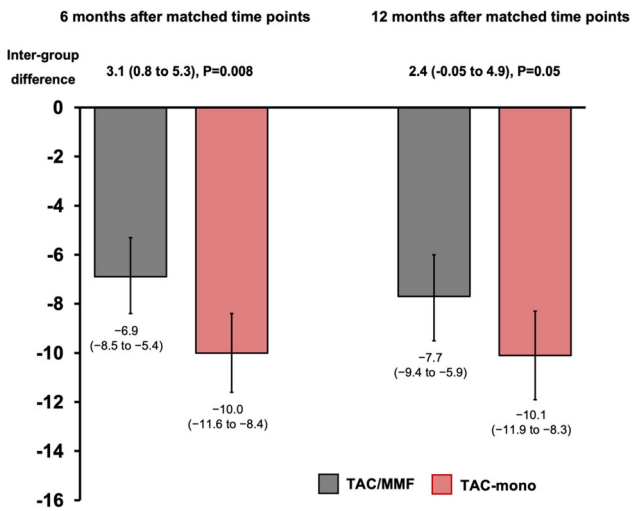
Objectives: The consequences of tacrolimus (TAC) monotherapy in liver transplantation (LT) have not been established in recent era since mycophenolate mofetil (MMF) was introduced. This study compared the safety of TAC monotherapy and TAC/MMF combination therapy when administered within the first 12 months after LT.
Materials and Methods: We retrospectively performed matched analysis on time-conditional propensity scores with LT recipients included in the Korean Organ Transplantation Registry. Patients receiving TAC monotherapy (TAC-mono group; n = 991) from 1-month, or switching from TAC/MMF to TAC-mono at 6-month, and 12-month after LT were chronologically matched to patients continuing to receive TAC/MMF (TAC/MMF group; n = 991) at corresponding time points of TAC-mono group. Outcomes within 12 months after matched time points were compared.
Results: Cumulative incidence of biopsy-proven rejection were similar between the TAC/MMF group (3.5%) and TAC-mono group (2.6%; P = 0.38). Graft failure rates were also similar between the TAC/MMF group (0.2%) and TAC-mono group (0.7%; P = 0.08). However, eGFR declines of TAC-mono group were 3.1 mL/min/1.73 m^2 (95% CI 0.8 to 5.3) greater at 6 months (P = 0.008) and 2.4 mL/min/1.73 m^2 (95% CI -0.05 to 4.9) greater at 12 months (P = 0.05) after matched time points compared to TAC/MMF group. TAC mono group also had higher TAC trough levels from matched time points to 12 months later.
Conclusion: TAC monotherapy within 12 months after LT is immunologically safe. However, it can lead to the higher required dose of TAC and more decline in renal function than continued TAC/MMF combination therapy.



Free Papers 07 (Portal HTN/Cirrhosis 1)

[OP-0523]

Experimental fibrosis alters matrix-bound vesicles cargo that do not revert after histologic recovery

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Objectives: Although it is now understood that hepatic fibrosis can resolve, potential therapies to enhance fibrosis resolution are lacking. MBV are nanometer-sized vesicles bound within the ECM collagen network. Changes in MBV cargo may contribute, at least in part, to the phenotypic changes driven by fibrosis and recovery.
Materials and Methods: Fibrosis was induced by injecting male C57BI/6 J mice with CCl_4 (1 ml/kg 2 × /wk 4wks); animals were sacrificed 1–28 days later. Liver injury and fibrosis was monitored by clinical chemistry, histology and gene expression. MBV were extracted from the livers of mice and the trypsinized MBV proteome cargo was analyzed by LC–MS/MS analysis using a Proxeon EASY-nLC 1000 UHPLC and nanoelectrospray ionization into an Orbitrap Elite mass spectrometer. Feature data were extracted and analyzed using Proteome Discoverer v2.4. Hierarchical clustering of significantly-changed MBV proteins was performed using StringDB and KEGG classification. To investigate the effect of MBV on the recovery of liver fibrosis, normal MBV from porcine urinary bladder (30 mg/mouse i.p.) were injected for up to 2 weeks after cessation of CCl_4.
Results: Fibrosis caused by CCl_4 rapidly resolved after cessation, reverting to almost normal histology and expression after 28d recovery. The amount and type of proteins associated with the MBV tended to decrease in fibrosis, which was not reversed even after fibrosis recovery. StringDB and KEGG analysis indicated that the proteins lost in fibrosis/recovery were predominantly RNA-binding proteins associated with the ribosome, which may also impact the RNA cargo of the MBV. Some mice injected with normal MBV accelerated the fibrotic resolution.
Conclusion: Liver MBV alter their protein cargo in response to experimental fibrosis. Importantly, these changes do not revert to baseline levels even after almost complete histological recovery of fibrosis. These data suggest MBV may be a novel prospect for mechanistic insight into hepatic disease progression and recovery.

[OP-0369]

Mesenchymal stem cells alleviate acute liver failure through promoting cell proliferation and inhibiting apoptosis

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Objectives: Acute liver failure (ALF) is a life- threatening clinical problem with high short-time mortality. Liver transplantation is an effective therapeutic option and improves the outcomes for patients with ALF. However, the application of liver transplantation is constrained due to the shortage of donor organ. Other interventions assisting to treat ALF are being explored. Mesenchymal stem cells (MSCs) are one of the attractive candidates for treating all kinds of diseases, including ALF. This study aimed to explore the potential mechanism of MSCs in attenuating ALF.
Materials and Methods: The mouse model of ALF was induced by stimultaneously intraperitoneal injection of lipopolysaccharide (LPS) and d- galactosamine (D- GalN), and MSCs were administered via tail vein before LPS/D-GalN treatment. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured. The expressions of inflammatory factors, tumor necrosis factor-α (TNF-α), IL-6 and IL- 1β were evaluated using ELISA, real- time PCR and western blotting. Hepatic apoptosis was detected by TUNEL assay and cleaved caspase-3 test. Apoptosis related protein expressions, including cleaved caspase-9, cleaved caspase-3, phospho- JNK, JNK, phospho- NF-κB and NF-κB were analyzed by western blotting. Meanwhile, immunohistochemic al (IHC) staining was conducted using Ki67 and PCNA to evaluate the proliferation in liver. And proliferation related protein expressions, including cyclinD1, phospho-AKT, AKT, phospho-ERK, ERK, phospho-p38 MAPK and p38 MAPK were assessed using western blotting.
Results: MSCs alleviated liver injury in the view of ALT and AST levels, pathological histology analysis and levels of inflammatory factors TNF-α, IL-6 and IL- 1β. MSCs transplantation decreased apoptotic cells and promoted proliferative cells in liver tissue. In addition, the expression of cleaved caspase-9, cleaved caspase-3, phospho-JNK and phospho-NF-κB were inhibited, while the expressions of cyclinD1, phospho- AKT, phospho-ERK and phospho-p38 MAPK were elevated in MSCs-treated mice.
Conclusion: MSCs can alleviate ALF through promoting cell proliferation and inhibiting cell apoptosis, and MSCs-based cell therapy may serve as an alternative option for patients with liver failure.

[OP-0337]

Magnetic resonance imaging improves stratification of fibrosis and steatosis in patients with chronic liver disease

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Objectives: Liver fibrosis and steatosis are common features in patients with chronic liver disease (CLD). The diagnostic accuracy of magnetic resonance (MR) imaging and transient elastography (TE) in assessing liver fibrosis and steatosis was compared in patients with CLD.
Materials and Methods: Patients who received liver biopsy or liver surgery at two academic hospitals between 2017 and 2021 were recruited. Stage of liver fibrosis and steatosis evaluated using histologic evaluation, liver stiffness assessed using MR elastography (LS_{MRE}) and TE (LS_{TE}), and liver steatosis assessed using proton density fat fraction (PDFF) and controlled attenuation parameter (CAP) were obtained.
Results: The mean age of the study population (n = 280) was 53.6 years and male gender predominated (n = 199, 71.1%). Nonalcoholic fatty liver disease was most prevalent (n = 127, 45.5%), followed by hepatitis B virus (n = 112, 40.0%). Hepatocellular carcinoma was identified in 130 (46.4%) patients. The proportion of F0, F1, F2, F3, and F4 fibrosis was 13.2%, 31.1%, 9.6%, 16.4%, and 29.7%, respectively. LS_{MRE} had a significantly higher area under receiver operating characteristic (AUROC) values than LS_{TE} in identifying F2-F4 fibrosis (0.846 vs. 0.781, P = 0.046), whereas LS_{MRE} and LS_{TE} similarly predicted F4 fibrosis (AUROC = 0.904 vs. 0.852, P = 0.093). Using a cutoff value of 3.1 kPa, LS_{MRE} had a sensitivity of 71.8%, specificity of 83.9%, positive predictive value of 84.8%, and negative predictive value of 70.3% for detecting significant fibrosis (F2-4). The proportion of S0, S1, S2, and S3 steatosis was 34.7%, 49.6%, 12.5%, and 3.2%, respectively. PDFF had significantly greater AUROC values than CAP in predicting S1-3 (0.922 vs. 0.806, P < 0.001) and S2-3 steatosis (0.924 vs. 0.795, P = 0.005). The best cutoff values of PDFF for detecting S1-3 and S2-3 steatosis were 4.2% and 11.9%, respectively.
Conclusion: MR imaging exhibited significantly higher diagnostic accuracy than TE for detecting significant fibrosis and mild or moderate to severe steatosis in patients with CLD.

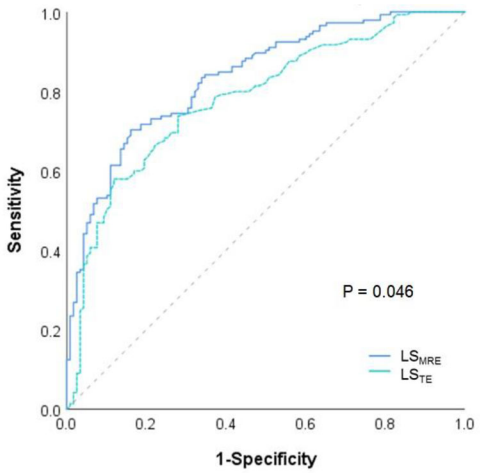

Figure 3. The area under the receiver operating characteristic curve of LS_{MRE} and LS_{TE} for the detection fibrosis stage F2-4.
LS_{MRE}, liver stiffness assessed using magnetic resonance elastography; LS_{TE}, liver stiffness assessed using transient elastography

[OP-0458]

Spleen volume based non-invasive criteria can identify patients with compensated cirrhosis at high risk of decompensation: A multi-centre study

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Objectives: Non-invasive criteria to stratify liver decompensation risk remained an unmet need in patients with compensated cirrhosis. Thus, we aimed to develop and validate a non-invasive model based on spleen volume and simple serum markers to predict decompensation in patients with compensated cirrhosis.
Materials and Methods: 239 patients with compensated cirrhosis were enrolled from three centers in China from January 2016 to June 2020 in this retrospective cohort study. They were followed up until the occurrence of liver decompensation or until the end of June 2021. Abdominal CT and Laboratory workup were collected at baseline. Spleen volume was measured automatically using an in-house AI algorithm with Dice > 0.98 in spleen segmentation. We used these data to develop a spleen volume-based model to determine the risk of decompensation in the first center comprising 66 patients (Training cohort). We validated it in the other two centers comprising 94 and 79 patients (Test cohort 1 and 2). And compared with Child–Pugh score, MELD, and FIB-4.
Results: 58 patients (24%) developed liver decompensation over a median follow-up of 25 months. Using a combination of spleen volume, PLT, GGT, and Hb, we developed a Spleen-Alert model (Model score > 2.14) to identify patients with compensated cirrhosis at risk of liver decompensation. HR for decompensation in patients with high risk was 13.4 in training and 6.1 and 12.2 in test respectively. The Spleen-Alert model has good performance to predict high-risk compensated patients at risk of liver decompensation (C- indexes of 0.82 in training and 0.82, 0.77 in two test cohorts), out performing traditional non-invasive tests (C- indexes from 0.51to 0.74).
Conclusion: This study shows that spleen volume is an accurate predictor of decompensation in compensated cirrhotic patients. Spleen-Alert model showed considerable performance in stratifying the individual risk of liver decompensation in patients with compensated cirrhosis as a simple and non-invasive criterion.

[OP-0079]

The diagnostic accuracy of LOGIQ S8 and E9 shear wave elastography for staging hepatic fibrosis, in compari-son with transient elastography

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Objectives: The aim of this study was to evaluate the usefulness of two different types of 2-dimensional shear wave elastography (2D-SWE) for predicting liver fibrosis stages in comparison to transient elastography (TE), using a histologic METAVIR scoring system as the reference method.
Materials and Methods: A total of 203 patients with chronic liver disease were prospectively enrolled in the study. Two different 2D-SWEs were assessed for liver stiffness in patients with chronic liver

diseases. Patients received 2D-SWE examinations with the S8 and E9 systems, and also underwent TE tests and liver biopsies on the same day.
Results: The most common etiology of chronic liver disease was non-alcoholic fatty liver disease (28.7%), followed by chronic hepatitis B (25.1%). Liver fibrosis stages consisted of F0 (22.6%), F1 (29.7%), F2 (16.9%), F3 (12.8%) and F4 (17.9%). Overall, S8 and E9 were well correlated with the histologic fibrosis stages. The optimal cut-off values for S8 and E9 to differentiate significant fibrosis ($\geq$ F2) were 6.70 kPa and 6.42 kPa, respectively, while the cut-off values for S8 and E9 in distinguishing liver cirrhosis were 9.15 kPa and 8.88 kPa, respectively. Among the 195 patients who had successful measurements in both S8 and E9, liver stiffness showed good inter-equipment correlation (ICC: 0.900, $p < 0.001$). Regarding diagnostic ability, upon comparison (FibroScan®), there were no significant differences between 2D-SWEs and TE for detecting every stage of liver fibrosis.
Conclusion: In comparison to TE, 2D-SWE with LOGIQ S8 and E9 (GE Healthcare) are useful non-invasive tools for predicting significant fibrosis and liver cirrhosis.

[OP-1007]

Diagnosis of clinically significant portal hypertension using deep learning model of 2D shear wave elastography images

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Corresponding author: Woo Kyoung Jeong, Radiology And Center For Imaging Science, Samsung Medical Center, Seoul, Republic of Korea

Objectives: We aimed to make a deep-learning model of 2D-shear wave elastography (SWE) images to detect clinically significant portal hypertension (CSPH) [DL-CSPH] using long short-term memory (LSTM) architecture, and to compare the diagnostic performance with conventional diagnostic method.
Materials and Methods: A retrospective study was conducted using 2D-SWE image data collected in a single center, and the subject were divided into training (n = 168) and test (n = 113) sets. CSPH was diagnosed by hepatic venous pressure gradient measurement. With the training set, the DL-CSPH model using convolution neural network (CNN) and long short-term memory (LSTM) architecture of the 2D-SWE measurement image was derived. Especially, sequential order of liver stiffness (LS) measurement was applied into the LSTM model and compared with the LSTM model with random selection. As a conventional diagnostic method, the cut-off value of LS was calculated via a receiver operating curve analysis in the training set and applied the cut-off value in the test set.
Results: In the prediction of CSPH using the deep-learning model, the LSTM model with sequential order showed better performance than the LSTM model with random selection (sensitivity: 94.3% VS 92.9%, specificity: 86.1% VS 83.7%, accuracy: 91.2% VS 89.4%). But, they did not show statistically significant difference. ($P < 0.99$, respectively) Conventional diagnostic method which the cut-off (13.5 kPa) of LS was applied showed no significant difference from DL-CSPH with sequential order. (sensitivity 94.5%, $P < 0.99$; specificity 85.0%, P = 0.5; accuracy 90.7%, $P < 0.99$).
Conclusion: DL-CSPH model shows the good overall performance in predicting CSPH. It has practical value in enabling non-invasive automated monitoring of portal pressure in patients with chronic liver disease in a robust and reproducible manner.

[OP-0354]

Sarcopenia is independently associated with death within 90 days in acute-on-chronic liver failure patients

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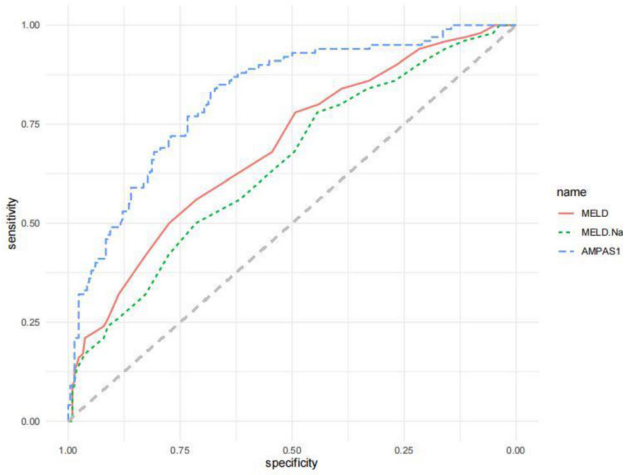
Objectives: Acute-on-chronic liver failure (ACLF) is characterized by the development of a syndrome associated with a high risk of short-term death in patients with acute decompensated cirrhosis. Better biomarkers are needed to predict these outcomes. Sarcopenia, as a common complication of cirrhosis, is tightly associated with poor prognosis and increased mortality of patients. The skeletal muscle index of ACLF patients was measured to determine whether sarcopenia combined with clinical parameters help to identify patients at high risk of death.
Materials and Methods: A total of 314 hospitalized ACLF patients were included and allocated into the survival group (n = 214) and the death group (n = 100) within 90 days. The muscle mass of patients was assessed based on skeletal muscle index. The optimal cut-off value of AMPAS1 (age, MELD score, platelet, alpha-fetoprotein, sarcopenia and more than one complication combination) for death prediction was identified using receiver operating characteristic (ROC) analysis.
Results: Sarcopenia prevalence was remarkably higher in the death group than that in the survival group (74.2% vs. 36.6%, P = 0.000). Through Cox proportional hazard model analysis, age, MELD score, platelet, alpha-fetoprotein, sarcopenia, and more than one complication were independent risk factors for death ($p < 0.05$). The area under the ROC curve was 0.908, and the cut-off value for death prediction was 0.21 (sensitivity 93.2%, specificity 71.1%).
Conclusion: We demonstrated that sarcopenia was an independent factor of death in ACLF patients. Moreover, AMPAS1 possessed high sensitivity and specificity in predicting death. Therefore, this model promises to be a useful tool to predict the poor prognosis of ACLF patients within 90 days.



[OP-0388]

Age, sex, and body mass index should be considered in assessing spleen length in patients with cirrhosis

Han Ah Lee[1], Soy Chang[1], Jihwan Lim[2], Seung Up Kim[3], Young-Sun Lee[2], Seong-Hee Kang[4], Young Kul Jung[1], Moon Young Kim[4], Ji Hoon Kim[1], Sang Gyune Kim[5], Ki Tae Suk[6], Soung Won Jung[5], Jae Young Jang[5], Hyung Joon Im1[2], Yeon Seok Seo[2]

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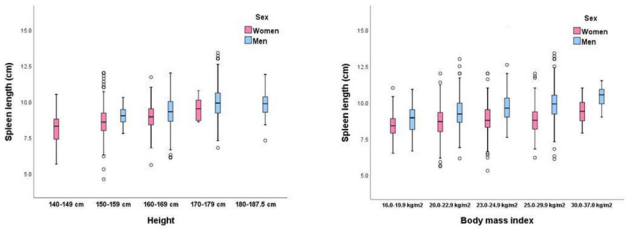
Objectives: The normal range of spleen length and its associated factors have not been well studied. Herein, we investigated the factors related to spleen length and the diagnostic accuracy of a prediction model using spleen length corrected by related factors for the prediction of varices needing treatment (VNT).
Materials and Methods: The maximum craniocaudal length of the spleen in healthy subjects who had undergone health checkups at two tertiary hospitals was measured, and the factors associated with spleen length were analyzed. Prediction models for VNT were evaluated in patients with compensated advanced chronic liver disease (cACLD).
Results: In 1,041 healthy subjects (518 women and 523 men), the median spleen length was significantly different between men and women (9.6 cm vs. 8.7 cm, $P < 0.001$). In the multivariate analysis, age (b = -0.027), sex (b = 0.762), and body mass index (BMI) (b = 0.097) were the significant factors for spleen length (all $P < 0.001$). The estimated spleen length was calculated using b values as follows: -0.027 ´ age (years) + 0.762 ´ sex (women, 0; men, 1) + 0.097 ´ BMI (kg/m^2) + 7.926. The ratio of the measured and estimated spleen lengths was calculated. VNTs were noted in 249 patients (20.4%) among 1,218 cACLD patients. Based on the binary regression analysis for the prediction of VNT, the liver stiffness (LS) value-spleen ratio to platelet ratio score (LSRPS) was calculated as follows: 0.027 ´ LS value (kPa) + 2.690 ´ measured/estimated spleen ratio – 0.011 ´ platelet count (cells ´ 10^9/L) – 4.215. The area under the receiver operating characteristic curve of the LSRPS for VNT was 0.820, which was significantly higher than the LS value-spleen diameter to platelet ratio score (0.797; P = 0.006).
Conclusion: Spleen length is influenced by age, sex, and BMI in Asian populations. The LSRPS based on the measured/estimated spleen ratio is useful in patients with cACLD.



[OP-0963]

External validation of APASL ACLF research consortium artificial intelligence model to predict mortality in acute-on-chronic liver failure patients

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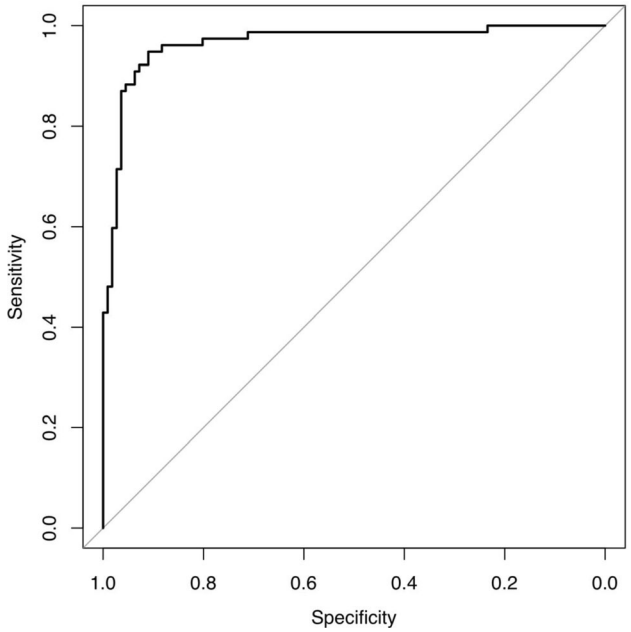
Objectives: We recently developed and validated an APASL-ACLF Research Consortium (AARC-AI) model with high accuracy for predicting short-term mortality in acute-on-chronic liver failure (ACLF) patients. Here we aim to validate the performance of the AARC-AI model in an external cohort.
Materials and Methods: We prospectively recruited ACLF patients (APASL definition) from ILBS, New Delhi, India, between January 2021 and September 2021 (n = 188) and followed them for 30 days. Their clinical data were fed in the pre-trained and pre-tuned AARC-AI model to predict 30-day mortality utilizing principles of supervised machine learning and MI-CLAIM criteria. The AARC-AI model was derived using feature importance and Shapley Additive Explanations of extreme gradient boosting-model (2481 patients). The features utilized for the model were admission day-7 parameters including creatinine, INR, circulatory-failure, HE-grade, leucocyte counts, platelet and sodium, and day-4 parameters including sepsis, platelet, and HE-grade.
Results: Patients aged 46.8 years (SD: 11.9), 154 (84%) males, commonly with an acute precipitant of alcohol associated hepatitis 93 (49.5%) or viral hepatitis 21 (12.7%) and chronic etiology of alcohol associated liver disease 101 (53.7%), or viral hepatitis 56 (29.7%) were recruited. Patients presented with jaundice 100%, ascites 65%, and hepatic encephalopathy 48%. The 30-day mortality of the cohort was 77 (41.0%). The area under the receiver operating curve (0.965;

95%CI: 0.939–0.992), accuracy (0.926; 95% CI: 0.878–0.959), sensitivity (0.909) and specificity (0.937) of AARC-AI model for 30-day mortality prediction in this cohort was excellent.
Conclusion: AARC-AI model is a robust, validated, and highly accurate model for outcome predictions in ACLF. Based on the admission day 4 and 7 parameters, the AARC-AI model can reliably predict the 30 day mortality and hence help in clinical decision making and prognostication of the patients. Large multi-centric studies should be undertaken to validate and refine AI models for predicting the mortality of ACLF patients.



Free Papers 08 (Portal HTN/Cirrhosis 2)

[OP-0871]

Prevalence of hepatic osteodystrophy in liver cirrhosis: A single center cross-sectional study

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Objectives: Hepatic osteodystrophy (HO) is frequently underdiagnosed in the clinical setting. This study determined the prevalence of HO among Filipino patients with liver cirrhosis. Secondary outcomes were: association of serum vitamin D, calcium, and bone mineral density (BMD); correlation of BMD, serum vitamin D, and calcium levels with the severity of liver disease; and comparison of the prevalence of HO among patients with hepatocellular carcinoma (HCC) and those without HCC.
Materials and Methods: This is a cross-sectional study that included all adult patients with liver cirrhosis seen from January 2019 to September 2021. Descriptive statistics was used to summarize demographic and clinical data. Statistical significance was determined using chi-square test or Fisher exact test. Pearson or Spearman correlation coefficient were computed for correlation analysis.
Results: Forty-six patients were included in the study (mean age: 59.96 ± 12.01, 60.9% males). HO and vitamin D deficiency were detected in 67.4% and 69.6% of patients, respectively. No significant difference on the prevalence of HO and vitamin D deficiency between patients with and without HCC. Non-alcoholic fatty liver disease was the most common etiology of liver disease in the low BMD group. Lumbar spine BMD and serum calcium had a positive correlation ($r = 0.340$, $p < 0.05$). In addition, a negative correlation between serum vitamin D and severity of liver disease assessed - through MELD-Na score ($\rho = -0.312$, $p < 0.05$) and Child–Pugh score ($\rho = -0.431$, $p < 0.05$) were reported.
Conclusion: HO and vitamin D deficiency are highly prevalent in patients with liver cirrhosis. Vitamin D level is inversely correlated with the severity of liver dysfunction. The absence of correlation between BMD and vitamin D in patients with liver cirrhosis probably reflects the multi-factorial etiology of osteodystrophy in these patients. Screening for HO with bone mineral densitometry and vitamin D deficiency can reduce the risk of morbidity.

[OP-0292]

The association of clot wave analysis with the severity of liver disease and risk of gastrointestinal bleeding in patients with cirrhosis

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Objectives: Conventional coagulation tests are unreliable for detecting the risk of bleeding in cirrhotic patients. Clot waveform analysis (CWA) provides a more comprehensive kinetic assessment of clot formation.
Materials and Methods: We examined the associations between CWA values of prothrombin (PT) and partial thromboplastin time (PTT) clotting assays and disease severity or the presence of gastrointestinal bleeding (GIB) in cirrhotic patients from June to September 2021. CWA values were performed on the CS-2500 (Sysmex, Beersel, Belgium).
Results: A total of 358 cirrhotic patients were consecutively enrolled. Of these, 123 had decompensated cirrhosis (34.4%), and 79 (22.1%) had GIB. The most common GIB was variceal bleeding (VB) (74.7%, n = 59). Table 1 shows the characteristics of patients. CWA of PT and PTT assays in patients presenting with GIB showed significantly lower maximum velocity (MV), maximum acceleration (MA), and maximum deceleration (MD) than patients without GIB ($p \leq 0.001$). In patients with INR < 1.5, the MV, MA, and MD of CWA of PT and

PTT were significantly lower in patients with GIB than those without GIB ($p \leq 0.01$). PTT ($p = 0.12$) and platelet counts ($p = 0.13$) were not different between patients with and without GIB. Prior history of VB was associated with lower all CWA values ($p \leq 0.005$). Based on PT and PTT assays, MV, MA, and MD of CWA were significantly lower ($p \leq 0.001$) in decompensated patients than those with compensated cirrhosis. Patients with MELD ≥ 15 exhibited lower MV, MA and MD during PT and PTT clotting reactions than patients with MELD < 15 ($p \leq 0.01$). CWA values of PT and PTT assays were significantly negative correlated with MELD scores in cirrhotic patients ($r = -0.36$ to -0.43, $p \leq 0.001$).
Conclusion: Patients with decompensated cirrhosis or GIB have more hypocoagulable profiles on the MV, MA, and MD of PT and PTT CWA tests. CWA plays a complementary role for predicting the risk of GIB in cirrhotic patients with INR < 1.5.

	No GI bleeding (n=279)	GI bleeding (n=79)	p-value
Age, years	58.4 ± 12.5	59.5 ± 16.6	0.65
Male, n (%)	168 (60.9%)	55 (71.4%)	0.09
Etiology of chronic liver disease, n (%)			
Hepatitis B virus	87 (34.0%)	10 (13.5%)	0.001
Hepatitis C virus	70 (27.3%)	16 (21.6%)	0.32
Alcohol	56 (21.9%)	26 (35.1%)	0.02
Hepatocellular carcinoma, n (%)	99 (35.5%)	28 (35.4%)	0.63
Hemoglobin, g/dL	11.7 ± 2.4	8.3 ± 2.2	<0.001
White cell count, 10^9/L	5.9 ± 8.8	8.0 ± 4.3	<0.001
Platelet count, × 10^9/L	122.7 ± 76.8	132.5 ± 76.5	0.13
INR	1.28 ± 0.26	1.49 ± 0.36	<0.001
Total bilirubin, mg/dL	2.63 ± 3.65	4.21 ± 7.65	0.02
Albumin, g/dL	3.6 ± 0.7	2.7 ± 0.7	<0.001
Creatinine, mg/dL	1.03 ± 1.17	1.57 ± 3.22	0.92
Sodium, mmol/L	136.5 ± 3.7	135.8 ± 4.6	0.03
MELD score	8.3 ± 6.0	12.8 ± 8.2	<0.001

GI; gastrointestinal bleeding

[OP-1018]

Direct oral anticoagulants in patients with LC: Trends of usage and its safety

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Objectives: Recently, the use of direct oral anticoagulants (DOAC) is steadily increasing. However, in most studies related to DOAC, there are insufficient reports of safety in liver disease, especially in liver cirrhosis (LC). The aim of this study is to determine trends in use of DOAC in patients with LC and its safety.
Materials and Methods: Among patients with LC, the subjects were 91 patients who used DOAC for more than 6 months and underwent blood tests before the start of treatment and after 6 months of treatment. Clinical observation of study subjects, adverse events, and safety according to the use of DOAC were investigated.
Results: There were 72 males (79.1%) and 19 females (20.9%). The child-Turcotte-Pugh (CTP) scores of the subjects were A 68 (74.7%), B 22 (24.2%), and C 1 (1.1%). The reasons for prescribing DOAC included atrial fibrillation 56 (61.5%), cerebrovascular accident 11 (12.1%), pulmonary thromboembolism 10 (10.9%), deep vein thrombosis 9 (9.9%), cardiovascular accident 3 (3.3%) and others. There were 19 subjects (20.8%) whose PT increased for more than 3 s during treatment. There were 7 subjects (7.7%) whose CTP score increased by 1 point or more. When the analysis was divided into two groups (group1: increased PT more than 3 s (19) vs. group 2: increased PT less than 3 s (72)), the use of rivaroxaban was significantly high in group 1. (group 1: rivaroxaban 52.6%, apixaban 21.1%, edoxaban 10.5%, dabigatran 15.8% vs. group 2: rivaroxaban 23.6%, apixaban 38.9%, edoxaban 22.2%, dabigatran 15.3%, $p = 0.083$). During treatment, 8 subjects discontinued DOAC and 7 subjects changed medication.
Conclusion: DOAC can be used relatively safely in patients with LC. However, it is recommended not to use rivaroxaban in DOAC selection, and blood test monitoring will be necessary during treatment in case of LC.

[OP-0744]

Fluoroquinolone-resistant strains in cirrhotic patients with spontaneous bacterial peritonitis: Microbiological and molecular aspects

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Objectives: This study aimed to determine the causative bacterial agents of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis and to define antibiotic-resistance patterns in addition to identifying the genetic mutations in the quinolone resistance determining regions (QRDRs).
Materials and Methods: Twenty milliliters of ascetic fluid was obtained from 51 patients with SBP. The antibiotic-sensitivity patterns of different strains were determined by the Kirby–Bauer method. Extracted bacterial DNA was used to determine the mutations in four different genes in QRDRs (gyrA, gyrB, parC, and parE) by sequencing after gene amplification by PCR.
Results: Gram-negative bacilli were detected in 60.7% of the patients. Escherichia coli was detected in 33.3% of the patients, and Staphylococcus aureus was detected in 21.6%. Gram-negative bacilli showed the best sensitivity to meropenem (90.3%), followed by amikacin (83.9%). Gram-positive cocci were sensitive to vancomycin and oxacillin at 90 and 80%, respectively. Fluoroquinolone resistance was detected in 27% of the bacterial strains. Mutations in the gyrA and parC genes were detected in quinolone-resistant strains (64.3 and 35.7%, respectively). Several mutations were found in the gyrA gene (Ser83Leu, Ser81Phe, and Ser-84Leu). Ser80Ile and Ser79Tyr mutations were detected in the parC gene. No mutation was detected in the parE gene.
Conclusion: Frequent use of antibiotics as prophylaxis against SBP leads to an increase in antibiotic resistance and changes the microbial pattern of causative agents. The gyrA gene mutation was the most common mutation detected in fluoroquinolone-resistant strains.

[OP-0264]

Risk factors of overt hepatic encephalopathy development in chronic hepatitis patients with minimal/covert hepatic encephalopathy

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Objectives: To analyze the relationship between common laboratory indicators and neuropsychological tests with MHE incidence and OHE development.
Materials and Methods: We prospectively incorporated 123 healthy controls and 266 patients with potential hepatic encephalopathy (HE) developing diseases (mainly cirrhosis) in our study. Data from healthy group was used to get the reference standard for diagnosis of MHE/CHE. All 266 patients were identified by the PHES, ANT, VNT, AVNT and 57 patients were assessed by Encephalstroop App. All patients were followed for the occurrence of OHE in 28 days.
Results: The prevalence rate of MHE diagnosed by the gold standard PHES was 27.1%. The risk of developing into OHE in patients with MHE (16/72, 22.2%) was over triple higher than those without MHE (13/194, 6.7%). Those who progressed for OHE suffered from decompensated liver cirrhosis (23, 79.3%), EASL-ACLF (9, 31.0%) and APASL-ACLF (26, 89.7%). Statistical analysis showed IBIL, LDH, eGFR were correlated with MHE ($p < 0.05$). Multivariate regression analysis indicated that age, ammonia and K (potassium) level at baseline were independent risk factors for MHE. Age, gender, comorbidity, primary OHE, GGT, TT at the time of study inclusion were correlated with OHE development ($p < 0.05$). Univariate regression analysis showed age, prior OHE, MHE, AVNT < 18, complications, HE treatments (including lactulose, LOLA, probiotics, etc.), MELD, IL6, L%, TBIL, DBIL, IBIL, TBA, eGFR, PT, PTA, APTT, Offtime, OffTime + OnTime were significant in OHE progression in 28 days ($p < 0.01$). However, after Multivariate regression analysis, there remained no significant independent risk factors for OHE development.
Conclusion: Age, ammonia and K (potassium) level at baseline were independent risk factors for MHE. Age, prior OHE, MHE incidence, abnormal neuropsychological test results (AVNT < 18, Offtime, OffTime + OnTime), complications, HE treatments, MELD, IL6, L%, bilirubin, TBA, eGFR, coagulation function (PT, PTA, APTT) were significant in OHE progression in 28 days.

[OP-1177]

Recurrence of portosystemic encephalopathy in cirrhotic patients and its risk factors

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Objectives: Portal systemic Encephalopathy (PSE) is a common complication of cirrhosis that places a high societal burden of illness and hospitalization. Identifying the patient's risk for PSE may allow closer monitoring to preserve the quality of life, reduce and manage risk factors so that appropriate prevention and prognostication can be done. Therefore this study is done to assess, the recurrence of PSE in cirrhotic patients, after the first episode and its risk factors.
Materials and Methods: It is a retrospective study done in the section of Gastroenterology, The Aga Khan University Hospital, Karachi, Pakistan from Jan 1, 2019, till December 31, 2019. Patients who were admitted first time with PSE and admitted within 3 months of index PSE were enrolled in the study. Grading of PSE Grade (I-VI), laboratory tests (Bilirubin, Albumin, Creatinine, and electrolytes), ascites with spontaneous bacterial peritonitis (SBP), gastrointestinal bleeding (GIB), acute kidney injury (AKI), Child-Turcotte-Pugh (CTP) score, and Model of End-Stage Liver Disease (MELD) Score were collected by chart review and analyzed by SPSS version 20.
Results: Total 61 patients were included in the study and 10 were lost to follow-up. The main comorbids were hypertension 33 (64%) and diabetes 28 (54%). As per etiology HCV (59%), HBV (27%), Alcohol (6%), others (7%). Out of 51 patients, 33 were readmitted with PSE while 22 patients remained stable on follow-up. On comparative analysis of both groups; infection, Meld score, low albumin, and raised total bilirubin showed significant P-value (< 0.05). The rest of the parameters were more or less the same in both groups.
Conclusion: We found ta hat high MELD score, raised total bilirubin level, low Albumin level, and infections were the risk factors for recurrence of PSE. Identification of risk factors during assessment can reduce the recurrence of PSE. We would recommend validating the results of our study on large scale prospectively.

[OP-0903]

Impact of low dose albumin infusion on outcome in patients with cirrhosis and sepsis—a randomized open label clinical trial

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Objectives: Primary objective—In-hospital mortality. Secondary objectives—Mortality at day 30 of randomisation and improvement in clinical and laboratory parameters among two groups at the time of discharge.
Materials and Methods: Consecutive patients with cirrhosis and sepsis were randomized in 2:1 ratio to two groups with group A (117) and group B (57) patients. In addition to antibiotics and standard medical therapy (SMT) group A was given albumin in a dose of 20 g /day for 5 days and group B was given recommended standard dose (1.5 g/kg/body weight and 1 g/kg body weight on day 1 and day 3 respectively).
Results: Of 174 patients, 101 (58%) had urinary tract infection, 45 (25.86%) had pneumonia, 21 (12.06%) had spontaneous bacterial peritonitis, 17 (9.77%) had lower limb cellulitis. The median duration of hospital stay in group A and B was 8 (5–11.5) and 8 (5.5–10) days (p = 0.520) respectively were similar in both the groups. The in-hospital mortality in group A and B was (12 [10.3%] vs 6 [10.5%], p = 0.956) and 30-day mortality (23 [19.7%] vs 17 [29.8%], p = 0.178) respectively were similar in both the groups. Further, the percentage of patients with improvement in MELD Na score > 2 in group A and B was (57.2% % vs 56.1%, p = 0.89) respectively was comparable in both the groups (see table).
Conclusion: Low dose albumin infusion in patients with cirrhosis with sepsis can have the same results as standard dose albumin and can be used in resource-limited situations.

Table: Comparison of baseline characteristics and outcomes in patients receiving low dose and standard dose albumin.

Variable	Group A n=117		Group B n=57		p value
Age (Mean±SD)	54.368±12.79		52.421±13.64		0.358[1]
Male n (%)	93 (79.5)		51 (89.5)		0.102[2]
Median duration of hospitalisation in days (IQR)	8 (5-11.5)		8 (5.5-10)		0.520[3]
MELD Na score on day 1 (Mean±SD)	21.99±6.32	p<0.001[5]	24.09±7.31	p=0.005[4]	0.053[1]
MELD Na score on day 5 (Mean±SD)	20.03±6.45		22.26±7.82		0.063[3]
Patients with improvement in MELD Na score ≥ 2 n (%)	67 (57.2)		32 (56.1)		0.89[2]
In Hospital Mortality n (%)	12 (10.3)		6 (10.5)		0.956[2]
Mortality within day 30 after randomisation n (%)	23 (19.7)		17 (29.8)		0.178[2]

[1] Independent t test [2] Chi-square test [3] Mann-Whitney U test [4] paired t test

[OP-1162]

Renal resistive index as a short-term predictor of hepatorenal syndrome in patients with decompensated cirrhosis

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Objectives: Hepatorenal Syndrome (HRS) is characterized by renal arterial vasoconstriction, which may precede clinically manifest renal dysfunction. Renal Resistive Index (RRI) is a measure of renal arterial vasoconstriction. The primary aim of our study was to obtain the best cut-off value of RRI in predicting HRS occurrence in decompensated cirrhosis over 6 months. We also assessed other factors associated with the development of HRS.
Materials and Methods: Methods: A prospective follow-up study of 136 decompensated cirrhotics admitted to our hospital. All underwent ultrasound Doppler with RRI measurement at initial admission. Baseline parameters were ascertained, and followed up for 6 months to look for the development of HRS.
Results: 16 patients were lost to follow-up amidst the pandemic. Selected variables of the remaining 120 patients were analysed. HRS occurred in 24 patients (20%). RRI cut-off of $\geq$ 0.77 at initial presentation predicted HRS over 6 months (AUROC: 0.895; Sensitivity 91.7%; Specificity 76%). On subgroup analysis, RRI $\geq$ 0.77 (AUROC: 0.910; Sensitivity 92.3%; Specificity 83.3%) & $\geq$ 0.82 (AUROC: 0.912; Sensitivity 90.9%; Specificity 87.5%) predicted HRS in NASH-related and non-NASH-related etiologies respectively. NASH-related etiology was found to be an independent predictor for HRS. Higher Urea and Creatinine, low Albumin, tense ascites at initial presentation were also associated with significant risk for HRS.We further compared RRI $\geq$ 0.77 vs < 0.77 (n = 45 vs 75). There was higher prevalence of tense ascites, higher Child status, MELDNa, Bilirubin, INR and lower Albumin (all $p < 0.01$), HE (p = 0.046), higher Urea (p = 0.035), Creatinine (p = 0.002); and low platelet counts (p = 0.087) in RRI $\geq$ 0.77. Mortality was also higher in RRI $\geq$ 0.77 ($p < 0.01$).
Conclusion: RRI is a simple diagnostic screening tool to predict short-term development of HRS in decompensated cirrhosis. This can aid early referral from primary care setting. NASH was an independent predictor for the occurrence of HRS.

[OP-0515]

Proton pump inhibitor treatment is associated with higher mortality and risk of spontaneous bacterial peritonitis in patients experiencing hepatic encephalopathy

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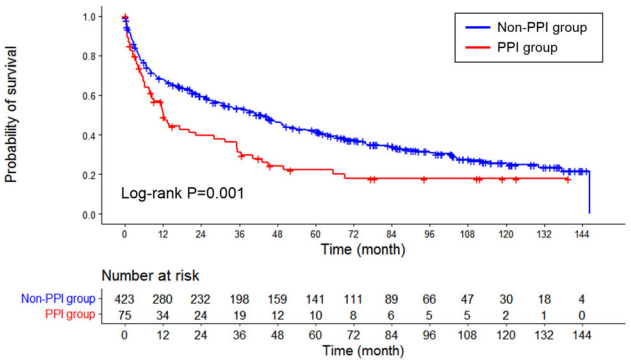
Objectives: Proton pump inhibitor (PPI) is widely used also in cirrhotic patients, but its use was reportedly associated with an increased risk of hepatic encephalopathy (HE) and spontaneous bacterial peritonitis (SBP). This study aimed to evaluate whether PPI was associated with the risk of death and cirrhotic complications.
Materials and Methods: We conducted an observational study that included 498 patients who experienced HE. The primary outcome was overall survival (OS) and secondary outcomes included the occurrence of SBP and recurrent HE. Each outcome was compared between patients who were treated with PPI of a mean defined daily dose

(mDDD) ≥ 0.5 (the PPI group) vs those who were treated with no PPI or PPI of mDDD < 0.5 (the non-PPI group).
Results: Among 498 patients, 423 were in the PPI group and 75 were in the non-PPI group. The PPI group showed significantly shorter OS than the non-PPI group (hazard ratio [HR], 1.60, 95% confidence interval [CI], 1.20–2.15, P = 0.001). In multivariable analysis, PPI was independently associated with higher mortality (adjusted HR [aHR], 1.59; 95% CI, 1.18–2.15; P = 0.002). The risks of SBP (aHR, 2.31; 95% CI, 1.52–3.53; P < 0.001) and recurrent HE (aHR, 1.80; 95% CI, 1.25–2.59; P = 0.002) were significantly higher in the PPI group than the non-PPI group. Patients who developed SBP had a significantly higher risk of death (P = 0.0009 by Z-test).
Conclusion: In cirrhotic patients, the use of PPI was independently associated with a higher risk of SBP, recurrent HE, and shorter OS.



Free Papers 09 (Liver Transplantation)

[OP-0532]

Twenty-year longitudinal follow-up after liver transplantation: A single-center experience with 251 consecutive patients

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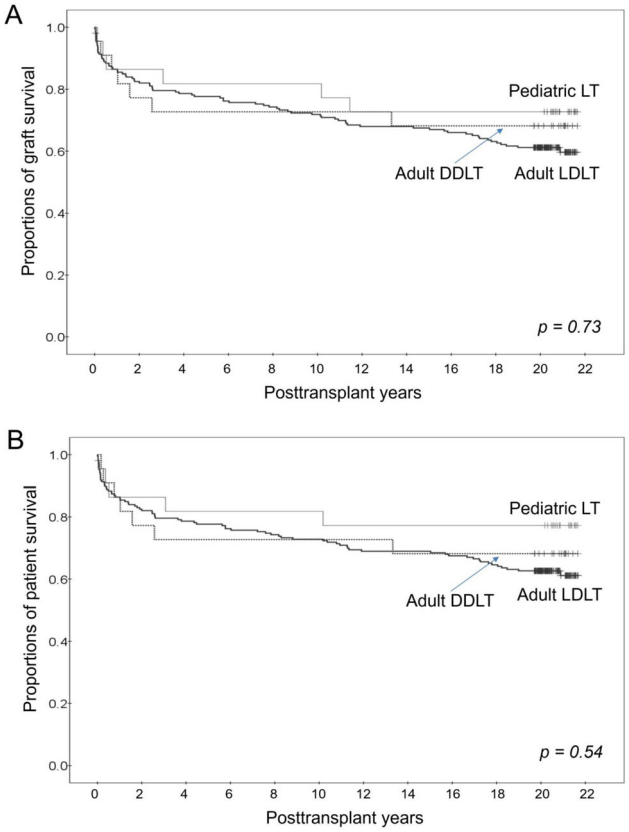
Objectives: The outcomes of liver transplantation (LT) have improved, but actual 20-year survival data are rarely presented.
Materials and Methods: Longitudinal follow-up data of 20-year LT survivors were retrospectively analyzed. LT database of our institution was searched to identify patients who underwent primary LT from January 2000 to December 2001. The study cohort of 251 patients was divided into three groups, including 207 adults who underwent living donor LT (LDLT), 22 adults who underwent deceased donor LT (DDLT), and 22 pediatric patients who underwent LT.
Results: Hepatitis B virus (HBV)-associated liver cirrhosis and biliary atresia were the most common indications for adult and pediatric LTs, respectively. Seven patients required retransplantation, including six who underwent DDLT and one who underwent LDLT. Twenty-two patients died within 3 months after LT and 69 died at later intervals. The overall patient survival rates at 1, 3, 5, 10, and 20 years were 86.4%, 79.6%, 77.7%, 72.8%, and 62.6%, respectively, in the adult LDLT group; 86.4%, 72.7%, 72.7%, 72.7%, and 68.2%, respectively, in the adult DDLT group; and 86.4%, 86.4%, 81.8%, 81.8%, and 77.3%, respectively, in the pediatric LT group (p = 0.545). Common immunosuppressive regimens at 20 years included tacrolimus monotherapy, tacrolimus–mycophenolate dual therapy, cyclosporine monotherapy, and mycophenolate monotherapy.
Conclusion: The present study is the first report of actual 20-year survival data in a Korean high-volume LT center. The graft and patient survival outcomes reflected the early experiences of LT in our institution, with long-term outcomes being similar regardless of graft type and patient age.



[OP-0953]

Safe use of hepatitis B surface antigen positive (HBsAg (+)) grafts in liver transplantation (LT): A nationwide study based on KOTRY (Korean Organ Transplantation Registry) Data

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Objectives: In the era of nucleos (t)ide analogues (ANs), we investigate the outcomes of liver transplantation (LT) using HBsAg (+) grafts using Korean national registry database.
Materials and Methods: Among 4265 LTs which were registered in KOTRY database between April 2014 and January 2020, 20 (0.5%) LTs using HBsAg (+) grafts were identified. We investigated the overall outcomes of LT using HBsAg (+) liver grafts (n = 4100, S (+) group) compared to those of HBsAg (-) liver grafts. S (+) group were compared to those for LT using HBsAg (-) & HBcAb (+) (n = 882, C (+) group) and HBsAg (-) & HBcAb (-) (n = 3132, SC (-) group) after propensity-score matching (1:1).
Results: Twenty HBsAg (+) grafts from deceased donors were transplanted to HBsAg (+) recipients. HBIG was maintained in 16 patients (80%). Most common NA was tenofovir. S (+) group showed comparable patient survival (26.5 ± 21.8 vs 22.8 ± 18.2 months, p = 0.332) and graft survival (26.5 ± 21.8 vs 21.3 ± 18.2 months, p = 0.152) compared to those of HBsAg (-) group. Age (HR = 1.03, p = 0.016), HCC (HR = 4.61, p < 0.001), MELD score (HR = 2.82, p = 0.001), ascites (HR = 2.14, p = 0.002) and encephalopathy (HR = 2.53, p < 0.001) were the risk factors affecting patient survival. For graft survival, HCC (HR = 4.01, p = 0.001), pre-operative treatment to HCC (HR = 0.54, p = 0.006), MELD score (HR = 2.14, p = 0.012), ascites (HR = 2.52, p < 0.001), and encephalopathy (HR = 1.99, p < 0.001) were significant factors. After PSM matching between S (+) and C (+), and S (+) and SC (-), there was no significant difference in patient survival (24.3 ± 20.7 vs 38.2 ± 23.0 months, p = 0.863, 24.3 ± 2.7 vs 38.2 ± 23.0 months p = 0.547), and graft survival (26.5 ± 21.8 vs 36.3 ± 17.4 months, p = 0.576, 26.5 ± 21.8 vs 36.3 ± 18.4 months, p = 0.327, respectively).
Conclusion: HBsAg (+) liver grafts can expand the donor pool without compromising the outcomes in the era of NA in the HBV endemic area.

[OP-0143]

Is liver resection still required for patients who have predictive factors for complete pathologic necrosis after downstaging for locally advanced hepatocellular carcinoma?

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Objectives: Liver resection is usually recommended in patients after tumor downstaging for locally advanced hepatocellular carcinoma (HCC) to induce complete remission. Whether liver resection is required in patients expected to have complete pathologic necrosis (CPN) after HCC downstaging or not is questionable.
Materials and Methods: From 2002 to 2019, 999 patients with locally advanced HCC underwent concurrent chemoradiotherapy (CCRT) or transarterial radioembolization (TARE). Among these patients, excluding liver transplantation, 94 patients who underwent hepatic resection (OP group) and 867 patients who did not undergo surgical treatment (non-OP group) were included in this study. Predictive factors of CPN in the OP group were analyzed by logistic regression analysis. Long-term outcomes were compared between the patients with CPN and patients with predictive factors for CPN in the non-OP group (CPN-PF group).
Results: Of the 94 patients in the OP group, thirty-eight patients (40.4%) were found to have CPN. In multivariable analysis, the predictive factors of CPN were complete radiologic response and tumor marker responder [Hazard ratio (HR) 1.00, p < 0.006; HR 3.698, 95% confidence interval (CI) 1.029–13.321, p = 0.045]. Among the non-OP group, twenty one patients belonged to the CPN-predictive factor (PF) group. There was no difference in disease-free survival (DFS) between the CPN-PF group and the CPN group (40.00 ± 18.25 vs. 60.00 ± 14.04, p = 0.838). In addition, the overall survival (OS) of the CPN group was not significantly higher than the OS of the CPN-PF group (144.00 ± 56.49 vs 97.00 ± 17.46, p = 0.328).
Conclusion: This study showed that surgical resection might not provide further advantages for long-term outcomes in patients with CPN predictive factors after HCC downstaging. However, this issue should be validated in large-scale and well-designed studies.

[OP-0171]

The identification of functional microbiomes affecting immune cellular homeostasis in long-term stable liver transplant patients

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Objectives: In this study, we examined and identified the gut microbial balance and functional microbiomes affecting immune homeostasis in the long-term post-LT patients.
Materials and Methods: A total of 16 long-term LT patients and 20 healthy volunteers were consecutively enrolled in our study. Included LT patients had normal liver function without history of rejection and underwent LT more than 3 years ago. Healthy controls have no medical diseases including metabolic and alcoholic disease. Fecal specimens and peripheral blood mononuclear cells (PBMCs) were collected in each patient, and we compared the microbial composition of LT patients to healthy controls.
Results: The mean age of LT patients was 61.6 years and the mean time from LT was 11.7 years. Of 16 included LT patients, 9 patients (56.2%) were male and 13 patients (81.2%) underwent living-donor LT. The long-term post-LT patients (LT group) showed a decrease in intraindividual diversity and overall diversity compared to healthy controls (control group). Moreover, there was a significant difference in abundant microbiome between the two groups. The LT group showed a significant decrease in Ruminococcaceae, potentially beneficial family, whereas an increase in Bacteroidaceae, potentially pathogenic family. At genus level, Faecalibacterium was significantly decreased with an increase in Bacteroides in the LT group compared to the control group. Moreover, the LT group demonstrated lower Tregs with higher Th17 cells than the control groups. In in vitro analysis, we demonstrated that the proportion of Treg was increased

with a decrease in IL-17 after treated with F.prausnitzii. and its metabolite, Butyrate.
Conclusion: In the long-term post-LT patients, gut microbial imbalance is still noted with a decrease in functional microbiomes represented as Faecalibacterium.

[OP-0094]

Prediction of hepatic steatosis by machine learning algorithms in living liver donor

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Objectives: Selecting an optimal donor for living donor liver transplantation (LDLT) is crucial for the safety of both the donor and recipient, and hepatic steatosis is one of the considerations. We aimed to build a prediction model to evaluate macrovesicular steatosis in potential donors using various prediction models with noninvasive variables.
Materials and Methods: The study population comprised potential living donors who had undergone donation workup, including percutaneous liver biopsy, in the Republic of Korea from 2016 to 2019. Meaningful macrovesicular hepatic steatosis was defined as > 5%. Whole data were divided into train and test sets based on the liver biopsy date. The algorithms of the random forest, support vector machine, regularized discriminant analysis, mixture discriminant analysis, flexible discriminant analysis, deep neural network as well as traditional logistic regression were employed.
Results: Of a total of 1,652 participants, 518 (31.4%) had macrovesicular steatosis > 5%. The train and test sets comprised 70.5% and 29.5%, respectively. The logistic model had the best prediction power and prediction performances; the accuracy rates for each of the sets were 80.0% and 80.9%, respectively; the sensitivity and specificity were 77.7% and 81.0%, respectively.
Conclusion: Our algorithm to predict macrovesicular steatosis with generally assessed parameters would be beneficial for identifying optimal potential living donors by avoiding superfluous liver biopsy.

Summary of Classification Model Performance for Identification of Hepatic Steatosis

	Train set*					Test set*				
	Discrimination		Calibration†			Discrimination		Calibration		
	Accuracy	AUROC (95% CI)	Chi-squared	DF	*P*-value	Accuracy	AUROC (95% CI)	Chi-squared†	DF†	*P*-value†
Logistic model	0.800	0.862 (0.839–0.885)	7.3	8	0.500	0.809	0.865 (0.830–0.900)	11.3	8	0.190
Random forest	1.000	1.000 (1.000–1.000)	136.5	8	< 0.001	0.793	0.851 (0.814–0.888)	17.2	8	0.030
Support vector machine	0.847	0.890 (0.867–0.912)	36.1	8	< 0.001	0.795	0.831 (0.790–0.872)	9.1	8	0.340
Regularized discriminant analysis	0.818	0.858 (0.834–0.882)	17.2	8	0.030	0.791	0.862 (0.827–0.897)	26.4	8	0.001
Mixture discriminant analysis	0.817	0.862 (0.838–0.885)	17.4	8	0.030	0.799	0.854 (0.818–0.890)	29.7	8	< 0.001
Flexible discriminant analysis	0.814	0.862 (0.839–0.885)	10.8	8	0.210	0.809	0.865 (0.830–0.900)	22.6	8	0.004
Deep neural network	0.776	0.953 (0.938–0.968)	2.5×10^5	8	< 0.001	0.776	0.830 (0.791–0.869)	3.4×108	8	< 0.001

* The train set comprised people who underwent pre-donation evaluation between January 2016 and January 2019; test set, between February 2019 and December 2019.
†Chi-squared, DF, and p-value were the results of Hosmer-Lemeshow test
Abbreviations: AUROC, area under the receiver operating characteristic; CI, confidence interval; DF, degrees of freedom

[ABST-0201]

The use of 18F-FDG positron emission tomography to predict tumour recurrence in hepatocellular carcinoma patients after hepatectomy

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Background: A reliable biomarker to predict hepatocellular carcinoma (HCC) recurrence after hepatectomy is lacking. We hypothesized that pre-operative 18F-fluorodeoxyglucose (18F-FDG) uptake on positron emission tomography (PET) predicted HCC recurrence after hepatectomy.
Methods: This was a retrospective study of prospective collected data between 2004–2019. The cut-off for 18F-FDG uptake on PET for HCC recurrence was determined by Youdens' index. Patients were stratified into PET + ve and PET-ve group. Baseline, pathological characteristics, disease-free and overall survival rates were compared.
Results: 267 patients underwent hepatectomy with preoperative PET scan. The cut-off for 18F-FDG PET positivity was 1.526 (AUC = 0.674, 95% CI 0.608–0.741, $P < 0.001$). 155 patients were PET-ve and 112 patients were PET + ve. The PET + ve group had larger tumors (8.25 vs. 3.5 cm, $P < 0.001$), more microvascular invasion (67 vs. 36.1%, $P < 0.001$), more poorly differentiated tumours (24.8 vs. 16.7%, $P = 0.03$) and higher AFP $\geq$ 100 ng/ml (49.1 vs. 23.2% $P < 0.001$). The time to recurrence was shorter in PET + ve patients (8.4 vs. 32.7 months, $P < 0.001$) and there was more extrahepatic recurrence (8.9 vs. 2.6%, $P < 0.001$). The PET-ve group had better overall and disease-free survival rates at 1-, 3- and 5-year respectively (96.1%, 84.9%, 79.8% vs. 78.2%, 54.9%, 43.1%, $P < 0.001$; 74.6%, 55.2%, 45.8% vs. 43%, 37.1%, 33.1%, $P < 0.001$).
Conclusions: PET + ve was associated with higher AFP and unfavourable tumour biology, with a higher risk of recurrence and inferior survival. 18F-FDG PET should be explored prospectively as a biomarker in HCC patients.

[OP-0660]

Impact of sarcopenia using L3 and thigh skeletal muscle index on clinical outcomes in liver transplantation recipient

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Objectives: Sarcopenia is defined as loss of muscle mass and function. It has been reported as a risk factor for outcomes after Liver transplantation (LT). Although there are various imaging modalities and measurement methods for diagnosing sarcopenia, the gold standard is not clear. The purpose of this study is to compare and analyze the impact of sarcopenia on outcomes in LT patients using third lumbar (L3)-skeletal muscle index (SMI) and thigh-SMI.
Materials and Methods: Two hundred eighteen patients who underwent LT in our center from Sep 2018 to Dec 2020 were analyzed. L3 and thigh-SMI were obtained by measuring preoperative computed tomography (CT) scans with semiautomatic software. The cutoff value of L3-SMI was referred to other studies, and the cutoff

value of Thigh-SMI was calculated by obtaining ROC curves from our cohort.
Results: The prevalence of sarcopenia diagnosed by L3-SMI in our cohort was 46% (101/218). Patient and graft survival rates in the sarcopenia group were significantly lower than in the non-sarcopenia group (P = 0.001 and P = 0.007). The cut-off values of thigh-SMI from the ROC curve were 38.9 for females (AUC = 0.856, P < 0.001) and 48.2 for males (AUC = 0.768, P < 0.001). Both the patient and graft survival rates in the sarcopenia group by thigh-SMI were lower than in the non-sarcopenia group, but patient survival was not statistically significant (P = 0.580, P = 0.032). As a result of Cox analysis of LT recipient, sarcopenia by L3-SMI were confirmed as one of the independent prognostic factors for survival after LT (HR, 2.595; 95% CI, 0.999–6.740; P = 0.05).
Conclusion: Sarcopenia by L3-SMI affected clinical outcomes in LT patients and was confirmed as an independent prognostic factor for patient and graft survival. On the other hand, Thigh-SMI is unfavorable for predicting clinical outcomes in LT patients. Therefore, L3-SMI can be a useful choice for the evaluation of sarcopenia in LT patients.

[OP-0093]

The clinical implication of hepatic venous territory mapping in living donor liver transplantation using right liver graft

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Objectives: We designed this study to evaluate the clinical implication of hepatic venous territory mapping in living donor liver transplantation.
Materials and Methods: LDLT cases performed using right liver graft since 2017 were included. Hepatic venous mapping using Volume viewer application in the AW server 3.2 (GE Healthcare, Chicago, IL, USA) was started since January 2019. Comparison between transplantation cases with venous mapping and cases without mapping were performed.
Results: Among 754 patients included to the study, 213 patients underwent hepatic venous mapping. Inferior hepatic vein reconstruction rate and patency rate were similar between the no mapping group and mapping group (25.2% vs. 28.8%, P = 0.402 and 92.5% vs. 96.8%, P = 0.412), respectively. While middle hepatic vein reconstruction rate was higher in the mapping group (67.3%) compared to the no mapping group, (55.8%, P = 0.013) patency rate was higher in the no mapping group (63.5%) compared to the mapping group (51.1%, P = 0.041). In patients with V5 reconstruction, median volume (177 cm^3, IQR 152–259 vs. 147 cm^3, IQR 113–199, P = 0.006) and median percentage of V5 territory (22.3%, IQR 17.1–29.7 vs. 18.4%, IQR 14.9–21.8, P = 0.001) were higher in the patent graft compared to occluded graft. A cut-off point of 150cm^3 (sensitivity = 0.824, specificity = 0.533, AUC = 0.680, P = 0.006) and 20.0% (sensitivity = 0.647, specificity = 0.711, AUC = 0.716, P = 0.001) were chosen based on Youden's index in area-under receiver operating characteristic analysis.
Conclusion: Hepatic venous mapping provided objective measure for performing venous outflow reconstruction in living donor liver transplantation using right liver graft with increased reconstruction rate of the middle hepatic vein territory.

[ABST-0446]

Analysis of a high-volume advanced liver program: Short-term outcomes and costs

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Background: Robotic liver surgery has shown an exponential growth worldwide. One of the remaining concerns about robotic surgery are its perceived higher costs. This study was undertaken to analyze outcomes and costs of a high-volume robotic liver surgery program.
Methods: With IRB approval, we followed 310 consecutive patients who underwent robotic hepatectomies at our institution. 'Major resection' was defined as resection of $\geq$ 3 Couinaud segments. Postoperative complications are noted if of Clavien-Dindo grade $\geq$ III. Data are presented as median (mean $\pm$ SD).
Results: Patients were 64 (62 $\pm$ 13.9) years-old with a BMI of 28 (29 $\pm$ 6.5) kg/m2, a MELD score of 7 (8 $\pm$ 3.4): 55% were women, 53% had previous abdominal operation (s), 57% required major resections, and 63% of operations had IWATE score $\geq$ 7. Operative duration was 247 (277 $\pm$ 124.2) minutes and blood loss was 100 (194 $\pm$ 233.0) mL. There were 6 (2%) conversions to 'open' operations [because of bleeding (2), extensive adhesions (3), lack of progress (1)] and 2 (1%) intraoperative complications [bleeding (2)]. There was a 5% postoperative complication rate and a 2% 90-day mortality rate (exacerbation of comorbidities (2), respiratory failure (1), sepsis (1), and GI bleed). Length of hospital stay (LOS) was 4 (4 $\pm$ 3.7) days with 18% readmittance within 30-days. Total cost was $27,912 (32,782 $\pm$ 26,543.07) with variable cost being $17,792 (20,651 $\pm$ 17,151.30), fixed direct cost being $2,111 (2,473 $\pm$ 2,022.52), and fixed indirect cost being $7,723 (9,580 $\pm$ 8,162.43). Hospital remuneration was $19,102 (38,975 $\pm$ 39,362.11) per operation.
Conclusions: Patients were generally older overweight women who had undergone previous abdominal operations and required major hepatectomies. Conversions to 'open', complications, LOS, readmissions, and deaths were few/short. Profit averaged over $6,000 per patient. Robotic liver surgery is safe, efficacious, and profitable.

Free Papers 10 (Hepatobiliary Surgery)

[OP-0782]

Robotic vs laparoscopic liver resection for hepatocellular carcinoma—short term and long term oncologic outcomes

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Objectives: There is growing evidence that supports the feasibility and safety of robotic liver resection, however, data concerning long-term oncologic outcomes in patients with liver malignancy are still lacking. In this study, we performed a matched comparison of short- and long-term oncologic outcomes between robotic and laparoscopic liver resection in patients with hepatocellular carcinoma (HCC).
Materials and Methods: We retrospectively reviewed all the cases of laparoscopic and robotic liver resection of hepatocellular carcinoma performed in our institute from 2006 to 2020. Three hundred-seven

patients who received laparoscopic liver resection and 44 patients who received robotic liver resection were included. A multivariable logistic model based on factors related to the patient, tumor and surgical procedure were then used to estimate a propensity score. Survival data were obtained using Kaplan–Meier method.
Results: The two groups did not differ significantly with respect to perioperative outcomes measured in terms of estimated blood loss, transfusion rate, conversion rate to open surgery, resection margins, perioperative complication rates, and length of hospital stay. All resections were R0 resections and no perioperative deaths were noted. There were notably longer operation times for the robotic group compared to the laparoscopic group (median:496.82 vs 238.56 min; P = < 0.0001). However, it was noted that more major resections were performed using the robotic approach compared to the laparoscopic approach (23.77% vs 75.0%; P = < 0.0001). After propensity score matching, the robotic group (n = 27) showed similar 1, 3, and 5-year disease- free (P = 0.696) and over-all survival rate (P = 0.869) compared to laparoscopic group (n = 27).
Conclusion: Robotic liver resection for hepatocellular carcinoma produced similar oncologic outcomes in terms of R0 resection rate, 5-year disease-free survival and over-all survival rate, and allowed for more major liver resections to be performed as compared to laparoscopic liver resection.

[OP-0268]

Acute kidney injury after liver resection: A systematic review, meta-analysis and metaregression of factors affecting it

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Objectives: This systematic review and meta-analysis aimed to study the incidence of acute kidney injury after liver resection and to analyze various factors affecting it by metaregression analysis.
Materials and Methods: The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (2020) and MOOSE guidelines. The meta-analysis was done using Review Manager 5.4 and the JASP Team (2020). JASP (Version 0.14.1) (University of Amsterdam). Weighted percentage incidence with 95% confidence intervals were used. Univariate metaregression was done by DerSimonian-Laird methods. Factors with a p-value less than 0.05 in the univariate metaregression model were entered in the multivariate metaregression model. Heterogeneity was assessed using the Higgins I^2 test. The random-effects model was used in meta-analysis.
Results: Total 14 studies including 15,510 patients were included in the final analysis. 1247 patients developed Acute Kidney Injury. Weighted Acute kidney injury percentage after liver resection was 15% with a 95% confidence interval of 11%-19%. On univariate metaregression analysis major hepatectomy (p = 0.001), Underlying cirrhosis of liver (p = 0.031), AKIN definition used (0.017), male sex ($p < 0.001$), open surgery (p = 0.032), underlying diabetes (0.026). On multivariate metaregression analysis major hepatectomy (p = 0.003), underlying cirrhosis ($p < 0.001$), male sex ($p < 0.001$), AKIN classification used for defining acute kidney injury ($p < 0.001$, independently predicted heterogeneity and hence acute kidney injury.
Conclusion: Liver resection is associated with a high incidence of acute kidney injury. Major hepatectomy, male sex, underlying cirrhosis were independently predicting acute kidney injury.

[OP-0977]

Clinical feasibility of laparoscopic liver resection for tumors in segment 7 or 8

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Objectives: Laparoscopic surgery has been established as the standard treatment for most liver resections, but for the lesions of right posterosuperior segments 7 and 8 (PSL), LLR have been compared to open liver resection (OLR) due to technical difficulties. However, various attempts are being made for PSL resection with the step-by-step development and accumulation of experience in LLRs, and results compared with OLR are reported.
Materials and Methods: This study included 98 patients who underwent LLR for PSL from September 2014 to August 2021. These LLRs were performed using 4 or 5 ports in left semi-lateral position and the flexible laparoscope and laparoscopic CUSA were routinely used. OLR cases (n = 48) for the same period were also included to identify the trend pattern to LLR and to compare the considerations for determining the optimal resection type.
Results: The criteria for the selection the liver resection type were tumor location, liver function (platelet, ICG R15, CTP score), resection margin involvement of right hepatic vein and the presence of right inferior hepatic vein. In 98 LLR cases, central bisectionectomy was 10 cases, posterior and anterior sectionectomy were 16 and 11 cases. 7/8 bisegmentectomy was 2 cases, wedge and segmentectomy were 37 cases. Bile leakage at the cut surface was observed in 2 cases after central bisectionectomy, resolved through PTBD and PCD insertion. Median overall operation time was 277.5 min in LLR and 280 min in OLR.
Conclusion: LLR for PSL is likely to be safe and feasible with the accumulation of experience and the advanced laparoscopic techniques and instruments. To select the optimal resection type of LLR for PSL, the degree of liver function, resection margin from tumor, the involvement of right hepatic vein, or the presence or absence of sizable RIHV are carefully considered. These considerations is the same as those in OLR, except in cases of vascular reconstruction.

[OP-0303]

Comparative long-term surgical outcomes for CC associated with non alcoholic fatty liver disease versus hepatitis B

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Objectives: The global burden of non- alcoholic fatty liver disease (NAFLD) and NAFLD-associated hepatocellular carcinoma (HCC) is steadily rising. Our objective was to compare surgical outcomes between NAFLD- and hepatitis B (HBV)-associated HCC.
Materials and Methods: Patients who underwent liver resection for HCC between January 2004 and December 2018 were included. Factors associated with recurrence in NAFLD-associated HCC were analyzed.
Results: The prevalence of NAFLD-associated HCC was 8.4%. A significant number of NAFLD patients had no cirrhosis (21 patients; 38.8%). Although NAFLD patients had a significantly better 5-year

survival (P = 0.033), NAFLD was not significantly associated with overall survival in multivariate analysis (P = 0.287). However, survival after 5 years declined in NAFLD patients and was similar to HBV. NAFLD was protective against systemic recurrence compared with HBV (P = 0.018), and this was confirmed in multivariate analysis (P = 0.044). Five-year systemic recurrence (P = 0.044) was significantly lower in NAFLD patients and decreased with time from surgery. Multivariate analysis revealed that anatomical liver resection was the only factor independently associated with decreased recurrence in NAFLD patients (HR = 0.347; P = 0.041).
Conclusion: Overall survival is similar between NAFLD-associated HCC and HBV-associated HCC. Despite there being no significant difference between liver function tests, type of surgery performed, liver cirrhosis, size of tumor, number of tumors, pathological factors like satellite nodules and Edmonson Steiner staging, NAFLD-associated HCC shows lower systemic recurrence compared to HBV-associated HCC.

[OP-0267]

Extent of liver resection is associated with incomplete liver restoration and splenomegaly a long period after liver resection

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Objectives: Little is known about the clinical significance and risk factors for incomplete liver resto- ration after partial hepatectomy, which is defined by a liver volume restoration of less than 100% of the original volume.
Materials and Methods: We retrospectively analyzed patients who underwent hepatic resection for liver tumors at the Kyoto University Hospital between January 2011 and October 2015 and survived without recurrence for more than 3 years. The preoperative and postoperative data, as well as liver and splenic volume after 3 postoperative years, were assessed.
Results: The percentage of resected liver was higher in the incomplete liver restoration group (n = 52, 41.6%) than in the complete liver restoration group (n = 73, 58.4%) (28 [3–78]% vs 14.5 [2–63]%, p = 0.0226). The percentage of resected liver was also higher in the splenomegaly group (defined by spleen volume increases of more than 35% of the original volume) than in the nonsplenomegaly group (40 [4–63]% vs 16.5 [2–78]%, p = 0.0002). Multivariate analysis demonstrated that the percentage of resected liver was a significant predictor of incomplete liver restoration (odds ratio = 9.75, p = 0.0043) and splenomegaly (odds ratio = 74.4, p = 0.0006). Incomplete liver restoration 3 years after hepatectomy was associated with lower serum albumin levels (4.0 [2.4–4.7] g/dL compared with 4.2 [2.6–4.8] g/dL in the complete liver restoration group, p = 0.0032). Splenomegaly was associated with a lower platelet count ($109.9 \pm 49.8 \times 10^3$/mL vs $163 \pm 58.1 \times 10^3$/mL, p = 0.0007) and lower serum albumin level (3.6 [2.6–4.4] g/dL vs 4.1 [2.4–4.8] g/dL, p = 0.0002).
Conclusion: An extensive resection of the liver parenchyma results in an increased risk for incomplete liver restoration and splenomegaly long after hepatectomy, which is associated with the clinical consequences of hypoalbuminemia and thrombocytopenia.

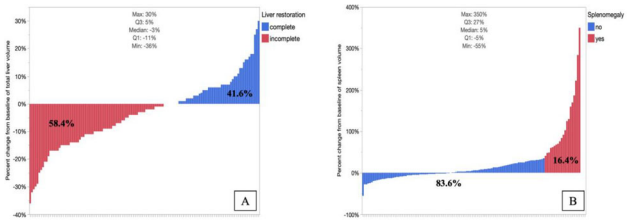

Figure: Waterfall plot of percent change from baseline of total liver volume (panel A) and spleen volume (panel B) after 3 years of hepatectomy.

[ABST-0257]

Future liver remnant less than 30% is not a contraindication to living donor right hepatectomy

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Background: The evidence for defining a safe remnant/total volume ratio (RTVR) for in living donors undergoing right hepatectomy for living donor liver transplantation (LDLT) is still not clear yet. The current practice of arbitrarily requiring an RTVR of at least 30% is based on the experience of early studies to keep donor safety. Recently, some centers reported that extended resection with RTVR less than 30% for living donor right hepatectomy but there is no consensus has been established for future remnant liver volume (FRLV) ratio limit. Herein, we describe out center's experience for living donor right hepatectomy with RTVR < 30% and evaluate the outcomes of living donors with RTVR < 30%
Methods: We retrospectively reviewed the outcomes of 473 living donor right hepatectomy (LDRH) which performed at our institution from January 2010 to December 2020. We performed right hepatectomy for living donors with RTVR < 30% under the following criteria; 1) Age ≤ 40 2) Preservation of MHV 3) No or Minimal fatty changes (< 15%) 4) Flat fish shaped left hemiliver 5) RTVR > 25% and FRLV/BW ≥ 0.45. The outcomes in these extended living donors were compared with those in living donors under conventional criteria.
Results: The mean RTVR in extended group was 27.1 ± 1.2% (range, 25.1–28.9). Posthepatectomy liver failure (PHLF) occurred in 50 donors (10.6%) and most cases were grade A except one case in conventional group and no clinically significant PHLF was not evident for these extended donor group. PHLF and major complications were not more frequent in living donor group with RTVR < 30%. In multivariate only the event for major complications was associated with PHLF but RTVR less than 30% was related to PHLF. To adjust for between-group differences, donors with FLR ≤ 30% and > 30% were matched based on baseline characteristics and overall complication rates and the incidence of PHLF were not different between the two groups.
Conclusions: LDRH under our extended criteria could be performed safely in donors with RTVR ratio < 30% under our strict criteria when no other donors are available and our extended criteria might be helpful to expand donor pools without adverse effects on donor safety.

[ABST-0214]

Non-invasive biomarkers, FIB-4 and APRI index, as predictors for prognosis of hepatocellular carcinoma patients after curative hepatectomy

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Background: Although many staging systems and liver reserve models were not developed to predict HCC recurrence and overall survival, the few studies, which have investigated their prognostic values in predicting prognosis of HCC patients after curative hepatic resection. Among those non-invasive biomarkers, we try to evaluate the value of FIB-4 and APRI as prognostic predictors.
Methods: Between 2006 and 2013, 973 patients were diagnosed with HCC and underwent hepatic resection at the Department of General Surgery of Samsung Medical Center, Korea. All biomarkers were calculated at the time of HCC diagnosis (FIB-4, APRI, AAR, AARPRI and ALBI). For all biomarkers, univariable and multivariable analysis was performed on recurrence-free survival and overall survival by binary division by the cut-off value of the ROC curve.
Results: FIB-4 and APRI, which had higher AUC values for RFS and OS, compared to other biomarkers, were included in multivariable analysis. The AUROC values for APRI were the largest for RFS and OS, 0.607 (95% CI, 0.572–0.640) and 0.623 (95% CI, 0.575–0.676), respectively. For FIB-4, they were 0.573 (95% CI, 0.536–0.612) and 0.568 (95% CI, 0.505–0.613), respectively. Those two indices are considered statistically significant risk factors for prognosis of HCC patients after hepatic resection. For APRI, HR for OS and RFS were 1.846 (95% CI 1.190–2.862, P = 0.006) and 1.762 (95% CI 1.357–2.287, P = 0.000), respectively, and for FIB-4, 1.559 (95% CI 1.002–2.425, P = 0.049) and 1.315 (95% CI 0.996–1.737, P = 0.053).
Conclusions: In our study, non-invasive biomarkers such as FIB-4 and APRI were statistically significant and meaningful as a predictor of prognosis after curative hepatectomy in HCC patients. Because post-operative complications, other models representing liver function reserve, and pathologic findings of HCC itself also influence the prognosis, rather than simply judging based on the above two indices, the significance of this study can be found in emphasizing the significance of a method that can be used as a reference when there is difficulty in predicting or making a decision using the conventional method in curative hepatectomy.

[ABST-0354]

Weight reduction of the donor in hepatic steatosis for living donor liver transplantation as a tool in expanding the donor pool

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Background: The obesity epidemic worldwide has made it increasingly common to encounter liver steatosis in the living as well as deceased donor candidate. The aim of our study was to review our experiences with right lobe (RL) adult living donor liver transplantation in donors who donated liver after confirming improvement of fatty liver through weight reductio (WR) and to investigate the feasibility, efficacy, and safety of using such donors on the donor, graft and recipient outcomes.
Methods: From January 2015 to December 2020, 150 living donors (LDs) donated RL after confirming improvement of hepatic steatosis through WR at a single center. We performed matching using a greedy method to compare the outcomes of the donors and recipients of this group to those of LDs with no WR.
Results: 150 patients in the WR group lost BW through diet and exercise for 113 (78—184) days for improvement of hepatic steatosis. The median (IQR) body weight gap from first visit to the operation in the weight reduction group were -13.22 (-16.58—-11.49) kg, and BMI were significantly reduced (27.8 ± 3.9 kg/m2 vs. 23.8 ± 3.1 kg/m2, P = < 0.0001) A notable result was the difference in graft volume (GV) gap between estimated GV e and real GV (WR group vs no WR group; -18.5 ± 93.3 vs -124.9 ± 148.9, P = < 0.0001). Post-operative complications in the WR group were significantly different compared to no WR group with a P-value of 0.0102 before matching, but were not statistically different after matching (P = 0.3185). The patient and graft survival rates of recipients in WR group showed no differences compared to donors with no WR group.
Conclusions: The appropriate short-term WR in potential living liver donors is an effective tool to expand the donor pool, enabling not only the conversion of marginal donors to low-risk donors, but also the transition from ineligible donors to eligible donors. However, since a decrease in liver volume due to BW reduction can affect graft-to-recipient weight ratio (GRWR), preoperative reevaluation is necessary in patients with expected marginal GRWR.

[ABST-0345]

Two distinct stem cell-like subtypes of resectable hepatocellular carcinoma with clinical significance and their therapeutic potentials

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Background: Hepatocellular carcinoma (HCC) is among the most common cancers worldwide. Stem cell-like characteristics, which drive early recurrence and therapy resistance, contribute significantly to poor prognosis even in the early stage with resectability. Therefore, a precise adjuvant treatment strategy for high-risk patients showing stem cell-like features is mandatory in the early stage HCC after surgical resection.
Methods: We integrated and analyzed gene expression data from human fetal liver cells and primarily resectable HCC tumors (n = 1231). We uncovered two clinically and biologically distinct hepatic stem cell (HS) subtypes, potential biomarkers associated with, and a possible new therapeutic intervention for these subtypes.
Results: By analyzing single-cell gene expression data from human fetal liver cells, we identified 609-, 2538-, and 1139-gene signatures for gestational 10-week fetal liver cells, 17-week fetal liver cells, and mature hepatocytes, renamed the gene signatures specific to the 10- and 17-week cells hepatic stem cell type 1 (HS1) and hepatic stem cell type 2 (HS2), respectively. The HS1 subtype was associated with the worst overall survival, the HS2 subtype exhibited moderate overall survival, and the DH subtype exhibited the best overall

survival ($P < 0.001$). The HS1 subtype showed higher rates of TP53 and RB1 mutations, while the HS2 subtype showed frequent IL6ST and CDKN2A mutations. Both HS subtypes showed high immune dysfunction with exclusion scores, suggesting that patients with either HS subtype would not benefit substantially from immunotherapy. YAP1 was highly activated in the HS1 subtype. Since YAP1 regulates HS and is associated with poor prognosis in HCC, we next examined the potential interaction of other transcription regulators with YAP1 by integrating the downstream target genes of each of the transcription regulators. JQ1 significantly reduced the viability and migration of HCC cells and tumor size in the patient-derived xenograft (PDX) mouse suggesting that JQ1 can inhibit the growth and invasion of HCC cells by suppressing YAP1.
Conclusions: Importantly, the HS1 subtype, which has a poor prognosis, appears to be sensitive to BET inhibitors. The newly identified serum markers associated with these subtypes may provide opportunities to develop marker-based clinical trials in the adjuvant setting. Furthermore, the potential marker genes we identified are well-preserved in PDX models, which shows promise for the development of accurate disease models for preclinical study.

Free Papers 11 (Viral Hepatitis 1)

[OP-0900]

Can FIB 6 non-invasive fibrosis index be used for HBV cases?

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Objectives: In patients infected with the hepatitis B virus (HBV), the stage of liver fibrosis is an important factor in determining prognosis and the need for care. Noninvasive alternatives to liver biopsies have been established for assessing liver fibrosis. We recently created and both internally and externally validated a noninvasive index (FIB-6) that integrates routine laboratory parameters for predicting the phase of hepatic fibrosis in patients with chronic hepatitis C. Aims: To evaluate the accuracy of the FIB-6 index in the diagnosis of HBV related fibrosis and cirrhosis.
Materials and Methods: This is a retrospective observational analysis of data obtained from seven sites (Egypt, KSA, Turkey, Greece, Oman, Qatar and Jordan) of HBV patients. The inclusion criteria include receiving adequate liver biopsy and complete dataset (in terms of biochemical and hematological data).
Results: In this study, 603 patients met the criteria, and their liver biopsy results were included for analysis. Using the optimal cutoffs in the data of FIB-6 indicated a reliable performance in diagnosing cirrhosis, severe fibrosis, and significant fibrosis. Sensitivity = 70.9%, specificity = 84.1%. PPV = 40.3% and NPP = 95.0% for diagnosis of cirrhosis. For diagnosis of severe fibrosis (F3 and F4), the results were 71.5%. 69.3%. 40.8% and 89.2% respectively, while for diagnosis of significant fibrosis (F2, F3 and F4), the results were 68.3%, 67.5%, 59.9% and 75.0%). Comparing of the results of FIB-6 rule-out cutoffs with those of FIB-4, APRI, and AAR showed that in ruling out severe fibrosis and cirrhosis, FIB-6 gave the highest sensitivity and NPV (89.1% and 92.4%), as compared to FIB-4 (63.8% and 83.0%), APRI (53.9% and 86.6%), and AAR (47.5% and 82.3%).
Conclusion: The FIB-6 index is valuable for detecting fibrosis stages in HBV-infected patients. It can be used in ruling out severe fibrosis and cirrhosis with good reliability.

[OP-0970]

Virological and histological characteristics of chronic hepatitis B virus patients with normal serum ALT

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Objectives: Patients with chronic hepatitis B virus (HBV) infection and persistently normal ALT levels have whether abnormal liver histology or not is crucial for treatment. At present worldwide available most of the guideline recommends treatment depending on serum ALT level, which may miss significant number of liver disease. We studied the ALT, HBV DNA levels, and spectrum of histologic lesions in such patients.
Materials and Methods: It was a cross sectional observational study among the chronic hepatitis B virus infected patients presented in the DMCH who shows persistently normal ALT and detected HBV DNA load. Total 104 patients were enrolled in the study and undergone liver biopsy (n = 104; hepatitis B e antigen [HBeAg +], 82; hepatitis B e antigen [HBeAg-] 22).
Results: Among 82 HBeAg negative cases, there were 12 (14%) moderate chronic hepatitis and 26 (31%) showed mild chronic hepatitis. HBeAg positive cases also 8 (27%) had moderate chronic hepatitis and 8 (36%) had mild chronic hepatitis. 62% of HBeAg-positive and HBeAg-negative patients persistent normal ALT had baseline HBV DNA levels of > 3.3 log copies/mL. Serum HBV DNA level and spectrum of histological changes doesn't correlate. 60 (73.1%) HBeAg negative and 14 (63.6%) HBeAg positive patients had Knodell score > 7.
Conclusion: A fair proportion of patients with chronic HBV infection with persistent normal ALT have HBV DNA > 3.4 log copies/ml and significant histologic fibrosis in both HBeAg positive and HBeAg negative groups. Use of ALT and HBV DNA levels without resorting to liver biopsy to define "inactive carrier state" in patients may miss histologically significant disease in a proportion of patients.

Table- Histological spectrum in HBeAg positive & HBeAg negative patients

Parameters	HBeAg Positive, n (%)	HBeAg negative, n (%)
Histological grade		
Minimal chronic hepatitis	8 (36.36%)	44 (53.66%)
Mild chronic hepatitis	8 (36.36%)	26 (31.7%)
Moderate chronic hepatitis	6 (27.28%)	12 (14.63%)
HAI score		
<3, n (%)	2 (9.1%)	16 (20%)
>3, n (%)	20 (90%)	66 (80.5%)
Knodell score		
<7	8 (36.36%)	22 (26.83%)
>7	14 (63.64%)	60 (73.17%)

[OP-1144]

Presence of liver inflammation and fibrosis in Asian patients with chronic hepatitis B in the grey zone

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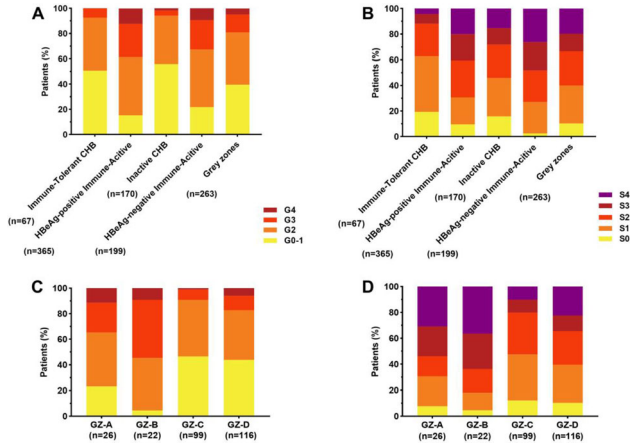
Objectives: Over a quarter of chronic hepatitis B (CHB) patients did not meet criteria of the traditional natural phases and hence classified as grey zone (GZ). However, few studies reported the liver inflammation and fibrosis of Asian CHB patients in the GZ.
Materials and Methods: This multicenter, retrospective study included 1,064 CHB patients underwent liver biopsy (LB). Phases of natural history were determined according the AASLD 2018 Guidance. GZ patients were divided into four categories: HBeAg-positive, normal ALT and HBV-DNA $\leq 10^6$ IU/ml (GZ-A); HBeAg-positive, elevated ALT and HBV-DNA $< 2 \times 10^4$ IU/ml (GZ-B); HBeAg-negative, normal ALT and HBV-DNA $\geq 2 \times 10^3$ IU/ml (GZ-C); HBeAg-negative, elevated ALT and HBV-DNA $< 2 \times 10^3$ IU/ml (GZ-D).
Results: 263 (24.7%) patients were in the GZ with the median age of 41.5 years and male of 67.2%. Among the GZ patients, GZ-D (44.1%) was the dominate category, followed by GZ-C (37.6%), GZ-A (9.9%) and GZ-B (8.4%). Surprisingly, as high as 60.4% of GZ patients had significant inflammation ($\geq$ G2) and 89.7% GZ patients had significant fibrosis ($\geq$ S2), which were higher than that of patients with immune-tolerant and inactive phases. Over half of patients had significant inflammation or fibrosis in each GZ category. GZ-B patients had the highest proportions of significant inflammation (95.5%) and fibrosis (81.9%) compared to other GZ categories (GZ-A: 76.9% and 69.3%; GZ-C: 53.5% and 52.5%; GZ-D: 56.1% and 60.4%, respectively).
Conclusion: A substantial GZ patients had significant liver inflammation or fibrosis, especially for CHB patients with GZ-B. Using liver biopsy to assess the liver histological activity should be encouraged in GZ patients.



[OP-0190]

High proportion of hepatic steatosis and metabolic risk factors among chronic hepatitis B patients: The multi-centre, prospective CAP-Asia study

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Objectives: We aimed to compare the characteristics of chronic hepatitis B (CHB) patients with hepatic steatosis, CHB patients without hepatic steatosis, and patients with non-alcoholic fatty liver disease (NAFLD).
Materials and Methods: Patients with NAFLD and CHB were prospectively enrolled from ten Asian centres. Fibroscan was performed for all patients and hepatic steatosis was defined based on controlled attenuation parameter > 248 dB/m.
Results: The data for 1063 patients were analysed (67.3% NAFLD, 32.7% CHB). A high proportion (59.2%) of CHB patients had hepatic steatosis. There was a significant stepwise increase in the proportion of patients with obesity, central obesity, diabetes mellitus, hypertension and dyslipidaemia, and significant stepwise increase in body mass index, waist circumference, alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transpeptidase, triglyceride, controlled attenuation parameter and liver stiffness measurement, from CHB patients without hepatic steatosis to CHB patients with hepatic steatosis to NAFLD patients (Table 1). The proportion with positive hepatitis B e antigen was similar between CHB patients with and without hepatic steatosis (16% vs 21%, p = 0.476); however, serum HBV DNA level was significantly lower among CHB patients with hepatic steatosis (29 [14 – 275] vs 45 [20 – 507] IU/mL, p = 0.040).
Conclusion: It is important to diagnose hepatic steatosis among CHB patients so that concomitant metabolic risks can be assessed and managed accordingly in these patients. (The study is supported in part by a grant from Gilead Sciences [IN-US-989–5334] and logistic support by Echosens).

	CHB patients without hepatic steatosis, n = 142	CHB patients with hepatic steatosis, n = 206	NAFLD patients, n = 715	p*	p**	p***
Age, years	53 (44 – 61)	56 (47 – 62)	56 (47 – 63)	0.267	0.052	0.964
Male, n (%)	86 (61)	127 (62)	393 (55)	0.838	0.220	0.088
BMI, kg/m^2	22.9 (21.3 – 24.8)	26.3 (24.2 – 28.5)	27.6 (25.5 – 30.8)	<0.001	<0.001	<0.001
Obese, n (%)	30 (21)	136 (66)	568 (79)	<0.001	<0.001	<0.001
DM, n (%)	11 (7)	44 (21)	302 (42)	0.001	<0.001	<0.001
HPT, n (%)	24 (17)	70 (34)	380 (53)	<0.001	<0.001	<0.001
Dyslipidemia, n (%)	40 (28)	84 (41)	412 (58)	0.016	<0.001	<0.001
WC, cm	82 (75 – 88)	93 (87 – 99)	95 (88 – 102)	<0.001	<0.001	0.035
Centrally obese, n (%)	34 (24)	129 (63)	549 (77)	<0.001	<0.001	0.025
SBP, mmHg	126 (114 – 138)	130 (120 – 144)	132 (123 – 144)	0.145	<0.001	0.167
DBP, mmHg	76 (67 – 82)	79 (71 – 86)	80 (72 – 87)	0.028	<0.001	0.499
Albumin, g/L	44 (42 – 46)	44 (42 – 45)	44 (42 – 46)	0.746	0.471	0.390
Bilirubin, μmol/L	13 (10 – 17)	14 (10 – 19)	13 (10 – 16)	0.087	0.154	0.001
ALP, U/L	78 (60 – 101)	75 (63 – 97)	78 (66 – 97)	0.538	0.336	0.270
ALT, U/L	21 (15 – 26)	29 (21 – 40)	46 (33 – 77)	<0.001	<0.001	<0.001
AST, U/L	22 (19 – 28)	26 (22 – 34)	35 (26 – 50)	<0.001	<0.001	<0.001
GGT, U/L	19 (14 – 24)	28 (18 – 47)	50 (32 – 80)	<0.001	<0.001	<0.001
Platelet, x10^9/L	215 (180 – 257)	234 (197 – 274)	227 (191 – 272)	0.038	0.022	0.464
FBS, mmol/L	5.3 (4.9 – 5.8)	5.4 (5.1 – 6.1)	5.9 (5.2 – 7.1)	0.083	<0.001	<0.001
HbA1c, %	5.6 (5.3 – 6.0)	6.4 (5.6 – 7.3)	6.3 (5.7 – 7.2)	<0.001	<0.001	0.959
TG, mmol/L	1.2 (0.8 – 1.9)	1.6 (1.1 – 2.3)	1.8 (1.3 – 2.8)	0.001	<0.001	0.001
TC, mmol/L	4.7 (4.3 – 5.3)	4.7 (4.2 – 5.4)	4.7 (4.1 – 5.3)	0.691	0.771	0.950
HDL, mmol/L	1.4 (1.2 – 1.7)	1.2 (1.1 – 1.4)	1.2 (1.0 – 1.4)	<0.001	<0.001	0.796
LDL, mmol/L	2.9 (2.5 – 3.4)	2.8 (2.4 – 3.4)	2.7 (2.2 – 3.3)	0.543	0.023	0.022
Creatinine, μmol/L	76 (62 – 88)	75 (63 – 88)	71 (59 – 83)	0.471	0.019	0.033
CAP, dB/m	184 (208 – 228)	297 (270 – 326)	321 (286 – 346)	<0.001	<0.001	<0.001
E, kPa	5.1 (4.2 – 5.9)	5.6 (4.7 – 7.3)	6.7 (5.1 – 8.9)	0.002	<0.001	<0.001

* CHB patients without hepatic steatosis compared with CHB patients with hepatic steatosis

** CHB patients without hepatic steatosis compared with NAFLD patients

*** CHB patients with hepatic steatosis compared with NAFLD patients

[OP-0981]

Baseline serum HBV RNA levels are associated with risk of hepatitis flare after stopping NA therapy in HBeAg-negative patients

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Objectives: Among HBeAg-negative CHB patients on NA therapy, treatment discontinuation has been associated with HBsAg loss, -durable virological suppression as well as hepatitis flares requiring NA to be restarted. However, the prediction of clinical outcomes remains challenging. Quantification of HBVRNA is a promising biomarker. We evaluated the role of serum HBVRNA levels to predict clinical outcomes in a cohort of patients enrolled in a prospective NA-STOP study.
Materials and Methods: The Melbourne HBV-STOP study was a prospective multi-centre study of NA discontinuation in 110 HBeAg-negative non-cirrhotic patients who had achieved long-term suppression. In a subset, we performed an exploratory analysis of serum HBVRNA levels for predicting clinical outcomes using the automated Roche cobas® HBVRNA Investigational Assay. Outcomes of interest included rates of hepatitis flare (ALT > 5xULN), disease remission (HBV DNA < 2000 IU/mL and ALT < 2xULN) and HBsAg loss, as well as rates of NA re-treatment.
Results: 65 patients had serum available at baseline and longitudinally off-treatment. Median age was 56yrs,54% male,75% Asian. Median HBsAg level was 701 IU/mL. Virological reactivation occurred in all participants, 38% experienced a hepatitis flare (ALT > 5xULN), 26% restarted NA, 6% (n = 4) lost HBsAg at 96 weeks. At baseline, HBVRNA was detectable in 16/65 (25%) and was associated with higher risk of hepatitis flare [63%vs31%, p = 0.03], as well as lower likelihood of sustained disease remission and HBsAg loss (baseline HBVRNA levels were undetectable in all HBsAg loss patients). Of patients HBVRNA negative at baseline, serum HBVRNA levels became detectable in 47/49 patients during follow-up. The time to detection of HBVRNA was shorter for patients stopping TDFvsETV (49vs90days,p = 0.02). HBVRNA > 10^3cp/mL off-treatment were associated with risk of ALT > 5xULN.
Conclusion: Detectable HBVRNA was uncommon in HBeAg-negative patients on long-term NA. The detection of any serum HBVRNA prior to stopping NA, and rising HBV RNA off-treatment, were associated with risk of subsequent hepatitis flare, as well as lower likelihood of HBsAg loss.

[OP-0491]

Lower level of hepatitis B core-related antigen associates with higher chance of spontaneous seroclearance of hepatitis B surface antigen

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Objectives: Clearance of hepatitis B surface antigen (HBsAg) indicates functional cure of hepatitis B virus (HBV) infection. However, little is known about of the association of hepatitis B core-related antigen (HBcrAg) level and HBsAg seroclearance.
Materials and Methods: We conducted a retrospective cohort study including 2614 CHB patients (2111 HBeAg-negative and 503 HBeAg-positive patients), who received long-term follow-up at the National Taiwan University Hospital. The primary endpoint was HBsAg seroclearance and we explored whether the baseline viral markers, including HBcrAg, could predict HBsAg seroclearance.
Results: There were 465 patients clearing HBsAg among 32,414.72 person-years of follow-up. HBcrAg levels were shown to be negatively associated with HBsAg seroclearance. Among viral markers, HBsAg was shown to be a better predictor for HBsAg seroclearance. When restricting to 1083 HBeAg-negative patients with HBsAg level > 1000 IU/mL, a lower HBcrAg level was shown to be associated with an increased chance of HBsAg seroclearance. After stratifying these patients by HBcrAg level of 10,000 U/mL, low-HBcrAg patients were more likely to clear HBsAg than those high-HBcrAg patients with an adjusted hazard ratio of 1.99 (95% CI: 1.36–2.91).
Conclusion: In patients with chronic HBV infection, HBsAg remains a better predictor for HBsAg seroclearance. However, in HBeAg-negative patients with higher HBsAg level, lower HBcrAg level is an independent factor predicting HBsAg seoclearance.

[OP-0555]

Functional cure of peginterferon treatment for HBeAg-positive chronic hepatitis B—a 15-year longitudinal study

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Objectives: We aimed to study the 15-year incidence of functional cure of hepatitis B e antigen (HBeAg)-positive chronic hepatitis B (CHB) patients who received peginterferon alfa-2b, compared to entecavir-treated patients.
Materials and Methods: We included HBeAg-positive CHB patients who received peginterferon alfa-2b 1.5 μg/kg/week for 32 weeks and lamivudine 100 mg/day for 52 or 104 weeks in years 2000–2004 from two randomized controlled trials, and compared them with those receivingentecavir treatment by 1:5 propensity score matching.Patients were censored upon retreatment. The cumulative incidence of virologic response, including functional cure, i.e.hepatitis B surface antigen (HBsAg) seroclearance, HBeAg seroconversion and serum hepatitis B virus (HBV) DNA suppression, were analysed.
Results: 85 HBeAg-positive patients in peginterferon group were followed for a median of 13.3 (4.0 – 16.5) years, compared to 5.8 (3.2 – 8.4) yearsin 425 patients in entecavir group. Seven and 9 patients (8% vs.2%) in the peginterferon and entecavir groups achieved HBsAg seroclearance. The cumulative incidences of HBsAg seroclearance were 1% and 2% at 5 years, and 5% and 4% at 10 years respectively (p = 0.429) (Fig. 1A). 71 patients (84%) in peginterferon group achieved HBeAg seroconversion, compared to 126 patients (30%) in entecavir group. The cumulative incidences of HBeAg seroconversion were 82% and 30% at 5 years, and 93% and 45% at 10 years respectively (p < 0.001) (Fig. 1B). 55 (65%) and 33 (39%) patients in the peginterferon group had sustained HBeAg seroconversion and HBV DNA < 2,000 IU/mL throughout. Genotype B (compared to genotype C) and undetectable HBV DNA at the end of peginterferon treatment were factors associated with sustained virologic response.
Conclusion: Peginterferon leads to high rates of HBeAg seroconversion and HBsAg seroclearance up to 15 years, offering an attractive option for functional cure in HBeAg-positive CHB patients.

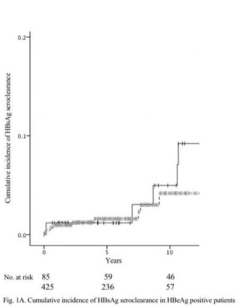

Fig. 1A. Cumulative incidence of HBsAg seroclearance in HBeAg positive patients

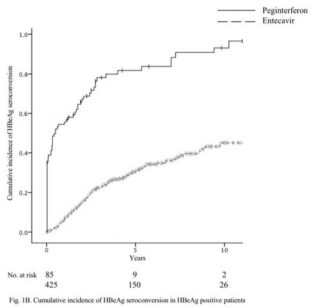

Fig. 1B. Cumulative incidence of HBeAg seroconversion in HBeAg positive patients

[OP-1093]

Efficacy of antiviral prophylaxis up to 6 or 12 months after completion of rituximab in resolved hepatitis B: A randomized controlled trial

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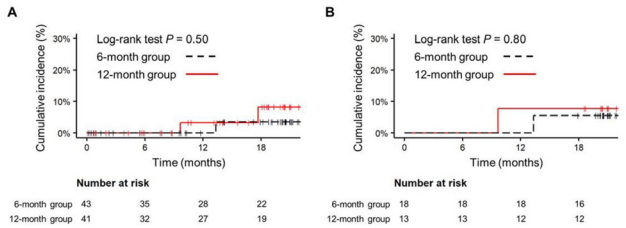
Objectives: Rituximab occasionally induces reactivation of hepatitis B virus (HBV) in patients with resolved HBV, at times with fatal consequences. The optimal duration of prophylactic antiviral therapy in this situation is unclear.
Materials and Methods: A multicenter, randomized, open-label, prospective study was conducted in HBsAg-negative and anti-HBc-positive non-Hodgkin's lymphoma patients treated with rituximab-based chemotherapy. A total of 90 patients were randomized and received prophylactic TDF from the initiation of rituximab until 6 months (the 6-month group) or 12 months (the 12-month group) after the completion of rituximab. The primary outcome was the difference in HBV reactivation. The secondary outcomes were the differences in hepatitis flare and adverse events between the two groups.
Results: In an intention to treat analysis, HBV reactivation occurred in 1 of 43 patients (2.3%) at a median of 13.3 months in the 6-month group and 2 of 41 patients (4.9%) at a median of 13.7 months in the 12-month group. The cumulative incidence of HBV reactivation was not significantly different between the two groups (P = 0.50). No hepatitis flare occurred in either group. The occurrence of adverse events was not significantly different between the two groups (9.3% in the 6-month group, 22.0% in the 12-month group, P = 0.19).

Conclusion: Prophylactic TDF up to 6 months after completion of rituximab-based chemotherapy is sufficient in terms of the efficacy and safety of reducing HBV reactivation in patients with resolved HBV.



[OP-0342]

Effectiveness of besifovir dipivoxil and tenofovir alafenamide on treatment-nave patients with chronic hepatitis B: A real world cohort

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Objectives: Besifovir dipivoxil maleate (BSV) and tenofovir alafenamide fumarate (TAF) were recently approved in Korea as the primary drugs for chronic hepatitis B. The outcomes of these drugs have not been fully elucidated yet based on real-world data. This study aims to compare the outcomes of two nucleotide analogues in treatment-naïve patients with chronic hepatitis B.
Materials and Methods: We retrospectively investigated the cohort of patients with chronic hepatitis B who received BSV and TAF as the first antiviral agent. The outcomes included achievement of laboratory endpoint as well as death and development of hepatocellular carcinoma (HCC).
Results: A total of 537 patients, 202 and 335 who received BSV and TAF, respectively, were followed-up up to 42 months. There were no significant differences in age, sex, BMI, presence of cirrhosis, hepatitis e antigen status, serum hepatitis B virus DNA level and liver function levels between two treatment groups. In terms of outcomes, there were no significant differences not only in virologic response, biochemical response, e antigen seroclearance, virologic breakthrough and kidney injury development but also in mortality and development of HCC between the two groups; During a median of 16.6 months (range, 1 – 42 months), two patients died, 10 were diagnosed with HCC. On multivariable analysis, older age [adjusted hazard ratio (aHR), 1.10], alcohol abuse (aHR, 2.08), and status of cirrhosis (aHR, 2.49) were independently associated with an increased risk of HCC development. The type of nucleotide analogues did not significantly affect the risk of mortality and HCC development. Even in the two subgroups with non-cirrhosis and cirrhosis, there was no significant difference in mortality and HCC development between those who received BSV and TAF.
Conclusion: The prognosis of patients with chronic hepatitis B were statistically similar between BSV and TAF.

Free Papers 12 (Viral Hepatitis 2)

[OP-0465]

Rapid HBsAg reduction in chronic hepatitis B virus infection: preliminary results from a phase 1 study evaluating a single dose of VIR-3434, a novel neutralizing, vaccinal monoclonal antibody

Carey Hwang[1], Man-Fung Yuen[2], Heiner Wedemeyer[3], Andre Arizpe[1], Ling Shen[1], Daniel Cloutier[1], Chin Tay[1], Sneha V. Gupta[1], Marie Fanget[1], Lillian Seu[1], Andrea L. Cathcart[1], Kosh Agarwal[4], Edward Gane[5]

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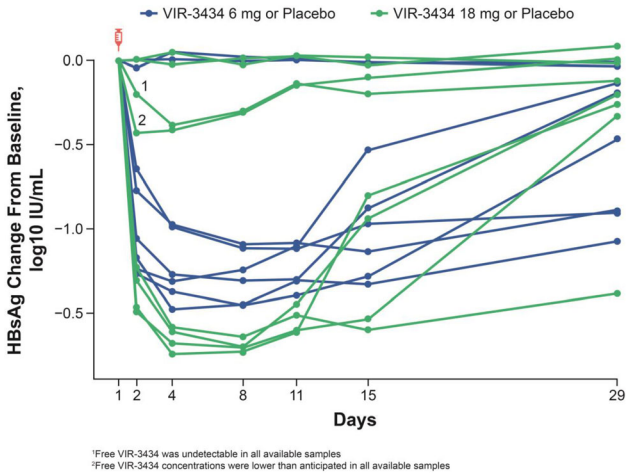
Objectives: VIR-3434 is an engineered human monoclonal antibody in development for chronic hepatitis B (CHB) with several potential modes of action. Single doses of VIR-3434 up to 3000 mg were generally well tolerated in healthy volunteers (Gupta et al., EASL 2021). Here, we report preliminary data from a randomized, double-blind, placebo-controlled, phase 1 single ascending dose study in participants with CHB.
Materials and Methods: Non-cirrhotic, virally suppressed, HBeAg-negative participants with HBsAg < 3000 IU/mL were randomized 3:1 to receive a single dose of VIR-3434 or placebo administered subcutaneously. Preliminary blinded safety, tolerability, and HBsAg results through Day 29 for cohorts evaluating a single dose of 6 mg or 18 mg are presented. Further dose escalation is ongoing.
Results: Eight participants per cohort were enrolled. In each cohort, 6 participants received a single dose of 6 mg or 18 mg VIR-3434, and 2 received placebo. Ten participants achieved ≥ 1 $\log_{10}$ IU/mL reduction from baseline in HBsAg within 7 days, with the largest reductions observed in the 18 mg cohort (Figure). Five adverse events (AEs) were reported: 4 grade 1 AEs, and 1 grade 2 AE. No serious AEs or clinically significant changes in safety laboratory parameters were observed. No participant developed evidence of immune complex disease.
Conclusion: A single dose of 6 mg or 18 mg of VIR-3434 was generally well tolerated and AEs were mostly mild. The rapid reductions in HBsAg following a single dose of VIR-3434 support the potential for VIR-3434 as a functional cure of CHB.



[OP-0615]

Preliminary results from a phase 2 study evaluating VIR-2218 alone and in combination with pegylated interferon alfa-2a in participants with chronic hepatitis B infection

Man-Fung Yuen[1], Young-Suk Lim[2], Daniel Cloutier[3], Vaidehi Thanawala[3], Ling Shen[3], Andre Arizpe[3], Chin Tay[3], Sneha V. Gupta[3], Andrea L. Cathcart[3], Carey Hwang[3], Edward Gane[4]

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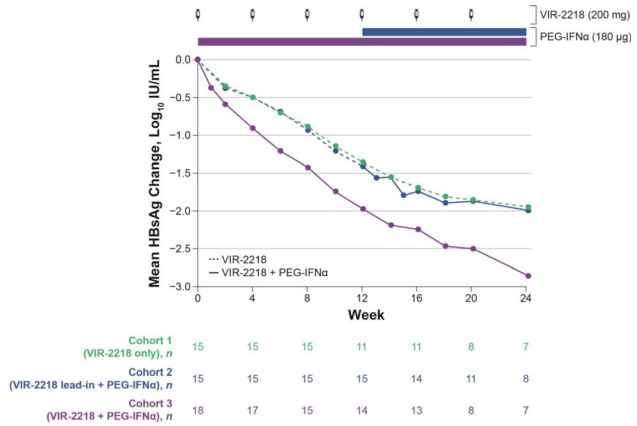
Objectives: VIR-2218 is a synthetic small interfering ribonucleic acid (siRNA) in development for chronic hepatitis B (CHB). Pegylated interferon alfa-2a (PEG-IFNα) is an approved immunomodulator for CHB; however, < 7% of patients achieve HBsAg loss after 48 weeks of treatment. We hypothesize that combining VIR-2218 with PEG-IFNα will increase rates of HBsAg loss in CHB patients.
Materials and Methods: In this ongoing phase 2, open-label study, noncirrhotic, virologically suppressed participants received 200 mg of subcutaneous VIR- 2218 every 4 weeks for 6 doses, either alone or in combination with 180 ?g subcutaneous PEG- IFNα administered either concurrently or starting at week 12.
Results: This preliminary analysis includes 22 participants who have completed the 24-week treatment period. VIR- 2218 alone or with PEG-IFNα starting at week 12 resulted in a mean HBsAg decline of 2.0 $\log_{10}$ IU/mL from baseline at week 24. Co- administration of VIR-2218 with PEG-IFNα for 24 weeks resulted in an earlier and more substantial HBsAg mean decline of 2.9 $\log_{10}$ IU/mL. Participants receiving PEG-IFNα with VIR-2218 experienced more adverse events (AEs) than with VIR-2218 alone. AEs were generally grade 1 or 2 and no treatment- related serious AEs were reported. Alanine aminotransferase elevations were more common in cohorts containing PEG-IFNα and coincided with reductions in HBsAg. One participant discontinued treatment due to PEG-IFNα- related AEs.
Conclusion: Co-administration of VIR-2218 with PEG- IFNα for 24 weeks resulted in an earlier and more substantial HBsAg decline, supporting the hypothesis that the antiviral activity of VIR- 2218 can be potentiated by concurrent administration of immunomodulators such as PEG-IFNα.



[OP-1122]

Real life study of bulevirtide in chronic hepatitis Delta: Preliminary results of the ANRS HD EP01 BuleDelta prospective cohort

Fabien Zoulim[1], Claire Fougerou-Leurent[2,3], Emmanuel Gordien[4], Caroline Scholtes[5], Sophie Metivier[6], Victor De Ledinghen[7], Vlad Ratziu[8], Laurent Alric[9], Nathalie Ganne-Carie[10], Veronique Loustaud-Ratti[11], Dominique Guyader[12], Vincent Leroy[13], Jerome Dumortier[14], Karine Lacombe[15], Georges-Philippe Pageaux[16], Anne Minello[17], Christelle Tual[2,3], Alain Renault[2,3], Estelle Le Pabic[2,3], Lucie Marchand[18], Dominique Roulot[19], Helene Fontaine[20]

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Objectives: The aim of the BuleDelta cohort, a French multicenter ANRS/MIE observatory was to analyze the efficacy and the safety of bulevirtide (BLV), available since September 2019, in patients with chronic hepatitis D (CHD).
Materials and Methods: This preliminary analysis was conducted in patients treated for at least 24 weeks (W24) on the biological (normalization of ALT), virologic (decrease of at least 2 log IU/mL or HDV RNA undetectability) and combined (association of both) responses.

Results: As of October 1st, 2021, 138 patients have been included in the cohort: 66% male, age 42 ± 11 years, 12% HIV-coinfected, 73% treated with nucleo (s)tides analogs (NUC), 42% with pegylated interferon-a (Peg-IFN). At baseline, the HDV RNA was in mean 6.1 ± 1.4 log IU/mL and above quantification threshold in 38 patients. The preliminary analysis included 98 patients: 74 (76%) treated with NUC, 44 (45%) with Peg-IFN. At W24, the mean decrease of HDV RNA was of 1.9 ± 1.4 log IU/mL (2.6 and 1.6 log IU/mL with and without Peg-IFN) and a virologic response was observed in 55 (56%) (80% and 37%, with and without Peg-IFN). Among these patients, the virologic response was observed in 8 (15%), 26 (47%) and 38 (69%) at W4, W8 W12, respectively. The biological response was observed in 36 (37%) (34% and 40%, with and without Peg-IFN), and the combined response in 25 (26%) patients (36% and 17%, with and without Peg-IFN).
Conclusion: In this first real-life study, a decrease of HDV viremia greater than 2 log IU/mL after 24 weeks of treatment of BLV was observed in more than half of patients with CHD, with a normalization of ALT in half of them. Updated results will be presented at the meeting.

[OP-0784]

Metabolic dysfunction-associated fatty liver disease subgroups and risk of hepatocellular carcinoma and mortality in patients with chronic viral hepatitis

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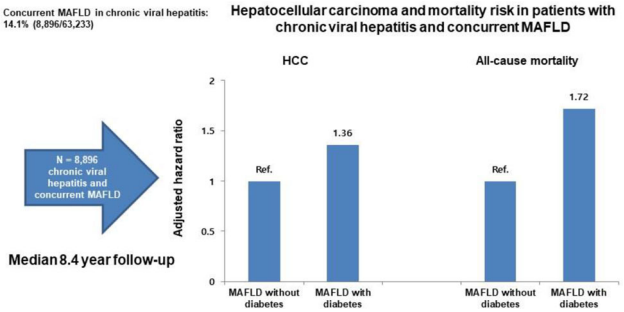
Objectives: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a recently proposed concept for fatty liver disease. However, heterogeneous disease severity and prognosis might exist even among the same disease category of MAFLD. We investigated the risk stratification of long-term outcomes according to MAFLD subgroups based on diagnostic criteria in patients with chronic viral hepatitis using a nationwide cohort.
Materials and Methods: We included 63,233 chronic hepatitis B and C patients who underwent health examinations in 2009. Hepatic steatosis was defined as a fatty liver index ≥ 60. MAFLD was defined as the presence of hepatic steatosis with any one of the following three conditions, overweight/obesity (body mass index ≥ 23 kg/m^2), diabetes, metabolic dysregulation (≥ 2). The primary endpoints of this study were incident hepatocellular carcinoma (HCC) and all-cause mortality.
Results: The prevalence of MAFLD was 14.1% (n = 8,896). During a median 8.4-year follow-up, we documented 3,732 HCC cases and 4,778 deaths. Compared to patients with no MAFLD, the risk of HCC and mortality was significantly higher in patients with MAFLD (adjusted hazard ratio [aHR] = 1.34, 95% confidence interval [CI] = 1.23–1.46) for HCC; aHR = 1.26, 95% CI = 1.17–1.36 for mortality). Among patients with MAFLD, 687 HCCs and 861 deaths were documented. The risk of HCC and mortality was significantly higher in patients with diabetes (aHR = 1.36, 95% CI = 1.16–1.59 for HCC; aHR = 1.72 95% CI = 1.50–1.97 for mortality) compared to patients with no diabetes, among patients with MAFLD. When we stratified patients with MAFLD according to the other criteria (overweight/obesity or metabolic dysregulation), the risk of HCC and mortality was not different across the groups (all P > 0.05).
Conclusion: Concurrent MAFLD was associated with higher risk of HCC and mortality in patients with chronic viral hepatitis. Our results suggest that diabetes can stratify the risk of HCC and mortality in patients with chronic viral hepatitis and concurrent MAFLD.



[OP-0804]

Association between daily aspirin therapy and hepatocellular carcinoma according to metabolic traits in patients with chronic hepatitis B

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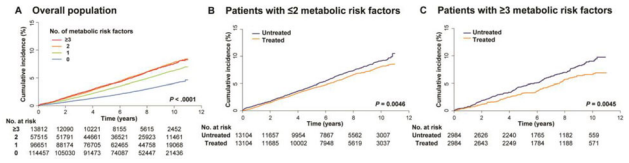
Objectives: Several studies have provided evidence supporting the chemopreventive effect of aspirin against hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients. Recently, we demonstrated that daily aspirin use was associated with reduced HCC risk in non-cirrhotics with CHB, but not in cirrhotics. To identify better candidates for daily aspirin therapy, we investigated the association of aspirin use with HCC risk according to metabolic traits, which is an independent risk factor of HCC, among non-cirrhotics with CHB.
Materials and Methods: We collected baseline data on metabolic risk factors, including obesity, high blood pressure, hypercholesterolemia, and diabetes, in 282,611 adult non-cirrhotics with CHB using the Korean National Health Insurance Service database. The study patients were stratified according to the number of metabolic risk factors, after which propensity score-matched cohorts were generated to balance baseline characteristics between aspirin users and nonusers. The risk of HCC was analyzed, accounting for competing risks.
Results: In the overall population, 11,024 patients developed HCC during a median follow-up period of 7.4 years. The cumulative incidences of HCC rose with increasing metabolic risk factor burden (P < 0.0001; panel A). Among patients with ≤ 2 metabolic risk factors (13,104 pairs), the cumulative incidences of HCC in aspirin users were significantly lower than in nonusers (P = 0.005; panel B); however, aspirin use was not associated with lower HCC risk after multivariable adjustment (adjusted hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.84–1.03; P = 0.18). Among patients

with ≥ 3 metabolic risk factors (2,984 pairs), aspirin users showed significantly lower cumulative HCC incidences compared to nonusers (P = 0.005; panel C) and aspirin use was associated with a 28% reduced risk of HCC (adjusted HR, 0.72; 95% CI, 0.57–0.91; P = 0.006).

Conclusion: In this Korean nationwide cohort study, daily aspirin use was associated with reduced risk of HCC in non-cirrhotic CHB patients with a higher burden of metabolic risk factors.



[OP-0887]

Fibrotic changes and HCC incidence after DAA treatment of F3 patients with chronic hepatitis C

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Objectives: Real-world data on the clinical outcomes in patients with baseline stage 3 liver fibrosis (F3) after sustained virologic response (SVR) are scare, most studies are retrospective with small cohorts. In practice, patients with F3 are screened for HCC in the same way that patients with compensated cirrhosis are. Aim: assessing the clinical outcomes following direct acting antiviral (DAA) treatment among hepatitis C F3 patients after SVR.

Materials and Methods: This study included 1517 chronic HCV patients with F3 fibrosis receiving DAAs in the out-patient clinics at the Egyptian Liver Research Institute and Hospital ELRIAH. We included patients 18 years or older with HCV who received DAA, have F3 by transient elastography, and have no history of HCC. Patients were followed up on every 6 months after finishing treatment using ultrasonography and laboratory tests.

Results: Significant improvement occurred in all parameters with decrease in ALT, AST, total bilirubin and AFP and increase in albumin, platelets, HgB and WBCs. Significant improvement of fibrosis with decrease in LSM, FIB-4, APRI and FIB-6 occurred. When changes in LSM was categorized depending on delta LSM, 873 patients (57.5%) showed regression, 454 (29.9%) are stable, while 190 patients (12.5%) showed progression of fibrosis. 33 cases developed HCC during follow up with incidence rate of 0.915/100 py (95% CI 0.64–1.27). Incidence was high with progression of liver fibrosis (6.17/100 py), than in patients with stable fibrosis (1.09/100 py) and regression of liver fibrosis (0.75/100 py). There are no significant differences as regards fibrosis indicators at baseline (LSM, FIB-4, APRI and FIB-6) between those who developed HCC and those who did not.

Conclusion: After a long-term follow-up of a cohort of F3 HCV-infected patients with DAA, significant improvement of liver functions and hematological parameters occurred. Patients showed high rate of regression of fibrosis, and decreased HCC incidence.

[OP-0855]

Noninvasive prediction of hepatocellular carcinoma development after oral antiviral therapy in patients with chronic hepatitis C: A multicenter study

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Objectives: Hepatocellular carcinoma (HCC) can still occur after achieving a sustained virologic response (SVR) to direct-acting antiviral (DAA) therapy in patients with hepatitis C. We aimed to identify non-invasive parameters that predict the HCC development for patients with chronic hepatitis C after SVR.

Materials and Methods: A total of 3,489 HCV patients who treated with DAAs and had achieved SVR from nine hospitals in South Korea were included in this study. Predictors of HCC occurrence and HCC risk scores were assessed.

Results: During a median follow-up of 2.3 years, HCC occurred in 158 patients (4.5%). LSM gradually decreased from baseline to SVR and 1 year after treatment (P < 0.001). Platelet count, bilirubin, and albumin levels also improved from before treatment to 1 year after treatment (all P < 0.05). Multivariate analysis using the Cox regression test identified that age (HR 1.055, 95% CI 1.036–1.074, P < 0.001), sex (HR 1.942, 95% CI 1.326–2.844, P = 0.001), platelet count (HR 0.987, 95% CI 0.984–0.991, P < 0.001), and albumin (HR 0.525, 95% CI 0.353–0.780, P = 0.004) at 1 year follow-up were independently associated with the risk of HCC. HCC risk scores including Modified PAGE-B scores (AUROC = 0.814) and aMAP risk score (AUROC = 0.826) at 1 year after SVR using age, gender, platelet counts, serum albumin levels can discriminate the risk of HCC.

Conclusion: In patients with chronic hepatitis C who have achieved SVR with DAAs, the use of HCC risk scores including Modified PAGE-B scores and aMAP risk score at 1 year after SVR accurately predicted the risk of HCC.

[OP-0251]

Towards hospital-based elimination of hepatitis C virus: HCV-HELP study

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Objectives: Scarce data are available on in-hospital hepatitis C virus (HCV) micro-elimination strategies. This pilot study was prospectively conducted to assess the outcomes of an HCV in-hospital micro-elimination program (HCV-HELP) in a single centre in Taiwan.

Materials and Methods: The study included the HCV reflex test for plans A (hospital personnel), B (outpatient surveillance), C (a call-

back system for anti-HCV + patients), and D (surveillance of cancer patients prior to chemotherapy). The primary outcome measurement was that > 80% of eligible patients were enrolled in linkage-to-treat; the secondary outcome measurement was the surveillance efficacy.
Results: We recruited 930, 6,072, 2,376 and 233 participants into plans A, B, C, and D, respectively, from Oct 2020 to May 2021. The anti-HCV-seropositivity prevalences were 0.22% for plan A, 4.3% for B, and 3.9% for D. Two staff members were identified as HCV-viremic in plan A; these staff members successfully achieved a sustained virological response (SVR). We identified 39, 95 and 2 HCV-viremic patients in plans B, C, and D, respectively. Of these 138 HCV-viremic patients, 135 (97.8%) received direct-acting antiviral therapy, and 134 achieved SVR. Two 4-month phases were stratified to compare efficacies in the liver clinic. In the late phase, the adjusted number of HCV-viremic patients was 4.36/10,000 outpatient visits (90/200,689), which was 3.18-fold higher than that of the early phase (1.37/10,000 outpatient visits [30/212,658], odds ratio = 3.18; 95% confidence interval = 2.10–4.81, $p < 0.0001$).
Conclusion: HCV micro-elimination is achievable at the hospital level as per the structured HCV-HELP study.

[OP-0869]

Establishment of a comprehensive people-centered outreach health-care system targeting HCV micro-elimination in hyperendemic areas of Taiwan

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Objectives: Gaps in the diagnosis, awareness and link-to-care are the main barriers toward hepatitis C virus (HCV) elimination in the era of directly-acting antivirals (DAA). We established a people-centered outreach health-care system aiming to target HCV micro-elimination in HCV-hyperendemic villages in Taiwan.
Materials and Methods: The COMPACT program, an "outreach HCV-checkpoint team" based on "door-by-door" strategy plus an "outreach HCV-eliminating team" to provide onsite-service for HCV screening/diagnosis, link-to-care and DAA therapy was implemented in Chidong and Chikan villages (Target group) between 2019 and 2021. The other participants were enrolled as Control group.
Results: By December 2020, 3,684 subjects were enrolled in the Target Group and 2,047 subjects in the Control group, with anti-HCV prevalence rates of 24.0% (n = 886) and 9.5% (n = 194), respectively ($P < 0.001$). The rates of HCV awareness, accessibility among aware subjects and treatment among accessed subjects at enrollment between Target and Control groups were 53.5% versus 61.9% ($P = 0.034$), 82.1% versus 74.2%, and 55.3% versus 58.4% with overall treatment uptake of 32.1% versus 36.5%, respectively. The HCV-viremic rates among anti-HCV-positive subjects was 42.7% and 41.2%, respectively, in both groups. After COMPACT engagement, 80.4% HCV-viremic subjects in the Target group were successfully linked-to-care, compared to 70% in the Control group ($P = 0.039$). All of the linked-patients received DAA therapy. The overall SVR12 rate by intention-to-treat and modified intention-to-treat analysis was 97.4% and 99.3%, respectively, in the Target, and 96.4% and 100%, respectively, in the Control. The overall community effectiveness was 76.4% in COMPACT campaign, significantly higher in Target than in Control (78.3% versus 67.5%, $P = 0.039$).
Conclusion: HCV remains a major health threat in the hyperendemic areas. We demonstrated that people-centered, outreach door-by-door screen strategy with onsite treatment programs greatly improved the HCV diagnosis and accessibility and scaled-up the HCV treatment uptake in HCV-hyperendemic areas and could serve as a model toward HCV elimination in high-risk marginalized communities.

Poster Presentation

Basic research

[OP-0035]

Tenofovir alafenamide fumarate alleviates non-alcoholic steatohepatitis by attenuating the phosphorylation of AKT in intrahepatic activated macrophages

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Objectives: The prevalence of nonalcoholic steatohepatitis (NASH) is rapidly increasing and effective therapy is still required. Tenofovir alafenamide fumarate (TAF) is a widely used antiviral drug against hepatitis B virus. In this study, we aimed to investigate the potential pharmacological effect of TAF in NASH.
Materials and Methods: The NASH mouse model was established by subcutaneous injection of streptozotocin (STZ; 0.2 mg) and feeding mice with high-fat, high-cholesterol (HFHC) diet. TAF (5 mg/kg) was administered per oral route for four weeks. Mice livers were homogenized and analyzed by multi-color flow cytometry and immunoblotting. $CD14^+$ monocytes were isolated from peripheral blood of healthy donors and treated with lipopolysaccharide (LPS) and TAF for some experiments.
Results: The serum levels of alanine aminotransferase and asparate aminotransferase in NASH mice treated with TAF were significantly lower than those in mock-treated, NASH mice. Livers from TAF-treated NASH mice showed attenuated infiltration of mononuclear cells compared with those from mock-treated mice. HLA-DR/PD-L1 were used as macrophage activation makers, and TAF-treated, NASH mice showed decreased infiltration of activated macrophages ($HLA\text{-}DR^+/PD\text{-}L1^+$) in their livers. In ex vivo experiments using sorted $CD14^+$ monocytes, we confirmed that TAF-treated, LPS-stimulated

monocytes showed decreased expression of phosphorylated AKT, compared to mock-treated, LPS-stimulated monocytes.
Conclusion: Overall, our data demonstrate that TAF has anti-inflammatory effects in NASH liver by attenuating the phosphorylation of AKT in intrahepatic activated macrophages. TAF may serve as new therapeutic option for NASH.

[OP-0202]

SF3B4 could be a non-invasive diagnostic marker and correlated with immune infiltration in hepatocellular carcinoma

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Objectives: This study aimed to identify the diagnostic value of the Splicing Factor 3b Subunit 4 (SF3B4) as a novel non-invasive biomarker for hepatocellular carcinoma (HCC) and the relationship between SF3B4 expression and immune cell infiltration in HCC.
Materials and Methods: Enzyme-linked immunosorbent assay (ELISA) was used to detect SF3B4 level in plasma samples of each patient with healthy control, with chronic hepatitis (CH), liver cirrhosis (LC), and HCC. Expression levels of auto-antibody, which can detect SF3B4, were measured in plasma samples of each group of patients. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to identify the expression levels of SF3B4 in serum small extracellular vesicle-derived (EV). TIMER database was used to investigate the correlation of SF3B4 expression and immune infiltration level in HCC.
Results: Among the three different measurement methods (ELISA, autoantibody, and serum small EV RNA qRT-PCR) using the patient's blood, the expression level of serum small EV- derived SF3B4 (EV-SF3B4) was increased in HCC patients compared to healthy control, CH patients, and LC patients. EV-SF3B4 showed significant discriminatory ability in the diagnosis of all-stage HCC (AUC = 0.884). Moreover, high SF3B4 expression was correlated with dysregulated immune infiltration such as CD8 + T cell, NK cell, Treg, and MDSC. Also, high expression of SF3B4 and correlated immune cell markers were associated with poor survival of patients.
Conclusion: EV-SF3B4 is a candidate novel non-invasive biomarker for diagnosing HCC and SF3B4 might induce tumor immune infiltration in HCC

[OP-0412]

Histogenesis of liver in human foetuses

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Objectives: Liver is having the extensive power of regeneration is an important compound gland having both exocrine and endocrine functions. Its main function is to store glycogen. In foetal life, it is an important site of haemopoiesis. Though, detailed study of adult liver is there but microscopic structure of liver at different stages in the foetal period is far and few. Hence the present study aims to find out the histogenesis of liver in foetal period.
Materials and Methods: Dissection of 100 normal human foetuses was done from January 2015 to December 2021 and histological features of foetal liver tissue was studied by using H and E stain. Important findings of foetal liver were noted with respect to gestational age. PAS stain was used to observe the glycogen granules in the foetal liver. The size of hepatic lobule was measured by using an ocular and a stage micrometer. The distance was measured between the portal triad and central vein.
Results: In the foetal liver, central veins appeared first at 16^{th} week, portal triad appeared at 18^{th} week, hepatocytes are arranged around the central vein in the form of radiating cords giving a lobular pattern, efferent and afferent structures were present at the periphery of the lobule in the form of portal triad and it shows an extensive haemopoiesis in mid gestation. Glycogen appeared in hepatic cells was noted in 14^{th} week. The size of hepatic lobule was 0.55 mm in 16^{th} week and 1.44 mm at 38^{th} week.
Conclusion: Our study on histogenesis of liver confirms the foetal haemopoietic function of liver regress towards the full term foetus at which the hepatocytes are occupied by plenty of glycogen deposits. It also provides new insights to the researchers and clinician for understanding the sequence of events in different weeks of gestation.

[OP-0577]

Targeting liver-resident CD8 + T cells based PLGA-particle with immune checkpoint blockade for effective anti-cancer immunotherapy

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Objectives: Hepatocellular carcinoma (HCC) often develops following chronic hepatitis B virus (HBV) infection and responds poorly to immune checkpoint blockade. CD8 positive Tissue-resident memory cells ($CD8^+$Trms) is a unique T cell type residing in non-lymphoid tissue that exerts local immune surveillance, however, the various antigen-specific (eg, tumor,virus) $CD8^+$Trms were highly exhausted. Here, tumor vaccine based Poly (lactic-co-glycolic acid) (PLGA) nano/micro particles (NP./MP.) with the multiple functions of PD-1 immune checkpoint treatment, antigen stimulation and the adjuvant effect of biomaterials was constructed, it is expected to activate the non-tumor antigen-specific $CD8^+$Trms, meanwhile promote the activation of DCs, macrophages, and other immune cells, thereby reversing the local immune suppression microenvironment and restoring liver cancer immunoresponse.
Materials and Methods: Anti-PD1 antibody (aPD1) were encapsulated into PLGA NP./MP. and surface condensed with negatively charged antigen ovalbumin $_{(257–264)}$ (OVA) to develop a tumor vaccine OVA/aPD1@NP./MP. Meanwhile, HCC with OVA-specific exhausted $CD8^+$Trms was established by sleeping beauty system and high-dose antigen immunization. The stability and immunotherapy effects of OVA/aPD1@NP./MP. in vivo or vitro were examined by ELISA, flow cytometry (FCM) and single-cell RNA sequencing after intravenous injection and also its immunomodulatory effect on $CD8^+$Trms were also examined by TCR sequence and FCM.
Results: OVA/aPD1@NP./MP.significantly promoted the expression of MHCII, CD86, CCR7 and the production of IL-12p70 of BMDCs, the uptake efficiency of OVA was improved significantly; it can also robustly activate OVA specific $CD8^+$Trms. Further, the tumor vaccine enhanced OVA-specific IgG immune response and the levels of

cytokines, induced a mixed Th1/Th2 immune response and the primary tumor growth retardation, prevention of metastases, and prolonged survival.
Conclusion: OVA/aPD1@NP./MP. have the potential to serve as an effective vaccine delivery and adjuvant system to induce vigorous and long-term immune responses by activating the exhausted $CD8^{+}$Trms, and also show that liver Trms may a promising target for the treatment of HCC.

[OP-0655]

Mesenchymal stem cells treatment restores liver macrophages homeostasis to alleviate acute liver injury

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Objectives: High doses of carbon tetrachloride (CCl_4) can cause severe and acute liver injury (ALI), leading immune cells infiltration and dysfunction with high mortality rate. Mesenchymal stem cells (MSCs) have shown promising therapeutic potential for treating acute liver injury due to their unique immunoregulatory properties. In this study, we focused on defining different liver macrophage subsets in acute liver injury and revealing the therapeutic effects of MSCs through restoring liver macrophages.
Materials and Methods: Wild-type C57BL/6L mice were intraperitoneally injected with CCl_4 for the ALI model and received injection through the tail vein with bone marrow-derived MSCs for therapy. The evaluation of the therapeutic effect of MSCs depended on survival rate, biochemical values, histopathology, and inflammatory chemokines levels. The proportion of liver macrophages at different time points was accessed by flow cytometry and the definition of different liver macrophages subsets and functional changes of them were accessed by single-cell RNA sequencing (scRNA-Seq). The major macrophage subsets and functional changes of them were validated by immunofluorescence and reverse transcription-polymerase chain reaction.
Results: Adoptive transfer of MSCs decreased mortality rate, improved liver pathology, and reduced liver enzyme levels and serum inflammatory chemokine levels, alleviated CCl_4-induced acute liver injury. Flow cytometry analysis indicated that the proportion of $Ly6C^{hi}$ monocytes/macrophages of the $CD45^{+}$ cells in the liver increased in ALI and MSCs treatment could mitigate monocytes/macrophages infiltration and promote their transition to the $Ly6C^{lo}$ population. scRNA-Seq results defined four different monocyte-derived macrophages that had an advantage over different periods of acute liver injury. Furthermore, the enrichment analysis of differentially expressed genes demonstrated MSCs enhanced the lysosome function of major macrophages subsets and attenuate their chemotaxis of neutrophils.
Conclusion: MSCs can effectively alleviate acute liver injury, mitigate monocytes/macrophages infiltration, and promote phenotypic transformation and functional maturity of major monocyte-derived macrophages, restoring liver macrophage homeostasis.

[OP-0735]

Viral hepatitis in Armenia

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Objectives: Our study is focused on seroepidemiological distribution of viral hepatitis in Armenia from 1993 to 2020.
Materials and Methods: This is an observational partially retrospective and prospective study. Evaluation of Armenian patients on viral hepatitis markers was conducted.
Results: Significant reduction (average $>$ 30 times) in the incidence of a 20-year period of viral hepatitis A (HAV) from 100,4 (1993) to 3,2 (2012): rate per 100 thousand, especially among children (50-fold) was observed. From 2013 to 2020 years documented cases of HAV are extremely rare. Armenia is not an endemic region for viral hepatitis E (HEV), thus single report of HEV was documented in 2006. Antibodies of HEV were defined in 2.5% of adults during serological screening in 2006. The number of HCV infected patients is decreasing and incidence rate of HCV infection per 100 000 population reached from 1.5% (2013) to 0.1% (2020). Predominant genotype of HCV is genotype 1 fallowing by genotype 3. Predominant genotype of HBV is genotype D (96%). During a 20-year period 60-fold reduction in morbidity is noted among children and sixfold among adults. Due to immunization (1999) of infants, isolated cases of acute HBV among children under 14 in recent years are recorded. According to the data of NCDC from 2013- 2020 the incidence rate of HBV infection per 100 000 population reached from 1.9% to 0.2%.
Conclusion: Identified seroepidemiological patterns of viral hepatitis are important for improving the system of regular epidemiological control of these infections which are the main reasons of liver damages in Armenia.

[OP-0964]

Immune therapy supported chemotherapy to counter experimental Visceral Leishmaniasis infection

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Objectives: Visceral leishmaniasis is a macrophage associated disorder which is linked with a profound decrease in the immunotherapeutic potential of the infected subjects leading to a marked reduction in the CD4 linked Th1 protective immune response. Simultaneously the patients in Bihar are showing unresponsiveness towards SAG which is still a first line of drug in many countries around the world against Visceral Leishmaniasis. We have previously reported down regulation of CD2 co receptor on the surface of CD4 cells in patients suffering from Visceral Leishmaniasis.
Materials and Methods: L.donovani parasites were grown at 24 °C in Schneider's medium supplemented with 20% heat inactivated Fetal calf serum. Six to Eight weeks old male BALB/c mice were chosen for the study. At the beginning of the study they were healthy and

active. Five mice were taken in each category. After confirming through DAT and Limiting Dilution Assay about the experimentally induced VL infection, SAG (20 mg/kg body weight) and CD2 (4 µl + 20 µl PBS 1x) were injected subcutaneously in two dosages in mice on 38th and 41st day. Likewise SAG alone was also administered in a dosage of 20 mg/kg body weight on 38th and 41st day. Mice were sacrificed on 42nd day and later evaluated for phenotyping, intracellular cytokine assay, nitric oxide assay.
Results: It has been found in the present set of studies that stimulation of CD2 co receptor along with along with therapeutic dose of SAG has led to the enhancement in the release of IFN-gamma which leads to the release of TNF-alpha and activates the macrophages. An increase in the NO mediated killing further observed by the activated macrophages leading to the reduction in the parasitic load.
Conclusion: The results indicate that enhancing immune potential of a VL patient will help in the better response of Sodium Antimony Gluconate which is the first line of drug against VL.

[OP-0984]

Coagulation-related genes negatively regulate the Heme and Xenobiotic metabolism progress of hepatocellular carcinoma

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Objectives: Cancer patients are more prone to develop dysfunction coagulation of venous thromboembolic complications (VTE), especially the risk of hypercoagulable liver cancer patients. The liver participates in the control of coagulation of the whole body. Conversely, the thrombus is related to the occurrence of complications of liver disease including high pressure of portal vein, dysfunction of blood perfusion in or out the liver, and the deadliest, formation of PVTT. However, the metabolic mechanism of dysfunctional coagulation is not clear. Here, we try to find some genetic explanation treatment of the dysfunction in hepatocellular carcinoma.
Materials and Methods: We downloaded the data from TCGA and normal liver tissues of GTEx, we focus on the coagulation-related genes from the Genecard database. We ran the GSEA and GSVA on the differential expression genes calculated by the packages of the R language. And we found two hallmark genesets that had a negative NES value according to the results means the negative regulation to coagulation. Data from TCGA were explored. Bioinformatics methods are used to analyze the genomics, transcriptomics, and clinical data.
Results: After utilizing the data from TCGA and GTEx, and genes filtered from Gencard Database were selected for further research. We ran the GSEA, and we found two negative enrichments in Biological Progress, " HALLMARK_HEME_METABOLISM ", and " HALLMARK_XENOBIOTIC_METABOLISM" are the only two that had negative normalized enrichment scores (NES) in Biological Process.
Conclusion: Our work revealed the importance of the Heme and Xenobiotic metabolism pathway inanition and development. It helps us to understand the mechanism of the Heme and Xenobiotic metabolism in the coagulation function of hepatocellular carcinoma. It also helps us to predict and prevent the complication of hepatocellular carcinoma. Heme and Xenobiotic metabolism will be a hopeful treatment to predict and prevent the incidence of coagulation-related complications, even the development of PVTT of hepatocellular carcinoma.

[OP-1070]

LOXL1/Fatty acid synthase (FASN) interaction attenuated lipid metabolism: Another face of ECM in fibroblast

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Objectives: Abnormal lipid metabolism in fibroblast accompanies the progression of liver fibrosis, during which extracellular matrix (ECM) is one of the key factors, but the mechanism is unclear. Lysyl oxidase (LOX) family is important in regulating ECM cross-linking, then affecting the stability and stiffness of ECM, especially Lysyl oxidase-like 1 (LOXL1). Our study aims to clarify whether LOXL1 can impact lipid metabolism in fibroblasts and further explore the mechanism by screening proteins interacting with it.
Materials and Methods: First, we over-expressed or silenced Loxl1 in NIH-3T3 cells, respectively, and inhibited LOXL1 function using inhibitor β-aminopropionitrile. We observed mRNA level of lipid synthesis-related genes to clarify role of LOXL1 in regulating lipid metabolism. Secondly, we identified and analyzed the proteins interacting with LOXL1 by co-immunoprecipitation and mass spectrometry combined with Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis. Finally, we verified the above targets by co-immunoprecipitation.
Results: After overexpressed Loxl1 in NIH-3T3 cells, lipid metabolism synthesis-related genes Fasn, Acaca, Scd1, and Scd2 were restrained by 2.2, 1.3, 1.6, and 1.8-fold, respectively, suggesting suppressed lipid metabolism synthesis. Treated NIH-3T3 cell with β-aminopropionitrile, mRNA level of Fasn, Acaca, and Scd1 increased 1.7 1.4 2.4-fold, respectively. Furthermore, Fasn, Acaca, Scd1, and Scd2 were increased 1.3, 1.3, 1.2-fold respectively after silenced Loxl1, indicating lipid synthesis enhancement in NIH-3T3 cell when inhibiting Loxl1. To further clarify the mechanism LOXL1 affecting lipid metabolism in fibroblasts, we found 772 proteins interacting with LOXL1 via co-immunoprecipitation and mass spectrometry. By KEGG enrichment analysis, 11 proteins (SGPL1, TECR, ECHA, FAS, ECHB, DHB12, GPCP1, CPT1A, LBR, GCDH, SOAT1) involved in the lipid metabolism pathway. Finally, we verified LOXL1 interacts directly with FAS by co-immunoprecipitation.
Conclusion: Our study demonstrates LOXL1 can affect lipid synthesis-related gene expression in fibroblasts and thus affect lipid metabolism. Also LOXL1 can interact with FAS.

[ABST-0112]

Transplantation of personalized 3D artificial bile duct with chemically reprogrammed hepatic progenitors

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Background: Cholangiopathy is a variety spectrum including chronic progressive bile duct disorders with limited treatment options. 3D bioengineering with stem cell-based is emerging as a new therapy tool for construction of functional tissues and hold great promise for regeneration medicine.
Methods: To demonstrate safety and adequacy for the in vivo transplantation, we manufactured 3D artificial bile duct (ABD) based on the MRI data of rabbit common bile duct (CBD). We manufactured tubular scaffold with nano- and micro- mixed fibrous using electrospinning to enhance hCdHs attachment of the inner electrospun fibrous layer as well as mechanical stability of outer layer. We previously reported that reprogrammed primary hepatocytes (hPHs) to human chemically derived hepatic progenitors "hCdHs" by using three small molecules (A-83-01, CHIR99021 and hepatic growth factor (HGF)). We seeded hCdHs inside of ABD and differentiated it to cholangiocyte (hCdH-Chols) undergo cholangiocyte differentiation medium (CDM) condition for 14 days. Finally, we transplantation the ABD with hCdH-Chols to middle in common bile duct of rabbit and monitored.
Results: First, we confirmed that hCdHs and hCdH-Chols showed each state markers expression and differentiation capacity hCdHs to hCdH-Chols by performing RT-qPCR and immunostaining. The hCdH-Chols showed cholangiocyte gene expression profiles and function in 2D and 3D. When cultured the hCdHs inside of ABD for 14 days with CDM, the hCdHs successfully differentiated to hCdH-Chols, showed line formation followed as inner layer that is one of biliary epithelium feature as well as cholangiocyte markers expression. Finally, we performed that resected mid portion of common bile duct (CBD) of rabbits and inserted the ABD with hCdH-Chols to demonstrate the stability and functionality of in vivo experiment. The complete blood count (CBC) and biochemistry results in blood displayed that the liver damage markers (AST, ALT and ALP) reduced as time goes on, while ductal damage marker (TBIL) was in reference range for 42 days. Notably, the rabbits that transplanted the ABD-hCdH-Chols was given survival capacity longer than control rabbits (empty ABD).
Conclusions: Our system could promise that provide a scalable and compatible platform for cholangiopathy, and it may contribute to manufacture patient-specific bile duct for clinical application.

[ABST-0114]

Expandable liver organoids generated from human chemically derived hepatic progenitor enable alcoholic liver modeling

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Background: As is currently well known, the organoid model is widely used for the study of disease modeling and drug screening. The generation of liver organoids is due to the presence of EpCAM + , which is expressed mainly in ductal cells. In our research group we develop chemically derived hepatic progenitors (hCdHs) cells, reprogrammed from human primary hepatocytes (hPHs) with EpCAM-positive characteristics, which gives them a better generation capacity for more than 6 months.
Methods: hPHs were cultured with reprogramming medium (HGF, A83-01 and CHIR99021) for 7 days to generate hCdHs. Human liver cells and hCdHs were cultured on Matrigel with organoid medium to generate human adult liver organoids (hALOs) as a control and hCdHs derived liver organoids (hCdHOs) respectively.
Results: hCdHO did not present morphological differences with the hALOs. Hepatic differentiation of organoids (hCdHO_DM) increased the expression of both hepatic and functionality markers, as well as the transcriptional analysis showed that hCdHO_DM were clustered with hPHs after hepatic differentiation. The transplantation of hCdHO into FRG mice increased the survival percentage compared to controls. The alcohol liver damage model in the organoids presented pathophysiological changes similar to those observed in patients.
Conclusions: hCdHOs show a potential to be an excellent organoid cell source to regenerative medicine and disease modeling studies.

[ABST-0241]

Serum biomarker signatures using integrated multi-omics analyses for post-hepatectomy liver failure in porcine hepatectomy models

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Background: Although post-hepatectomy liver failure is a fatal complication, clinical diagnosis can only be made on or after post-operative day 5. This study aimed to identify earlier biomarkers for predicting the PHLF using integrated multi-omics analysis.
Methods: Twenty domestic female crossbreed pigs underwent sham operation (n = 6), 70% (n = 7) and 90% (n = 7) partial hepatectomy (PH). Serum samples from all the animals were collected at five-time points (pre-operation, 6 h, 14 h, 30 h, and 48 h after the operation). A comprehensive multi-omics analysis was conducted on 164 proteins, 184 qualified lipids, and 109 metabolites derived from each omics study.
Results: An unsupervised Z-score heatmap clustering of all molecules showed a distinct trend between the sham, 70% PH, and 90% PH groups at each different time point. A supervised Z-score heatmap found 75 molecules not expressed in the sham group but showed significant changes between the 70% PH and 90% PH groups. Among them, seven potential biomarkers with an extreme difference (> twofold change) between the 70% PH and 90% PH groups were derived. Creatinine, methionine sulfoxide, and hypoxanthine showed significant different changes at 14 h between the groups (early markers). Lysophosphatidylethanolamine 22:4, oxalic acid, adiponectin, and angiotensinogen showed an increasing trend in the 90% PH group than in the 70% PH group, finally showing a significant difference at 48 h between the groups (late markers).
Conclusions: Integrated multi-omics analyses revealed new potential biomarkers for predicting PHLF. We expect future clinical studies using these candidates may open new paths to earlier diagnosis for PHLF and become a basis for applying various treatments trials.

[ABST-0279]

Liquid biopsy from bile-circulating tumor DNA in patients with biliary tract cancer

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Background: Although Liquid biopsy of blood is useful for cancer diagnosis and prediction of prognosis, diagnostic and prognostic value of ctDNA in bile fluid for BTCs are not clear yet. We evaluate determine whether liquid biopsy for circulating tumor DNA (ctDNA) can replace tissue biopsy when assessing somatic mutations in biliary tract cancers (BTCs).
Methods: Bile samples were obtained from 42 patients with BTC. Matched formalin-fixed paraffin-embedded (FFPE) samples were obtained from 20 of these patients and matched plasma samples from 16 of them. Droplet digital PCR (ddPCR) was used for detection KRAS somatic mutation.
Results: KRAS mutations were identified in the bile ctDNA of 20 of 42 (48%) patients. Patients with mutant KRAS showed significantly worse survival than those with wild-type KRAS (2-year survival rates: 0% vs 55.5%, respectively; $P = 0.018$). There was 80.0% mutational concordance between the paired bile ctDNA and FFPE samples, and 42.9% between the plasma and FFPE samples. On transcriptomic sequencing of one set of paired bile and FFPE samples, expression level of KRAS-associated signaling oncogenes in the bile and tissue samples showed a strong positive correlation ($r = 0.991$, $P < 0.001$).
Conclusions: Liquid biopsy of bile reliably detect mutational variants within the bile ctDNA of BTC patients. These results suggest that bile is an effective biopsy fluid for ctDNA analysis and can replace tissue biopsy in BTC patients.

[ABST-0390]

A novel defined lactate-related gene signature for predicting the prognosis of liver cancer

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Background: The large amount of lactic acid produced by glycolysis in the tumor microenvironment was previously thought to be merely a metabolic waste product. However, more and more studies have shown that lactic acid can play a role in promoting tumor progression.
Methods: In this study, We obtained liver cancer data from The Cancer Genome Atlas (TCGA) database and identified 50 lactate-related genes that were differentially expressed between liver cancer and normal liver tissues. Based on these differentially expressed genes (DEGs), all liver cancer cases could be divided into two subtypes.
Results: The prognostic value of each Lactate-related gene for survival was evaluated to construct a multigene signature using TCGA cohort. By applying the least absolute shrinkage and selection operator (LASSO) Cox regression method, a 2- gene signature was built and classified all liver cancer patients in the TCGA cohort into a low- or high-risk group. Liver cancer patients in the low-risk group showed significantly higher survival possibilities than those in the high-risk group ($P < 0.001$). Utilizing the median risk score from the TCGA cohort, Liver cancer patients from a Gene Expression Omnibus (GEO) cohort were divided into two risk subgroups, and the low-risk group had increased overall survival (OS) time. Combined with the clinical characteristics, the risk score was found to be an independent factor for predicting the OS of liver cancer patients.
Conclusions: lactate-related genes play an important role in tumor progression and can be used to predict the prognosis of HCC patients.

Hepatitis B—Basic

[OP-0261]

Exogenous IFN mediated exosomes deliver declined MiR-27b-3p from hepatocytes to macrophages promoting synthesis of endogenous IFNα by targeting RIG-I/TBK1 signaling

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Objectives: Evidence suggests that interferon alpha (IFNα) plays an essential role in treating chronic hepatitis B (CHB) caused by the hepatitis B virus (HBV). However, the immunological mechanisms of the antiviral response of IFNα-based treatment remain unclear.
Materials and Methods: Differently expressed exosomal microRNA were found through exosomes microRNA sequencing and verified by RT-PCR assays. THP-1 derived macrophages were stimulated by exosomes from the serum of peg-IFNα-treated responders or from the supernatant of IFN treated HepAD38 cells.
Results: Through serum exosomes microRNA sequencing, we discovered 6 distinctly declined miRNAs in responders at week 12 compared with that at baseline. In further RT-PCR assays the responders were confirmed with distinctly reduced miR-27b-3p and miR-493-5p in exosomes among these 6 miRNAs at week 12 than baseline, and both of miRNAs were upregulated in the non-responders at week 12 compared to the responders. Exosomes extracted from the serum of peg-IFNα-treated responders or from the supernatant of IFN treated HepAD38 cells improved the activation of endogenous IFNα synthesis by activating phosphorylation of interferon regulatory factor 3/7 (IRF3/7). The overexpression of miR27b-3p in HepAD38 cells suppressed endogenous IFNα synthesis in macrophages, resulting in insufficient ability to eliminate HBV, whereas the inhibitory effect could be blocked by two inhibitors of exosomes release. The knockdown of miR27b-3p in hepAD38 cells restored the production of endogenous IFNα in macrophages, which inhibited HBV replication. Last, the luciferase and mutation experiments showed RIG-I and TBK1 are the target genes of miR-27b-3p interference.
Conclusion: Exogenous IFNα mediated the declined miR-27b-3p in exosomes derived from HBV-infected hepatocytes, and subsequently triggered an elevated expression of RIG-1/TBK1 signaling and innate immune response in recipient macrophages, thus more endogenous IFN was produced and formed positive feedback of amplifying effect

against HBV. Serum exosomal miR-27-3p represents a potential biomarker and therapeutic target for patients with CHB.

[OP-0478]

Hepatitis B splice variants vary across HBV genotypes and phases of chronic hepatitis B natural history

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Objectives: Chronic hepatitis B (CHB) infection is characterized by different phases, which on rare occasions resolves as a functional cure, characterized by hepatitis B surface antigen (HBsAg) loss. Although not necessary for HBV replication, there is evidence that HBV splice variants are associated with liver disease.
Materials and Methods: Next generation sequencing data from 404 patient samples were analysed for differences in splice variants across CHB Phase I, II, and IV for HBV genotype A, B, C, or D.
Results: Splice variants detected differed across phases of CHB and HBV genotype. The highest proportion of patients harbouring splice variants was detected in Phase II (123/165 patients, 75%) followed by Phase I (69/99 patients, 70%). The proportion of patients positive for any splice variant was lowest in Phase IV (60/140 patients, 43%, $p < 0.001$). Genotype A patients had a significantly higher proportion of splice variants in phase II compared to phase IV ($p < 0,001$). Genotype B patients had a significantly higher proportion of splice variants in phase II compared to both phase I and phase IV ($p = 0.046$ and $p = 0.01$ respectively). Genotype D patients had a significantly lower proportion of splice variants in phase IV compared to phase II ($p < 0.001$). For genotype C, there was no significant difference in the proportion of patients with splice variants across CHB phases. The most commonly detected splice variants were Sp1 and Sp13, detected in all HBV genotypes. In contrast, Sp5 and Sp9 were the least commonly detected splice variants, being restricted to genotypes B and C. HBsAg loss was significantly associated with reduced frequency of SP1 and SP13 variants ($p = 0.0014$ and 0.0156, respectively).
Conclusion: HBV splice variants detected in patient serum differed markedly by HBV genotype and phase of CHB natural history, and were generally highest in phase II, the so-called "immune clearance" phase of CHB natural history.

[OP-0567]

Hepatitis B surface antigen (HBsAg) is significantly reduced by the HBV small interfering RNA (siRNA) ALG-125755 in HBV-infected cells and the AAV-HBV mouse model

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Objectives: Currently approved therapies for the treatment of chronic hepatitis B (CHB) infrequently achieve a functional cure in patients, which requires a sustained loss of hepatitis B surface antigen (HBsAg). In CHB patients, HBV siRNAs have demonstrated significant reductions of HBsAg, indicating a potential for use in a curative therapeutic regimen. Here, stabilization chemistries were applied to siRNA sequences targeting highly conserved regions of the HBV genome in the HBsAg open reading frame to assess the modifications effect on the reduction of serum HBsAg in AAV-HBV mice when compared to parent sequences.
Materials and Methods: HBV siRNAs were transfected into HepG2.2.15 cells, PLC/PRF/5 cells, and a primary human hepatocyte live HBV infection model. HBsAg was quantified by ELISA and cell viability was assessed using Cell Titer Glo. In the AAV-HBV mouse model, siRNAs were administered subcutaneously (SC) with blood collected every 5 days for HBsAg and ALT assessments. An in vitro Ago2 cleavage assay and Northern blot of HBV RNA extracted from the AAV-HBV mouse livers were used to evaluate on-target activity.
Results: In several HBV-infected cell lines, ALG-125903, the parent unconjugated siRNA, showed picomolar EC_{50} values for inhibition of HBsAg release. Further, the anti-sense strand of ALG-125903 efficiently cleaved target RNA sequences in the Ago2 cleavage assay. In AAV-HBV mice dosed with a single 5/mg/kg/dose ALG-125755, a maximal 1.5 $\log_{10}$ IU/mL reduction of serum HBsAg was observed. ALT levels were not impacted with dosing. Furthermore, sustained HBsAg reduction was noted for 90 days post-last dose with HBV RNA species significantly reduced in the livers.
Conclusion: ALG-125755 demonstrated significant and sustained HBsAg knockdown in the AAV-HBV mouse model. Further development of ALG-125755 is ongoing.

[OP-0574]

A novel cell culture model to interrogate the in vitro replication phenotype of hepatitis B virus (HBV) splice variant Sp1

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Objectives: Although not required for HBV replication, HBV spliced variants have been shown to impact replication of genome length HBV on which they rely for their replication. Until now it has not been possible to study the replication cycle of authentic splice variants in cell culture in the absence of wild-type HBV. We have developed a greater than genome length in vitro model, permitting "rescue" of Sp1 RNA, to analyse replication phenotype and its impact on WT HBV replication. Previous studies have shown that a modified precore protein expressed by Sp1 impacts WT HBV replication.
Materials and Methods: Splice variant Sp1 (genotype D3) was transfected into permissive Huh7 and HepG2 cells, with either (i) polymerase expression "rescue" plasmids which supplied the HBV polymerase in trans, or (ii) WT HBV. HBV replicative phenotype was analysed by southern and northern blotting, immunoblotting and quantitative serology.
Results: HBV splice variant Sp1 was incapable of autonomous replication, but replication was "rescued" by HBV Pol supplied in trans, in the absence of genomic length HBV. Sp1 expressed HBeAg and HBcAg, but did not express HBsAg or polymerase. Importantly, Sp1 also expressed HBx mRNA and protein. When co-transfected with genome length WT HBV, Sp1 reduced HBV replication. Knocking out the Sp1 precore and core proteins, but not the precore protein alone, partially restored replication of WT HBV. Knocking out expression of Sp1 HBx protein further reduced core-associated HBV DNA levels.
Conclusion: We have developed a cell culture model permitting interrogation of the complete replication phenotype of HBV splice variant Sp1 in the absence of genomic length HBV DNA. HBV splice variant Sp1 had a negative impact on genome length HBV replication. The mechanism for this is still unclear, as knockout studies targeting the Sp1 PC protein did not restore HBV replication to WT levels, contradicting previous findings.

[OP-0583]

Determining the effect of HBV splice variant 9 (Sp9) on wildtype HBV replication

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Objectives: Over 296 million people are currently living with chronic hepatitis B which can lead to the development of liver cirrhosis and hepatocellular carcinoma (HCC). Prior to nuclear export, the pregenomic RNA (pgRNA) can be spliced by the host cell spliceosome to form shorter RNA sequences known as splice variants. 17 splice variants have been characterised thus far, and whilst the role of splice variants currently remains unknown, an increased proportion in patient sera has been associated with the development of HCC. Furthermore, different splice variants have been shown to have different effects on wildtype HBV replication. Due to the deletions in the open reading frames, splice variants can encode novel fusion proteins, and some novel fusion proteins have been found to play a role in their respective splice variant's effect on wildtype HBV replication. It remains unknown how the second most common splice variant, Sp9 and its novel fusion proteins, affects wildtype HBV replication.
Materials and Methods: A greater than genome length (1.3mer) Sp9 clone was co-transfected with a replication competent wildtype HBV clone. Sp9 novel fusion protein overexpression plasmids and mutant Sp9 clones that knocked out Sp9's novel fusion proteins were also co-transfected with WT HBV. The replication phenotype of wildtype HBV was analysed five days post-transfection.
Results: Co-transfection of Sp9 with WT HBV markedly reduced HBV DNA, pgRNA and S mRNA production, intracellular HBV core and S protein production and intracellular and secreted HBV E and S antigen levels. Cytotoxicity assays confirmed that Sp9 is not cytotoxic to the cells. Co-transfection of WT HBV with Sp9 novel protein knockout clones partially restored HBV replication.
Conclusion: The role of HBV splice variants in HBV replication and pathogenesis remains unclear. This study shows that Sp9 significantly reduces HBV replication, which may be due to the novel fusion proteins expressed by Sp9.

[OP-0652]

Higher expression of Hepatitis B virus entry receptor and presence of replication marker suggest that placenta act as a reservoir

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Objectives: Sodium taurocholate co-transporting polypeptide (NTCP), facilitates the binding of the virus on surface of hepatocytes. Expression of NTCP in extrahepatic cells may make these cells susceptible to HBV infection and support cellular proliferation akin to hepatocytes. Placental replication of HBV is not well explored. In this study we have assessed the expression of NTCP on placental cells and investigated if these cells may act as reservoir for HBV.
Materials and Methods: Ten healthy (Control) and 20 HBsAg + ve pregnant women were enrolled. The later were further grouped on the basis of HBV viral load, $\geq$ 2000 (n = 10) as High Viral Load (HVL) Group and $<$ 2000 IU/ml (n = 10) as Low Viral Load (LVL) Group. HBV DNA in placenta was detected by qPCR using primers for X and core ORF. Expression of NTCP in placenta was analyzed by qRT-PCR and was further investigated by immunohistochemistry (IHC) along with HBV replication biomarkers, HBsAg, HBeAg, and HBcAg.
Results: HVL and LVL females showed increased expression of NTCP in trophoblasts of placenta compared to control group. Furthermore, significant difference in NTCP expression was also observed between HVL and LVL group and it was correlated with the maternal HBV DNA load. Membranous and/or Cytoplasmic immunostaining of NTCP, and cytoplasmic staining of HBeAg and HBcAg in trophoblasts along with presence of HBV DNA indicated that trophoblasts are not only susceptible to HBV infection but may also be a probable site for viral replication.
Conclusion: Here, for the first time we demonstrated expression of NTCP on placenta which may facilitate the entry of HBV. We establish the presence of HBeAg in trophoblasts indicating these cells may act as replication host/reservoir. Correlation of NTCP expression with maternal viral load and presence of HBeAg in placenta indicates

its probable role in vertical transmission of HBV. Our finding suggest that NTCP blocking strategy may be used for therapeutic intervention.

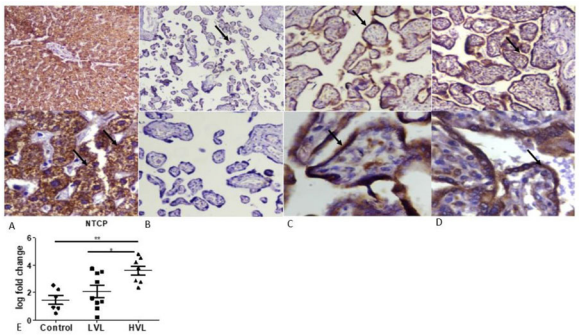

Fig. (A-D) NTCP Expression at 100X and 400X. A. NTCP expression in liver. B. NTCP expression in placenta of control. C. NTCP expression in placenta of Group B. D. NTCP expression in placenta of Group A. E. NTCP mRNA fold change among groups.

[OP-0682]

Characterization of circulating Hepatitis B virus RNAs in vitro and chronic hepatitis B patients

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Objectives: Circulating HBV RNA (CirB-RNA) is a promising non-invasive biomarker for cccDNA transcriptional activity. However, the molecular characteristics and circulating particles containing cirB-RNA in vitro and in vivo remain to be fully defined.
Materials and Methods: Supernatants from cultured hepatocytes infected by HBV and treated or not with lamivudine, and sera from 9 untreated [4 HBeAg (+) and 5 HBeAg (-)] and 1 HBeAg (+) ETV-treated chronic hepatitis B (CHB) patients were subjected to Iodixanol/Sucrose ultracentrifugation for buoyant density. Each density fraction was analyzed for HBV DNA/RNA by specific qPCR and droplet digital (dd)PCR. Viral and extracellular vesicles (EVs)-associated proteins were detected by ELISA and Western Blotting. 5' RACE PCR followed by ONT MinION sequencing was used to identify CirB-RNA species. Longitudinal serum samples before and at two time points after NUC therapy initiation were obtained from two additional patients [HBeAg (+) TDF-treated CHB and HBeAg (-) ETV-treated CHB].
Results: After ultracentrifugation, CirB-RNA was mainly detected in core-associated virion-like particles, in 2 log10 less amount than HBV DNA. However, CirB-RNA was the predominant species in lighter density fractions (1.17–1.18 g/ml) deprived of viral proteins, both in cell supernatant and in serum. The enrichment for EVs in these fractions was confirmed by detection of CD9 and CD81 by Western Blotting, immunoprecipitation assay, Nanoparticle tracking analysis and Transmission Electron Microscopy. Distribution of CirB-RNA did not differ significantly according to HBeAg status, while in a patient with low HBsAg level, CirB-RNA was mainly detected in the EVs-enriched fractions. Lastly, CirB-RNA profiling by 5' RACE and ONT MinION sequencing identified different proportions of pgRNA-derived transcripts according to HBeAg status and HBsAg level.
Conclusion: Our results indicate that EVs-enriched compartment also contributes to the circulation of HBV-RNAs. Moreover, different HBV-RNA transcripts in addition to pgRNA can be detected in vivo. Altogether, these data could significantly contribute to the characterization of cirB-RNAs as new viral biomarker.

Hepatitis B—Clinical

[OP-0086]

Increased risk of hepatocellular carcinoma and mortality in chronic viral hepatitis with concurrent fatty liver

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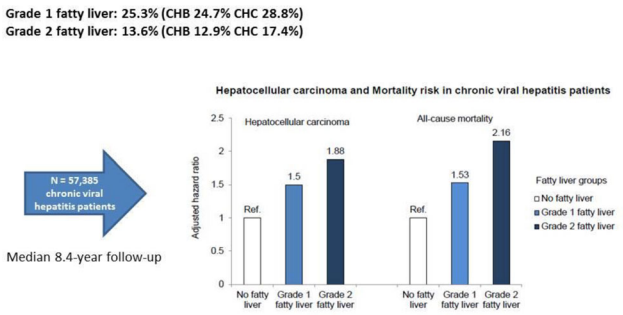
Objectives: Population-based data are lacking regarding whether fatty liver is a risk factor for hepatocellular carcinoma (HCC) and mortality in patients with chronic viral hepatitis. We investigated the association of concurrent fatty liver with HCC incidence and mortality in patients with chronic viral hepatitis using a nationwide cohort.
Materials and Methods: We included 57,385 chronic hepatitis B (CHB) and chronic hepatitis C (CHC) patients who underwent health examinations in 2009. The patients were divided into three groups: no fatty liver, fatty liver index (FLI) < 30; grade 1 (G1) fatty liver, $30 \leq$ FLI < 60; and grade 2 (G2) fatty liver, FLI > 60. To investigate the effect of the change in fatty liver on the risk of HCC and mortality, we additionally analyzed 39,204 subjects who had undergone health examinations in both 2009 and 2011.
Results: During a median 8.4-year follow-up, we documented 3,496 HCC cases and 4,146 deaths. Compared to patients with no fatty liver (n = 35,018), the risk of HCC was significantly higher in patients with G1 fatty liver (n = 14,544) (adjusted hazard ratio [aHR] = 1.50, 95% confidence interval [CI] = 1.38–1.64) and G2 fatty liver (n = 7,823) (aHR = 1.88, 95% CI = 1.67–2.12). The risk of mortality significantly increased in patients with G1 fatty liver (aHR = 1.53, 95% CI = 1.41–1.66) and G2 fatty liver (aHR = 2.16, 95% CI = 1.94–2.42) compared to patients with no fatty liver. The risk of HCC and mortality was significantly higher in patients with fatty liver at follow-up, compared to patients with persistent no fatty liver ($P < 0.001$).
Conclusion: Concurrent fatty liver was associated with a higher risk of HCC and mortality in patients with chronic viral hepatitis. Our

results suggest the importance of management of fatty liver to reduce the risk of HCC and mortality in patients with chronic viral hepatitis.



[OP-0263]

Quick assessment of minimal/covert hepatic encephalopathy by the combination tool of the animal and vegetable naming test, number connection test B, ammonia and lactic acid

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Objectives: To standardize the naming tests in the Asian group and find a new screening tool combined neuropsychological tests and laboratory results that is easy and quick to implement in daily clinical work.
Materials and Methods: We prospectively incorporated 123 healthy controls and 266 patients with potential hepatic encephalopathy (HE) developing diseases (mainly cirrhosis) in our study. 123 healthy controls underwent the psychometric hepatic encephalopathy score (PHES), and 119 of them underwent three naming tests, including the animal naming test (ANT), the vegetable naming test (VNT), and the animal and vegetable naming test (AVNT). All 266 patients were identified by the PHES, ANT, VNT, AVNT and 57 patients were assessed by Encephalstroop App. All patients were followed for the occurrence of OHE in 28 days.
Results: The study achieved normalization of the PHES and equivalent scores of the ANT, VNT, AVNT in Asian group. The prevalence rate of MHE diagnosed by the gold standard PHES was 27.1%. The risk of developing into OHE in patients with MHE (16/72, 22.2%) was over triple higher than those without MHE (13/194, 6.7%). The AVNT (adjusted num. (if education $\leq$ 12, num. + 3) < 18) had a better diagnostic performance than the ANT and VNT ($p < 0.001$) with an area under the curve (AUC) of 0.82, 81.94% sensitivity and 71.35% specificity. The combination tool of adjusted num. below 18 for the AVNT, below -1 for the NCT-B, above 66 umol/L for the ammonia and equal or lesser than 1.53 mmol/L assessed patients with MHE with AUC of 0.97, 92.31% sensitivity and 96.77% specificity. The average time to complete the combination tool was 193 ± 78 s, compared 401 ± 192 s for the integrated PHES.
Conclusion: The combination tool (adjusted AVNT < 18 + NCT-B < -1 + ammonia > 66 umol/L + LAC < = 1.53 mmol/L) is easy and quick to implement for identifying patients with MHE in daily clinical work.

[OP-0363]

Serum levels of pgRNA and HBcrAg are associated with viral relapse after cessation of nucleotide analogues therapy in chronic hepatitis B patients

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Objectives: Whether NAs can be safely ceased remains a difficult and topical clinical issue. Our study aimed to investigate the role of serum pre-genomic RNA (pgRNA), hepatitis B core-associated antigen (HBcrAg), and HBsAg levels at end of treatment in predicting safe discontinuation of NAs treatment.
Materials and Methods: This is a prospective cohort study. Sixty-four CHB patients who met criteria for stopping treatment recommended by Chinese hepatitis B management guideline were enrolled in the West China Hospital of Sichuan University. The serum HBcrAg level was quantitatively measured using the fully automated CLEIA system. The HBV RNA was detected by RNA simultaneous amplification testing method (HBV-SAT). Serum HBcrAg and pgRNA were tested at the time of discontinuation of NAs treatment. All enrolled patients followed up every 3 months for 12 months or until virological relapse (VR).
Results: Among the 64 patients, 36 patients were HBeAg positive and 28 patients were HBeAg negative at the start of treatment. At one year of discontinuation, 33 patients (51.5%) had a virological relapse. Serum pgRNA positivity at the end of treatment (EOT) (OR = 14.59) and higher HBcrAg at EOT (OR = 14.14) were found to independently predict the risk of VR. To predict VR, the ROC value was 0.817 for higher serum HBcrAg and 0.651 for serum pgRNA positivity. Interesting, the combination of higher HBcrAg and pgRNA positivity had a higher ROC value (0.857) for predict virological relapse, than the other parameters alone predicted.
Conclusion: Serum pgRNA positivity and higher HBcrAg state at the EOT could predict virological relapse after treatment discontinuation. Combining serum HBcrAg and pgRNA can better help us assess whether patients can safely cease NAs treatment.

[OP-0476]

Study on mechanism of phyllanthus against hepatitis B virus based on bioinformatics and molecular docking

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Objectives: To explore the mechanism of Phyllanthus against hepatitis B virus (HBV) based on bioinformatics and molecular docking.
Materials and Methods: Through pharmmapper database, CTD database and gene card database, the active ingredients of Phyllanthus and the potential molecular targets of against HBV were obtained. Serial interaction analysis of target proteins was carried out, and cytoscape 3.7.1 was used to complete the construction of network map. KOBAS database was used for GO and KEGG enrichment

analysis. Using discovery studio software to dock drug molecules and target proteins.
Results: A total of 6 effective molecules of Phyllanthus were obtained, and 36 common targets of Phyllanthus against HBV were screened. The key targets involved AKT1, CASP3, mapk8, MMP9, SRC. GO and KEGG enrichment analysis revealed 12 signal pathways involved in hepatitis B and hepatocellular carcinoma, as well as biological processes associated with cell proliferation, apoptosis, signal transduction, and drug response. Phyllanthus molecules have good binding activity with these target proteins.
Conclusion: Phyllanthus may play an against HBV role through PI3K-Akt, MAPK and JAK/STAT pathways.

[OP-0480]

Study on molecular mechanism of matrine against hepatitis B virus based on bioinformatics

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Objectives: To explore the molecular mechanism of matrine against hepatitis B virus.
Materials and Methods: Using PubChem (https://pubchem.ncbi.nlm.nih.gov/), the chemical structure of matrine was obtained. Applying pharmmapper (http://www.lilabecust.cn/pharmmapper/), the target of matrine was obtained. Retrieving TCMSP database (https://old.tcmspe.com/tcmsp.php), the target of matrine was obtained. Taking hepatitis B as the keyword, retrieved CTD (https://ctdbase.org/) and genecards database (http://www.Genecards.org/), Hepatitis B related targets were obtained. Taking the intersection after merging target sites and the associated targets of the hepatitis B, the potential targets and scoring of matrine against hepatitis B were obtained. Through string online analysis tool (https://stringdb.org/cgi/input.pl), the target protein interaction diagram was obtained and analyzed with Cytoscape visualization software. The components, functions and pathway information of these targets were obtained by GO and KEGG analysis.
Results: We found that in the IL-17A/F signal pathway, intervening IL-17 expression can down regulate the expression levels of TRAF6, p38 and AP-1, inhibit HBV DNA replication and reduce inflammatory factors IL-6, TNF α, IL-1 and p38 levels as well as chemokines CXCL1, CXCL2, CXCL5, CXCL8, CXCL10, CCL2, CCL7, CCL20 levels. Stimulating IL-6 and TNF α can down regulate HNF1 α and HNF4 α, inhibiting the synthesis of hepatitis B virus pgRNA, preventing the generation of HBeAg, further down regulating the expression of MyD88, TRAF6, p38 and AP-1, as well as inhibiting the replication of DNA.
Conclusion: Matrine may play an immunomodulatory role by down regulating the expression of IL-17A/F signaling pathway related factors and inhibiting the release of inflammatory factors.

[OP-0503]

Comparative study of treatment of HBV decompensated cirrhosis of liver patients by tenofovir and entecavir

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Objectives: Decompensated cirrhosis is defined in patients with cirrhosis as an acute deterioration of their liver function and is characterized for jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome (HRS) and varices. The aim of the study was to compare of Treatment of HBV decompensated Cirrhosis of Liver Patients by Tenofovir and Entecavir.
Materials and Methods: The study was carried out both at the inpatient department of hepatology, Bangabandhu Sheikh Mujib Medical University Hospital and Kurmitola General Hospital, Dhaka, Bangladesh. The study enrolled 100 treatment-naive patients with HBV decompensated cirrhosis of liver on entecavir or tenofovir disoproxil fumarate from January 2013 to December 2018.
Results: There are three follow up taken, first follow up was three month after medication. Second and third follow-up was after 06 month and 12 month completion of the treatment. In 3rd follow up (after one year), 100.0% patients was found undetected HBV DNA in tenofovir group and 97.56% in entecavir group. The difference was not statistically significant ($p > 0.05$) between two groups. At 01 year total death was found 12 patients, out of them 03 was tenofovir group and 06 was entecavir group. In tenofovir patients, Mean Child Pugh score was found 12.1 ± 1.3 in pretreatment and 5.8 ± 1.3 at 01 year. Mean MELD score was found 25.0 ± 3.1 in pretreatment and 9.3 ± 3.2 at 1 years. In entecavir patients, Mean Child Pugh score was found 12.0 ± 1.5 in pretreatment and 9.3 ± 0.9 at 01 year. Mean MELD score was found 26.5 ± 2.0 in pretreatment and 17.0 ± 2.1 at 1 years. The difference of MELD and CTP score improvement was statistically significant ($p < 0.05$) between two groups.
Conclusion: Entecavir and Tenofovir both are good antiviral drugs for the treatment of HBV infection. In treatment of decompensated cirrhosis of liver entecavir and tenofovir both are significantly improved liver function, HBV DNA undetection and also patient's survival. But Tenofovir shown more improvement.

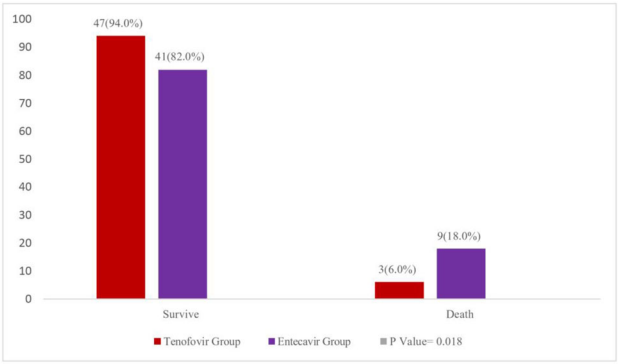

Figure I: Outcome of the decompensated patients after the antiviral therapy.

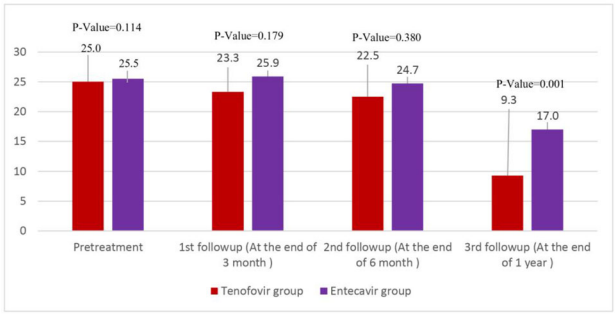

Figure II: Bar diagram showing MELD score in different follow up.

[OP-0621]

Active site polymerase inhibitor nucleotides induce sustained HBV RNA suppression following treatment cessation

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Objectives: The active site polymerase inhibitor nucleotide (ASPIN) clevudine was associated with potent and prolonged HBV DNA suppression in patients and animal models, with decreases in replication intermediates, including RNA and cccDNA, observed in animal models. In patients, cccDNA activity can be approximated by circulating HBV RNA, and end-of-treatment RNA negativity is associated with better off-treatment responses. The impact of the next-generation ASPIN ATI-2173 on HBV RNA was evaluated.
Materials and Methods: ANTT101 (phase 1b portion) and ANTT201 (phase 2a portion) were randomized, double-blind trials of 28-day ATI-2173 monotherapy versus placebo (ANTT101) or 90-day ATI-2173 + TDF versus placebo + TDF (ANTT201) in chronic HBV-infected patients conducted in Moldova and Ukraine. Data from the 25- and 50-mg cohorts are presented. Antiviral activity was measured at baseline; end of treatment; and months 1, 3, and 6 off treatment. HBV RNA was measured by Roche Cobas 6800 (LLOQ = 10 copies/mL; investigational use, not approved in any market).
Results: One-month ATI-2173 and 3-month ATI-2173 + TDF treatment induced rapid HBV RNA declines that mirrored HBV DNA kinetics and persisted off treatment. ATI-2173 monotherapy led to 0.6-$\log_{10}$ declines in HBV RNA over 28 days, with 5/9 patients undetectable at end of treatment; 0.8-$\log_{10}$ declines were observed at 1 month off treatment, with all patients becoming undetectable. Sustained off-treatment suppression was observed for 24 weeks. In the dual therapy study, 6/13 patients had undetectable HBV RNA at end of treatment with ATI-2173 + TDF versus 2/3 with placebo + TDF, with prolonged off-treatment suppression observed. Change from baseline in RNA was –1.23 versus –1.15 $\log_{10}$ at end of treatment and –1.5 versus –1.21 $\log_{10}$ at 1 month off treatment with ATI-2173 + TDF and placebo + TDF, respectively.
Conclusion: ASPINs decrease circulating HBV RNA with similar kinetics to HBV DNA and induce prolonged off-treatment HBV RNA suppression.

[OP-0658]

Comparison of HBV reactivation in HCC patients who received TKI and TKI with PD-1 inhibitor

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Objectives: To explore the relationship between hepatitis B virus reactivation and PD-1 inhibitors and other influencing factors.
Materials and Methods: The retrospective analysis was performed on data collected at the 5th Medical Center of the PLA General Hospital from March 2017 to March 2021, gathered from inpatients who received either TKI or TKI combined with PD-1 inhibitor. All subjects were treated with standard antiviral therapy. The primary endpoint was the occurrence of HBV reactivation. HBV reactivation was defined as an increase of $\geq$ 1 log for HBV DNA from baseline, or as seropositive for HBV DNA but undetectable serum HBV DNA at baseline.
Results: A total of 499 eligible patients were included, among whom 296 patients received TKI monotherapy and 203 patients received TKI combined with PD-1 inhibitor. The median follow-up time was 4.7 (2.8,8.9) months. The 3 months,6 months, 9 months cumulative incidence of HBV reactivation in TKI and TKI combined with PD-1 inhibitor groups was 6.2%,20.4%,33.4% and 13%,30.8%,44.3% (P = 0.01),respectively. The Cox proportional hazard model indicated that combination therapy, ALT > 40U/L, and tumor size > 5 cm were independent risk factors for HBV reactivation. 90 patients (59.2%) with HBV reactivation had tumor progression, and 102 patients (29.4%) without HBV reactivation had tumor progression during the follow-up period (P = 0.001).All patients with reactivation without tumor progression were divided into adjusted antiviral regimen treatment group and original regimen treatment groupand and were followed up for

3 months.The group of adjusting the antiviral regimen significantly reduced the tumor progression rate (P = 0.008).
Conclusion: Patients who received TKI combined with PD-1 inhibitor had a greater risk for HBV reactivation and patients with HBV reactivation had a higher rate of tumor progression.Timely adjustment of antiviral regimen can reduce the rate of tumor progression.

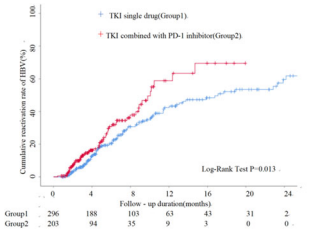

Figure a, Cumulative reactivation rate of HBV

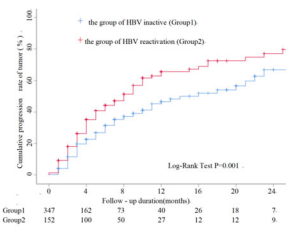

Figure b, Cumulative progression rate of tumor

	Tumor progression	Tumor non progression	P
TKI plus PD-1inhibitor			
Adjusted antiviral regimen	1	9	0.036
Original antiviral regimen	4	2	
TKI			
Adjusted antiviral regimen	1	8	0.176
Original antiviral regimen	6	8	
Total			
Adjusted antiviral regimen	2	17	0.008
Original antiviral regimen	10	10	

Figure c, Comparison of tumor progression rate between the original antiviral regimen group and the adjusted antiviral regimen group in all HBV reactivation patients after 3 months of follow-up

[OP-0704]

Effect of Biejiajian Pill on intestinal microbiota in patients with hepatitis B cirrhosis/liver fibrosis

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Objectives: In this study, a prospective, randomized controlled study was conducted to analyze the effects of Biejiajian pill, a classic and famous prescriptions, on intestinal microbiota of patients with hepatitis B cirrhosis/liver fibrosis, and to explore its relationship with liver fibrosis.
Materials and Methods: This study is a randomized double-blind placebo controlled trial. Patients with chronic hepatitis B cirrhosis/liver fibrosis in Beijing Ditan Hospital, Capital Medical University from January 2018 to December 2020 were randomly assigned (1:1) to receive entecavir combined Biejiajian Pill (BJJP) or entecavir combined with placebo (simulant as control, SC) respectively for 48 weeks. Blood and stool samples were collected from the patients at baseline and week 48 of treatment. Liver function, renal function and hematological indexes were detected in the laboratory of Beijing Ditan Hospital, Capital Medical University. Fecal samples were analyzed by 16S rDNA V3-V4 high-throughput sequencing technology, the changes of intestinal microbiota in the two groups before and after treatment were compared, and its correlation with liver fibrosis was analyzed.
Results: Weighted Unifrac distance based principal coordinate analysis (PCoA) showed significant differences in intestinal microbiota community diversity before and after BJJP treatment (P = 0.0001 and P = 0.003). After 48 weeks of treatment, the abundance of beneficial bacteria (Bifidobacteria, Lactobacillus, Faecalibacterium, Blautia, etc.) increased, the abundance of potential pathogenic bacteria (Escherichia coli, Bacteroides, Ruminococcus, Parabacteroides and Prevotella) decreased, among which, Ruminococcus and Parabacteroides were significantly positively correlated with the degree of liver fibrosis. The microbiota in the SC group did not change significant through the whole process of treatment.
Conclusion: BJJP has a certain regulatory effect on intestinal microbiota of patients with hepatitis B cirrhosis/liver fibrosis, which may be related to the mechanism of anti-liver fibrosis.

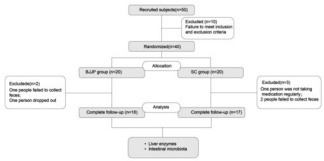

Figure 1. Research object screening process

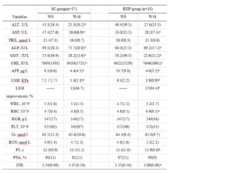

Table 1. Therapeutic effect of BJJP

Data are expressed as frequency counts (percentage of total) or mean (SD).
a P < 0.05 W0 vs. W48.
b P < 0.05 SC group vs. BJJP group.

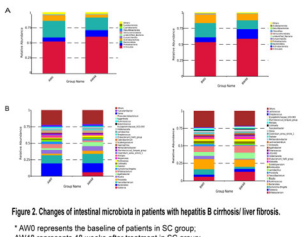

Figure 2. Changes of intestinal microbiota in patients with hepatitis B cirrhosis/ liver fibrosis.

* AW0 represents the baseline of patients in SC group;
AW48 represents 48 weeks after treatment in SC group;
BW0 represents the baseline of patients in BJJP group;
BW48 represents patients in the BJJP group after 48 weeks of treatment.

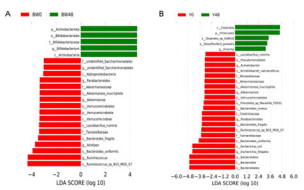

Figure 3. Changes of intestinal microbiota in patients with hepatitis B cirrhosis/ liver fibrosis.

* BW0 represents the baseline of patients in BJJP group;
BW48 represents patients in the BJJP group after 48 weeks of treatment.

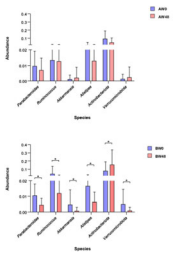

Figure 4. Difference of microbiota in in SC group and BJJP group at baseline and after treatment.

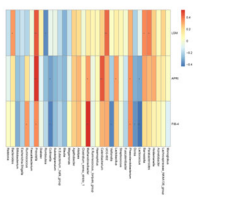

Figure 5. Spearman correlation analysis of intestinal microbiota and fibrosis score in hepatitis B cirrhosis/fibrosis.

[OP-0747]

Identification and characterization of besifovir-resistant hepatitis B virus isolated from a chronic hepatitis B patient

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Objectives: Hepatitis B virus (HBV) is known to cause liver diseases such as acute or chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Chronic HBV (CHB) infection is a major health problem with over 250 million individuals infected worldwide. Currently, nucleos (t)ide analogs (NAs) and IFN-α are treatments for HBV infection. NAs are potent antiviral agents that inhibit HBV replication. Besifovir dipivoxil maleate (BSV) is a newly developed NA against HBV. BSV is an acyclic nucleotide phosphonate that is available for oral administration similar to adefovir and tenofovir. BSV competes with dGTP for binding to HBV polymerase and blocks viral reverse transcription. Until now, resistance to BSV treatment has

not been reported. In this study, we found a CHB patient who showed viral breakthrough in HBV DNA levels after 64 weeks treatment with BSV.
Materials and Methods: We isolated HBV DNA from patient's serum and cloned into replication-competent HBV 1.2mer to analyze the sequence of reverse transcriptase (RT) domain of polymerase and drug susceptibility.
Results: Several mutations were identified in HBV RT domain. Among them, mutants harboring ten RT mutations showed resistance to BSV treatment in vitro susceptibility assay. The ten mutations include rtV23I (I), rtH55R (R), rtY124H (H), rtD134E (E), rtN139K (K), rtL180M (M), rtM204V (V), rtQ267L (L), rtL269I (I) and rtL337M (M). To identify the responsible mutations for BSV resistance, we further performed in vitro drug susceptibility assay using several artificial clones. As a result, our study revealed that rtL180M (M) + rtM204V (V) mutations, already known as lamivudine-resistant mutations, confer resistance to BSV in CHB patients.
Conclusion: Although the use of BSV as CHB therapy was very successful for more than 60 weeks because of a high genetic barrier to resistance, we herein report that HBV isolated from patients who developed phenotypic resistance during BSV therapy showed genotypic resistance in an in vitro study.

[OP-0774]

Prevalence of depressive disorder among patients with hepatitis B virus infection in the United States: A cross-sectional epidemiological study

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Objectives: Depression is one of the common and overwhelming mental disorder among individuals with hepatitis B virus (HBV)infection. This study aimed to assess the prevalence of depressive disorder among patients with HBV infection in the United States.
Materials and Methods: Using 1999–2018 National Health and Nutrition Examination Survey data, we calculated the prevalence of depressive disorder among adults with HBV infection in the United States. Depression was assessed by using Composite International Diagnostic Interview Version2.1 (CIDI-Auto2.1) and Patient Health Questionnaire-9 (PHQ-9). Data were weighted according to the age–sex–residence distribution data from census population survey to adjust for differential probabilities of selection and differential response, as well as to post-stratify the sample to match the population distribution. The data were entered into Python and analyzed by the statistical package.
Results: From 1999–2018, 27,744 respondents (13,655 [49.2%] men and 14,089 [50.8%] women) completed the survey. The weighted prevalence of depression among HBV surface antigen (HBsAg) positivity patients was 10.3% (95% CI 5.9–14.7%), compared with 7.6% (95% CI 7.3–7.9%) among HBV surface antigen negativity patients. We estimated that 9.2% (95% CI 8.0–10.4%) of HBV core antibody (anti-HBc) positivity patients, and 7.5% (95% CI 7.2–7.8%) of anti-HBc negativity patients, while 7.0% (95% CI 6.4–7.6%) of HBV surface antibody (HBsAb) positivity patients were suffering depressive disorder. This includes 123.6 (95% CI 70.8–176.4) thousand noninstitutionalized civilian adults in the United States were suffering depressive disorder and a current HBV infection.
Conclusion: An early depression-focused regular screening for HBV surface antigen positivity persons should be carried out by mental health service providers. Further research was needed to identify strategies for preventing and treating depression in HBV past or current infected patients.

[OP-0829]

SAVE-1: Phase 2a results of ATI-2173, a novel active site polymerase inhibitor nucleotide, combined with TDF in chronic hepatitis B patientssite polymerase inhibitor nucleotides induce sustained HBV RNA suppression following treatment cessation

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Objectives: ATI-2173 is a novel phosphoramidate liver-targeted prodrug of clevudine that functions as an active site polymerase inhibitor nucleotide. In Phase 1, ATI-2173 demonstrated potent HBV activity with sustained off-treatment responses 4 to 24 weeks after discontinuation. The SAVE-1 Phase 2a trial evaluated the safety and efficacy of ATI-2173 + tenofovir disoproxil fumarate (TDF) in treatment-naive chronic HBV–infected (CHB) patients.
Materials and Methods: A randomized, double-blind, placebo-controlled trial was conducted at sites in Moldova and Ukraine. Each cohort had 10 CHB patients randomized 8:2 to receive either 25 mg or 50 mg of ATI-2173 + TDF or placebo (PBO) + TDF daily for 90 days. HBV DNA and HBV RNA were measured using a Roche Cobas 6800 (lower limit of quantification; LLOQ = 10 IU/mL, and 10 copies/mL respectively). HBsAg was measured using a Roche Elecsys (LLOQ = 0.05 IU/mL).
Results: All patients completed 90 days of dosing with no serious adverse events or study drug discontinuation. Treatment-emergent adverse events are presented in the Table. Most patients were HBeAg − (90%). Virologic responses at day 90 for TDF alone (N = 4), 25 mg (N = 8) and 50 mg of ATI-2173 + TDF (N = 8) were − 3.53, − 3.72 and -3.54 $\log_{10}$ IU/mL, respectively. HBV RNA responses mirrored HBV DNA responses on treatment. No changes in HBsAg were observed. At 1 month off treatment, 1/4 in the TDF alone, 4/8 in the 25-mg cohort and 5/8 in the 50-mg cohort had HBV DNA below the limit of quantification (< 10 IU/mL). Preliminary pharmacokinetic analysis showed no drug interactions between ATI-2173 and TDF.
Conclusion: ATI-2173 + TDF was safe and well-tolerated. Similar on-treatment HBV DNA antiviral activity was observed between the 25-mg and 50-mg cohorts of ATI-2173 + TDF and TDF alone arms. HBV DNA rebounded quickly in the TDF arm off treatment while remaining suppressed in the ATI-2173 + TDF arms of the study.

Table. Treatment-Emergent Adverse Events

MedDRA System Organ Class Preferred Term	Pooled TDF (n=4) n (%)	TDF + 25 mg ATI-2173 (n=8) n (%)	TDF + 50 mg ATI-2173 (n=8) n (%)
Subjects with any TEAE	0	3 (37.5)	2 (25)
ALT/AST increase	0	1 (12.5)	1 (12.5)
Blood creatine phosphokinase increase	0	2 (25)	0
Headache	0	0	1 (12.5)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TDF, tenofovir disoproxil fumarate.

[OP-0941]

Aspirin use and risk of hepatocellular carcinoma in patients with chronic hepatitis B with or without cirrhosis

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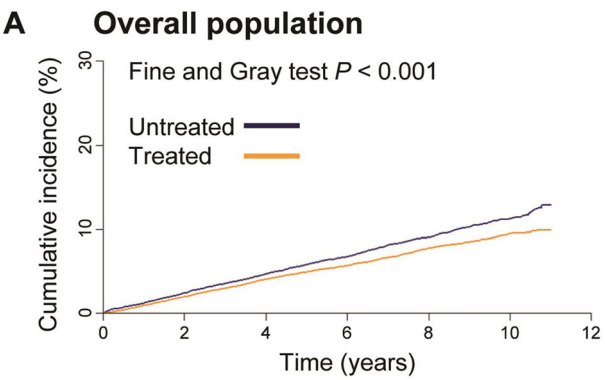
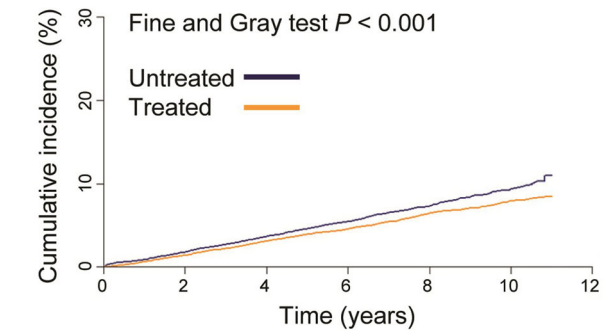
Objectives: Studies on differential effect of aspirin therapy on hepatocellular carcinoma (HCC) risk across the spectrum of liver diseases are lacking. We investigated the association between aspirin use and risks of HCC, liver-related death, and major bleeding in chronic hepatitis B (CHB) patients with or without cirrhosis.
Materials and Methods: We identified 329,635 eligible adults with CHB from 2007 through 2017, using the Korean National Health Insurance Service database, including patients who received aspirin for ≥ 90 consecutive days (n = 20,200) and patients who never received antiplatelet therapy (n = 309,435). The risks of HCC, liver-related mortality, and major bleeding were estimated in a propensity score-matched cohort (19,003 pairs), accounting for competing risks.
Results: With a median follow-up of 6.7 years, the 10-year cumulative incidence of HCC was 9.5% in the aspirin-treated group and 11.3% in the untreated group (adjusted subhazard ratio [aSHR], 0.85; 95% confidence interval [CI], 0.78–0.92). However, among cirrhotics (2,479 pairs), an association of aspirin use with HCC risk was not evident (aSHR, 1.00; 95% CI, 0.85–1.18). The cirrhosis status had a significant effect on the association between aspirin use and HCC risk ($P_{interaction}$ = 0.04). Aspirin use was also associated with lower liver-related mortality (aSHR, 0.80; 95% CI, 0.71–0.90). Moreover, aspirin use was not associated with major bleeding risk (aSHR, 1.09; 95% CI, 0.99–1.21).
Conclusion: Aspirin use was associated with reduced risks of HCC and liver-related mortality in adults with CHB. The cirrhosis status had a substantial effect on the association between aspirin use and HCC risk.



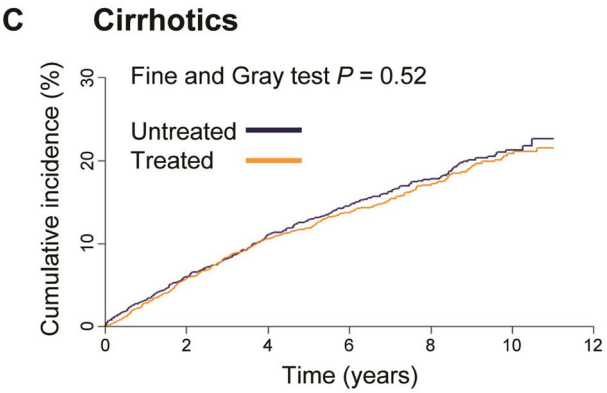
Number at risk

Untreated	19,003	16,489	13,800	10,642	7,246	3,665
Treated	19,003	16,582	13,937	10,811	7,372	3,748



Number at risk

Untreated	16,507	14,585	12,418	9,728	6,687	3,415
Treated	16,507	14,645	12,484	9,837	6,785	3,481



Number at risk

Untreated	2,479	1,920	1,444	970	573	252
Treated	2,479	1,922	1,449	971	590	275

[OP-0972]

Management of patients with hepatitis B virus reactivation PostDAA treatment of chronic hepatitis C virus infection In HCVHBV coinfected patients with pretreatment HBeAg seroconversion

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Objectives: Hepatitis C virus (HCV)–HBV coinfection is a significant health problem with rapid progression of liver disease without precise diagnosis and treatment. Weaimed in this study to identify if there were any role of HBV antiviral therapy in patients with HBV reactivation after direct-acting antiviral therapy in HCV–HBV coinfected patients.
Materials and Methods: A prospective random study was carried out on 140 patients presenting with chronic HCV and chronic HBV coinfection. All patients had pretreatment HBeAg seroconversion, HBV DNA $<$ 2,000 IU/mL, normal liver enzymes, and F0/F1 hepatic fibrosis. They treated with sofosbuvir 400 mg and daklatasvir 60 mg once daily for 3 months. All patients underwent pretreatment hepatic fibrosis assessment using Fibro Scan and laboratory investigations: platelet count, liver-function tests, quantitative HCV PCR, HBsAg, HBc IgG, HBeAg, and HBeAb. All patients were followed up at 1, 3, 6, and 12 months from the start of HCV therapy.
Results: The study enrolled 140 HCV–HBV coinfected patients: 55% were F0 and the rest F1. All our patients had negative HCV PCR at 1 month post treatment and had achieved sustained virologic response with negative HCV PCR 3 months after treatment end. Four patients showed HBV reactivation with raised HBV DNA PCR and liver enzymes. Their mean age was 23.7 $\pm$ 2.7 years, and three were male. Regarding patients with HBV reactivation, at 12 months posttreatment they showed significant decreases in liver enzymes, bilirubin, and INR, with increased platelet count (P = 0.001), each with undetectable HBV PCR (P = 0.001).
Conclusion: HBV–HCV coinfected patients with no/mild hepatic fibrosis, HBeAg seroconversion, and HBV DNA $<$ 2,000 IU/mL can complete direct-acting antiviral therapy without HBV antiviral treatment with close monitoring.

[OP-0973]

Impact of long-term oral antiviral treatment on hepatocellular carcinoma risk in immune-tolerant (IT) and immune-active (IA) chronic hepatitis B patients (CHB) utilizing modified PAGE-B SCORE

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Objectives: CHB is a leading cause of Hepatocellular Carcinoma (HCC), and oral antivirals (OAVs) can reduce but not eliminate HCC risk. The mPAGE-B score (age, gender, platelets, and albumin) is a tool validated in Asian CHB patients on OAVs to predict 5-year HCC risk. We utilized Modified PAGE-B (mPAGE-B) to assess HCC risk in patients enrolled in tenofovir (TFV)-based trials.
Materials and Methods: Data from a Phase 2 study of TFV disoproxil fumarate (TDF) vs. TDF/emtricitabine (FTC) in IT patients and 2 Phase 3 studies, comparing tenofovir alafenamide (TAF) vs. TDF in IA patients, were used to generate mPAGE-B scores at baseline and over 192 (IT), or 240 (IA) weeks. Shifts in risk categories (low-risk [0 $\leq$ 8], medium-risk [9–12], and high-risk [$\geq$ 13]) were evaluated.
Results: Of 126 (64 TDF; 62 TDF/FTC) IT patients (49% male, 92% Asian or Pacific Islander (PI), 99% HBeAg-positive). Mean (range) baseline (BL) mPAGE-B score was 5.2 (0–16); 106 (84%), 19 (15%) and 1 (0.8%) were low?, medium?, or high?risk. At Week 192, mean (range) change in mPAGE-B was -0.5 (-4 to 3); Majority remained categorically unchanged or improved (Table). No IT patients

developed HCC. Of 1631 (1092 TAF; 539 TDF) IA patients (65% male, 83% Asian/PI, 64% HBeAg-positive), mean (range) BL mPAGE-B was 8.0 (0–18); 901 (55%), 588 (36%), and 142 (9%) were low-, medium-, or high-risk. At Week 240, mean (range) change in mPAGE-B was ?0.6 (-6 to 3); majority remained unchanged or improved; only 22 (2%) patients shifted to higher risk. Overall, 22 HCC cases developed (0.2%, 1.2%, and 9.2% in the low-, medium-, and high-risk groups at BL).
Conclusion: Use of mPAGE-B risk scores support few IT or IA patients at low risk for HCC at treatment initiation progressed to higher risk, while many medium- or high-risk patients improved to a lower risk after long-term treatment.

Table. Shifts in HCC Risk from Baseline to End of Treatment (EOT) for IT or Week 240 for IA by mPAGE-B Categories

	Immune-Tolerant CHB (N=126)			Immune-Active CHB (N=1631)		
	Baseline			Baseline		
n (%)	Low-risk (n=106)	Medium-risk (n=19)	High-risk (n=1)	Low-risk (n=901)	Medium-risk (n=588)	High-risk (n=142)
Week 192 (EOT)						
Low-risk	83 (100)	8 (44.4)	0			
Medium-risk	0	9 (50)	0			
High-risk	0	1 (5.6)	1 (100)			
Missing	23	1	0			
Week 240						
Low-risk				651 (97.5)	105 (21.6)	1 (0.9)
Medium-risk				17 (2.5)	377 (77.4)	44 (40.7)
High-risk				0	5 (1)	63 (58.3)
Missing				233	101	34

[OP-1030]

Antiviral therapy does not improve clinical outcomes of decompensated cirrhosis patients with undetectable hepatitis B virus DNA

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Objectives: Antiviral therapy (AVT) is not recommended in chronic hepatitis B (CHB) patients with decompensated cirrhosis and undetectable serum hepatitis B virus (HBV) DNA. We compared the clinical outcomes of those patients who had and had not undergo AVT.
Materials and Methods: Treatment-naive, HBsAg-positive cirrhotic patients with decompensation who were referred to two academic teaching hospitals between 2000 and 2017 were recruited. Liver transplant (LT)-free mortality and hepatocellular carcinoma (HCC) development were evaluated between the patients who started AVT (AVT group) and patients who did not (non-AVT group). Propensity score (PS) matching was performed to balance the groups.
Results: In total, 429 patients were analyzed (50 patients [11.4%] in AVT group vs. 379 patients [86.1%] in non-AVT group). The mean age was 54.1 years, and 305 patients (71.1%) were male. The baseline characteristics of both groups were comparable (all $P > 0.05$). During a median follow-up period of 49.6 months, 98 patients (22.3%) died, 40 patients underwent LT, and 105 patients (23.9%) developed HCC. The LT-free mortality rates were similar between AVT (8.1%, 10.3%, and 17.7% 1-, 2-, and 5 years, respectively) and non-AVT groups (11.4%, 14.8%, and 26.3%, respectively) (P = 0.295). In multivariate analysis, presence of diabetes, lower albumin level, higher MELD score, and presence of ascites were associated with higher LT-free mortality (all $P < 0.05$) while AVT was not (P = 0.342). The LT-free mortality rates were not different between PS-matched AVT (n = 49) and non-AVT groups (n = 98) (P = 0.111). The HCC occurrence rates were similar between AVT (8.6%, 15.8%, and 26.4% at 1-, 2-, and 5 years, respectively) and non-AVT groups (1.6%, 7.7%, and 24.4%, respectively) (P = 0.958). In multivariate analysis, only higher age was associated with higher risk of HCC (P = 0.001). The HCC rates were not different between PS-matched AVT and non-AVT groups (P = 0.133).
Conclusion: AVT does not improve LT-free mortality and HCC development in decompensated patients with undetectable HBV DNA.

[OP-1136]

A novel non-invasive index for the prediction of liver fibrosis in chronic hepatitis B patients with concurrent nonalcoholic fatty liver disease

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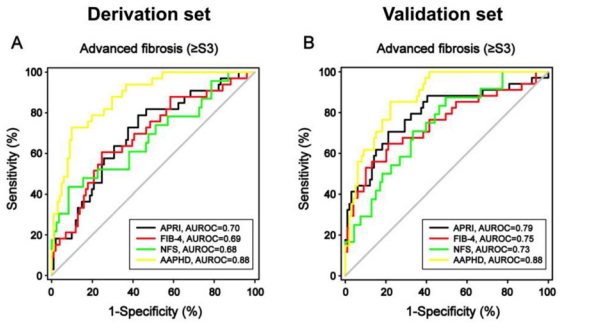
Objectives: Few accurate non-invasive indexes are available to evaluate liver fibrosis in chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease (NAFLD). We aimed to establish a predictive index for advanced fibrosis in CHB patients with NAFLD.
Materials and Methods: A total of 267 treatment-naïve CHB patients with NAFLD underwent liver biopsy were enrolled from four hospitals and randomly divided into a derivation set (n = 134) and a validation set (n = 133). Receiver operating characteristic (ROC) curve was used to compare predicting accuracy of different indexes.
Results: In the derivation set, alanine aminotransferase, aspartate aminotransferase (AST), prothrombin time, presence of hypertension, and type 2 diabetes were significantly associated with advanced fibrosis ($\geq$ S3). Based on these parameters, a novel index namely AAPHD for predicting advanced fibrosis was developed. The areas under the ROC curves (AUROCs) of AAPHD index in predicting advanced fibrosis was 0.88 (95%CI:0.82–0.94). The optimal cut-off value of AAPHD was -2.870, with a sensitivity of 72.73% and a specificity of 90.10%. The predicting accuracy of AAPHD for advanced fibrosis was significantly superior to AST-to-platelet ratio index (APRI) (AUROC = 0.70), fibrosis-4 score (FIB-4) (AUROC = 0.69), and NAFLD fibrosis score (NFS) (AUROC = 0.68). In the validation set, the AUROCs of AAPHD (AUROC = 0.88) remains significantly higher than that of FIB-4 and NFS, while it was comparable with APRI for predicting advanced fibrosis.
Conclusion: AAPHD is a promising non-invasive index for predicting advanced fibrosis with high accuracy in CHB patients with NAFLD. The application of AAPHD may reduce the necessary for liver biopsy in CHB patients with NAFLD.



Hepatitis C—Clinical

[OP-0322]

The efficacy and safety of sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir in HCV infected Korean patients

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Objectives: Despite the availability of pangenotype direct acting antivirals (DAAs) for chronic hepatitis C in Korea, there are still unmet needs for patients with advanced liver disease, complex drug interactions and those who failed previous DAA treatment. This study investigated the efficacy and safety of Sofosbuvir (SOF)/Velpatasvir (VEL) and SOF/VEL/Voxilaprevir (VOX) for 12 Weeks in HCV infected Korean patients (ClinicalTrials.gov Identifier: NCT04211909).
Materials and Methods: In this Phase 3b multicenter, open-label study, patients were enrolled to 2 cohorts. In Cohort 1, adult subjects with genotype (GT) 1 or 2 HCV infection who were treatment-naive or treatment-experienced with interferon-based treatments received SOF/VEL 400/100 mg daily for 12 weeks. In cohort 2, adult subjects with GT 1 HCV infection who previously received a nonstructural protein (NS) 5A inhibitor-containing regimen of at least a 4-week duration received SOF/VEL/VOX 400/100/100 mg daily for 12 weeks. Patients with decompensated cirrhosis were excluded from this study.
Results: A total of 87 patients were enrolled at 22 sites in this study. Of the 54 patients in cohort 1, 53.7% were female, mostly older (mean (SD) age 60 ± 12.6) and non-cirrhotic (79.6%), with ALT ≤ 1.5xUpper Limit Normal (ULN) at baseline (79.6%). 50% had GT 1 HCV infection and 50% had GT 2 infection. Of the 33 patients in cohort 2, 54.5% were female, non-cirrhotic (72.7%) with mean (SD) age 62 ± 12.6 and ALT ≤ 1.5xULN at baseline (78.8%). The majority of patients had GT 1b (97%) with one GT 2 patient who was inadvertently randomized into Cohort 2. 87.9% had failed prior treatment with an NS5A + NS3 ± NS5B regimen. Of the 53 patients treated with SOF/VEL, 52 patients (98.1%) achieved SVR12. The single patient who did not achieve an SVR experienced an asymptomatic Grade 3 ASL/ALT elevation on day 15 and discontinued treatment. The event resolved without any intervention, and the patient remained asymptomatic during the entire event. All 33 patients (100%) treated with SOF/VEL/VOX achieved SVR 12.. Overall, treatment with SOF/VEL or SOF/VEL/VOX was generally safe and well tolerated. 3 patients (5.6%) of cohort 1 and 1 patient (3.0%) of cohort 2 had SAEs and none were considered treatment-related. No deaths or grade 4 laboratory abnormalities were reported.
Conclusion: Treatment with SOF/VEL and SOF/VEL/VOX was safe and resulted in high SVR 12 in Korean HCV patients.

[OP-0501]

Metformin use greatly reduced the risk of hepatocellular carcinoma after antiviral therapy among diabetic chronic hepatitis C patients: A nationwide study on Taiwanese chronic hepatitis C cohort

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Objectives: Diabetes mellitus (DM) is associated with an increased risk of hepatocellular carcinoma (HCC) among chronic hepatitis C (CHC) patients. We aimed to evaluate whether metformin could reduce the risk of HCC in diabetic CHC patients after antiviral therapy.
Materials and Methods: CHC patients with interferon-based therapy were enrolled in a large-scale, multicenter cohort in Taiwan (T-COACH). HCC, decompensated cirrhosis and liver-related complications after antivirals were identified by linking to the catastrophic illness and cancer registry databases.
Results: Of the 11,012 CHC patients enrolled in the study, 2,374 (21.6%) patients had diabetes with 12.6% metformin users and 77% patients achieved a sustained virological response (SVR). During a median follow-up of 4.1 years, 474 patients developed new-onset HCC. The 5-year cumulative HCC incidence in DM non-metformin users, DM metformin users and non-DM patients were 13.2%, 3.4% and 3.9%, respectively. Advanced fibrosis, DM non-metformin use, non-SVR, older age, male and higher body mass index were significantly associated with HCC risk. Compared to non-DM patients, the adjusted hazard ratio (aHR) was 2.7 for DM non-metformin users and 0.6 for DM metformin users. With a simple risk score constructed by advanced fibrosis, DM non-metformin use and non-SVR, the HCC risk increased with the risk score (aHR: 3.1, 6.0 and 13.9) for scores 1,2, and 3, respectively, with score 0 as reference). The benefits of metformin use were consistently observed on decompensated cirrhosis and liver-related complications.
Conclusion: Metformin use greatly reduced the HCC risk after antiviral therapy in diabetic CHC patients. A simple risk score composed of advanced fibrosis, DM non-metformin use and non-SVR could predict the risks of HCC and major liver complications after antiviral therapy among CHC patients.

[OP-0945]

Prevalence of depressive disorder following hepatitis C virus infection: A nationwide population-based study

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Objectives: To estimate the prevalence of depressive disorders among Hepatitis C virus (HCV) infected adults aged $\geq$ 18 years in the United States.
Materials and Methods: We analyzed 1999–2018 data from the National Health and Nutrition Examination Survey (NHANES) to estimate the prevalence of HCV in the noninstitutionalized civilian population, Data were weighted according to the age–sex–residence distribution data from census population survey to adjust for differential probabilities of selection and differential response, as well as to post-stratify the sample to match the population distribution. The data were entered into Python and analyzed by the statistical package.
Results: We estimated that during 1999–2018,19.4% (95% CI 16.2–22.6%) of HCV antibody-positive (indicating past or current infection) adults in the United States, approximately 0.8 (0.7–0.9) million persons, were suffering depressive disorders, and 21.6% (95% CI 17.6–25.6%) of HCV RNA-positive (indicating current infection) adults, approximately 0.5 (0.4–0.6) million persons, were suffering depressive disorders. The weighted prevalence of depression with HCV antibody-negative in the United States was 7.3% (95% CI 7.0–7.6%), compared with 8.1% (95% CI 7.7–8.5%) among HCV RNA-negative patients.
Conclusion: The likelihood of developing depressive disorders is greater among HCV RNA-positive patients than patients without HCV antibody-positive. Efforts on multiple fronts are needed to combat the symptoms of depression in patients with past or current HCV infection, including increasing capacity for and access to HCV testing, mental health service, and cure.

[OP-0968]

Daclatasvir and sofosbuvir therapy enhance monocyte phenotypic changes in naive chronic hepatitis C patients: A prospective cohort study

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Objectives: Liver inflammation influences monocyte function, recruitment, and consequently inflammatory and fibrogenic responses. We aimed to investigate changes in the circulating monocyte phenotypes in response to Daclatasvir-Sofosbuvir (SOF/DCV) therapy in chronic hepatitis C (CHC) and relate findings to the viral kinetics and the fibrosis score.
Materials and Methods: A longitudinal study involving 100 treatment-näıve patients and 30 healthy controls, tested for liver function, fibrosis scores (AST to platelet ratio index, FIB-4), and blood monocyte subsets based on CD14/CD16 expression by flow cytometer.
Results: CHC patients had significantly lower albumin, higher ALT, AST, alkaline phosphatase, and increased fibrosis scores [Fib-4 (1.85 ± 0.98) and AST to platelet ratio index (APRI) (0.6 ± 0.35)], higher monocyte and eosinophil counts and lowered neutrophil to monocyte ratio (NMR), and lymphocyte to monocyte ratio (LMR) compared to week 12 and control. CHC patients had significantly increased median [classical (52.2% versus 25.8%, $P = 0.004$) and inflammatory CD16 + monocytes (23.1% versus 13.58%, $P = 0.035$)]. Therapy results in achievement of sustained virological response in 92% of cases, liver function improvement, and normalization of the inflammatory monocytes subsets. Monocyte counts showed positive correlation with viral load, calculated fibrosis scores (APRI and FIB-4 score), AST, ALT, ANC, and inverse correlations with serum albumin, leukocyte, eosinophil, NMR, and LMR.

Multivariate regression found eosinophil count as predictors of CD16 + monocyte count in CHC patients.
Conclusion: CHC infection promotes a proinflammatory and profibrotic monocytes profile. SOF/DCV therapy efficiently decreases viral load, reduces fibrosis potentials, attenuates monocyte activation, normalizes monocytes phenotypic abnormalities, and modulates monocyte subsets recruitment and differentiation later in the liver.

Nonalcoholic Fatty Liver Disease—Basic

[OP-0209]

Simultaneous analysis of plasma metabolomics and genetic variants

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Objectives: The aim of this study was to investigate the effects of genetic variants on pediatric NAFLD and analyze metabolic differences between NAFLD patients and controls in a pediatric population.
Materials and Methods: NAFLD was defined if hepatic steatosis was shown on ultrasound. A total 166 (105 NAFLD and 61 control) children were enrolled for metabolomic analysis. Four variants of PNPLA3 (rs738409), TM6SF2 (rs58542926) and SAMM50 (rs2073080, rs3761472) were genotyped by TaqMan allelic discrimination assay. The plasma metabolome was quantified using a Biocrates AbsoluteIDQ p400 kit and Thermo Q Exactive Plus Orbitrap mass spectrometer. P-values were corrected for multiple testing by controlling the false discovery rate (FDR) for metabolomic analysis.
Results: NAFLD patients showed a higher plasma levels of branched chain amino acids (BCAAs, leucine, isoleucine, valine), tyrosine, phosphatidylcholines (PCs), sphingomyelins (SMs), diglyceride, triglycerides (TGs) than control. Some of these metabolites including BAAA, glutamate, PCs, SMs had positive association with homeostasis model assessment-estimated insulin resistance (HOMA-IR). Plasma levels of glutamine, glycine and serin were lower in NAFLD patients than control. Glutamine and glycine showed negative correlation with HOMA-IR. The carries of TM6SF2 variants significantly showed lower plasma PCs, SMs and TG compared to wild type and the distribution of these metabolites was reversed to the NAFLD. Metabolomic differences among PNPLA3 and SAMM50 genotypes were not significant after FDR correction.
Conclusion: A total of 49 metabolites showed significant differences between subjects with NAFLD and control, are associated with insulin resistance. While variants of TM6SF2 results in lower plasma lipids, other variants did not show significant differences in metabolome.

[OP-0944]

Therapeutic effects of human endometrial stem cell secretome in a non-alcoholic steatohepatitis model

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Objectives: Recently, secretome-based therapies have emerged as a promising approach to overcome the limitations related to cell-based therapies. Endometrium is recently introduced as an available source of mesenchymal stem cells, and therapeutic roles of human endometrial stem cell secretome (hESC-secretome) are still unclear. The aim of study was to evaluate the effects of the hESC-secretome in non-alcoholic steatohepatitis (NASH) model.
Materials and Methods: C57BL/6 N mice were fed normal chow diet for 12 weeks (G1, n = 9), western diet (WD) + CCl4 [0.2 μl (0.32 μg)/g of body weight] for 12 weeks (G2, n = 9), and WD + CCl4 for 12 weeks treated with weekly intraperitoneal injections of hESC-secretome (G3, n = 9). Pathologic evaluations were made based on the NASH Clinical Research Network score. In vitro study, LX-2 cells were exposed to conditioned media (CM) from palmitate-treated hepG2 cells.
Results: The hESC-secretome ameliorated the plasma levels of AST [244 ± 129 (G2) vs. 136 ± 39 (G3), P = 0.038] and ALT [100 ± 38 (G2) vs. 67 ± 24 (G3), P = 0.048] as well as NAFLD activity score [7.3 ± 0.9 (G2) vs. 6.0 ± 0.7 (G3), P = 0.003], particularly the lobular inflammation score component [2.6 ± 0.5 (G2) vs. 1.7 ± 0.5 (G3), P = 0.002] in WD + CCl4 model. The hESC-secretome reduced the mRNA expressions of TNF-α ($P < 0.001$) and IL-1b (P = 0.04) in palmitate-treated hepG2 cells. The hESC-secretome also reduced the mRNA expressions of TGF-β (P = 0.008), TIMP-1 (P = 0.004), and collagenIα (P = 0.003) in LX-2 cells exposed to CM from palmitate-treated hepG2 cells.
Conclusion: The hESC-secretome ameliorated the pathologic hepatic inflammation in murine NASH model, and reduced the inflammation and fibrosis-related markers in vitro model of NASH. The hESC-secretome administration may be considered as a new therapeutic strategy for NASH.

[OP-1001]

Identifying therapeutic targets of NAFLD through in vivo functional genetic screens

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is emerging as the most common cause of chronic liver disease. The massive growth in NAFLD is being fuelled by an increase in global overnutrition and obesity; however, it remains an underrepresented disease with the absence of current approved pharmacological treatments. To address this, we are combining in-depth patient samples' transcriptomic profiling with mouse models of the disease to identify potential therapeutic targets by our established capability in in-vivo functional genetic screens.
Materials and Methods: We analyzed the transcriptomic data of 130 patients, covering different stages of NAFLD. Based on the dysregulated genes, a focused-shRNA library targeting these genes was generated. A functional genetic screen using shRNA constructs expressing in hepatocytes was conducted in the diet-induced NAFLD mice models with normal chow-fed animals as a control. At the end of diet treatment, livers were harvested, and the abundance of each shRNA was determined by NGS. Subsequently, the enriched shRNAs were validated for their potential therapeutic impact in mice that every hepatocyte expresses the shRNA of interest. The mice were exposed to a NAFLD-inducing diet, and fibrosis development was evaluated.
Results: Our in-vivo functional genetic screen, using shRNA libraries based on NAFLD patient transcriptomics, identified highly enriched shRNAs. So far, two targets have been validated for reducing liver fibrosis in the aggressive CDHFD NAFLD model. Various assays showed promoted regeneration of hepatocytes without tumor developments by candidate genes silencing.
Conclusion: We show that the combination of human patient disease-related gene expression data, mouse in vivo functional genetic screening, and our validation system can pinpoint new therapeutic targets. We identified and validated through this approach new targets for treating NAFLD. We are currently investigating the underlying molecular mechanisms. Our study may contribute to new insights about the therapeutic development of the disease in the near future.

Nonalcoholic Fatty Liver Disease - Clinical

[OP-0090]

Metabolic Dysfunction-associated fatty liver disease and risk of incident chronic kidney disease: A nationwide cohort study

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Objectives: The recently proposed metabolic dysfunction-associated fatty liver disease (MAFLD) has been suggested to better reflect the metabolic components of fatty liver disease (FLD), compared to nonalcoholic fatty liver disease (NAFLD). This study investigated whether MAFLD identifies a higher proportion of individuals at risk of developing chronic kidney disease (CKD).
Materials and Methods: 268,946 participants aged 40–64 years, who underwent National Health Insurance Service health examinations between 2009 and 2015 were included. Participants were categorized by presence of FLD, according to MAFLD or NAFLD. In participants with FLD, participants were categorized into three groups: non-metabolic risk (non-MR) NAFLD, MAFLD but not NAFLD, and overlapping FLD. Incident CKD was defined as the occurrence of eGFR < 60 mL/min/1.73m^2 or proteinuria ($\geq$ trace) on two consecutive health examinations.
Results: 73,726 (27.4%) and 88,762 (33.0%) participants had NAFLD and MAFLD, respectively. During a median follow-up of 5.1 years, CKD occurred in 8,335 (6.2/1,000 person-years) participants. Compared to non-NAFLD participants, the adjusted hazard ratio (aHR) for incident CKD was 1.20 (95% CI, 1.14–1.26; $P < 0.001$) for participants with NAFLD. Compared to non-MAFLD participants, the aHR for participants with MAFLD was 1.31 (95% CI, 1.24–1.39; $P < 0.001$). When the analysis was confined to participants with FLD, compared to non-MR NAFLD participants, the aHRs for participants with MAFLD but not NAFLD, and those with overlapping FLD were 1.24 (95% CI, 1.08–1.43; $P = 0.002$) and 1.38 (95% CI, 1.22–1.57; $P < 0.001$), respectively.
Conclusion: MAFLD identified a higher proportion of individuals at risk of developing CKD than NAFLD.

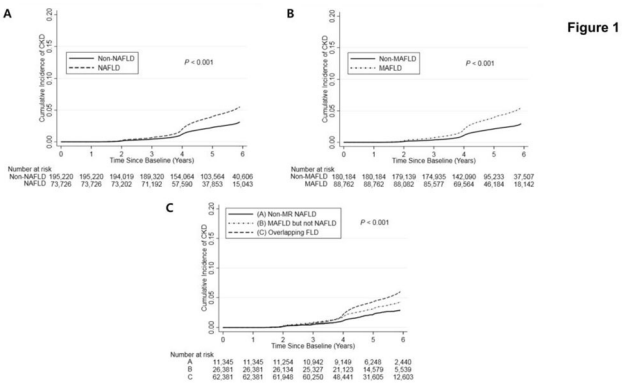

Figure 1

[OP-0106]

Nonalcoholic fatty liver disease is a precursor of new-onset metabolic syndrome in metabolically healthy young adults: A nationwide population-based study

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is associated with metabolic syndrome (MetS). However, the temporal relationship between NAFLD and MetS has yet to be evaluated, especially in young adults. In this study, we investigated whether NAFLD could be a precursor for MetS in metabolically healthy young adults.
Materials and Methods: Using the Korean nationwide health screening database, we analyzed subjects aged 20–39 years who were free from any component of MetS between 2009 and 2012. A total of 1,659,192 subjects without excessive alcohol consumption or concomitant liver disease were categorized into three groups according to

the fatty liver index (FLI): (1) NAFLD (FLI $\geq$ 60); (2) borderline NAFLD (30 $\leq$ FLI $<$ 60); and (3) control (FLI $<$ 30). The outcome was the development of MetS during follow-up.
Results: During the 6,699,462 person-years of follow-up, 109,239 subjects developed MetS (16.3 per 1000-person-years). The NAFLD group and the borderline NAFLD group were associated with a higher risk of MetS than the control group (incidence rate ratios, 2.9 [95% confidence interval (CI), 2.7–3.1] for the NAFLD group and 2.1 [95% CI, 2.1–2.2] for the borderline NAFLD group, respectively). In addition, all of the metabolic components were positively associated with FLI in a dose-dependent manner.
Conclusion: NAFLD is associated with the future onset of MetS in young adults. Therefore, active lifestyle intervention is required for young adults diagnosed with NAFLD to prevent MetS and other metabolic diseases.

[OP-0231]

Nonalcoholic fatty liver disease in individuals with mild or no metabolic abnormalities and the risk of incident metabolic syndrome.

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Objectives: A change of the terminology from nonalcoholic fatty liver disease (NAFLD) to metabolic associated fatty liver disease (MAFLD) has been proposed. Using these two definitions (MAFLD and NAFLD), some people fulfill diagnostic criteria of NAFLD but not MAFLD. The clinical outcome of people with NAFLD but not MAFLD is not well-known.
Materials and Methods: A cohort of 7,212 men and women of 20 years of age or older with no or minimal metabolic abnormalities were analyzed. NAFLD was defined with ultrasonography and excluding secondary causes. Metabolic abnormalities were defined for people with (a) overweight/obesity, (b) type 2 diabetes, and (c) metabolic dysregulation (that means at least 2 factors amongst increased waist circumference, hypertriglyceridemia, low serum HDL-cholesterol levels, hypertension, impaired fasting plasma glucose, insulin resistance and chronic subclinical inflammation), which is used to define MAFLD.
Results: Among 7,212 participants with no or minimal metabolic abnormalities, 400 participants were NAFLD. Incidence rate of metabolic syndrome per 100,000 person was 7,800 for those with NAFLD (n = 400), while it was 2,504 for those without NAFLD (n = 6,812). The fully adjusted hazard ratio (95% confidence interval) for metabolic syndrome by NAFLD status was 1.73 (1.39, 2.15). The increased risk of incident metabolic syndrome for participants with NAFLD was observed for all pre-defined subgroups.
Conclusion: NAFLD even in absence of no or minimal metabolic abnormalities were at higher risk of developing metabolic syndrome. This suggests NAFLD, but no MAFLD, cannot be considered completely benign condition.

[OP-0240]

Clinical features and factors associated with significant fibrosis of non-obese nonalcoholic fatty liver disease in patients with chronic hepatitis B

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Objectives: The burden of nonalcoholic fatty liver disease (NAFLD) is increasing in patients with chronic hepatitis B (CHB). Although a non-obese phenotype has been noted in NAFLD patients, little is known about non-obese NAFLD in patients with CHB.
Materials and Methods: A total of 1,008 NAFLD patients with CHB were prospectively recruited. NAFLD was diagnosed by transient elastography and defined as controlled attenuation parameter $\geq$ 248 dB/m. The Asian body mass index (BMI) cutoff of 25 kg/m^2 was defined as non-obese NAFLD. Significant fibrosis was defined as liver stiffness $\geq$ 8 kPa. The presence of hypertension, diabetes, dyslipidemia or hyperuricemia defined metabolic abnormalities. Propensity score matching (PSM) was used to control potential confounders.
Results: Among 1,008 recruited NAFLD patients with CHB, 43.3% (436/1008) were non-obese. Although non-obese and obese patients had comparable HBV viral load, non-obese patients had lower incidences of significant fibrosis (6.2% vs 15.0% in treatment-naïve patients, P $<$ 0.001; 19.7% vs 31.0% in nucleos (t)ide analogue (NA) treated patients, P = 0.008) and metabolic abnormalities (69.5% vs 79.9% in treatment-naïve patients, P = 0.006; 70.5% vs 80.3% in NA-treated patients, P = 0.018). These findings remained persisted after adjusting for age, gender, NA treatment and duration by PSM analysis. By multivariate analysis in non-obese patients, higher AST (OR 1.077, P = 0.016) and older age (OR 1.078, P = 0.004) were independently associated with significant fibrosis in NA-treated patients, while higher AST (OR 1.069, P = 0.040) and lower albumin (OR 0.694, P = 0.026) in treatment-naïve patients.
Conclusion: Non-obese NAFLD in patients with CHB had less severe disease than obese NAFLD. Higher AST, older age and lower albumin were the risk factors associated with significant fibrosis in non-obese patients.

[OP-0244]

The impact of pylorus preservation on the development of nonalcoholic fatty liver disease after pancreaticoduodenectomy and its pathophysiology; A Historical Cohort Study

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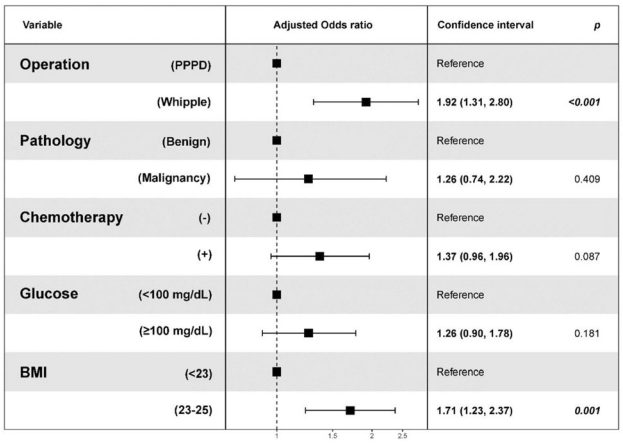
Objectives: Previous literature revealed that the patients who received pancreaticoduodenectomy (PD) frequently develop nonalcoholic fatty liver disease (NAFLD) postoperatively. As long-term survival has become achievable in these patients, there is growing attention to the quality of life after PD including prevention of NAFLD. We aimed to investigate the factors, including operational type, for NAFLD development after PD in a large cohort.
Materials and Methods: This historical cohort study included 786 consecutive patients treated either with classic Whipple operation or pylorus-preserving pancreaticoduodenectomy (PPPD) in Korea between 2012 and 2018. Development of NAFLD was defined when median hepatic attenuation on non-enhanced CT was lower than 40 hounsfield units (HU) or at least 10 HU lower than that of spleen. The patients were divided into two groups according to operation types: PPPD group and Whipple group. Incidence of NAFLD, demographics, and laboratory results were compared between the two groups. Logistic regression analysis was additionally used to find out risk factors for the development of NAFLD.
Results: Among 786 patients, 216 patients (27.5%) developed into NAFLD. The incidence of newly detected NAFLD at 0.5, 1, 1.5, and 2 years were 13 (1.7%), 41 (5.2%), 48 (6.1%), and 114 (14.5%), respectively. Whipple group showed a significantly higher NAFLD development than PPPD group (40.3% vs 24.5%, $p < 0.001$). Severe fatty liver with abnormal liver enzymes occurred in 17 (2.2%) patients. By multivariable analysis, Whipple operation (versus PPPD) was independently associated with a higher risk of NAFLD development (adjusted odds ratio [AOR]: 1.92, confidence interval [CI]: 1.31–2.80, $p < 0.001$) as well as pre-operative high body mass index (versus normal BMI) (AOR: 1.71, 95% CI: 1.23–2.37, $p = 0.001$) (Fig. 1).
Conclusion: Whipple operation compared with PPPD and pre-operative high BMI were significantly associated with the development of de novo NAFLD. De novo NAFLD should be paid more attention as a long-term complication after PD.



[OP-1015]

Investigating Non-Alcoholic Fatty Liver Disease in Asian Americans Using the Steatosis-Associated Fibrosis Estimator (SAFE) Score

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Objectives: The Steatosis-Associated Fibrosis Estimator (SAFE) score was developed and validated to rule out clinically significant (> stage 2) fibrosis among subjects with non-alcoholic fatty liver disease (NAFLD). The score includes BMI regardless of the subject's race, whereas obesity-related metabolic dysfunction may be seen at a lower BMI in Asians. We compare the test characteristics of the SAFE score in Asian versus non-Asian subjects with NAFLD.
Materials and Methods: The 2017–2018 National Health and Nutrition Examination Survey represents a population-based survey among US civilians, which included vibration-controlled transient elastography (VCTE). Adults (≥ 18 years) with NAFLD were selected based on controlled attenuation parameter (CAP) of ≥ 240 dB/m with other chronic liver diseases excluded (e.g., viral hepatitis and alcohol-associated liver disease). Each subject's SAFE score was calculated based on the established formula (medcalculators.stanford.edu/safe). Individuals were classified into high- and low-risk fibrosis groups based on liver stiffness measurement (LSM) threshold of 7 kPa. The negative predictive value (NPV) of the SAFE score was compared across races.
Results: A total of 2,575 individuals, including 412 Asians, met the inclusion criteria. In the Table, Asians happened to be the youngest and had the lowest BMI, whereas the prevalence of type 2 diabetes was similar in all races. When categorized by race-appropriate BMI thresholds, the proportions of overweight (29%) and obese (60%) subjects were not different between Asian and other races. Overall, Asians had the lowest SAFE score, whereas LSM was similar. When gauged by NPV, the SAFE score was most predictive of low-risk fibrosis in Asians (NPV = 94.3%) compared to other races (87.7%).
Conclusion: While the degree to which BMI reflects metabolic dysfunction associated with insulin resistance and NAFLD may differ among different racial groups, a SAFE score of < 0 may exclude clinically significant fibrosis nearly 95% of the time among Asian subjects with NAFLD.

Characteristics of study subjects. Data are shown as n (%) or median (IQR).

Characteristics	Total (n = 2,575)	NH Asian (n = 412)	NH White (n = 935)	NH Black (n = 554)	Hispanic (n = 674)
Age in years	56 (41 - 66)	52 (40 - 63)	60 (44 - 72)	56 (43 - 65)	54 (39 - 63)
Men, n (%)	50	51	53	47	49
Type II Diabetes, n (%)	20	20	19	21	20
BMI in kg/m^2	31 (27 - 35)	27 (24 - 30)	31 (27 - 36)	34 (29 -39)	31 (28 – 34)
LSM in kPa	5.3 (4.3 - 6.6)	5.1 (4.2 - 6.1)	5.3 (4.3 -6.7)	5.4 (4.3 - 6.9)	5.3 (4.3 - 6.7)
CAP Score in dB/m	295 (268 - 331)	289 (264 - 325)	299 (270 - 335)	289 (264 - 325)	298 (271 - 330)
SAFE score	27 (-48 - 85)	-9 (-67 - 54)	22 (-49 - 88)	41 (-17 - 102)	14 (-55 - 81)
NPV	89	94	88	89	85

Abbreviations: BMI, body mass index; LSM, liver stiffness measurement; kPa, kilopascals; CAP, controlled attenuation parameter; dB/m, decibels per meter; SAFE, Steatosis-Associated Fibrosis Estimator; NPV, negative predictive value

[OP-1094]

Ssaroglitazar, a new paradigm in the management of advanced liver fibrosis in NAFLD: A single-arm prospective study

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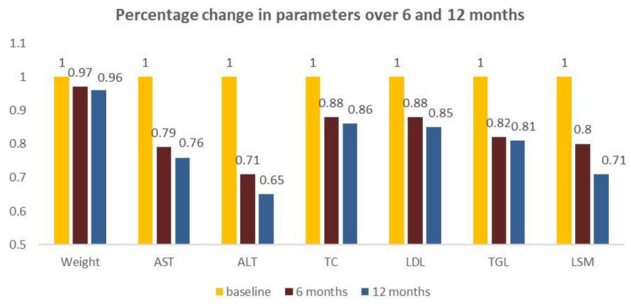
Objectives: NAFLD is fast becoming the leading cause of cirrhosis worldwide. But the pharmacotherapy of NASH remains elusive. This trial was conducted to study the effects of the dual PPAR agonist Saroglitazar on liver fibrosis, transaminases and lipid profile in NAFLD patients.
Materials and Methods: Investigator initiated single arm prospective study. Consecutive patients of NAFLD (2016 EASL Clinical Practice Guidelines) with transaminitis and liver stiffness (LSM) $\geq$ 7 kPa (by Transient Elastography) were started on Tab Saroglitazar 4 mg daily. Patients with pregnancy and lactation were excluded. AST/ALT, Lipid profile and LSM were measured at baseline, 6 months and 1 year.
Results: 90 patients were started on Saroglitazar. Data was analysed for all patients at 6 months and for the 57 patients who completed 1 year of therapy. At 6 months and 1 year, there was a significant reduction in transaminases (20.8% and 23.6% reduction for AST, 29.5% and 35.4% reduction for ALT, p = 0.00006). Mean liver stiffness reduced from 11.6 kPa at baseline to 9.4 at 6 months and 8.3 at 12 months (21.5% and 28.7% reduction, respectively, p = 0.000001). For those with advanced liver fibrosis at baseline (TE $\geq$ 9.9 kPa, n = 52), the reduction in LSM was 28.2% and 36% at 6 and 12 months, respectively. Total cholesterol, LDL and triglycerides reduced significantly (14.5%, 15.3% and 18.6% respectively at 1 year, $p < 0.05$). Therapy was also associated with significant weight reduction, both at 6 and 12 months (3.3% and 3.9% reduction respectively, p = 0.00004). No serious adverse effects were noted in any of the patients while on therapy.
Conclusion: Saroglitazar seems to be a promising option for reduction of liver stiffness and transaminitis in NAFLD with advanced fibrosis. Whether there is similar effect on liver histology remains to be proven by biopsy-based studies.



[OP-1104]

Azonal steatosis correlates with disease severity and poor outcome of non-alcoholic fatty liver disease

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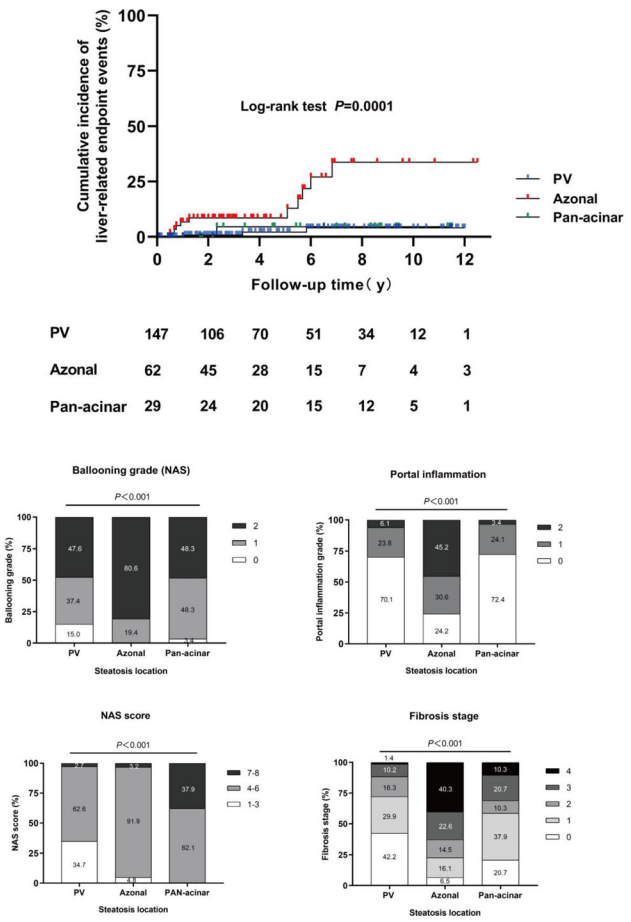
Objectives: Hepatic steatosis is an essential parameter for histological evaluation in NAFLD. However, the influence of the steatosis distribution pattern on the severity of disease and its prognostic value is still unclear. We aimed to evaluate the clinicopathological characteristics and the long-term prognosis of patients with different patterns of steatosis distribution.
Materials and Methods: The clinical and histological data of 238 biopsy proved NAFLD patients were reviewed. Both NASH-CRN and SAF/FLIP pathological systems were applied. Kaplan–Meier analysis was used to compare the cumulative incidence of liver-related endpoint events. Logistic regression was used to analyze the affecting factors of steatosis distribution.
Results: The cohort members were divided into three groups according to the distribution of steatosis: the PV (pericentral vein) group (n = 147, 62%), the Azonal group (n = 62, 26.1%), and the Pan-acinar group (n = 29, 12.1%). The ballooning grade, disease activity in the Azonal group were significantly higher than the PV and Pan-acinar groups ($p < 0.05$). In addition, the Azonal group had a higher fibrosis level than the other two groups ($p < 0.001$). Over a median follow-up of 3.7 years, we found the cumulative incidence of liver-related endpoint events in the Azonal group was significantly higher (HR 8.0; 95% CI, 2.34–27.35). Multivariate analysis showed that PNPLA3 rs738409 with CG /GG genotype (OR 3.717; 95%CI, 1.045–13.220), and age (OR 1.102; 95%CI, 1.053–1.152) were associated with the "Azonal steatosis" distribution pattern.
Conclusion: NAFLD patients with "Azonal steatosis" distribution pattern had higher disease activity, fibrosis stage and were more susceptible to have poor outcomes.



Alcoholic Liver Disease

[OP-0024]

Intestine-derived miRNAs in inflammation of distance organs

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Objectives: Ethanol (EtOH)-induced organ injury occurs at multiple molecular levels such as penetration of endotoxins, circulation of cytokines, release of pro-inflammatory RNAs, and even directly by EtOH in the blood stream. Circulating microRNAs (miRNAs) are generated by a number of tissues and organs. However, after exposure to EtOH, the intestine is the most prominent source of exosomal miRNAs. Although specific miRNAs released from intestines have previously been described, their exact release mechanisms have not been investigated.
Materials and Methods: Argonaute (AGO) proteins have been the focus of miRNA studies but we observed AGO-free mature miRNAs directly interacting with RNA-binding proteins. To investigate microRNA-binding proteins (miRBPs) globally, we used high-density protein arrays to identify RBP quaking (QKI) as a novel miRBP for let-7b.
Results: QKI inhibits exosomal release of let-7b likely by controlling the availability of let-7b for loading into exosomes, via additional miRBPs such as AU-rich element RNA-binding protein 1 (AUF1) and hnRNPK. The accelerated exosomal release of let-7b after QKI depletion activates the Toll-like Receptor 7 (TLR7), and promotes the production of proinflammatory cytokines in recipient cells resident in liver and brain leading to inflammatory responses.
Conclusion: Moreover, our miRNA-seq data of serum exosomes from heavy alcohol drinkers revealed that serum level of let-7b correlates with severity of liver injury implicating a prognostic marker of alcohol-induced organ injury.

[OP-0909]

Temporal multiomics analysis characterizes circulating molecular determinants associated with poor outcome in patients with severe alcoholic hepatitis

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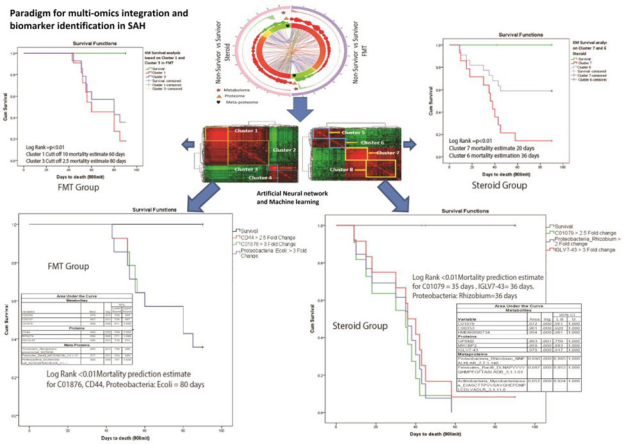
Objectives: Severe alcoholic hepatitis (SAH) has high morbidity, with steroid therapy providing 65% 28-day survival. Steroid non-responders (NR) have higher incidence of infections and mortality. Faecal microbiota transplant (FMT) is another emerging therapy for SAH patients. We investigated whether multi-omic studies and machine learning (ML) approaches could identify non-responders to corticosteroid or FMT at baseline.
Materials and Methods: Thirty SAH patients randomized in ongoing steroid vs. FMT protocol (Gov-no.NCT03091010) received either prednisolone (40 mg/day-7 days, responders for 4 weeks, n = 13) or FMT (daily; nasoduodenal-tube for 7 days, n = 17). Multi-omic analysis was performed at baseline, day-7 and day-28. Molecular determinants linked with non-response (NR) to steroid or FMT were identified and validated for survival outcomes in separate 70-SAH (NR = 21) patients using artificial neural networking (ANN) and ML.
Results: Baseline characteristics of derivative and validation cohorts were comparable. FMT temporally increased amino-acid metabolism, primary bile-acid biosynthesis, energy metabolism ($p < 0.05$). Steroid therapy temporally induced vitamin/fat metabolism ($p < 0.05$). Circulating meta-proteome alpha/beta diversity was temporally increased by FMT with increase in bacterial species; orientia, geobacter and streptococci. Steroid therapy added ($p < 0.05$) desulfovibro, clostridales and other species at day28. Compared with steroid therapy, FMT significantly reduced arachidonic acid and tryptophan metabolism, TLR and immune-cell activation, complement cascade and prostaglandin synthesis ($p < 0.05$) and increased antioxidant, vitamins, and energy metabolism ($p < 0.05$). Multi-omics profile of FMT non-survivors was distinct, and showed highest alpha-diversity with increase in actinobacteria and firmicutes ($p < 0.05$). Using multi-omics integration along with ANN and ML, specific molecular clusters were identified in non-survivors. Cluster-1 specific to complement, coagulation and leukotriene biosynthesis, cluster-3 (P38-MAPK) in the FMT arm and cluster-7 (complement, TLR activation) in the steroid arm significantly predicted mortality (Norm Imp > 95%, AUC > 0.90, log-rank < 0.01). Of these clusters; > 3Fold increase in molecules; CD44, 3-Oxosteroid and Proteobacteria; Ecoli for FMT and protoporphyrinogen-IX, MYCBP2, Proteobacteria; rhizobium for steroid arm were associated to higher mortality (AUC > 0.95; log-rank < 0.01).

Conclusion: Baseline levels of panel; CD44, 3-Oxosteroid, proteobacteria; E.coli, rhizobium protoporphyrinogen-IX and MYCBP2 can predict NR and non-survival in SAH patients.



Autoimmune and Cholestatic Disease

[OP-0505]

Add-on immunosuppressive therapy did not improve the long-term outcomes of primary biliary cholangitis with autoimmune phenomenon

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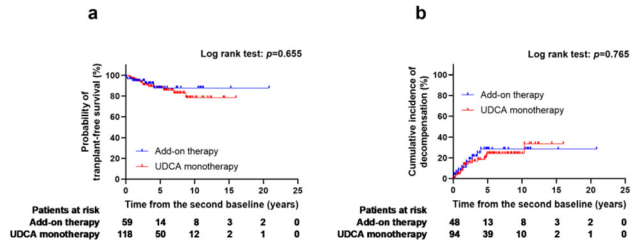
Objectives: Most primary biliary cholangitis (PBC) patients have elevated levels of transaminase or immunoglobulin G (IgG) but do not fulfill the criteria of PBC with autoimmune hepatitis (AIH) features in clinical practice. Whether this population would benefit from add-on immunosuppressive therapy is controversial.
Materials and Methods: We retrospectively analyzed all PBC patients with autoimmune phenomenon which was defined as PBC patients with higher IgG and/or transaminase, but did not fulfill the criteria of PBC with AIH features. We grouped these patients according to the use of add-on immunosuppressants and balanced their characteristics using 1:2 propensity score matching (PSM). Biochemical responses and long-term outcomes were compared in the matched cohorts.
Results: A total of 707 PBC patients with autoimmune phenomenon were included in the present study, with a median follow-up duration of 4.08 years (interquartile range: 1.83–7.25). After PSM, 59 patients in the add-on immunosuppressive therapy group were strictly matched with 118 patients in the UDCA (ursodeoxycholic acid) monotherapy group based on age, sex, cirrhosis, transaminase, IgG, and total bilirubin. After 1 year of add-on therapy, patients in the add-on therapy group had a higher biochemical rate based on normalization of transaminase and IgG ($p = 0.008$), but similar response rates per the Paris I, Paris II, and GLOBE criteria. Furthermore, no differences were observed in the cumulative incidence of decompensation and transplant-free survival between the two groups.

Conclusion: Add-on immunosuppressive therapy for PBC patients with autoimmune phenomenon improved the rate of transaminase and IgG normalization, but did not improve the long-term outcomes.



[OP-1123]

Liver inflammation activity in autoimmune hepatitis patients with normal ALT and IgG levels

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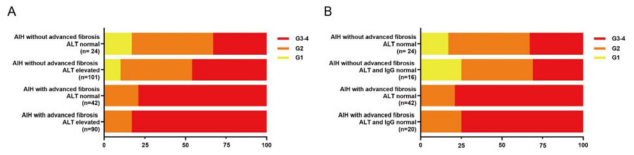
Objectives: Serum alanine transaminase (ALT) and IgG levels are considered as surrogate markers for histological activity in autoimmune hepatitis (AIH). We assessed the inflammatory activity in AIH patients with normal ALT and IgG levels.
Materials and Methods: 257 AIH patients underwent liver biopsy (LB) were retrospectively included from four medical centers. Liver inflammation and fibrosis were estimated by Scheuer scores. The definitions of advanced inflammation and fibrosis were $G \geq 3$ and $S \geq 3$, respectively.
Results: 163 (63.3%) AIH patients had advanced inflammation, while 125 (48.6%) patients had advanced fibrosis. The proportion of advanced inflammation was 62.1% in patients with normal ALT and 55.6% in patients despite normal ALT and IgG. The proportion of advanced inflammation was 44.0% in patients without advanced fibrosis and was 81.8% in those with advanced fibrosis. Of patients with advanced fibrosis, 78.6% (33/42) of patients with normal ALT presented advanced inflammation, which was 75.0% in patients with normal ALT and IgG. Among patients without advanced fibrosis, the proportion of advanced inflammation was as high as 33.3% in those with normal ALT and 31.3% in those despite normal ALT and IgG. Red cell distribution width was independently associated with advanced inflammation (OR: 1.521, 95%CI: 1.193–1.938, P = 0.001) in entire patients.
Conclusion: High proportion of advanced inflammation was found in AIH patients despite normal ALT and IgG levels even for those without advanced fibrosis. Though fibrosis can be ruled out by non-invasive methods in AIH patients with normal ALT and IgG, LB is encourage to assess inflammatory activity.



Metabolic and Genetic Disease

[OP-0260]

Hepatoprotective activity of pyrroloquinoline quinone and Gymnema sylvestre on oxidative stress and antioxidant status in diabetic mice

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Objectives: Pyrroloquinoline quinone (PQQ) and G.sylvestre leaves extract both are known to possess high antioxidative properties and can protect against several types of oxidative damages in diabetes mellitus (DM). However, the hepatoprotective activity of PQQ with compare to G.sylvestre in DM practically nothing has been studied so far. In the present investigation, we compare the hepatoprotective effects of PQQ with G.sylvestre in STZ-induced diabetic mice with an emphasis on oxidative damages and antioxidant status in the liver of diabetic mice.
Materials and Methods: Animals were randomly divided into 4 groups. Group I receiving only citrate buffer served as control; groups II to IV were rendered diabetes by a single dose of STZ (150 mg/kg), following which PQQ (20 mg/kg) and G.sylvestre (600 mg/kg) was administered to the animals of group III and IV respectively for 15 days. At the end of experimentation, alterations in the levels of diabetic indices; liver tissue peroxidation & antioxidants; and relevant serum indices including SGPT, SGOT, cholesterol & lipids, urea, etc. were evaluated.
Results: STZ-treated animals developed oxidative stress in the liver as indicated by a significant increase in tissue lipidperoxidation, serum SGPT, SGOT, glucose, cholesterol, triglyceride and urea, with a parallel decrease in the levels of tissue antioxidants and serum insulin. When diabetic animals received doses of PQQ & G.-sylvestre in groups III and IV respectively, these adverse effects were ameliorated. However, PQQ appeared to be more effective than G.-sylvestre extracts to ameliorate oxidative damages in the liver of diabetic mice.
Conclusion: These findings revealed for the first time that PQQ has better potential than G.sylvestre to mitigate STZ-induced oxidative damages in the liver of mice.

[OP-0983]

Genomic features of metabolic kinetics from early chronic liver disease to acute-on-chronic liver failure

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Objectives: Acute-on-chronic liver failure is a disease that develops in patients with acutely decompensated chronic liver disease which has an extremely high mortality. The prediction and prevention are important parts of the treatment. However, the metabolic molecular features during the progression from healthy, early chronic liver disease, compensated cirrhosis, decompensated cirrhosis to acute-on-chronic liver failure are still unclear. Here, we developed a disease progress-related metabolic genomic kinetics model to investigate metabolism-related molecular changes from healthy to acute-on-chronic liver failure. The metabolic kinetics model reveals the dynamic changes of liver metabolism in different stages of liver dysfunction.
Materials and Methods: We downloaded the data from the NCBI GEO database and begin the analysis of the GSE139602. After extracting the genes under the "Metabolism" category in KEGG database. We constructed a disease-progress-depended dynamic model by utilizing the R programing language, including vegan, limma, and Mfuzz packages. We divided the metabolism genes into different clusters according to the Calinsky criterion. After that, Gene set enrichment analysis is performed to find the important biological functions or modules in the different progress of the liver disease.
Results: By using the bioinformatics method, we defined 6 different clusters according the Calinsky criterion. The central line of found 270 differently expressed genes (DEGs) in the progress of formation of Non-alcoholic fatty liver disease. Gene set enrichment analysis is performed to find the enriched functions. We found that 13 metal ion transport or metabolism-related and 3 chemokine-related genes were enriched.
Conclusion: Our work revealed that there is another important role of LLPS, except for the cellular transcription-related, it's also metabolism-related. It helps us to understand more comprehensively the function of LLPS in the cancer cells, vice versa, metabolism may have a role in the progress of LLPS.

[OP-1128]

Variation and relationship of three dimensional structure like human liver, evaluation method of hepatotoxicity and conjugate like human liver

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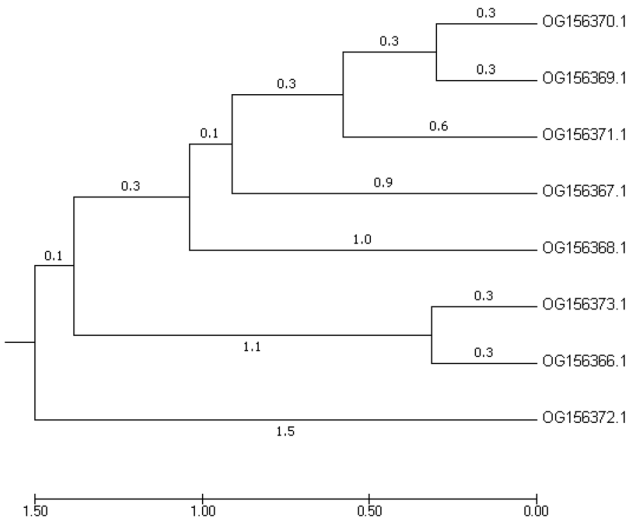
Objectives: DNA arrays capable of simultaneously measuring expression of thousands of genes in clinical specimens from affected and normal individuals have the potential to provide information about superior characteristics gene from organism. Genes can be used as markers for cell recruitment and activation molecules. This study aims to evaluate the variation and relationship of variation and relationship of three dimensional structure like human liver, evaluation method of hepatotoxicity and conjugate like human liver.
Materials and Methods: Data obtained from 8 nucleotide sequences on secondary data form on https://www.ncbi.nlm.nih.gov/. The phylogeny analysis of variations and relationships of DNA sequences Constructed with Neighbor Joining using MEGA 7.0 software.
Results: Based on the analysis of variations and relationships, it is known that on the dendogram, 8 sequences were divided into 2 main groups, namely groups A consisting of 7 specimens and groups B consisting of 1 specimens. The optimal tree with the sum of branch length = 7.53041418 is shown. The tree is drawn to scale, with

branch lengths (next to the branches) in the same units as those of the evolutionary distances used to infer the phylogenetic tree. This grouping is based on the existence of a similar genetic makeup equation with a high bootstrap value indicating the degree of kinship between specimens and the strength of the philogenous trees. Specimens that are in the same sub-groups show a degree of close kinship. On the other hand, specimens from different sub-groupss display distant kinship. Grouping was achieved on the basis of differences in expression levels across individual specimens.

Conclusion: It can be concluded that the variation and relationship of three dimensional structure like human liver, evaluation method of hepatotoxicity and conjugate like human liver sequence have highly variation. Information about kinship can be used as an informative source to assembly of superior genes in living of human cells.



Fibrosis and Cirrhosis

[OP-0508]

Anti-fibrotic properties of extracellular globins in vitro and in vivo: Old globins, new function

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Objectives: Anti-fibrotic therapy remains an unmet medical need in human chronic liver diseases. Recently, Cytoglobin (CYGB) was reported to inhibit hepatic stellate cells (HSCs) activation and their collagen production. We aim to study anti-fibrotic property of 4 human "Globins", i.e. tetramer Hemoglobin (HB), monomer-Myoglobin (MB), -CYGB, and -Neuroglobin (NG).

Materials and Methods: We produced recombinant human CYGB and NG. MB and HB were obtained from commercial source. We traced their bio-distribution after in vitro and in vivo administration and assessed their biological activities in cultured human HSCs (HHSteCs) or in mice with cirrhosis induced by intraperitoneal 0.5 ml/kg BW of Carbon tetrachloride (CCl_4) for 6 weeks.

Results: In a cell-free system, all globins demonstrated total antioxidant capacity higher than glutathione (0.5 mM). IC_{50} values of ROS-scavenging activity of human HB, MB, CYGB and NG were 0.43, 0.38, 2.4, and 25.2 μM, respectively. Cellular fractionation revealed that extracellularly added MB, NG, and CYGB, but not HB, penetrated HHSteCs and located in membrane, cytoplasm and cytoskeletal fractions. Extracellularly added MB, CYGB and NG, but not HB, dose dependently suppressed type I collagen production in spontaneous or TGFβ1-stimulated HHSteCs. RNA-seq analysis of MB, NG or CYGB-treated HHSteCs revealed the common downregulation of extracellular matrix-encoding and fibrosis-related genes, and the upregulation of antioxidant genes or inactivated markers of HSCs including GATA, EST2, and PPARγ. Disruption of disulfide bond in NG decreased heme activity, superoxide-scavenging activity, and collagen inhibition capacity. Intravenously injected MB or NG (1 mg/kg BW, twice/week for last two weeks of CCl_4) both markedly suppressed mouse liver fibrosis indicated by reducing collagen content, and αSma expression in the liver.

Conclusion: These findings revealed an unexpected and profound role for MB, NG and CYGB in maintaining HSCs in deactivated status and protect the mouse liver against cirrhosis, proposing the "globin therapy" as a new strategy to combat fibrotic liver disease.

[OP-0647]

Sarcopenia as A predictor of mortality and complications in cirrhosis patients-A prospective cohort study

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Objectives: To study the predictive role of sarcopenia on mortality and complications in cirrhosis patients. Sarcopenia is a promising tool for prognostication of cirrhosis.EWGSOP2 guidelines define sarcopenia based on muscle strength,muscle quantity or quality and physical performance.Many previous studies didn't use a standardized definition of sarcopenia and was based on skeletal muscle measurement by CT or MRI.Ultrasound guided thigh muscle thickness (TMT) measurement is a validated,cost effective and easy method for assessment of muscle quantity.There is paucity of Indian studies analysing prognostic role of sarcopenia in cirrhosis.This study was aimed at the same.

Materials and Methods: This was a prospective cohort study with 120 consecutive patients each in 'sarcopenia' and 'no sarcopenia groups'.Sarcopenia was diagnosed based on EWGSOP2 guidelines using ultrasound guided measurement of TMT.They were followed up for 6 months.Kaplan–Meier analysis with LogRank test was used to compare survival and Cox proportional-hazards model was used for multivariate analysis to determine risk factors of mortality.

Results: Cirrhosis patients with sarcopenia[N_1 = 120,M:F = 80:40,Median age-58yrs (51–64)] and without sarcopenia[N_2 = 120,M:F = 93:27,Median age-54yrs (46.25–60)] were enrolled.Six month cumulative survival was 56.7% and 76.7% in sarcopenia and no sarcopenia groups respectively (p = 0.001).Six month cumulative survival in severe and non severe sarcopenia was 23.9% and 70% respectively (p = 0.001).Age,sex,nutritional status, sarcopenia status, CTP score, MELD score, Bilirubin, Albumin, INR and Sodium were significantly associated with survival.A multivariate analysis showed sarcopenia (HR = 1.283,95%CI 1.092–2.130,p = 0.031),female sex (HR = 1.851,95%CI 1.106–3.097,p = 0.019), CTP class C (HR = 1.447,95%CI 1.252–1.794,p = 0.002) and MELD score > 15 (HR = 1.116,95%CI 1.056–2.203,p = 0.05) as independent predictors of mortality. Development of complications like ascites,HE,Covid infection and UGI bleed were significantly higher in

sarcopenia group, while SBP,AKI,cellulitis,UTI,HCC and ACLF were not statistically significant between two groups.
Conclusion: Sarcopenia is an independent prognostic marker of mortality in cirrhosis and is associated with increased risk of complications like ascites, HE, Covid infection and UGI bleed. Severe sarcopenia has even poorer outcome. It appears that addition of sarcopenia to existing scoring systems of cirrhosis will improve prognostication of patients.

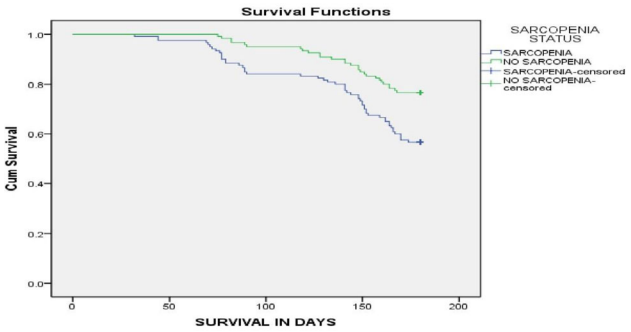

FIGURE 1.Survival curves in both groups(Log rank p=0.001)

[OP-0728]

Distinct functions of PSMP/MSMP in liver fibrogenesis and hepatocarcinogenesis.

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Objectives: Chemokines are a family of cytokines that orchestrate the migration and positioning of immune cells within tissues and are critical for the function of the immune system. PC3 secreted microprotein (PSMP) or microprotamine (MSMP) is a novel chemotactic cytokine discovered through genome-wide bioinformatics analysis and chemoattractant platform screening, which can act as a CCR2 ligand to recruit peripheral blood monocytes and lymphocytes. In the present study, we investigated the expression and role of PSMP in liver fibrosis/cirrhosis and hepatocellular carcinoma (HCC).
Materials and Methods: PSMP expression was studied in patients and murine models of fibrosis/cirrhosis and HCC. The role of PSMP in vivo was evaluated in PSMP gene knockout mice. The direct effects of PSMP on macrophages, hepatic stellate cells and tumor cells were studied in vitro.
Results: In this study, we found that PSMP is highly expressed in fibrotic/cirrhotic tissues from patients with multiple etiologies. PSMP is also overexpressed in human liver cancer-adjacent tissues, and its expression level is positively correlated with patients' survival. PSMP deficiency ($Psmp^{-/-}$) resulted in a marked amelioration of hepatic fibrosis, but promoted liver tumor growth in mice. In CCl_4-induced hepatic injury, the infiltration of $CCR2^+$ monocytes and macrophages into the liver is significantly decreased in $Psmp^{-/-}$ mice. In addition, knockout of PSMP can inhibit the infiltration of tumor-infiltrating $CD8^+$ lymphocytes and promote M2-polarization of tumor-associated macrophages (TAMs) in mice. At the cellular level, we found that PSMP can directly promote the M1 polarization of bone marrow-derived macrophages and the activation of LX-2 cells, and also inhibit the proliferation and migration of HCC cells.
Conclusion: In conclusion, PSMP can promote liver fibrosis, while inhibit liver carcinogenesis. These results indicate that PSMP may play different or even opposite functions in different stages of liver disease, suggesting that PSMP is a potential target for the treatment of chronic liver disease and HCC.

[OP-0766]

Alteration of gut microbiota and fecal short-chain fatty acids are associated with liver fibrosis in HIV and HIV/HCV co-infection

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Objectives: The alteration of gut microbiota is associated with human immunodeficiency virus (HIV) infection. Nevertheless, the relationships between HIV/HCV-coinfection, gut dysbiosis and short-chain fatty acids (SCFAs) including butyrate, are not well-characterized.
Materials and Methods: Fecal sample specimens obtained from 25 healthy controls, 46 patients with HIV, and 24 patients with HIV/HCV-coinfection were examined. Gut microbiome profiles and butyrate level (butyryl-CoA:acetateCoA-transferase gene) were assessed by 16S rRNA sequencing and quantitative PCR, respectively.
Results: Our data showed that microbial alpha diversity (Chao1) and butyrate levels in the HIV and HIV/HCV groups were declined compared with healthy controls. Moreover, butyrate levels were significantly associated with the abundant of SCFAs-producing bacteria including Blautia ($r = 0.327$, $P = 0.006$), Roseburia ($r = 0.483$, $P < 0.001$), Lachinopira ($r = 0.325$, $P = 0.006$), and Eubacterium ($r = 0.390$, $P = 0.001$). The reduction in these bacteria was also correlated with elevated serum aminotransferase, severity of liver fibrosis (FIB-4, APRI and transient elastography) and declined mucosal-associated invariant T (MAIT) cells. Additionally, the level of fecal butyrate was negatively correlated with liver stiffness assessed by transient elastography ($r = -0.248$, $P = 0.047$).
Conclusion: Decrease in fecal butyrate and the abundance of SCFAs-producing bacteria were correlated with the severity of liver fibrosis. These data suggest that gut dysbiosis and reduced SCFAs may involve in the pathogenesis of HIV and HIV/HCV infection.

Portal Hypertension and its complications

[OP-0861]

Safety and efficacy of large volume paracentesis in patients of cirrhosis with ascites and acute kidney injury (a pilot study)

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Objectives: We carried out a randomized controlled trial of conservative treatment versus Large Volume Paracentesis (LVP) in patients having cirrhosis with ascites and acute kidney injury (AKI) to study safety and efficacy of LVP in presence of AKI. (CTRI number: CTRI/2020/02/023602).
Materials and Methods: Consecutive patients of cirrhosis with ascites and AKI were randomized into two groups in ratio 1:1. Group A underwent LVP along with standard medical treatment (SMT) while Group B only received SMT, which included albumin, terlipressin and antibiotics. Apart from age, sex and etiology of cirrhosis, following parameters were also recorded for each patient at baseline, on day 1, 3 and 5, mean arterial pressure, heart rate, urinary output, serum urea, serum creatinine plasma renin activity and renal resistive index. Comparison between two groups was done by unpaired student t test (for continuous variables). $P < 0.05$ was considered statistically significant.
Results: A total of 50 patients were randomized into Group A (n = 26) and group B (n = 24) patients. All baseline parameters in the two groups including, sex ratio, etiology of cirrhosis, CTP, and MELD score were similar. The summary of the results is given in the table. Both the groups had shown significant improvement in clinical and renal functional parameters from baseline. The mean heart rate and mean arterial pressure fell in both groups as the treatment progressed. Average urine output progressively increased, and serum creatinine progressively decreased in both groups. No significant difference was noted between groups A and B.
Conclusion: LVP in presence of AKI does not lead to any adverse effect on clinical recovery, rise in urine output and fall in serum creatinine levels.

Table 1: Comparison of parameters between the groups

Variables	Group A				Group B			
	Baseline	Day 1	Day 3	Day 5	Baseline	Day 1	Day 3	Day5
Heart rate	86.00 ±5.33	83.02 ±5.05	81.15 ±5.09	79.30 ±5.15	86.29 ±5.01	84.08 ±5.05	82.45 ±5.05	80.83 ±4.54
Mean arterial pressure	80.11 ±11.57	75.44 ±5.05	71.36 ±5.09	69.88 ±11.11	79.95 ±9.65	76.29 ±5.05	72.39 ±5.05	71.33 ±9.15
Urine output(ml)	823.07 ±95.11	1025.02 ±97.74	1240.02 ±175.84	1388.46 ±359.25	841.67 ±97.43	985.61 ±107.33	1176.47 ±156.28	1275.00 ±375.61
Serum creatinine (mg/dl)	2.08 ±0.53	1.85 ±0.84	1.72 ±0.84	1.62 ±0.84	2.11 ±0.95	1.94 ±0.93	1.81 ±0.93	1.78 ±0.93

Group A- LVP + Standard medical treatment

Group B- standard medical treatment only

Acute Liver Failure and ACLF

[OP-0258]

Fibrinogen-like protein 2 promotes fulminant hepatitis by inducing neutrophil activation and neutrophil extracellular traps formation

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Objectives: We aim to investigate the role of fibrinogen-like protein 2 (fgl2) in regulating neutrophil and neutrophil extracellular traps (NETs) in fulminant hepatitis (FH).
Materials and Methods: Neutrophil amount and NETs formation were detected in serum and liver of wild type and $fgl2^{-/-}$ mice following murine hepatitis virus-3 (MHV-3) infection. Bone marrow-derived neutrophils were stimulated with MHV-3 in vitro to investigate the underlying mechanism of NETs formation.
Results: Concomitant with histopathology lesions and increased ALT and AST, abundant neutrophil accumulation and NETs formation were observed in mice following MHV-3 infection. NETs depletion significantly increased the survival rate (from 4 to 28%) of infected mice, implying that NETs contribute to FH progression. $Fgl2^{-/-}$mice showed remarkable reduction of myeloperoxidase levels, along with improved histopathology damage, decreased liver enzymes and expression of inflammatory cytokines. The expression of fgl2 on neutrophils was upregulated post MHV-3 infection. Fgl2 destruction reduced neutrophil accumulation in liver of the infected mice, and downregulated expression of hepatic ICAM-1, CXCL1, CXCL2 and CXCR2. Both in vivo and in vitro studies revealed that fgl2 promoted NETs generation through the ROS-dependent PAD4 pathway. Moreover, fgl2 directed fibrin deposition in NETs area, aggravating the following coagulation cascade and tissue lesions.
Conclusion: Fgl2 promotes FH progression partially via boosting hepatic neutrophil accumulation as well as facilitating NETs formation and subsequent liver injury. Thus, fgl2 might serve as a potential therapeutic target in FH.

[OP-0858]

The use of granulocyte-colony stimulating factor in patients with acute-on-chronic liver failure: A meta-analysis

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Objectives: Treatment options for acute-on-chronic liver failure (ACLF) remain limited at this time. Initial studies on the use of granulocyte colony-stimulating factor (G-CSF) shows promising results in decreasing mortality rates in ACLF. This study determined the efficacy of using G-CSF in addition to standard medical therapy (SMT) versus SMT alone in reducing mortality in patients with ACLF. The primary outcome of this study was mortality among patients with ACLF. Secondary outcomes include 90-day mortality, mortality due to gastrointestinal bleeding, and mortality due to sepsis.
Materials and Methods: A systematic search in MEDLINE, Cochrane CENTRAL, SCIENCEDIRECT, and SCIENCEOPEN - from inception up to October 2021 was made to identify randomized controlled trials that compare the use of G-CSF in addition to SMT versus SMT in the treatment of adults patients with ACLF. Random and fixed-effects model for dichotomous data using Mantel–Haenszel and Peto odds method were reported at 95% confidence interval (CI).
Results: Four randomized controlled trials involving 292 participants were analyzed (Fig. 1). Administration of G-CSF did not reduce overall mortality (RR 0.64, 95% CIs [0.38, 1.07], p = 0.09, I^2 = 74%, moderate certainty of evidence), 90-day mortality (RR 0.44, 95% CIs [0.12, 1.56], p = 0.02, I^2 = 73%, moderate certainty of evidence), mortality secondary to GI bleeding (OR 0.58, 95% CIs [0.25, 1.33], p = 0.20, I^2 = 43%, moderate certainty of evidence) and mortality secondary to sepsis (OR 0.50, 95% CIs [0.20, 1.26], p = 0.14, I^2 = 0%, moderate certainty of evidence).
Conclusion: This meta-analysis shows that the use of GCSF in ACLF shows no benefit and cannot be recommended as a standard of care for patients with ACLF. LT remains the definitive treatment for ACLF; however, these patients may present with numerous disease complications making LT futile. Further studies evaluating the effectiveness of G-CSF in patients with ACLF are recommended.

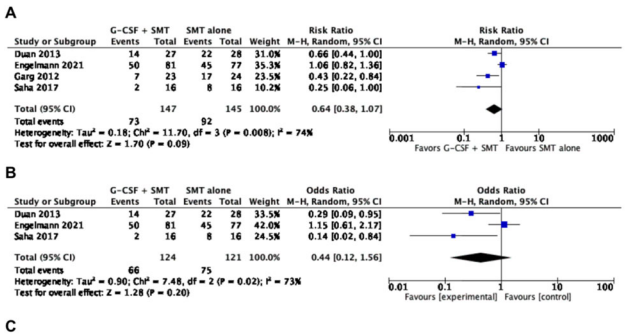

Figure 1. A. Forest plot of comparison: Over-all mortality between G-CSF + SMT and SMT alone in ACLF. **B.** Forest plot of comparison: 90-day mortality between G-CSF + SMT and SMT alone in ACLF. **C.** Forest plot of comparison: deaths due to GI bleeding between G-CSF + SMT and SMT alone in ACLF. **D.** Forest plot of comparison: deaths due to sepsis between G-CSF + SMT and SMT alone in ACLF.

[OP-0888]

Etiology and prognosis of acute liver failure in Korea: A nationwide multicenter study

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Objectives: Acute liver failure (ALF) is rare, but a disease with a high mortality rate. In this study, we evaluated clinical features, presumed etiology, and outcomes of patients with ALF in Korea. In addition, we compared the performance of various prognostic models of ALF.
Materials and Methods: A total of 653 ALF patients who admitted at 26 nationwide centers in Korea from January 2010 through December 2019 were included in the study.
Results: Acute hepatitis A was the most common cause of ALF (n = 215, 32.9%), followed by herb/supplemental agents use (15.5%, n = 101), acute hepatitis B (15.3%, n = 100), and drug-induced liver injury (8.9%, n = 58). Approximately, 10% of cases remained unknown (indeterminate, n = 70). Of the 642 traceable patients, 232 (36.1%) survived without transplantation more than 1 month after diagnosis of ALF. Transplant-free survival rates varied according to the etiologies, which was higher than 60% in acetaminophen, hepatitis A and pregnancy-induced, and lower than 20% in Wilson's disease, hepatitis B and autoimmune-related cases. A risk-prediction model for hepatitis A-related ALF (ALFA score) showed the highest discrimination in prediction of transplant or death at 1 month (c-statistic, 0.853; 95% confidence interval [CI], 0.816–0.891) versus

Model for End-stage Liver Disease (c-statistic, 0.807; 95% CI, 0.764–0.849), U.S. Acute Liver Failure Study Group index (c-statistic, 0.801; 95% CI, 0.758–0.844) and King's College criteria (c-statistic, 0.704; 95% CI, 0.663–0.746) (all $P < 0.01$).
Conclusion: Acute hepatitis A, herb/supplemental agents, and acute hepatitis B were most common causes of ALF in Korea recently. The ALFA score may be helpful to predict early outcome and manage patients with ALF.

Liver Cancer—Clinical

[OP-0031]

A novel mRNA signature associated with immune microenvironment to predict survival and response to immunotherapy in hepatocellular carcinoma

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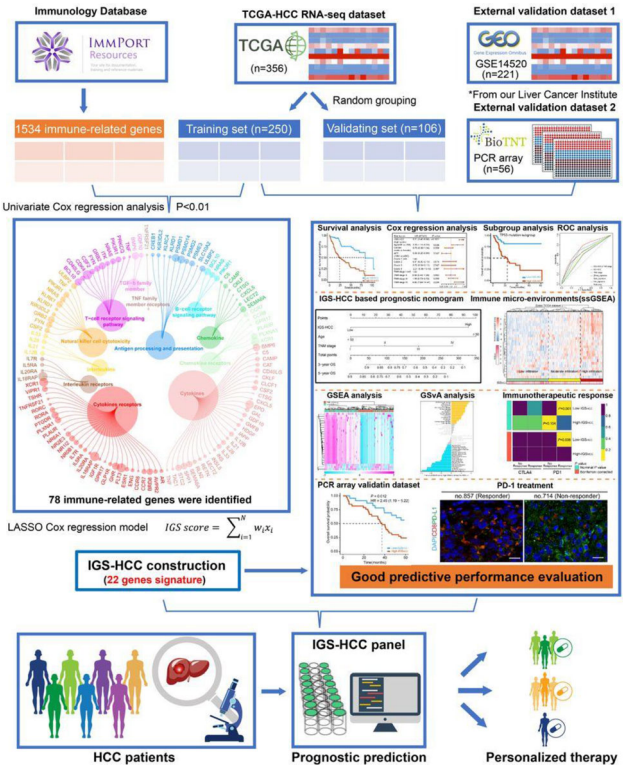
Objectives: Hepatocellular carcinoma (HCC) is the most common primary liver cancer with increasing incidence and mortality rates. Given the limited treatments of HCC and promising application of immunotherapy for cancer, we aimed to identify an immune-related prognostic signature that can predict overall survival (OS) rates and immunotherapy response in HCC.
Materials and Methods: The initial signature development was conducted using a training dataset from The Cancer Genome Atlas followed by independent internal and external validations from this resource and the Gene Expression Omnibus. A signature-based nomogram was generated using multivariate Cox regression analysis. The associations of signature score with tumor immune phenotype and response to immunotherapy were analyzed using single-sample gene set enrichment analysis and tumor immune dysfunction and exclusion algorithm. A cohort from Zhongshan Hospital was employed to verify the predictive robustness of the signature regarding prognostic risk and immunotherapy response.
Results: The prognostic signature, named IGS_{HCC} and consisting of 22 immune-related genes, possessed independent prognostic ability with training and validation cohorts. Also, IGS_{HCC} stratified HCC patients with different outcomes in subgroups. The prognostic accuracy of IGS_{HCC} was better than three reported prognostic signatures. The IGS_{HCC}-based nomogram exhibited high accuracy and significant clinical benefits in predicting 3- and 5-year OS likelihood. IGS_{HCC} may have reflected distinct immunosuppressive phenotypes in low- and high-score groups. Patients with low IGS_{HCC} scores were more likely than those with high scores to benefit from immunotherapy.
Conclusion: IGS_{HCC} is a powerful signature for predicting HCC prognosis and response to immunotherapy, contributing to individualized clinical management.



[OP-0101]

Sorafenib versus nivolumab after failed lenvatinib treatment in patients with advanced hepatocellular carcinoma

Yuna Kim[1], Jae Seung Lee[1], Hye Won Lee[1], Beom Kyung Kim[1], Jun Yong Park[1], Do Young Kim[1], Sang Hoon Ahn[1], Myung Ji Goh[2], Wonseok Kang[2], Seung Up Kim[1]

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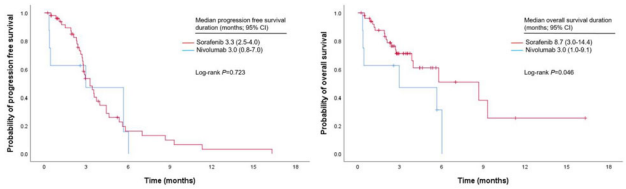
Objectives: An optimal sequential anti-hepatocellular carcinoma (HCC) agent that can be used after failed lenvatinib treatment has not been established. Here, we compared the outcomes of sorafenib and nivolumab as second-line agents after failed lenvatinib treatment in patients with advanced HCC.
Materials and Methods: Patients with advanced HCC who had received sorafenib or nivolumab as second-line agents after failed lenvatinib treatment were recruited from two Korean tertiary institutions between November 2018 and June 2020.
Results: The median age of the 60 participants (52 treated with sorafenib and eight treated with nivolumab) at baseline was 56.8 years. The demographic, laboratory, and tumor variables, as well as lenvatinib treatment duration, were similar between the two groups. The median durations of sorafenib and nivolumab treatment were 1.2 and 2.6 months, respectively ($p = 0.164$). Twenty-four (40.0%) patients died during the follow-up period (median, 15.8 months). The median overall survival (OS) of the study population was 5.8 months. The median OS of patients treated with sorafenib was significantly longer than the median OS of patients treated with nivolumab (8.7 vs. 3.0 months, $p = 0.046$, log-rank test). Sorafenib treatment (vs. nivolumab) was independently associated with a lower risk of mortality (hazard ratio = 0.194, 95% confidence interval: 0.053–0.708; $p = 0.013$). Worse ECOG performance status,

larger maximal tumor size, lymph node metastases, and higher total bilirubin levels were independently associated with increased mortality risk (all $p < 0.05$).
Conclusion: Lenvatinib-sorafenib sequential treatment resulted in significantly better survival did than lenvatinib-nivolumab sequential treatment in patients with advanced HCC. Larger studies are needed to validate our results.



[OP-0142]

Factors predicting extrahepatic metastasis of hepatocellular carcinoma after curative surgical resection

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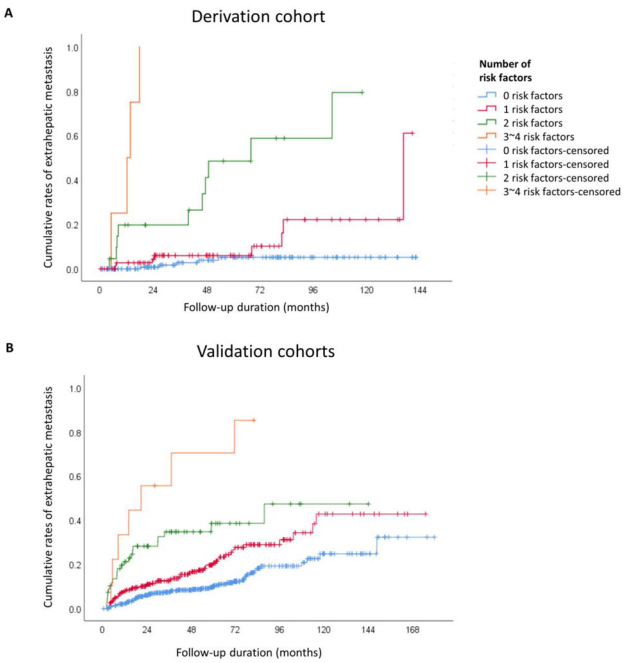
Objectives: Factors associated with extrahepatic metastasis (EHM) after curative treatment of hepatocellular carcinoma (HCC) have rarely been investigated. This study was aimed to evaluate the EHM after curative resection in patients with HCC.
Materials and Methods: We retrospectively reviewed data from treatment naïve HCC patients and enrolled patients who underwent curative resection for the treatment of HCC from 2004 to 2019 at three tertiary hospitals. We evaluated the characteristics of recurrence after resection and analyzed the predictors associated with EHM. The predicting factors were internally validated in JBNU cohort and then externally validated in other cohorts.
Results: A total of 1,069 HCC patients (derivation cohort 278 and validation cohort 791) treated with surgical resection were enrolled for the study. The mean age was 59.1 ± 10.2 years and 85.8% of patients were male. Baseline characteristics were generally similar between the derivation cohort and the validation cohort. During the follow-up period, there were 165 EHM cases (derivation cohort 27 and validation cohort 138). Multivariate Cox regression analysis for EHM was performed in the derivation cohort, and non-single tumor, serosal invasion, vascular invasion, and ALBI grade ≥ 2 were independently associated factors with statistical significance. The cumulative rate of EHM was well distinguished by the aforementioned factors. Of note, the cumulative rate of EHM was well distinguished even when divided by the number of risk factors. Next, the EHM probability was evaluated in the validation cohort by the risk factors analyzed in the derivated cohort, and the results were also well distinguished by the number of risk factors.
Conclusion: Non-single tumor, serosal invasion, vascular invasion, and ALBI grade ≥ 2 were risk factors for EHM in patients with HCC who underwent curative resection. The cumulative rate of EHM was significantly distinguished in both derivation and validation cohorts, depending on the accompanying number of risk factors.



[OP-0178]

Role of The Prophagocytic Signal Calreticulin in Hepatitis C Virus-Related Hepatocellular Carcinoma: Relation to Tumor Progression

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Objectives: Programmed cell removal (PrC is a process of macrophage-mediated immunosurveillance by which tumor cells are recognized and phagocytosed. Calreticulin (CALR) is one of the key players in the activation of PrCR and when expressed on the cell surface, it acts as a "eat-me" signal for multiple human cancers initiating phagocytosis. The aim of the present work was to study the role of the prophagocytic signal CALR in hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC) in relation to tumor progression.
Materials and Methods: 55 treatment-naïve patients with HCV-related liver cirrhosis (25 patients without HCC and 30 patients with HCC) and 15 healthy subjects were enrolled in the study. Quantification of CALR levels in serum was performed using enzyme-linked immunosorbant assay. The staging of HCC was determined according to the Barcelona Clinic Liver Cancer staging system (BCLC). Liver specimens were obtained from 19 patients without HCC and 23

patients with HCC. Tumor histological grading was performed according to Edmonson and Steiner's criteria. Immunohistochemical staining for cirrhotic and HCC tissues was done using mouse monoclonal antibody against CALR and was scored semi-quantitatively according to the intensity of the staining (score 0–3).
Results: Serum CALR levels were significantly higher in cirrhotic patients with and without HCC than in healthy subjects and in patients with HCC than in those without HCC ($P < 0.001$). HCC tissues showed a significant increase in CALR expression compared with tissues obtained from cirrhotic patients without HCC and the surrounding non-neoplastic liver tissues ($P < 0.05$). Serum CALR levels and intratumoral CALR expression in patients with HCC were positively correlated and both showed inverse correlations with serum alpha fetoprotein, BCLC stage and tumor maximum diameter and histological grade (table 1).
Conclusion: Calreticulin was upregulated in HCV-related HCC and negatively regulated tumor growth. Enhancing CALR function could be a promising target for HCC immunotherapy.

Table 1: Statistical correlations ("r" value) between serum calreticulin (CALR) levels (ng/ml), tumor CALR expression and other parameters in cirrhotic patients with hepatocellular carcinoma.

	Serum CALR (ng/ml) (n = 30)		Tumor CALR expression (n = 23)	
	r	P	r	P
Age (years)	-0.353	0.056	-0.294	0.173
Serum AST (U/L)	-0.500	0.005	-0.531	0.009
Serum ALT (U/L)	-0.611	<0.001	-0.615	0.002
Serum GGT (U/L)	-0.533	0.002	-0.480	0.020
Serum HCV RNA (x10^3 IU/ml)	-0.619	<0.001	-0.582	0.004
Serum AFP (ng/ml)	-0.591	0.001	-0.535	0.009
Child-Pugh score	-0.571	0.001	-0.702	<0.001
MELDNa score	-0.422	0.020	-0.485	0.019
HCC maximum diameter (cm)	-0.455	0.012	-0.487	0.018
BCLC stage	-0.420	0.021	-0.541	0.008
Histological activity grade	-0.689	<0.001	-0.461	0.027
Steatosis grade	-0.326	0.129	-0.255	0.241
HCC histological grade	-0.638	0.001	-0.543	0.007
Tumor CALR expression	0.456	0.029	-	-

[OP-0185]

Sarcopenia predict the outcomes in patients with hepatocellular carcinoma treated by trans-arterial radioembolization

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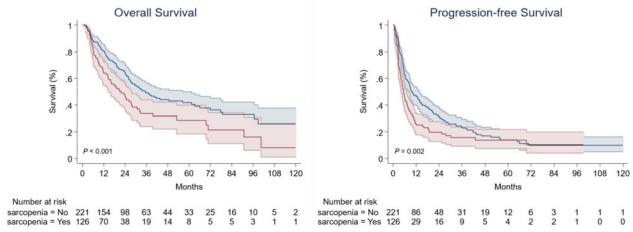
Objectives: Trans-arterial radioembolization (TARE) is a form of radiation therapy performed by selective intra-arterial injection of microspheres loaded with Yttrium-90 in hepatocellular carcinoma (HCC). The aim of this study is to identify prognostic factors for overall survival (OS) and progression free survival (PFS) in patients with HCC undergoing TARE.
Materials and Methods: This is a multi-center retrospective study on consecutive HCC patients undergoing TARE from Jul 2009 to May 2019. Using pre-treatment plain computed tomography imaging, the total cross-sectional area (cm2) of abdominal skeletal muscle at the third lumbar vertebra was measured. The skeletal muscle index (SMI) was calculated by normalizing muscle area to patient height.
Results: A total of 347 patients were included in the study (mean age 66 years, 284 male patients). 107 patients (30.8%) had portal vein tumor thrombus (PVTT). 126 patients (36.3%) were classified as sarcopenia. Median 5-year OS was 31.3 months (95% CI 24.7–37.9) and median 12-month PFS was 9.7 months (95% CI 8.0–11.4). Sarcopenia (HR, 1.44; 95% CI, 1.01–2.04, p = 0.04), PVTT (HR, 1.70; 95% CI, 1.13–2.56, p = 0.01), hypoalbuminemia ($\leq$ 3.5 g/dL) (HR 1.64; 95% CI 1.17–2.30, $p < 0.01$), and prior treatment experience (HR 1.61; 95% CI 1.00–2.57, p = 005) were independently associated with poor 5-year OS by multivariate Cox regression analysis. Sarcopenia, PVTT, multifocal tumor, and prior treatment experience were independent predictors of PFS in multivariate analysis.
Conclusion: TARE is an effective therapy for patients with advanced HCC. In patients undergoing TARE, Sarcopenia and PVTT are independent predictors of both OS and PFS.



[OP-0226]

A Real-world comparative analysis of transarterial chemoembolization plus external beam radiotherapy vs sorafenib in hepatocellular carcinoma with macroscopic vascular invasion

Myung Ji Goh[1], Jong-In Chang[1], Dong Hyun Sinn[1], Moon Seok Choi[1], Wonseok Kang[1], Geum-Youn Gwak[1], Yong-Han Paik[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1]

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Objectives: Transarterial chemoembolization plus external beam radiotherapy (TACE-RT) had shown better outcomes compared to sorafenib for hepatocellular carcinoma (HCC) with macroscopic vascular invasion in a randomized clinical trial. This study aimed to compare clinical outcomes between TACE-RT and sorafenib in real-world practice setting.
Materials and Methods: A total of 241 treatment-naïve patients with liver-confined HCC showing macroscopic vascular invasion, and received TACE-RT (n = 190) or sorafenib (n = 51) as an initial treatment were analyzed. Overall survival (OS) and progression-free survival (PFS) based on modified Response Evaluation Criteria in Solid Tumors (mRECIST) were evaluated.
Results: TACE-RT showed significantly better OS compared to sorafenib (54.0% vs. 19.6% at 12-months, $P < 0.001$). However, patients treated with sorafenib showed poorer performance status, poorer liver function and more advanced tumor characteristics than patients treated with TACE-RT. In the multivariable-adjusted analysis, TACE-RT was an independent prognostic factor for OS (hazard ratio [HR] 0.53, 95% confidence interval [CI] 0.36–0.78, P = 0.001). Early treatment discontinuation was observed for 7 (3.7%) patients in TACE-RT group and 15 patients (29.4%) in sorafenib group (who discontinued sorafenib within a month). Among 219 patients who completed TACE + RT or one month of sorafenib treatment, TACE-RT showed significantly better OS compared to sorafenib (56.1% vs. 22.2% at 12-months, $P < 0.001$).
Conclusion: In this real-world cohort study, TACE-RT showed better OS than sorafenib for liver-confined HCC showing macroscopic vascular invasion, which cannot be explained by differences in

baseline characteristics. This suggest TACE-RT can be preferred option over sorafenib for these patients.

[OP-0315]

Comparison between stereotactic body radiotherapy and radiofrequency ablation as first therapy for small hepatocellular carcinoma

Baek Gyu Jun[1], Han Ah Lee[1], Young Don Kim[2], Gab Jin Cheon[2], Sae Hwan Lee[3], Hong Soo Kim[3], Jeong-Ju Yoo[4], Sang Gyune Kim[4], Young Seok Kim[4], Soung Won Jeong[5], Jae Young Jang[5], Young Chang[5]

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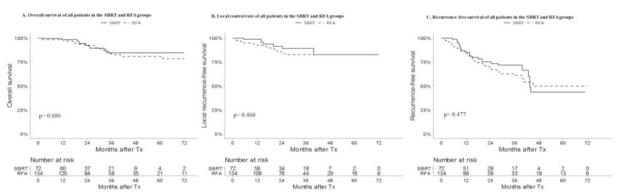
Objectives: Resection or ablative therapy is not indicated for many patients with hepatocellular carcinoma (HCC) because of advanced cirrhosis or tumor location. Stereotactic body radiotherapy (SBRT) may be an alternative treatment for these patients. This study compared the therapeutic effects of radiofrequency ablation (RFA) and SBRT in patients with small ($\leq$ 3 cm) HCC.
Materials and Methods: Data of HCC patients who underwent SBRT or RFA as an initial treatment at four tertiary referral hospitals between March 2011 and February 2017 were reviewed. The patient inclusion criteria were a single nodule measuring $\leq$ 3 cm in size and not suitable for resection.
Results: SBRT and RFA were performed in 72 (SBRT group) and 134 (RFA group) patients, respectively. The 1-, 3- and 5-year overall survival rates were 9.0%, 84.4%, and 84.4%, respectively, in the SBRT group compared with 97.9%, 83.9%, and 80.8%, respectively, in the RFA group, with no significant difference between the two groups (P = 0.686). The estimated five-year local control (LC) rate were 82.7% in the SBRT group and 82.8% in the RFA group (P = 0.460). In the SBRT group, 34 patients received SBRT only and 38 patients received SBRT combined with transarterial chemoembolization (TACE). There were no difference between SBRT only and SBRT with TACE in overall survival (p = 0.591) and LC rate (p = 0.380).
Conclusion: SBRT is an effective and safe treatment method for small HCCs, with survival and tumor recurrence rates similar to those of RFA.



[OP-0338]

Predictors of survival in untreated hepatocellular carcinoma patients in Korea: Analysis of a Nationwide Cancer Registry Database

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Objectives: There have been few studies regarding the natural history of untreated HCC patients. In this retrospective cohort study, we aimed to determine the natural history and the predictors of survival in patients with untreated HCC in an endemic area of HBV infection, using a large national cancer registry database.
Materials and Methods: We identified 1,045 untreated HCC patients registered at the Korean Primary Liver Cancer Registry between 2008 and 2014, with follow up ending in 2018, who had not received any treatments. Clinical characteristics between groups of patients who survived under 12 months and over 12 months were analyzed. Cox proportional regression model was used to identify variables associated with patient survival.
Results: The mean age of untreated patients at HCC diagnosis was 59.55 years and most patients had hepatitis B virus infection (52.1%). Most untreated patients (94.2%) died within the observation period; the median survival time was 3.0 months. Median survival times for each BCLC stage were 31.0 months for stage 0/A (n = 123), 10.0 months for stage B (n = 96), 3.0 months for stage C (n = 599), and 1.0 month for stage D (n = 227). Univariate analyses demonstrated that BCLC stage, Child–Pugh class, MELD score, serum AFP level, ECOG performance status, ascites, encephalopathy, tumor number, tumor size, portal vein invasion were highly significant predictors of overall survival ($P < 0.0001$). Multivariable cox regression analysis demonstrated that BCLC stage D (HR = 4.282, $P < 0.0001$), MELD score $\geq$ 10 (HR = 1.484, $P < 0.0001$), serum AFP level $\geq$ 1,000 (HR = 1.506, $P < 0.0001$) were associated with worse survival outcome in untreated HCC patients.
Conclusion: This is the first report demonstrating the factors affecting the survival outcomes of the untreated HCC patients in Korea. Advanced BCLC stage, serum AFP level $\geq$ 1,000 and MELD scores $\geq$ 10 were significantly associated with overall survival in untreated HCC patients.

[OP-0421]

Radiofrequency ablation and other local interventions for non-surgical cases of early hepatocellular carcinomas: A network meta-analysis of randomized controlled trials

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Objectives: Although various interventional and radiation techniques with differential pros and cons have challenged RFA for early hepatocellular carcinomas (HCCs), there is neither clear evidence nor consensus on their hierarchy for therapeutic indication and

effectiveness. We aimed to quantitatively evaluate whether RFA should be still considered as a single primary option in such patients using a network meta-analysis.
Materials and Methods: We systematically searched MEDLINE, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials databases for randomized trials concerning the efficacy of loco-regional therapies for HCCs < 5 cm of any number without extrahepatic spread or portal invasion. Primary outcome of interest was the pooled hazard ratio (HR) for overall survival (OS); and secondary outcomes included overall and local progression-free survival (PFS). A Bayesian network meta-analysis was performed and relative ranking of therapies was assessed with surface under the cumulative ranking (SUCRA) probabilities.
Results: Overall, 19 studies comparing 11 different strategies in 2,793 patients were included. Compared with RFA alone, chemoembolization plus RFA was ranked best for improving OS (HR 0.52, 95% confidence interval [CI] 0.33–0.82; SUCRA = 0.951). Pair-wise comparisons demonstrated comparable effects on OS between RFA and other single modalities such as cryo-, microwave-, and laser ablations, and proton-beam therapy. For overall PFS, only chemoembolization plus RFA had significantly better than RFA in a network pooling 10 trials reporting 8 treatment options (HR 0.61, 95% CI 0.42–0.88; SUCRA = 0.964), albeit not for local RFS. Therapies pooled in the networks other than percutaneous ethanol or acetic acid injection did not have any difference in both progression outcomes when compared with RFA.
Conclusion: Statistical comparisons using a network method suggest that chemoembolization combined with RFA is the best option that should be primarily considered to locally treat early HCCs. Cases with potential contraindications for RFA may benefit from a tailored approach using other effective thermal or radiation modalities.

[OP-0469]

External validation of the FSAC model using on-therapy response of noninvasive fibrosis markers in patients with chronic hepatitis B; A multicenter study

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Objectives: Potent antiviral therapy (AVT) induces not only regression of non-invasive fibrosis markers (NFMs), bur also reduction of hepatocellular carcinoma (HCC) risk among chronic hepatitis B (CHB) patients. We externally validated predictive performances of a recently suggested HCC prediction model using on-therapy NFM response, i.e. FSAC model, among the independent cohort.
Materials and Methods: Our multicenter study consecutively recruited treatment-naive CHB patients receiving potent AVTs for > 18 months between 2007 and 2018. Patients with decompensated cirrhosis or HCC at baseline were excluded. The predictive performances of FSAC model were assessed using Harrell's c-index, in comparison with other HCC risk-prediction models.
Results: Among the entire population (n = 3026), the median age was 50.0 years with male predominance (61.3%) and 1391 (46.0%) patients had cirrhosis. During follow-up (median 64.0 months), HCC developed in 303 (10.0%) patients. Patients with low FIB-4 or APRI at 12 months showed significantly lower HCC risk than those with high NFMs at 12 months (all $P < 0.05$). Cumulative 3-, 5-, and 8-year HCC probabilities were 0.0%, 0.3% and 1.2% in low-risk group (FSAC score $\leq$ 2), 2.1%, 5.2%, and 11.1% in intermediate-risk group (FSAC score 3 − 8), and 5.2%, 15.5%, and 29.8% in high-risk group (FSAC score $\geq$ 9), respectively (both $P < 0.001$ between each adjacent pair). Harrell's c-index of FSAC score (0.770) was significantly higher than those of PAGE-B (0.725), modified PAGE-B (0.738), modified REACH-B (0.737), LSM-HCC (0.734), and CAMD (0.742). Simplified version of FSAC score, i.e. FSAC (2) including only NFMs at 12 months also showed high c-index (0.763).
Conclusion: This external validation study showed that FSAC model which includes on-therapy response of NFMs had the better predictive performances than the models using only baseline parameters. For predicting HCC development, accurate measurement of intra-hepatic fibrotic burden during adequate AVT is necessary.

[OP-0538]

Prognostic impact of serum soluble PD-1 and ADV score for living donor liver transplantation in patients with previously untreated hepatocellular carcinoma

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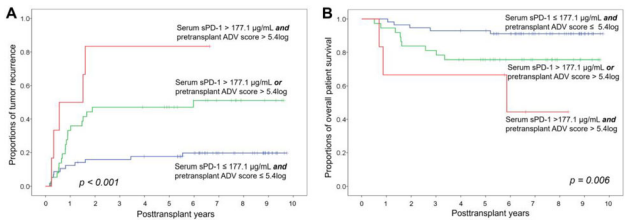
Objectives: The programmed death protein 1 (PD-1) pathway is the critical mechanism in development of hepatocellular carcinoma (HCC). The present study analyzed the prognostic impact of pre-transplant serum soluble PD-1 (sPD-1) concentration and α-fetoprotein– des-γ-carboxyprothrombin–tumor volume (ADV) score in patients with previously untreated HCC undergone liver transplantation (LT).
Materials and Methods: This retrospective single-center study enrolled 100 patients with HCC who underwent living donor LT from 2010 to 2016. Concentrations of sPD-1 were measured in stored serum samples.
Results: Receiver operating characteristic curve analysis of 2-year tumor recurrence resulted in an sPD-1 cutoff of 177.1 μg/mL, which was associated with higher rates of tumor recurrence ($p = 0.022$), but not with overall patient survival ($p = 0.460$). The derived cutoff for pretransplant ADV score was 5.4log, which was associated with higher tumor recurrence rate ($p < 0.001$) and lower overall patient survival rate ($p < 0.001$). Both sPD-1 > 177.1 μg/mL (hazard ratio [HR] = 2.26, $p = 0.020$) and pretransplant ADV score > 5.4log (HR = 3.56, $p < 0.001$) were independent risk factors for post-transplant HCC recurrence. The combination of these two factors enabled the stratification of patients into three groups, with groups having 0, 1 and 2 risk factors differing significantly in the prognosis of tumor recurrence ($p < 0.001$) and overall patient survival ($p = 0.006$).
Conclusion: Both sPD-1 concentration and ADV score have prognostic impacts in patients who underwent LT for untreated HCCs. These factors, both individually and combined, can help in predicting post-transplant prognosis.



[OP-0587]

Risk factors and Long-term prognosis of beyond-Milan recurrence after hepatectomy for BCLC stage 0/A hepatocellular carcinoma: A multicenter observational study

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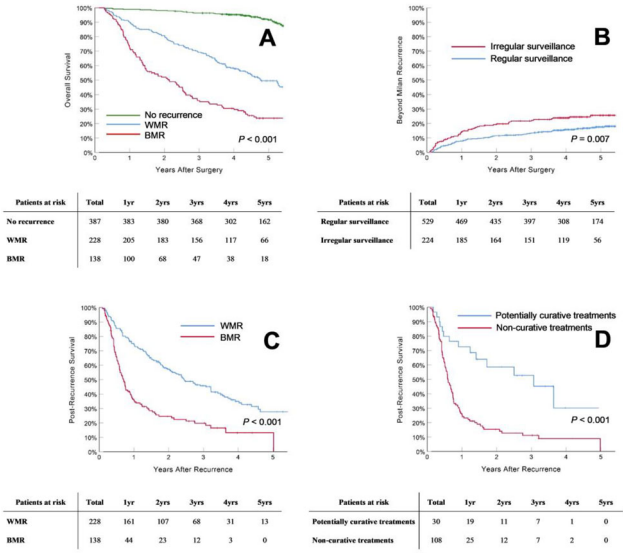
Objectives: In-depth understanding of the extent pattern of recurrence is critical to improve long-term surgical efficacy for patients with hepatocellular carcinoma (HCC). This study aimed to identify risk factors and long-term prognosis of beyond-Milan recurrence (BMR) after hepatectomy for early-stage (BCLC stage 0/A) HCC.
Materials and Methods: Multicenter data of patients who underwent curative hepatectomy for BCLC 0/A HCC were retrospectively analyzed. Risk factors of BMR and predictors of post-recurrence survival (PRS) in patients with BMR were identified by univariate and multivariate Cox-regression analyses.
Results: Among 753 analytic patients, 138 (18.3%) developed BMR at a median follow-up of 51.8 months. Among these 138 patients, 53 (38.4%) didn't receive regular recurrence surveillance, which was defined as surveillance every < 3 months within 1 year after surgery and every < 6 months in the subsequent years. Independent risk factors of BMR included preoperative alpha-fetoprotein level > 400 ng/mL, tumor size > 5.0 cm, multiplicity, microvascular invasion, and no/irregular recurrence surveillance. The median PRS of patients with BMR was only 8.4 months (95%CI: 7.0–9.8). Multivariate analysis showed that Child–Pugh grade B/C, early recurrence within 1 years after surgery, macrovascular invasion and/or distant metastasis, and non-curative treatment for recurrence were independent predictors of poorer PRS for patients with BMR.
Conclusion: Nearly 1 in 5 patients occurred BMR following hepatectomy for early-stage HCC with very poor post-recurrence prognosis. No/irregular recurrence surveillance was identified as an independent risk of BMR. As such, enhancing regular surveillance strategy is an important controllable measure to reduce BMR and improve long-term prognosis for patients undergoing hepatectomy for HCC.



Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
No recurrence	387	383	380	368	302	162
WMR	228	205	183	156	117	66
BMR	138	100	68	47	38	18

Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
Regular surveillance	529	469	435	397	308	174
Irregular surveillance	224	185	164	151	119	56

Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
WMR	228	161	107	68	31	13
BMR	138	44	23	12	3	0

Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
Potentially curative treatments	30	19	11	7	1	0
Non-curative treatments	108	25	12	7	2	0

[OP-0663]

Proper position of Single and Large (≥ 5 cm) Hepatocellular carcinoma in Barcelona Clinic Liver Cancer stage

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Objectives: The purpose of this study was to evaluate proper position of single large hepatocellular carcinoma (HCC) in Barcelona Clinic Liver Cancer Stage system (BCLC).
Materials and Methods: The data was collected from the nationwide multicenter database of the Korean Liver Cancer Association. Patients with single large (^{3} 5 cm) HCC was separated from BCLC A group and designated as group X. And remained BCLC Group A was renamed as Group A and BCLC Group B as Group B. Survival outcomes of propensity score-matched groups were compared.
Results: Among the 3965 randomly selected patients, Group X was 414, Group A (2787) and Group B (760). TriMatch analysis allowed us to obtain 116 well-balanced triplets. The 1-,3- and 5-year overall survival rates in the Group X was worse than Group A (91%, 71% and 48% Vs 90%, 78% and 64%, respectively; $P < 0.000$). But it was not different compared to Group B (91%, 71% and 48% Vs 90%, 69% and 48%, respectively; $P < 0.09$). In multivariable analysis, Group X, Group B, Age over 60 years, and prothrombin time international normalized ratio and Creatinine levels were independent predictors of worse overall survival.
Conclusion: Our findings suggest that Group X should be relocated to group BCLC B rather than BCLC A stage.

[OP-0712]

Perfluorobutane-enhanced ultrasonography with a Kupffer phase: Improved diagnostic sensitivity for hepatocellular carcinoma

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Objectives: In diagnosing hepatocellular carcinoma (HCC) in at-risk patients, the ideal diagnostic criteria for a definitive diagnosis of HCC on perfluorobutane contrast-enhanced ultrasonography (CEUS) are still controversial. We aimed to evaluate diagnostic accuracy of perfluorobutane CEUS for HCC and to explore how accuracy can be improved compared to conventional diagnostic criteria.
Materials and Methods: A total of 123 hepatic nodules ($\geq$ 1 cm) from 123 at-risk patients (mean age, 61.5 years $\pm$ 11.7; 98 men) who underwent perfluorobutane CEUS between 2013 and 2020 at three institutions were retrospectively analyzed. 93% of subjects (n = 114) had pathological results, except benign lesions stable in follow-up images. We evaluated presence of arterial phase hyperenhancement (APHE), washout time and degree, and Kupffer phase (KP) defects in target observations. KP defects are defined as hypoenhancing lesions relative to liver in KP. We diagnosed the lesion as HCC in two ways: 1) vascular phase criteria defined as APHE and late ($\geq$ 60 s)/mild washout, and 2) KP criteria defined as APHE and KP defect. To find grayscale features that could cause misdiagnosis of HCC and increase diagnostic accuracy, we explored grayscale images of each observation and reflected them to adjust the diagnostic criteria. Diagnostic performance was compared using McNemar's test.
Results: There were 77 HCCs, 15 non-HCC malignancies, and 31 benign lesions. An ill-defined margin without hypoechoic halo on grayscale image caused the misdiagnosis, which were not considered HCC in analysis. Regarding perfluorobutane CEUS diagnosis of HCC, sensitivity of KP criteria (83.1%; 95% confidence interval [CI]: 72.9%?90.7%) was higher than that of vascular phase criteria (75.3%; 95% CI: 64.2%?84.4%; P = 0.041). Specificity was 91.3% (95% CI: 79.2%?97.6%) in both groups.
Conclusion: On perfluorobutane CEUS, diagnostic criteria for HCC using KP defect with adjustment by grayscale findings had higher diagnostic performance than conventional criteria without losing specificity.

[OP-0765]

Plasma extracellular vesicle-derived microRNAs for diagnosis of patients with nonalcoholic fatty liver disease and hepatocellular carcinoma

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Objectives: Extracellular vesicle-derived microRNAs (EV miRNAs) are used as promising sources of circulating biomarkers in diseases and cancers. However, there is a lack of study of EV miRNA biomarkers in nonalcoholic fatty liver disease (NAFLD) and NAFLD-associated hepatocellular carcinoma (NAFLD-HCC). In the present study, we investigated the EV miRNAs as diagnostic biomarkers for NAFLD and NAFLD-HCC by miRNA profiling using the NanoString miRNA Expression Assay in a discovery set and validating in an independent set of plasma samples by quantitative RT-PCR.
Materials and Methods: Pre-treatment plasma samples of NAFLD and NAFLD-HCC along with healthy controls were collected to isolate EVs and characterized by nanoparticle tracking analysis, western blot, and transmission electron microscopy. The expression profiles of EV miRNAs in the plasma of the patients with NAFLD and NAFLD-HCC to healthy controls were compared (n = 9 per group).
Results: Differentially expressed miRNAs were observed from the discovery set, and the most significant upregulated miRNA in the NAFLD-HCC group compared with the other groups, miR-19b-3p, was identified. To examine the expression level of miR-19b-3p from the plasma EVs in the validation cohort, a total of 70 participants were preliminary enrolled. miR-19b-3p from plasma EVs showed significantly higher in the NAFLD-HCC group (n = 22) than in the NAFLD (n = 28) ($p < 0.001$) and the healthy control group (n = 19) (p = 0.012).
Conclusion: Our data demonstrated that the expression profiles of EV miRNAs of patients with NAFLD and NAFLD-HCC were different from the healthy control group. Indeed, EV miRNA miR-19b-3p might act as a biomarker for the diagnosis of NAFLD-HCC.

[OP-0771]

Utility of CT/MR surveillance in LI-RADS Visualization Score-assessed Liver cirrhosis patients

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Objectives: International guidelines for hepatocellular carcinoma (HCC) surveillance suggest the use of CT or MR when visualization of the liver by ultrasonography (US) is limited. But its effectiveness has not been studied systematically, especially in real-world practice.
Materials and Methods: We conducted a retrospective cohort study of 2045 liver cirrhosis patients who had undergone abdominal US for HCC surveillance with LI-RADS visualization score assessed at least once at our institution from April 2003 to December 2020. A 1:1 propensity score matching with CTMR surveillance group and US-only surveillance group was done including age, sex, etiology of cirrhosis, laboratory values, chronic disease status, Child–Pugh score, and LI-RADS visualization score. The size, stage (BCLC, mUICC), mRECIST treatment response (initial, overall), and recurrence free survival of HCC patients were compared before and after propensity score matching. The two groups were also compared in LI-RADS visualization score subgroups.
Results: Of 2045 patients with liver cirrhosis, 1458 patients were classified as CTMR surveillance group and 587 patients were classified as US-only surveillance group. 56 patients developed HCC. Even after propensity score matching, HCC was more detected in CTMR surveillance group than in US-only surveillance group (6% vs. 1%). The HCC detected in CTMR surveillance group had smaller size (2.0 cm vs. 2.4 cm) and higher complete response (CR) rate (91% vs. 57%) in initial treatment. However, the stage (BCLC, mUICC), overall mRECIST treatment response, recurrence free survival of HCC were statistically insignificant between the two groups. The

result was similar when analyzed in LI-RADS visualization score subgroups.
Conclusion: Surveillance by CT or MR detects HCC better and in smaller size than US, but its clinical benefit is not evident.

[OP-0916]

Extending the criteria for curative surgical resection to intermediate stage hepatocellular carcinoma: A novel approach that accounts for heterogeneity in BCLC B and the dispersion of tumour

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Objectives: This study aims to provide granular clinical outcomes data for surgical resection in early and intermediate stage HCC divided based on sub-groups of the modified Barcelona Clinic Liver Cancer (BCLC) staging system and the dispersion of tumour.
Materials and Methods: A single-centre retrospective cohort study of patients with early and intermediate stage HCC who underwent surgical resection for HCC between 1st January 2000 to 30th June 2016. Patients were divided into 6 groups based on the Milan Criteria (MC), the "Up-to-7" (Ut7) criteria, and presence of bilobar tumours as per table 1. Separately, survival analysis was conducted for solitary HCC lesions stratified by size to: S1 (within MC), S2 (Out of MC + within Ut7), S3 (Out of MC + out of Ut7).
Results: 794 of 1043 patients met the study criteria. Groups A (65.3%), B (64.9%) and C (57.7%) had 5-year cumulative overall survival (OS) rates above 50% after surgical resection and median OS exceeding 60 months (P = 0.04). There was a sharp decline in the 5-year cumulative recurrence-free survival rates (RFS) as the disease severity progressed from group C to E (37.9% to 24.6% respectively) (P = 0.00). In the analysis of solitary lesions, the 5-year cumulative OS for the subgroups were S1 (65.8%), S2 (56.0%) and S3 (47.6%) (P = 0.50). Compared to S1, there was also a significant trend towards relatively poorer OS as the lesion sizes increased in S2 (HR 1.46, 95%CI 1.03 – 2.08) and S3 (HR 1.65, 95%CI 1.25 – 2.18).
Conclusion: We adopted a novel approach combining the modified BCLC B sub-classification and dispersion of tumour to show that surgical resection in intermediate stage HCC can also be robustly prognosticated. We found that resection with curative intent in intermediate HCC may be offered to unilobar lesions within the "up-to-7" criteria subgroup of patients and that size prognosticates resection outcomes in solitary tumours.

Table 1: Baseline demographics and clinical variables

Variable	Milan Unilobar (n= 448) Group A	Milan Bilobar (n=25) Group B	B1 - Out of Milan Within Upto7 Unilobar (n= 112) Group C	B1 - Out of Milan Within Upto7 Bilobar (n= 20) Group D	B2 - Out of Milan Out of Upto7 Unilobar (n=145) Group E	B2 - Out of Milan Out of Upto7 Bilobar (n= 44) Group F	p value
Age (years)							
Mean (SD)[1]	62 (10)	64.85 (10.61)	63.5 (11.53)	63.2 (11.2)	63.7 (13.24)	63.7 (16.3)	0.4527
Median (Range)[2]	63 (30, 85)	65.4 (39, 82)	64.1 (26 , 88)	64.3 (41, 84)	67 (16 , 86)	68 (15, 88)	0.0416
Gender, n (%)							
Male	345 (77)	14 (56)	86 (76.8)	16 (80)	118 (81.4)	34 (77.3)	0.16
Female	103 (23)	11 (44)	26 (23.2)	4 (20)	27 (18.6)	10 (22.7)	
Hepatitis B, n (%)	329 (73.43)	17 (68)	69 (61.6)	9 (45)	74 (51.03)	21 (47.72)	<0.0001
Hepatitis C, n (%)	45 (10)	3 (12)	20 (17.86)	3 (5)	10 (7)	4 (9.1)	0.11
Child-Pugh Score, n (%)							
5	348 (77.68)	18 (72)	80 (71.42)	16 (80)	83 (57.24)	30 (68.18)	0.001
6	81 (18.08)	7 (28)	30 (26.79)	3 (15)	55 (37.93)	13 (29.55)	
7_9	19 (4.24)		2 (1.79)	1 (5)	7 (4.83)	1(2.27)	
Albumin-bilirubin (ALBI) score							
Mean (SD)[1]	-2.5 (.43)	-2.50 (.40)	-2.46 (.39)	-2.59 (.44)	-2.36 (.45)	-2.4 (.378)	0.001
Median (Range)[2]	-2.6 (-3.4, -0.8)	-2.6 (-3.3, -1.7)	-2.5 (-3.7, -1.2)	-2.7 (-3.3, -1.6)	-2.4 (-3.4, -1.2)	-2.4 (-3.1, -1.2)	0.0006
Alpha-Fetoprotein (AFP) (ng/mL)							
Mean (SD)[1]	395.22 (1928.64)	527.8 (1758.6)	1948.55 (8149.63)	474.94 (1279.06)	7572.58 (20778.81)	12952.23 (25026.11)	<0.0001
Median (Range)[2]	10.45 (0.8, 29483)	31.2 (1.8, 8739)	13.1 (1.4, 70700)	16.1 (3, 4306)	77.4 (0.6, 175000)	58.35 (1.3, 70700)	0.001
Tumour Capsule, n (%)							
Not encapsulated	139 (31.03)	8 (32)	31 (27.7)	5 (25)	31 (21.38)	16 (36.36)	0.82
Completely encapsulated	115 (25.67)	4 (16)	28 (25)	4 (20)	39 (26.9)	9 (20.45)	
Partially encapsulated	137 (30.6)	8 (32)	38 (33.93)	8 (40)	54 (37.24)	15 (34.09)	
Micro Vascular Invasion, n (%)	90 (20.09)	5 (20)	32 (28.57)	7 (35)	83 (57.24)	22 (50)	
Number of nodules, n(%)							
1	425 (94.87)	13 (52)	68 (60.71)	5 (25)	113 (77.93)	17 (38.64)	0.001
2	21 (4.69)	10 (40)	32 (28.57)	11 (55)	16 (11.03)	12 (27.27)	
3_5	2 (0.45)	2 (8)	12 (10.71)	4 (20)	12 (8.28)	11 (25)	
>5	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	4 (2.76)	4 (9.09)	
Maximum size nodules, n (%)							
<3 cm	176 (39.29)	9 (36)	40 (35.71)	12 (60)	2 (1.38)	2 (4.55)	0.001
3_5 cm	272 60.71)	16 (64)	1 (0.89)	0 (0.00)	0 (0.00)	1 (2.27)	
>5 cm	0 (0.00)	0 (0.00)	71 (63.39)	8 (40)	143 (98.62)	41 (93.18)	

Note: p-values for categorical variable are based on Pearson's Chi2 test and for continuous variables p-values are base on ANOVA1 test or Kruskal-Wallis rank test2

[OP-0992]

A new therapeutic strategy using circulating tumor DNA that predicts drug resistance of atezolizumab + bevacizumab for the treatment of advanced hepatocellular carcinoma

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Objectives: tezolizumab + bebacizumab (atezo + bev) therapy was indicated for unresectable hepatocellular carcinoma (HCC) as the first combined immunotherapy. Compared with existing molecular-targeted drugs, significant prolongation of OS and PFS was observed in atezo + bev therapy. However, there are not a few cases with poor effect, and therefore, the timing of switching to conventional molecular-targeted drugs is important. Therefore, there is an urgent need to develop a biomarker for early determination of atezo + bev

resistance. The aim of this study is to analyze circulating tumor DNA (ctDNA) as a biomarker for early diagnosis of treatment resistance of atezo + bev.
Materials and Methods: For unresectable hepatocellular carcinoma with Child–Pugh A performed at our hospital, 16 cases with CR/PR and 18 cased with PD on atezo + bev were registered. CtDNAs from serum were analyzed using digital PCR before and after administration of atezo + bev. These mutations and clinical parameters were analyzed for the detection of drug resistance of atezo + bev.
Results: In patients with hepatocellular carcinoma, 45% of TERT mutations (228C > T or 250C > T) were found in serum cfRNA before atezo + bev treatment. The CTNNB1 mutations (396A > T or 407 T > G) were 42% in serum. TERT mutations and CTNNB1 mutations in serum before atezo + bev treatment in PD cases were significantly higher values ??than those in CR/PR cases. In the multivariate analyses of gene mutations and clinical parameters using ctDNA in serum before administration of atezo + bev, both TERT and CTNNB1 had a significant correlation in resistance. By quantifying ctDNA mutations in pre-administration serum, it was possible to predict the resistance of atezo + bev.
Conclusion: CtDNA was suggested to be effective as a biomarker for diagnosing the resistance of atezo + bev.

[OP-1025]

Neutrophil-to-lymphocyte ratio and interleukin-6 are associated with survival in hepatocellular carcinoma patients receiving atezolizumab/bevacizumab

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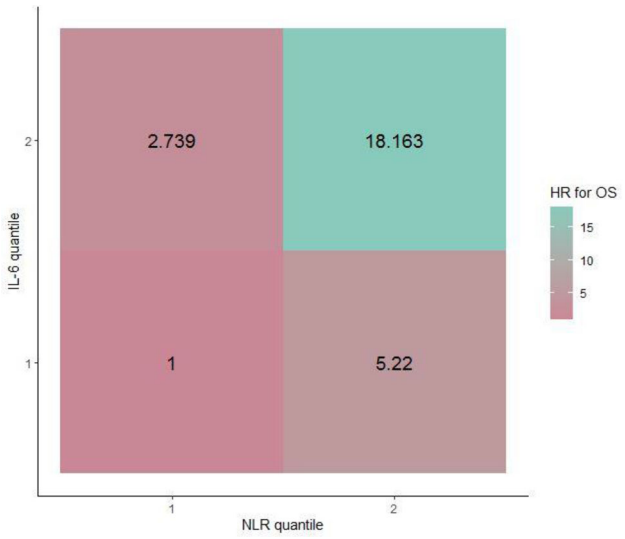
Objectives: The impact of blood biomarkers on the outcomes of patients with hepatocellular carcinoma (HCC) treated with atezolizumab/bevacizumab (atez/bev) has not been clearly demonstrated.
Materials and Methods: This is a retrospective analysis of unresectable HCC patients who received atez/bev at two hospitals from Jun 2020 to May 2021. The primary endpoint was overall survival (OS) and progression-free survival (PFS). Objective response (complete or partial response) and clinical benefit (objective response or stable disease for > 6 months) were also assessed. Inflammatory biomarkers and circulating cytokines were measured at baseline. Cox proportional hazards models were used to identify predictive factors for OS and PFS. The cut-points for blood biomarkers were determined.
Results: A total of 125 patients (mean age, 63 years; 82.4%, male; and 90.4%, Child–Pugh A) were identified. The majority of patients received curative or locoregional therapy before atez/bev (77.6%), had hepatitis B virus infection (69.8%), and had liver cirrhosis (76.0%). The median OS was not reached as of Oct 2021 and median PFS time was 6.8 months (95% confidence interval [CI], 3.3?10.3 months). The OS time was shorter in patients with higher neutrophil-to-lymphocyte ratio (NLR; hazard ratio [HR], 1.22; 95% CI, 1.09?1.36; P = 0.001) and higher interleukin-6 (IL-6) levels (HR, 1.03; 95% CI, 1.01?1.04; P < 0.001). The results with regard to PFS were consistent. When patients were classified into four groups according to the cut-points for NLR (2.65) and IL-6 (4.78), the worst OS and PFS were observed in the high risk group (NLR high/IL-6 high). Additionally, objective response (12.0% vs. 37.2%; P = 0.026) and clinical benefit (31.8% vs. 64.7%; P = 0.007) were significantly lower in the high risk group than in the low-to-intermediate risk group.
Conclusion: NLR, when combined with IL-6, can be a useful tool to sort out patients with HCC who are least likely to be benefited from atez/bev chemotherapy.



[OP-1081]

Outcomes of surgical resection and transarterial chemoembolization in elderly patients with hepatocellular carcinoma: A meta-analysis

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Objectives: Treatment options for early to intermediate hepatocellular carcinoma (HCC) in the elderly remain controversial due to concerns about safety and clinical outcomes. This meta-analysis aimed to evaluate the overall survival (OS), disease-free survival (DFS), and complications of surgical resection (SR) and transarterial chemoembolization (TACE) in elderly compared to non-elderly patients with HCC.
Materials and Methods: A systematic search in Ovid, MEDLINE, Cochrane Library, Scopus, and SCIENCEDIRECT from inception up to October 2021 was made to identify comparative studies with outcomes of SR and TACE in elderly and non-elderly patients with HCC.
Results: A total of 19,784 patients in thirty-nine studies were included. Of these, 16,556 patients underwent SR, while 3,228 patients underwent TACE. The elderly group had more cardiovascular and respiratory comorbidities. Among those who underwent SR, there were more post-operative complications in the elderly than the non-elderly (OR 1.14; 95%CI 1.02, 1.27, p = 0.03). However, there was no significant difference in postoperative mortality between the groups (OR 1.27; 95%CI 0.96, 1.68, p = 0.10). OS was similar in the first year (OR 0.94; 95%CI 0.75, 1.19, p = 0.062), third year (OR 0.97; 95%CI 0.87, 1.08, p = 0.55), and fifth year (OR 0.82; 95%CI 0.68,1.00, p = 0.05). DFS was also similar in the first year (OR 1.08; 95%CI 0.91, 1.28, p = 0.37), third year (OR 1.02; 95%CI 0.87,1.19)

and fifth year (OR 1.04; 95%CI 0.86,1.26, p = 0.67). Among patients who underwent TACE, post-procedure complications were similar (OR 0.95; 95%CI 0.71, 1.26, p = 0.72). OS was also similar in the first year (OR 1.30; 95%CI 0.84, 2.02, p = 0.24), third year (OR 1.32; 95%CI 0.97, 1.80, p = 0.07), and fifth year (OR 0.75; 95%CI 0.43, 1.29, p = 0.29).

Conclusion: Despite a higher number of postoperative complications in elderly patients who undergo surgical resection, survival outcomes are similar to non-elderly patients. Hence, surgical resection and TACE are successful treatment options for elderly patients with HCC after preoperative clinical assessment.

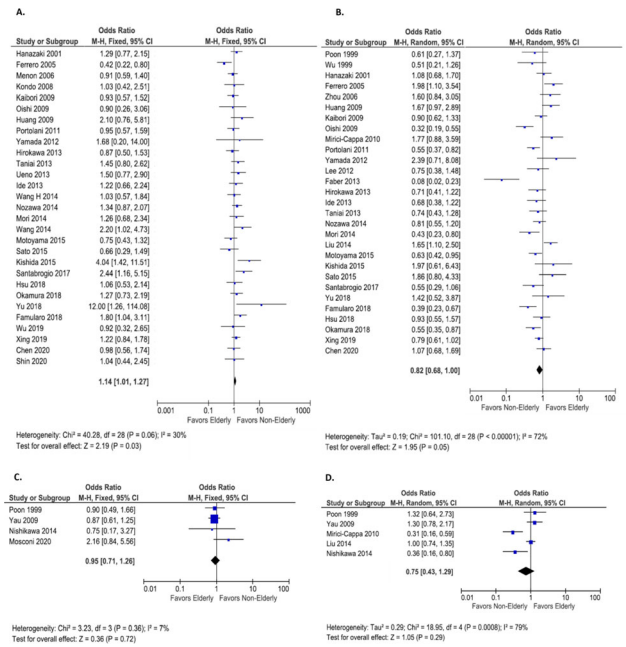

Figure 1. A. Post-operative complications of elderly vs non-elderly patients with Hepatocellular Carcinoma after surgical resection. B. 5-Year Overall Survival of elderly vs non-elderly patients with Hepatocellular Carcinoma after surgical resection. C. Post-procedure complications of elderly vs non-elderly patients with Hepatocellular Carcinoma after transarterial chemoembolization. D. 5-Year Overall Survival of elderly vs non-elderly patients with Hepatocellular Carcinoma after transarterial chemoembolization

[OP-1087]

Variceal bleeding in hepatocellular carcinoma patients treated with atezolizumab/bevacizumab

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Objectives: Variceal bleeding is a major cause of morbidity and mortality in patients with liver disease. We aimed to evaluate the incidence of variceal bleeding and its predictors in patients who received atezolizumab/bevacizumab (atez/bev) for unresectable hepatocellular carcinoma (HCC).

Materials and Methods: In this retrospective cohort study, HCC patients who were started with atez/bev chemotherapy from Jun 2020 to Oct 2021 at our institution were analyzed. Baseline data including endoscopic findings were collected. The primary outcome was occurrence of variceal bleeding during atez/bev chemotherapy. Logistic regression analysis was used to identify factors associated with variceal bleeding.

Results: Among 194 patients (mean age, 62 years; 85.6%, male; 74.7%, cirrhosis; and 15.5% Child–Pugh B) included in the analysis, 8 (4.6%) patients experienced variceal bleeding. The bleeding group had more portal vein tumor thrombosis (PVTT; Vp4, 50.0% vs. 12.9%; P = 0.025) and a higher proportion of high-risk varices on baseline endoscopy (83.3% vs. 13.1%; P < 0.001). Age (odds ratio [OR], 0.94), platelet counts (OR, 0.99), Vp4 PVTT (OR, 3.98), infiltrative tumor (OR, 3.49), and Child–Pugh score (OR, 2.32) were associated with high-risk varices at baseline (all Ps < 0.05). Presence of high-risk varices (OR, 33.08; 95% confidence interval [CI], 3.58?306.03; P = 0.002) and Vp4 PVTT (OR, 6.75; 95% CI, 1.58?28.80; P = 0.010) predicted variceal bleeding. Prophylactic endoscopic variceal ligation (EVL) tended to reduce the bleeding events in patients with high-risk varices (OR, 0.21; 95% CI, 0.02?2.48; P = 0.22). Among 8 patients who were treated with prophylactic EVL, only 1 patient experienced variceal bleeding when the progression of PVTT was identified and the decision to stop atez/bev was made.

Conclusion: Variceal bleeding occurred in less than 5% of patients receiving atez/bev for unresectable HCC. High-risk varices on baseline endoscopy and presence of Vp4 PVTT predicted variceal bleeding; however, bleeding events tended to be decreased in those treated with prophylactic EVL.

[ABST-0194]

Y-90 radioembolisation for large unresectable hepatocellular carcinoma as a bridge to surgery—a 5-year single institute's experience In Hong Kong

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Background: Hepatocellular carcinoma has a high incidence rate in Hong Kong due to the high prevalence of chronic hepatitis B infection. It was the fifth commonest cancer and accounted for 5.3% of all new cancer cases in 2019. By the time of diagnosis, it is not uncommon that HCCs are unresectable. We present short term outcomes of patients with large (> 8 cm) unresectable hepatocellular carcinoma who received Y-90 radioembolization. Cases were determined unresectable due to inadequate residual liver volume or close margins after discussion in our multidisciplinary meetings.

Methods: This was a single-center retrospective analysis on the outcomes in patients who received Y-90 radioembolization as a bridge to surgery between 1 May, 2017 and 31 May 2021 at Princess Margaret Hospital, Hong Kong.

Results: 39 patients were enrolled in receiving pre-treatment technetium-99 m labeled macroaggregated albumin (MAA) scan, and 25 (64%) patients were eligible to receive Y-90. The most common cause of MAA failure was lung shunting (71%) One patient who initially passed was excluded due to deteriorating functional status. Of the 24 patients who received Y-90, 16 (66%) had complete or partial response and eventually 8 patients underwent hepatectomy. Univariate analysis was performed for predictors of passing MAA scan and complete/partial responders to Y-90 and revealed the absence of ascites (p = 0.038) and the percentage of lung shunting (p = 0.009) were prognostic factors respectively.

Conclusions: Y-90 radioembolization with the intention as a bridge to surgery is a safe and feasible option for large unresectable hepatocellular carcinomas.

[ABST-0260]

Effectiveness and safety of sorafenib 400 mg vs 800 mg initial dose on survival in patients with advanced and intermediate stage hepatocellular carcinoma: A systematic review and meta-analysis

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Background: Sorafenib is a multi-tyrosine kinase inhibitor that has been shown to improve survival in patients with advanced-stage hepatocellular carcinoma (HCC). Based on the search to date, there are quite a number of studies evaluating the effectiveness of the modified dose of sorafenib (400 mg) compared to the standard dose (800 mg) on the survival of patients with advanced HCC, but the previous studies have shown varying results. This SR aimed to determine the effectiveness of initial dose sorafenib 400 mg compared with initial dose sorafenib 800 mg on survival in patients with advanced HCC and its side effects in both groups.
Methods: This systematic review is conducted by following the PRISMA standard. We searched PubMed, Embase, EBSCOhost, and Proquest through April 30, 2021. Secondary searching was done by snowballing method manual searching through global index Medicus, GARUDA, SINTA, and several digital libraries of universities in Indonesia. The selection was carried out on RCTs (Randomized Controlled Trials) and NRSIs (Non-randomized Studies of Interventions) studies that included patients with advanced stages who received initiation therapy of sorafenib at a dose of 800 mg and a dose of 400 mg which assessed overall survival and side effects. Of the 603 articles, there were 5 NRSI studies that met the eligibility criteria.
Results: Administration initial dose of sorafenib 400 mg was significantly more effective on overall survival compared to the initial dose of sorafenib 800 mg in patients with advanced HCC (HR 0.84; 95% CI 0.71–0.98; p = 0.03). There was no difference in the overall incidence of adverse events to varying degrees in the two groups (pooled OR 0.93; 95% CI 0.67–1.30; p = 0.68).
Conclusions: sorafenib 400 mg initial dose has a better effectiveness on overall survival with no significant difference in the incidence of adverse events compared to sorafenib 800 mg initial dose in patients with advanced and intermediate HCC.

Liver Transplantation

[OP-0092]

Complete transition from open to laparoscopy: 8-year experience with more than 500 laparoscopic living donor hepatectomy

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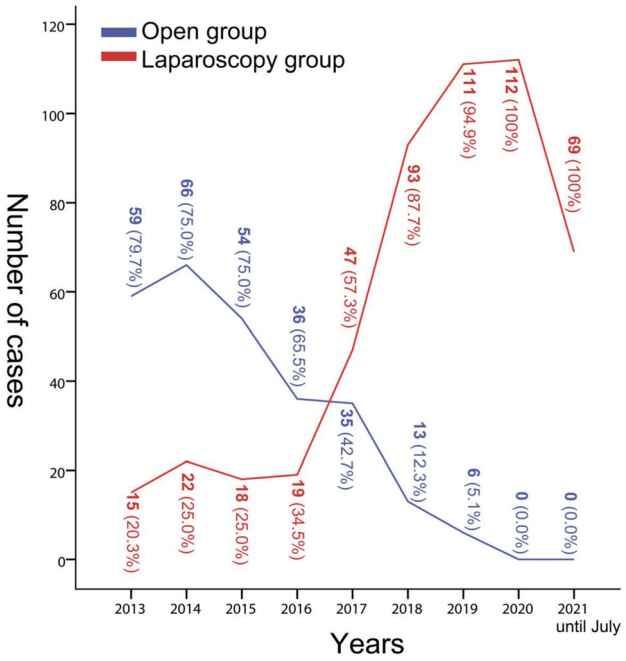
Objectives: We designed this study to comprehensively review the laparoscopic living donor liver transplantation of our institution.
Materials and Methods: Living donor liver transplantation cases performed since the first laparoscopic living donor hepatectomy, until reaching 500th laparoscopic cases were reviewed. Laparoscopic cases were compared to open cases in a yearly basis, regarding the donor selection, donor morbidity, recipient morbidity and operation time.
Results: Between 2013 to July 2021, 775 living donor liver transplantations, 506 laparoscopic and 269 open cases were performed. Complete transition to laparoscopy was achieved in 2020. Variation of bile duct type of donor became similar in 2018. (P = 1.000) There were no differences in the occurrence of grade III complication of donor and recipient throughout the study period. Mean donor operation time were significantly longer in the laparoscopy group which became similar since 2017 (P = 0.313) There were no differences in the mean operation time of recipients throughout the study period. Regarding graft survival and overall survival of the recipient, there were no difference between the two group throughout the period.
Conclusion: In the initial period, donor selection existed especially for bile duct variation maintaining the safety of the donor and recipient. However, with accumulated experience, complete transition to laparoscopy became possible.



[OP-0191]

Long-term clinical outcomes and predictive factors for living-donor liver-transplant recipients with biliary strictures

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Objectives: Biliary strictures frequently occur in LDLT recipients. However, long-term clinical outcomes, including overall and graft survivals and their associated factors, have not yet been elucidated.
Materials and Methods: We analyzed an historical cohort of 228 recipients who underwent LDLT from January 2006 to July 2020 and were subsequently diagnosed with biliary strictures. ERCP or PTBD

were performed to treat biliary strictures. Patients that experienced persistent jaundice (> 3 mg/dL) over 3 months after the initial treatment, including those who developed LC, underwent re-transplantation, or who died due to the hepatic failure were defined as remission-failure groups.
Results: Median observation period of total cohort was 8.5 years after the diagnosis of biliary stricture. The 15-year OS rate was 70.6%, and 15-year rate of developing LC was 26.1% in the total group. Remission-failure occurred in 25.0% (57/228) of study participants. In multivariate logistic-regression, biopsy-proven acute rejection, and portal vein/hepatic artery abnormalities were independent risk factors for remission-failure. Developing LC (35/57, 61.4% vs. 0/171, 0%, $p < 0.001$), re-transplantation (11/57, 19.3% vs. 0/171, 0%, $p < 0.001$), and death (32/57, 56.1% vs. 18/171, 10.5%, $p < 0.001$) were significantly more frequent in the remission-failure group. Remission-failure (HR = 2.4, p = 0.022) and LC (HR = 3.0, p = 0.001) were associated with poor OS. In multivariate Cox-regression, hepatic artery abnormality (n = 15) was a common significant factor that was associated with a poor OS (HR = 2.9, p = 0.010) and development of LC (HR = 9.9, $p < 0.001$). Furthermore, biloma (n = 33) was also significantly observed in the multivariate Cox-regression, which was associated with poor OS (HR = 2.0, p = 0.049) and development of LC (HR = 2.7, p = 0.016).
Conclusion: Insufficient blood supply reflected by hepatic artery abnormality and biloma might be the most important factors that can predict poor long-term overall and graft survivals in LDLT patients with biliary strictures. Future large-scale prospective studies are needed to validate our observations.

[OP-0537]

Usability of intraoperative cine-portogram during liver transplantation in young pediatric patients with biliary atresia

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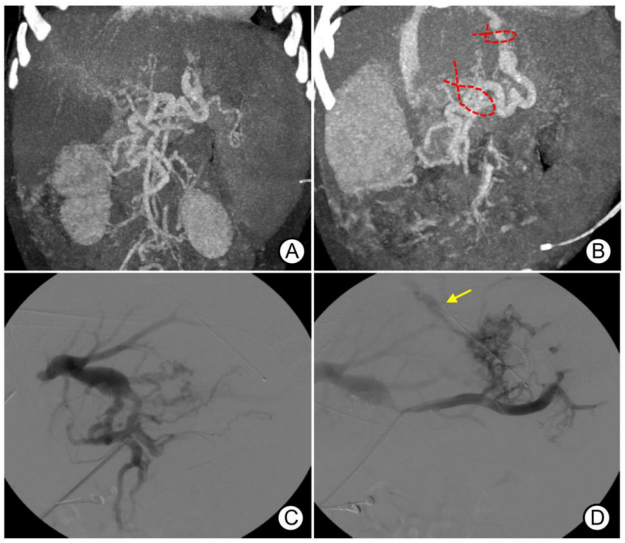
Objectives: Pediatric patients with biliary atresia (BA) often present liver cirrhosis-associated portal hypertension and portal vein (PV) hypoplasia. For successful liver transplantation (LT), it is essential to maintain sufficient PV inflow through stenosis-free PV reconstruction with effective ligation of collateral veins. The aim of this study was to assess the clinical usability of intraoperative cine-portogram (IOCP) in young pediatric patients who underwent LT for BA.
Materials and Methods: Medical records of pediatric patients younger than 10 years who underwent primary LT for BA from 2018 to 2020 were reviewed.
Results: A total of 31 patients had undergone Kasai portoenterostomy soon after birth. Their median ages at Kasai portoenterostomy and LT were 1 month and 11 months, respectively. Types of LT were living donor LT in 13, deceased split LT in 15, and deceased whole LT in 3 patients. PV interposition using iliac vein homograft was performed in 28 patients receiving partial liver grafts. Side-to-side PV unification venoplasty was performed in 3 patients undergoing whole LT. All patients underwent ligation of collateral veins. IOCP was performed in 6 (19.4%) patients. Four showed no or faint residual venous collaterals. Collateral vein embolization and endovascular stenting were performed in one patient each. PV insufficiency-free survival rate was 100% at 1 year and 93.8% at 3 years. All patients are currently alive with a median follow-up period of 23 months.
Conclusion: IOCP can be a useful method for identification and embolization of residual portosystemic collateral veins in young pediatric patients who undergo LT for biliary atresia.



[OP-0616]

Optimizing fatty liver allograft potential for transplantation using the NRF2 axis

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Objectives: Due to the exponential rise in fatty liver disease, there has been an increase in the prevalence of hepatic steatosis in the liver donor pool. Transplantation using steatotic allografts is a recognized risk factor because of the increased susceptibility to ischemia reperfusion injury. This study seeks to assess the role of the nuclear factor-erythroid 2-related-factor-2 NRF2 axis in steatotic allografts using novel ex-vivo preservation techniques.
Materials and Methods: Hepatic NRF2 expression levels were measured and quantified by immunoblotting in discarded lean and steatotic human allografts (n = 40). Livers (n = 8)were then studied separately following 6 h of normothermic machine preservation (NMP). A fatty liver rodent model was designed to assess the effects of pharamacologic NRF2 modulation during NMP.
Results: Hepatic steatosis was associated with lower hepatic NRF2 expression levels (p = 0.002) which appeared to decrease sharply when 40% steatosis was exceeded. Hepatic NRF2 levels increased in lean samples following NMP exposure, while steatotic samples failed to boost NRF2 activity (p = 0.031) and demonstrated wider transaminase derangements at the end of perfusion (ALT 11,329 IU vs 6,592 IU, p = 0.04; AST 28,056 IU vs 13,166 IU p = 0.14). NRF2-treated fatty rat livers observed increased levels of hepatic NRF2, when compared to the steatotic group receiving vehicle control

(p = 0.043), and were associated with significantly improved liver enzymes following NMP.
Conclusion: The NRF2 axis appears impaired in steatotic livers which could explain their resistance to the effects of NMP. Weaknesses in antioxidant physiology within steatotic and discarded livers may present a molecular opportunity for future therapeutic targeting.

[OP-0642]

Pure laparoscopic versus open right donor hemi-hepatectomy including the middle hepatic vein: A comparison of outcomes and safety

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Objectives: Pure laparoscopic donor hepatectomy is now commonly accepted as a safe and feasible surgery. Inclusion of the middle hepatic vein (MHV) to the liver graft to prevent graft congestion is sometimes needed and performed in current practice. But the data and studies related to outcomes and safety related to pure laparoscopy in donor hepatectomies with MHV inclusion are limited to date. In this study, we aimed to compare the outcomes of donor right hemi-hepatectomy including the MHV when performed laparoscopically against open surgery.
Materials and Methods: Prospectively collected data from living donors who received donor right hemi-hepatectomy at Seoul National University Hospital between 2012 January and 2020 December was retrospectively analyzed. The baseline characteristics, intraoperative events and parameters, postoperative complication rates of the Laparoscopic donor right hemihepatectomy with MHV inclusion (LDRHM) group were compared to the Open donor right hemihepatectomy with MHV inclusion (ODRHM) group and Laparoscopic donor right hemihepatectomy without MHV inclusion (LDRH) groups.
Results: Compared to the ODRHM group, the LDRHM group demonstrated less Clavien Dindo class I complications (p = 0.022), and Clavien Dindo class II, III, IV complications had no difference between the groups. The LDRHM group also had a shorter mean hospital stay (7.03 days vs 8.00 days, p = 0.004) but had larger postoperative increases in total bilirubin and ALT, AST levels ($p < 0.001$). This larger increase in lab results was also seen in the LDRH group, which had similar mean differences in total bilirubin, ALT, ans AST as the LDRHM group. The ODRHM group had 5/10 complications (such as intra-abdominal infection, pneumonia, ileus, pleural effusion) and the LDRHM group had 3/40 complications (wound seroma, intra-abdominal fluid collection, biliary stricture).
Conclusion: Pure laparoscopic donor right hemi-hepatectomy with the inclusion of the MHV is safe when performed by surgeons experienced in laparoscopic surgery, with favorable complication rates compared to open donor right hemi-hepatectomy.

[OP-0726]

Surgical site infection among liver transplant patients: Evidence from real-world studies

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Objectives: Surgical site infection (SSI) is a common and postoperative complication in patients who underwent solid organ transplant and it makes extensive healthcare burden. So far, the pooled prevalence and microorganisms causing SSI among liver transplantation has not been reported well. This evidence based systematic literature review and meta-analytic approach aimed to find the pooled prevalence of SSI.
Materials and Methods: A systematic literature search on PubMed/Medline, Embase was conducted to identify the study determining the prevalence of SSI among patients who underwent liver transplantation. We calculated pooled prevalence (%) with 95% confidence interval (CI) with random-effect model. A meta-analysis was performed using "meta" package through R 3.5.0. software.
Results: A total of 16 studies with 6,012 studied patients were included in this analysis. The rate of SSI was ranged between 9.0% and 96.4%. The pooled prevalence of SSI was 28.52% (95% CI: 17.19 to 41.01%) with high degree of heterogeneity ($I^2 = 99\%$, heterogeneity-$p < 0.01$). The included studies reported higher percentage of organ-space SSI (70.2%), followed by incisional, superficial and deep SSI. The incidence rate of SSI was ranged from 0.34–10.3 episodes per 100 transplantation. Staphylococcus aureus (76.5%) was the most common pathogen identified, followed by Coagulase-negative staphylococci (35.0%), Escherichia coli (21.25%), Enterococcus faecium and Staphylococcus epidermidis (12.5%), and Candida albicans (6.25%).
Conclusion: The current result suggests the overall prevalence of SSI infection was noted high. However, due to high degree of heterogeneity, resulting considerable amount of clinical uncertainty regarding the prevalence of SSI among patients underwent liver transplantation. Therefore, studies are required to confirm the present findings.

[OP-0785]

Impact of previous abdominal surgery on laparoscopic donor hepatectomy for living donor liver transplantation

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Objectives: Laparoscopic donor hepatectomy (LDH) has many advantages over open donor hepatectomy. However, previous abdominal surgical history can be considered to cause difficulties in laparoscopic surgery. Few studies have evaluated the impact of previous abdominal surgery (PAS) on LDH. Therefore, we studied the effect of PAS on LDH.
Materials and Methods: This study is a retrospective study conducted at a single center. We reviewed the data of 361 patients who underwent LDH at Samsung Medical Center from January 2017 to December 2020. These patients divided into 72 patients with previous abdominal surgery (PAS) group and 289 patients with non-previous abdominal surgery (non-PAS) group. Two groups were compared with respect to operation factors such as estimated blood loss,

operation time, and intraoperative blood transfusion. Postoperative outcomes such as length of hospital stay, postoperative complications, AST, ALT, INR, albumin, and total bilirubin trends (preoperative, peak-postoperative and after 1 month) were also compared.
Results: 72 patients has previous abdominal surgical history [cholecystectomy (4), splenectomy (1), pyloromyotomy (1), cesarean Sect. (28), appendectomy (19), uterine surgery (8), ovarian surgery (7), hernia repair (3), laparoscopic anterior resection (1)]. There was no statistical difference in estimated blood loss and operation time between the two groups. No donors received intraoperative blood transfusion. Complications occurred in 7 patients (9.7%) in the PAS group and in 26 patients (9%) in the non-PAS group, and there was no statistical difference between the two groups. There were no significant differences in the changes in AST, ALT, INR, albumin, and total bilirubin (preoperative, postoperative and 1 month). All donors fully recovered and returned to their normal activities.
Conclusion: The outcomes of our study show the feasibility and safety of LDH in patients with previous abdominal surgical history. Therefore, even if there is a history of PAS, LDH can be performed safely enough, so it is not a contraindication.

[OP-0908]

A new avatar mouse model to predict the liver immune homeostasis and histologic inflammation of long-term stable liver transplant patients

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Objectives: Although liver transplantation (LT) patients have the possibility of rejection or tolerance, there have been no reliable models to predict the liver immune homeostasis of LT patients, which may give clinicians the chance to assess liver immunity and guide future treatment plans. Here, we developed a new patient-derived mouse model to predict the liver immune homeostasis of LT patients.
Materials and Methods: The patient-derived avatar model was developed by injection of peripheral blood mononuclear cells from healthy controls (HCs) or LT patients with stable, rejection, or tolerance into NSG mice, followed by human hepatic stellate cells and CCl_4 injections. After seven weeks of transferring the cells, the patient's T-cell engraftment and liver inflammation of the avatar model were evaluated and compared to the liver histology of LT patients.
Results: The CXCR3-dependently engrafted patient's T cells caused different liver inflammation in our model according to the status of the LT patients. The livers of avatar models from rejection patients had severe inflammation with more T helper 17 and fewer regulatory T cells compared to that of the models from tolerance and HCs showing only mild inflammation. Moreover, our model could classify stable post-LT patients into severe and mild inflammation groups, which correlated well with the liver immunity of these patients.
Conclusion: Using our new patient-derived avatar model, we could predict real liver immune homeostasis and histologic inflammation in stable LT patients without liver biopsy.

[OP-0932]

Steatosis following liver transplantation for Nonalcoholic Steatohepatitis is associated with a higher rate of cardiovascular complications

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Objectives: Introduction: Cirrhosis secondary to Nonalcoholic Steatohepatitis (NASH) is projected to become the leading indication for liver transplantation (LT) worldwide. Objectives: to evaluate the prevalence of metabolic syndrome and long term outcome of patients transplanted for NASH related cirrhosis.
Materials and Methods: Methods: All patients transplanted for NASH related cirrhosis at our institution from 2001–2016 were included in this study. Patients data were collected from our prospectively collected database.
Results: Results: 108 patients were transplanted for NASH related cirrhosis at our institution. Sixteen (15%) patients had pretransplant hepatocellular carcinoma. Pretransplant obesity (BMI $>$ 30), diabetes, hyperlipidemia and hypertension were present in 37 (34%), 55 (51%), 20 (19%), and 30 (28%) patients, respectively. Following LT patients were followed for an average of 103 months (range 54–203 months). Post-transplant diabetes, hyperlipidemia and hypertension were present in 73 (67.6%), 25 (23%) and 51 (47%) patients, respectively. 58 (53.7%) patients developed disease recurrence with significant fatty infiltration on various imaging modalities. Additionally, 48 (44%) patients developed renal impairment (GFR $<$ 60). Sixteen patients were treated for mild rejection and only one patient developed ductopenic rejection resulting in graft loss. Eighteen (16.6%) patients developed severe cardiovascular complications. Overall survival during the follow period was 83%. One and three year survivals were 92.5% and 87% respectively. Sepsis was the commonest cause of death in our patient population. Three patients died secondary to acute cardiovascular events. In Univariate and multivariate analysis recurrence of steatosis was associated with cardiovascular complications.
Conclusion: Conclusion: Disease recurrence in our patient population was common and was associated with a higher rate of cardiovascular complications; however, post-transplant cirrhosis remains rare. The prevalent metabolic syndrome negatively impacted renal function and resulted in cardiovascular complications.

[OP-0947]

Long-term outcomes of liver transplantation (LT) using grafts from donors with active and chronic hepatitis B Virus (HBV) infection; Multi-center cohort study

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Objectives: We report the long-term outcome of liver transplantation (LT) using grafts from donors with active and chronic hepatitis B virus infection using Hepatitis B immunoglobulin (HBIG) and Nucleos (t)ide analogues (NA).
Materials and Methods: Among 2260 LTs performed in Seoul National University Hospital, SNU Bundang Hospital, and SNU Boramae Hospital between January 2000 and April 2019, 26 (1.2%) grafts from donors with HBsAg (+), HBeAb (+) or HBV DNA (+) were referred as active and chronic HBV hepatitis grafts and reviewed retrospectively. HBV reactivation redefined as the increase of viral DNA for HBsAg (+) grafts and HBsAg positive seroconversion for chronic hepatitis grafts. Also, we adopted the stage of chronic HBV infection to evaluate and manage of recipients transplanted HBV infected grafts.
Results: Sixteen deceased donor LT were performed with active HBsAg (+) grafts. Ten living donor LT were performed with inactive HBV infected grafts; 8 patients in inactive hepatitis; HBsAg (-), HBcAb (+) & HBV DNA (+), and 2 patients in chronic HBV hepatitis with seroconversion; HBsAg (-), HBsAb (+) and HBeAg (+). Average follow-up period was 82.6 ± 60.1 months. NA and HBIG were administered during perioperative period depending on donor and recipient's serology. Deaths (n = 8) were occurred 2.0–47.3 months after transplantation. Comparing LT using non-hepatitis virus-infected grafts, there was no difference in patient survival (30.8% vs. 18.6%, p = 0.247). Most common causes of death were infection (n = 4) and HCC recurrence (n = 3). HBV reactivation (n = 1) resolved without additional management. All 10 LDLT recipients survived and were in good condition during follow-up. Survivors were in inactive or resolved status for HBV infection under the HBIG and NA. Fourteen patients followed-up more than 5 years were stable and no increase in HCC recurrence was observed 5 years after transplantation.
Conclusion: Considering long-term outcome, liver grafts with active and chronic HBV infection can be safely used in HBV endemic area.

[ABST-0123]

Efficacy and safety of adhesion barrier in living-donor liver transplantation using right lobe graft for preventing post-operative delayed gastric emptying: A propensity score matching analysis

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Background: Delayed gastric emptying (DGE) is a common complication after living donor liver transplantation. The aim of this study was to clarify the efficacy and safety of application of adhesion barrier (Seprafilm), for preventing DGE in living-donor liver transplantation (LDLT).
Methods: This retrospective study included 257 patients who underwent LDLT using right lobe graft between January 2018 and August 2019 and the incidence of post-operative DGE and complications were compared between patients in whom Seprafilm was used (147 patients, Seprafilm group) and was not used (110 patients, non-Seprafilm group). We performed 1:1 propensity score matching between two groups and 83 patients were included in each group. The severity and definition of DGE followed the International Study Group of Pancreatic Surgery (ISGPS) classification.
Results: The use of Seprafilm was significantly associated with lower overall incidence of post-operative DGE in LDLT (34.7 vs 19.1%; p = 0.006), including grade A (24.4 vs 10.0%; p = 0.009) and grade B (8.8 vs 2.7%; p = 0.045) and grade C (1.9 vs 2.7%; p = 0.265). After propensity score matching, the similar results were showed in the overall incidence of DGE (33.7 vs 19.3%; p = 0.035), including grade A (24.9 vs 8.4%; p = 0.010), grade B (8.4 vs 3.6%; p = 0.192) and grade C (2.4 vs 7.2%; p = 0.147). The univariate and multivariate analysis showed significant correlation between the use of Seprafilim and low incidence of DGE. There were no significantly statistical differences in post-operative complications between two groups.
Conclusions: Application of adhesion barrier could be safe and feasible to reduce the incidence of post-operative DGE in LDLT.

[ABST-0124]

The novel surgical technique using gastroepiploic vein for restoration of portal inflow in living donor liver transplantation for patient with diffuse portomesenteric thrombosis

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Background: For restoration of portal inflow in patients with diffuse portomesenteric vein thrombosis (DPVT) without available enlarged portosystemic collaterals, cavoportal hemitransposition is a proposed surgical option in deceased-donor liver transplantation but rarely indicated in living-donor liver transplantation (LDLT), which requires splanchno-portal inflow for regeneration of partial liver graft. In the presence of engorged gastroepiploic vein (GEV) without available collaterals for portal inflow, venous interposition graft using fresh cadaveric inferior vena cava (IVC) from GEV could be valid surgical management for portal flow reconstruction. This is the first report of a successful restoration of portal inflow using GEV.

Methods: A 52-year-old male patient with cirrhosis due to hepatitis B underwent LDLT from his son due to recurrent esophageal varices rupture and increased ascites. In pre-operative computed tomography, total portomesenteric thrombosis and dilated GEV 8 mm without large splenorenal shunt were identified. Portal anastomosis was established by venous interposition graft using fresh cadaveric IVC from GEV.
Results: At one-year post-operative follow-up, the patient had well regenerated graft with enough portal inflow through the enlarged GEV.
Conclusions: Portal anastomosis using venous interposition graft from engorged GEV could be a useful surgical option for LDLT selectively in patient with DPVT.

[ABST-0183]

Is it acceptable to perform duct to duct anastomosis during living donor liver transplantation in patients with hepatocellular carcinoma treated with radiotherapy before?

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Background: Radiotherapy (RT) has been proved to provide acceptable oncologic outcomes in the selected patients with hepatocellular carcinoma (HCC) followed by adult living donor liver transplantation (LDLT). The study aims to evaluate the biliary stricture after LDLT in patients with HCC treated with RT.
Methods: We retrospectively enrolled 50 patients with HCC treated with RT, who underwent duct to duct anastomosis during LDLT using a single right graft between January 2019 and December 2020. The perihilar RT was defined as RT including a 10 mm expansion area surrounding the right, left, and common hepatic duct. We identified the risk factors for biliary stricture by analyzing the LDLT and RT factors.
Results: During a median follow-up period of 23.2 months (range, 6.3–35 months), a total of 17 (34%) patients presented biliary stricture after LDLT. In a comparative analysis between biliary stricture and no stricture groups, the patients with perihilar RT in the biliary stricture group were significantly more than those in the no stricture group (47.1% vs. 15.2%, $p = 0.021$). In a univariate analysis of risk factor for biliary stricture, warm ischemic time [odd ratio (OR), 1.06; 95% confidence interval (CI) 1.00–1.14, $p = 0.08$] and perihilar RT (OR, 4.98; 95% CI 1.33–20.47, $p = 0.019$) were significantly associated with biliary stricture. In a multivariate analysis, perihilar RT was identified as the only significant risk factor for biliary stricture (OR, 4.37; 95% CI 1.13–18.4, $p = 0.036$).
Conclusions: Perihilar RT for HCC before LDLT can lead to biliary stricture of duct to duct anastomosis. Hepaticojejunostomy may be an eligible option for the prevention of biliary stricture after LDLT for patients with HCC treated with a perihilar RT.

[ABST-0215]

Short-term outcomes of flipped left lobe graft implantation to right side in adult living donor liver transplantation

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Background: Orthotopic implantation is naturally considered as a standard option for living donor liver transplantation (LDLT) regardless of the graft type. In literature, however, LDLT using left lobe graft tends to have more venous outflow complications, small for size syndrome, early satiety, and the possibility of surgical difficulty with anastomosis. Herein, we reported our early experience of flipped left lobe graft implantation (FLGI) to the right side of the recipients.
Methods: A total of 926 adult LDLTs, right lobe grafts were 900 and left lobe grafts were 26. Out of left lobe grafts, we have performed 7 cases of FLGI including two extended left lobe grafts. The left hepatic vein was anastomosed to the right side of IVC. V4 was reconstructed with a dacron graft except for an extended left lobe graft. We retrospectively analyzed the outcomes of the patients.
Results: Vascular anastomosis including HV, PV, and HA was easier than orthotopic left liver transplantation because the vascular axis particularly in PV and HA anastomosis were parallel to the recipient main PV and HA. There was one in-hospital mortality, who had a 40 MELD score and massive gastric varix bleeding just before liver transplantation. There was one bile leak after liver transplantation, which was resolved by ERBD insertion. All others were discharged without postoperative complications. Post-operative CT scan showed well-positioned in the right subphrenic area without any vascular complication (Fig. 1).
Conclusions: FLGI is an easier and feasible technique when we use left lobe graft in living donor liver transplantation. Long-term follow-up will be needed.

[ABST-0320]

Effect of donor against recipient one-way mismatch on graft-versus-host-disease after liver transplantation

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Background: Graft-versus-host-disease (GVHD) after liver transplantation (LT) is a rare but fatal disease. The risk factor and treatment of GVHD still has a lot to be investigated. The aim of this study is to evaluate the effect of human leukocyte antigen (HLA) relationship between donor and recipient to graft and patient survival and GVHD after LT.
Methods: LT recipients who had evaluated HLA typing together with donor were all included in study. The number donor against recipient ($D \rightarrow R$) one-way mismatch was evaluated and recipient against donor ($R \rightarrow D$) mismatch numbers were categorized as 0–1, 2–3 and ≥ 4. Patients who were confirmed of GVHD by pathologic biopsy due to the symptoms of diarrhea, cytopenia or rash were

evaluated and described of whole treatment period. HLA relationships along with patient's characteristics such as age, sex, HCC, MELD score, re-LT, HBV, HTN and DM are analyzed as variable factors of GVHD, graft survival, patient survival and T-cell mediated rejection.
Results: Total 994 living donor LT (LDLT) patients and 393 deceased donor LT (DDLT) patients were involved. A total nine patients were confirmed as GVHD including five patients in LDLT. All GVHD patient except one in LDLT had died. Among seven patients with D → R one-way mismatch at 3 loci, four patients developed GVHD (57.1%). Cox regression analysis showed D → R one-way mismatch at 3 loci was related to high GVHD incidence (HR = 787, $p < 0.001$, multivariate). D → R one-way mismatch at 3 loci was also related to graft failure ad patient death in LDLT patients (HR = 6.02 with $p = 0.020$ and HR 8.05 with $p < 0.001$, respectively, multivariate). On the contrary, low number R → D mismatch (0 or 1) showed relative low graft survival in Kaplan–Meier analysis ($p = 0.032$) but not in Cox regression analysis ($p = 0.137$). Re-LT was associated with TCMR, graft failure and patient death in LDLT (HR 7.59 with $p = 0.001$, HR 4.46 with $p = 0.051$ and HR 6.68 with $p < 0.001$).
Conclusions: D → R one-way mismatch at 3 loci greatly increased the incidence of GVHD after LT leading to patient death. Low R → D HLA mismatch numbers (0 or 1) was related decreased graft survival in LDLT.

[ABST-0326]

Outcomes of ABO-incompatible adult living donor liver transplantation for patients with hepatocellular carcinoma beyond the Milan criteria

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Background: Given the organ scarcity, ABO incompatible (ABOi) living donor liver transplantation (LDLT) emerged as a treatment option for hepatocellular carcinoma (HCC) and underlying liver disease. Milan criteria became standard criteria but expansion beyond the Milan criteria have resulted in similar post-transplant outcomes, thus suggesting LT is a viable treatment option for HCC presenting beyond the Milan Criteria. However, there was few reports the outcome of the patients receiving ABOi LDLT in beyond the Milan Criteria. The aim of our study was to review the HCC-related survival outcomes in the ABOi and ABO compatible (ABOc) groups in the beyond Milan Criteria.
Methods: We retrospectively reviewed the medical records of patients undergoing LDLT for HCC from January 2000 to July 2021 at two tertiary centers in Korea. In total of 114 patients underwent ABOc and 25 patients underwent ABOi LDLT for HCC presenting beyond the Milan Criteria. The eligibility of the beyond Milan Criteria was assessed using preoperative findings by imaging study.
Results: There was no significant difference in pre-transplantation tumor staging, recipient and donor demographics between groups. In terms of operative outcomes and pathologic outcomes, there was no significant difference in both groups. The overall patient survival at 1-,3-, and 5-year was 88.4%, 72.0% and 69.9% after ABOc LDLT and 58.9%, 58,9% and 58.9% after ABOi LDLT, respectively ($P = 0.139$). The recurrence free survival at 1-,3-, and 5-year was 94.7%, 86.6% and 82.7% after ABOc LDLT and 87.5%, 60.0% and 48.5% after ABOi LDLT ($P < 0.001$). Recurrence type (intrahepatic versus extrahepatic) was no significant difference in both groups.
Conclusions: Although, recurrence free survival was significant poor in ABOi LDLT for patients with HCC presenting the beyond Milan Criteria than ABOc LDLT, overall survival was comparable between groups. ABOi LDLT may be a option for HCC with beyond Milan Criteria.

[ABST-0364]

Changes in the trend of deceased donors in Korea: Establishment of the regional trauma center and KODA

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Background: South Korea shows extremely high activity in living donor liver transplantation because it has been selected as an alternative to overcome the shortage of deceased donors. With the establishment of the Korea organ donation agency (KODA) as an independent organ procurement organization (IOPO), a large number of donor-managing hospitals were selected as a policy. Separately, the nationwide regional trauma center project was carried out in earnest from 2015. This study aims to analyze how the trend of deceased donor recruitment and donation has been changed according to national policy factors such as IOPO activities and the establishment of regional trauma centers.
Methods: From 2010 to 2019 Among the KONOS data, deceased donors were discovered and managed by hospitals and analyzed in relation to the establishment of regional trauma centers and the activities of IOPO.
Results: A total of 62 centers had 4,395 cases of deceased donors, and a total of 3,863 recipients underwent deceased donor liver transplantation. Cerebrovascular events were the most common cause of death among donors, and head trauma-related death accounted for 26.1%, accounting for the second most common cause. When the increased rate of deceased donors was analyzed by dividing into the early period (2010–2014) and the late period (2015–2019) based on 2015 when regional trauma centers began to be active. 53 non-traumatic centers had cases from an average of 29.3 cases to 31.0 cases (6.2% increase). On the other hand, 9 regional trauma centers showed a statistically significant increase from an average of 39.8 cases to 70.3 cases (75.9% increase).
Conclusions: In Korea, according to the national policy, the pattern of hospitals where deceased donors occur is changing. It is necessary to communicate with regional trauma centers staff for recruiting more deceased donors through the discovery of potential deceased donors.

[ABST-0387]

Risk factors for biliary complication-free survival after living donor liver transplantation in the era of laparoscopic donor hepatectomy

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Background: Biliary complication (BC) remains the most common postoperative complications after liver transplantation (LT) despite the advancement of surgical techniques and management. Biliary reconstruction after living donor liver transplantation (LDLT) is technically more demanding than deceased donor LT due to multiple duct openings, small and short graft duct. Herein, we analyzed the risk factor of BC-free survival after LDLT including considerable cases of laparoscopic living donor hepatectomy.
Methods: From August 2011 to December 2019, 824 recipients underwent adult LDLT in Seoul National University Hospital. BC was defined as a bile leakage (BL) or a biliary stricture (BS) requiring interventions. Median follow-up period was 63.5 months.
Results: BC was developed in 272 cases (34.3%) at a median time of 4 months (range 1–81); 64 (8.1%) cases of BL and 253 (31.9%) cases of BS. Pure laparoscopic donor hepatectomy (PLDH) was done in 358 cases (43.5%), open hepatectomy (OH) in 435 cases (52.9%), and laparoscopic-assisted hepatectomy in 30 cases (3.6%). BC-free survival rates were significantly lower in PLDH group (59.8%) than in OH group (70.6%) ($P < 0.001$). PLDH and donor warm ischemic time were one of the risk factors for BC after LDLT in univariate analysis ($P = 0.001$ for both), however, none of these factors were associated risk factors on multivariate analysis. Preoperative radiofrequency ablation history, hepaticojejunostomy (HJ), multiple anastomosis of bile duct, postoperative transfusion during hospital stay, and use of inotropics during hospital stay were found to be significant risk factors for biliary complication in multivariate analysis.
Conclusions: PLDH for LT is considered a feasible option, however, there are increased possibility for BC in the recipient. Therefore, maximal effort should be exerted to avoid associated risk factors for BC, i.e. reducing donor warm ischemic time, postoperative transfusion, and use of inotropics postoperatively, and close surveillance for BC is required in this specific group.

[ABST-0449]

Outcomes of long-term survival in liver transplantation using small-for-size graft: A systematic review and meta-analysis

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Background: The standard graft-to-recipient weight ratio (GRWR) $\geq 0.8\%$ widely is accepted in liver transplantation (LT), however the indications of LT are gradually expanding selectively to patients adopting small-for-size graft (SFSG) with predicted GRWR $< 0.8\%$. The aim of this study was to compare the long-term outcomes following LT according to GRWR.
Methods: Electronic databases were searched from January 1995 to January 2022 for studies comparing long-term outcomes between patients adopting a small volume of graft (GRWR $< 0.8\%$, SFSG group) and a sufficient volume of graft (GRWR $\geq 0.8\%$, non-SFSG group). The hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using the random-effects model.
Results: Twelve studies comprising 2787 patients were included. Regarding patient survival rate, SFSG group had poor 3-year overall survival (OS) (HR 1.45, 95% CI [1.01, 2.08], $p = 0.005$) but there were no significant differences between SFSG and non-SFSG group in 1-year OS (HR 1.51, 95% CI [1.00, 2.27], $p = 0.009$) and 5-year OS (HR 1.40, 95% CI [0.95, 2.08], $p = 0.02$). In graft survival (GS) rate, there were no significant differences between two groups in 1-year (HR 1.30, 95% CI [1.00, 1.69], $p = 0.07$), 3-year (HR 1.33, 95% CI [0.97, 1.82], $p = 0.02$), and 5-year GS (HR 1.17, 95% CI [0.95, 1.44], $p = 0.71$).
Conclusions: Expanding the indications of LT to small livers graft with a GRWR $< 0.8\%$ can be acceptable in terms of comparable long-term survival rates after careful recipient selection.

[ABST-0462]

Learning curve of robotic living donor right hepatectomy: A cumulative sum analysis

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Background: Robotic living donor right hepatectomy is a challenging procedure and only a few experienced centers are available with this technique. However, the use of robotic donor hepatectomy has proved its feasibility and safety with consecutive studies. No current study is reported about the learning curve of robotic donor right hepatectomy. In this study, we evaluated the learning curve of robotic living donor right hepatectomy (RLDRH).
Methods: From 2016 to 2021, ninety-nine patients underwent RLDRH by a single surgeon. We divided robotic procedure time into 5 steps to confirm learning curve of each steps. The learning curve was evaluated using the cumulative sum (CUSUM) analysis based on operation time.
Results: The mean age of donor group was 30.74 years and the mean BMI was 22.74. Anatomical variation of portal vein was found in 12 (12.12%) donors and bile duct variation was found in 27 donors (27.28%). The mean operation was 460.91 ± 82.53 min without significant disability of graft. The CUSUM of total operation time explained a learning curve of 17th cases of RLDRH. The mean console time was 389.77 ± 77.89 min and a learning curve of 19th case was demonstrated. The mean parenchymal dissection time was 184 ± 50.94 min and a learning curve was 14th case. The mean graft out time was 366.31 ± 87.67 and a learning curve was 19th case. However, Hilum dissection time (mean, 57.99 ± 13.55 min) and warm ischemic time (mean, 15.49 ± 5.58 min) showed no significant discriminative pattern. No significant risk factor was found in learning curve of operation time.
Conclusions: This study is the first trial which enables to evaluate the learning curves of RLDRH with detailed division of operation procedures. Parenchymal dissection time was the determining factor of learning curve for RLDRH. Fine approach and skilled movement are particularly requested in the hilum dissection step which didn't showed specific discrimination time in learning curve. This result proved robotic hepatectomy as a safe and feasible method. These learning curves could build the basis for successful development of minimally invasive LDLT program.

[ABST-0471]

Application of proximal splenic vein embolization to interrupt complicated large splenorenal shunts in adult living donor liver transplantation

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Background: In adult living donor liver transplantation (ALDLT) for a patient who has large splenorenal shunts (SRS), their interruption is utmost important to maintain adequate portal flow by avoidance of portal flow steal through the preexisting SRS. We effectively managed most of the recipients with surgical ligation and/or additional radiologic embolization using by intraoperative cine-portogram (IOP). However, when complete interruption is not achieved in a few recipients having complicated large SRS, it may leave a chance of lethal portal flow steal in the recipient afterwards. The aim of present study is to evaluate efficacy and safety of proximal splenic vein embolization (PSVE) for liver transplant recipients having complicated large splenorenal shunts.
Methods: PSVE was performed in 13 patients between April 2014 and November 2017. We performed a retrospective analysis of preoperative images, postoperative graft and recipient outcomes, and presence of isolated portal hypertension.
Results: Ten patients underwent PSVE as an additional secondary method because of for portal steal syndrome through the remaining SRS after surgical interruption and/or embolization, and 3 patients underwent PSVE only as a primary method of SRS interruption. In all 13 patients, portal steal on the final IOP completely disappeared after PSVE. All patients recovered with satisfactory regeneration of the partial liver graft without the reappearance of portosystemic collaterals, and there were no procedure-related complications.
Conclusions: PSVE is an effective and safe procedure to secure adequate portal flow without portal steal for patients with complicated large SRS arising from multiple sites of the splenic vein or escaping to multiple terminal ends.

[ABST-0472]

Efficacy and safety evaluation after conversion from twice-daily to once-daily tacrolimus in stable liver transplant recipients: A phase 4, open label, single center study

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Background: Simplifying immunosuppressive therapy after liver transplantation may improve patient compliance, thereby preventing acute rejection and graft loss. This phase 4, open label, single center study was conducted to evaluate the efficacy and safety of twice-daily to once-daily tacrolimus conversion in stable liver transplant recipients.
Methods: Between May 2017 and January 2019, twice-daily tacrolimus was converted to once-daily tacrolimus in 101 stable recipients at least 12 months post-liver transplantation in Asan Medical Center. The doses of both drugs was converted to 1:1, and the target trough level was 5–10 ng/ml. We prospectively analyzed graft function, drug compliance, and adverse reactions after switching regimen for 24 weeks.
Results: There was no acute rejection confirmed histologically within 24 weeks, which was the primary endpoint, and there was no chronic rejection, fatal deterioration of liver function or death in any patient during this period. After conversion, the trough level of tacrolimus decreased, and the differences between the trough level and baseline level were 1.46 (± 2.41) ng/mL, 0.43 (± 2.08) ng/mL, and 0.07 (± 2.73) ng/mL at 3, 12, and 24 weeks after conversion, respectively. Despite transient fluctuations of the trough level, there was no evidence of rejection or graft dysfunction. There were 37 adverse reactions after conversion; most of them were mild, and thrombocytopenia developed in one patient as an adverse drug response. Drug compliance improved after conversion, according to questionnaire-responses.
Conclusions: The conversion to once-daily tacrolimus in stable liver transplant recipients is an effective and safe therapeutic strategy improving drug compliance.

[ABST-0522]

Risk factors for pneumocystis jirovecii pneumonia (PJP) in liver transplantation recipients

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Background: Pneumocystis jirovecii pneumonia (PJP), a potentially life-threatening infection occurring in immunocompromised patients, has been rarely studied in liver transplant recipients in respect to its incidence and risk factors. The aim of this study was to evaluate risk factors for PJP after liver transplantation and to address high-risk group that can possibly benefit from prolonged prophylaxis.
Methods: This is a single-center, retrospective study involving 860 patients who underwent liver transplantation at Severance Hospital between January 2009 and December 2019. The incidence, risk factors and outcome of PJP were retrospectively reviewed.
Results: Among 100 patients who did not receive trimethoprim/sulfamethoxazole (TMP/SMX), 15 patients (15%) were diagnosed with PJP, of which 80% occurred within three months after transplantation. Upon prescription of TMP/SMX, 25 of 760 (3.3%) suffered PJP. In multivariate analysis, old age (≥ 65) (HR 2.842, 95% CI 1.061–7.609), P = 0.038), CMV viremia (HR 3.410, 95% CI 1.510–7.701, P = 0.003), and use of everolimus (HR 2.708, 95% CI 1.206–6.078, P = 0.016) were found as risk factors of diagnosis with PJP. PJP-related mortality was as high as 32% (8/25) in this subgroup.
Conclusions: Late onset PJP occurs even after six to twelve months of TMP/SMX prophylaxis. This study addresses that old age, CMV viremia and use of everolimus may be risk factors for late onset PJP in liver transplant recipients. Extended duration of prophylaxis targeting high-risk recipients may be a more cost-effective strategy.

[ABST-0237]

Development and validation of a deep learning model for the prediction of hepatocellular cancer recurrence after transplantation: An international study

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Background: Identifying patients at high risk for hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) represents a challenging issue. The present study aims at developing an accurate post-LT recurrence prediction calculator using the machine learning method (Time_Radiological-response_Alpha-feto-proteIN_Artificial-Intelligence, TRAIN-AI).
Methods: 3,381 patients with HCC listed for LT from 2000 to 2018 and coming from 17 centers from North America, Europe, and Asia were included in the study. The original dataset was split to generate the two main data sets used for the research. The Training Set was composed of 70% of the records of the original dataset, and the Test Set was composed by the remaining 30%. Using the Training Set data, a prognostic model for HCC recurrence was developed with a Deep Surv model, and a Cox proportional hazards deep neural network was constructed. Validation of the model was done using the Test Set. The TRAIN-AI was compared using the DeLong test with Metroticket 2.0 Score, AFP-French Model, Milan Criteria, San Francisco Criteria, Up-to-Seven Criteria, TRAIN Score, NYCA Score, and HALT-HCC Score.
Results: The developed TRAIN-AI model showed an escellent c-statistics, with an AUC = 0.78 (95%CI = 0.73–0.82). The TRAIN-AI always outperformed the other scores: Metroticket 2.0 Score AUC = 0.66, $P < 0.0001$; AFP-French Model AUC = 0.65, $P < 0.0001$; Milan Criteria AUC = 0.63, $P < 0.0001$; San Francisco Criteria AUC = 0.61, $P < 0.0001$; Up-to-Seven Criteria AUC = 0.60, $P < 0.0001$; TRAIN Score AUC = 0.59, $P < 0.0001$; NYCA Score AUC = 0.58, $P < 0.0001$; HALT-HCC Score AUC = 0.57, $P < 0.0001$.
Conclusions: The proposed TRAIN-AI score showed higher accuracy than other available risk scores in terms of post-LT recurrence risk. Further validation is required. A web calculator has been developed for improving the user-friendly availability of the model.

[ABST-0498]

Factors associated with "Difficult Bile Duct Stricture" following living donor liver transplantation

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Background: Biliary stricture is the most common and important complication after living-donor liver transplantation (LDLT). Moreover, among patients with biliary stricture, there are patients who present with protracted disease course and require multiple sessions or treatment modalities for disease resolution or fail to respond to treatment. This study aimed of identify factors that are associated with the "difficult bile duct stricture" following LDLT.
Methods: We reviewed the records of one hundred and twenty-nine adults who received LDLT between January 2010 and December 2021. We evaluated the incidence of post-LDLT biliary stricture and the long-term outcome of treatment for biliary stricture. We divided the patients with biliary stricture into 2 groups (simple vs complicated). Patients with a protracted disease course who required more than 3 months for successful treatment or failed to respond to treatment were included in the complicated group.
Results: Biliary strictures developed in 20 (15.8%) patients. Of these, 15 patients were in the complicated group. The cold ischemic time (165.94 ± 53.86 min) was shorter and the graft-to-recipient weight ratio (GRWR) was lower (0.97 ± 0.17) in the complicated group. As expected, the mean number of intervention performed per patient was higher (7.00 ± 6.89) in the complicated group. In addition, all non-anastomotic strictures were included in the complicated group. Contrary to our expectations, the rate of ductoplasty or ABO incompatible LDLT was not associated with "difficult bile stricture". However, patients requiring interventions due to insufficient graft inflow such as hepatic artery or portal vein insufficiency significantly presented with a protracted disease course ($p = 0.041$). The graft survival was significantly shorter in the complicated group (92.68 ± 14.06 months vs 122.06 ± 5.17 months).
Conclusions: Patients with low GRWR requiring interventions due to insufficient graft inflow such as hepatic artery or portal vein insufficiency are at risk for developing "difficult bile duct stricture" that does not respond well to treatment.

Hepatobiliary Surgery

[OP-0534]

Diagnostic and prognostic impact of fluorodeoxyglucose-positron emission tomography in diagnosing intraductal papillary neoplasms of the bile duct of the liver

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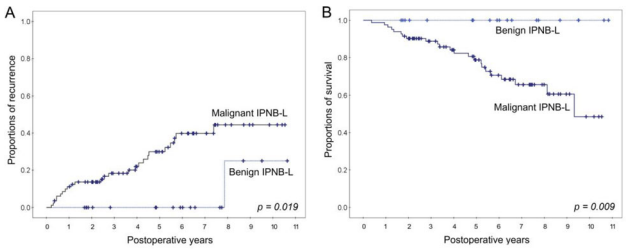
Objectives: Malignant intraductal papillary neoplasm of the bile duct of the liver (IPNB-L) cannot readily be diagnosed through preoperative computed tomography or magnetic resonance imaging, but fluorodeoxyglucose-positron emission tomography (FDG-PET) is a viable alternative. This study evaluated the diagnostic and prognostic impacts of FDG-PET in patients with IPNB-L.
Materials and Methods: This was a retrospective single-center study of 101 IPNB-L patients who underwent hepatectomy between 2010 and 2019.
Results: Mean age was 64.4 ± 8.3 years and 76 (75.2%) were male. Anatomical hepatic resection was performed in 99 (98.0%). Concurrent bile duct resection and pancreaticoduodenectomy were performed in 41 (40.1%) and 1 (1.0%), respectively. R0 and R1

resections were performed in 88 (87.1%) and 13 (12.9%), respectively. Low-grade intraepithelial neoplasia and high-grade neoplasia/invasive carcinoma were diagnosed in 19 (18.8%) and 82 (81.2%), respectively. Median FDG-PET maximal standardized uptake values (SUVmax) in low-grade neoplasia and high-grade neoplasia/carcinoma were 3.6 (range: 1.7–7.6) and 5.2 (range: 1.5–18.7; p = 0.019), respectively. Receiver operating characteristic curve analysis of SUVmax showed area under the curve of 0.674, with sensitivity of 84.2% and specificity of 47.4% at SUVmax cutoff of 3.0. This cutoff had no significant influence on tumor recurrence (p = 0.832) or patient survival (p = 0.996) in patients with IPNB-L of high-grade neoplasia or invasive carcinoma.

Conclusion: IPNB-L is a rare type of biliary neoplasm and encompasses a histological spectrum ranging from benign disease to invasive carcinoma. An FDG-PET SUVmax cutoff of 3.0 appears to effectively discern high-grade neoplasia/carcinoma from low-grade neoplasia, which will assist with the surgical strategy for these cases.



[OP-0535]

Clinicopathological features and long-term outcomes of intraductal papillary neoplasms of the bile duct of the liver: Single-institution experience with 146 patients

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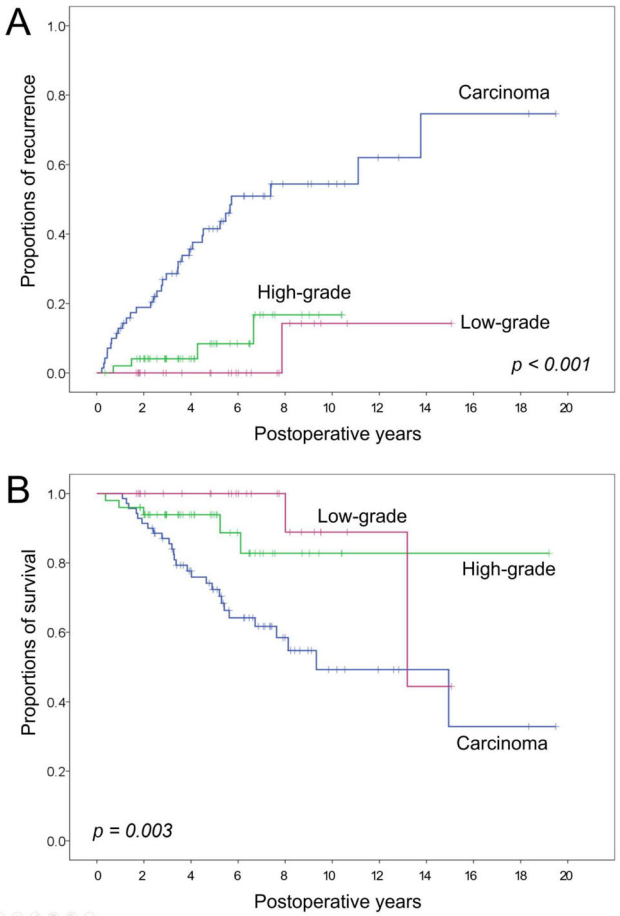
Objectives: Intraductal papillary neoplasm of the bile duct (IPNB) has wide range of histopathology and intra- and extrahepatic tumor locations.

Materials and Methods: This retrospective single-center study evaluated the clinicopathological features and long-term outcomes of 146 patients with IPNB of the liver (IPNB-L) who underwent hepatic resection between January 2002 and June 2019.

Results: The 146 patients included 97 (66.4%) men and 49 (33.6%) women, of mean age 64.3 ± 8.0 years. Seventy-two (49.3%) patients were incidentally diagnosed, with no specific symptoms, and 18 (12.3%) were found to have hepatolithiasis. Sixty-one (41.8%) and two (1.4%) patients underwent concurrent bile duct resection and pancreaticoduodenectomy, respectively, and 130 (89.0%) underwent R0 resection. Low-grade and high-grade intraepithelial neoplasia, and invasive carcinoma were identified in 26 (17.8%), 50 (34.2%), and 70 (47.9%) patients, respectively. Five-year tumor recurrence and patient survival rates were 8.4% and 93.9%, respectively, in patients with high-grade neoplasia, and 41.5% and 72.3%, respectively, in patients with invasive carcinoma. CA19-9 > 37 U/mL and R1 resection were independent risk factors for tumor recurrence and reduced survival in patients with carcinoma. The combination of hypermetabolic fluorodeoxy-glucose-positron emission tomography (FDG-PET) or elevated CA19-9 showed a sensitivity of 91.8% and a specificity of 61.9% for prediction of IPNB-L with high-grade neoplasia and carcinoma.

Conclusion: IPNB-L is a rare type of intrahepatic biliary neoplasm can range histologically from benign disease to invasive carcinoma. Surgical curability is the most important prognostic factor, with aggressive resection highly recommended to achieve R0 resection. FDG-PET and CA19-9 expression may help in preoperatively diagnosing malignant IPNB-L.



[OP-0589]

Relaparotomy and repeated mini-invasive interventions in hepatobiliary surgery

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Objectives: Improving the immediate results of surgical treatment of liver and biliary tract diseases through the rational use of minimally invasive technologies.

Materials and Methods: The study materials are based on an analysis of 420 patients with postoperative intra-abdominal complications after surgery on the liver (n = 224) and biliary system (n = 196). The patients were divided into two groups. The first control group included 150 (35.7%) patients who were treated in the period from 1997 to 2005, before the introduction of modern technologies into clinical practice and for the diagnosis and treatment of whom traditional

relaparotomy was used. The second (main) group included 270 (64.3%) patients who were in the period 2005–2020 for diagnosis and treatment, who were used modern technologies and improved surgical tactics.
Results: Correction of postoperative intra-abdominal complications of the hepatobiliary zone in patients of the main group in 56 (20.7%) cases was performed by various mini-invasive interventions under ultrasound control, in 50 (18.5%)—endoscopic hemostasis, in 114 (42.2%)—laparoscopic, in 5 (1.8%)—a combination of laparoscopy with minilumbotomy laparotomy, in 27 (10.0%)—minilaparotomy approaches, in 18 (6.7%)—developed bilio-shunting (n = 4) and Y-shaped hepaticojejunoanastomoses according to the methods developed in the clinic. At the same time, postoperative complications in the main group amounted to 18.1%, on the contrary, 29.3% in the control group, and mortality, respectively, was 8.9% and 16.0%.
Conclusion: Comparative indicators of repeated traditional operations with minimally invasive interventions, as well as the use of improved methods of surgical tactics, in patients with pathologies of the hepatobiliary zone, show the high efficiency of the methods used in the main group of patients.

[OP-1005]

Enhanced liver fibrosis score as a predictive factor for perioperative surgical outcome after liver resection for the patient with hepatocellular carcinoma

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Objectives: Liver fibrosis is well-known factor affecting surgical outcomes for the patient with hepatocellular carcinoma (HCC) after liver resection. The enhanced liver fibrosis (ELF) score is extracellular matrix marker set consisting of tissue inhibitor of metalloproteinases 1, amino-terminal propeptide of type III procollagen and hyaluronic acid having good correlations with fibrosis stages in chronic liver disease. Thus, this study aimed to figure out the predictive value of ELF score for the patients with HCC after liver resection.
Materials and Methods: From April 2015 to December 2020, preoperative ELF score was collected for 141 patients with HCC having liver resection. The patients were grouped according to ELF score as 10.3. Perioperative outcomes including post-hepatic insufficiency were compared between two groups. Prognostic factors for disease-free survival were analyzed.
Results: Patients over 10.3 of ELF score had significantly higher liver stiffness (19.7 vs 8.04 kPa, $p < 0.001$), lower albumin level (4.15 vs 4.56, $p < 0.001$), higher rate of post-hepatic insufficiency (32.4% vs 15.9%, $p = 0.036$), higher rate of intraoperative transfusion (14.7% vs 3.7%, $p = 0.023$), and higher rate of pathologic liver cirrhosis (67.6% vs 35.5%, $p = 0.001$). Patient under 60 year-old (Hazard ratio (HR) = 0.240, $p < 0.001$), larger than 5 cm tumor (HR = 4.816, $p < 0.001$), presence of micro-vessel invasion (HR = 2.982, $p = 0{,}002$), and over 10.3 of ELF score (HR = 5.422, $p < 0.001$) were significant predictive factors for disease-free survival in multivariable analysis.
Conclusion: ELF score over 10.3 was correlated with poor perioperative outcomes. In addition, ELF score was the significant prognostic factor for disease-free survival for the patients after liver resection.

[ABST-0094]

Liver trauma at Dr George Mukhari Academic Hospital

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Background: The evolution of management of hepatic trauma has followed a course from mandatory exploration for all patients to selective non-operative management and presently, to non-operative management with selective operation. There is, however, in specialized referral centers in countries with a high volume of trauma and limited access to facilities such as interventional radiology, still a role for major surgical resection in the management of the complex grades of liver injury. We report on our experience in a tertiary academic hospital in South Africa.
Methods: A retrospective analysis of all patients with liver injuries following trauma (blunt and penetrating) at a single referral center (Dr George Mukhari Academic Hospital) was performed. The data was obtained from a prospectively maintained database from January 2018 till November 2021. Data on identified patients was analyzed for demographic information, mechanisms of injury, associated injuries, hemodynamic stability on presentation, need for damage control surgery, overall management route (nonoperative vs operative), and outcome. All complications were analyzed and reported using the Clavien-Dindo scoring system.
Results: A total of 212 patients were managed at our center over the 4-year period. There were 57 blunt trauma patients (27%) and 155 penetrating trauma patients (73%). Non-operative management rate was 75% in blunt group vs 7% in penetrating group. Those patients who were managed operatively, 90% had associated injuries, 55% had liver injuries that could be managed by simple measures (diathermy and suturing) and 45% had high grade injuries that required more complex maneuvers (hepatotomy and vessel ligation, resectional debridement, lobar resection, perihepatic packing and relaparotomy, hepatic isolation). Overall mortality was 15% and was highest in the blunt injury group (20%) compared to penetrating trauma. Complications occurred in 72 (41%) out of 181 surviving patients. The complications correlated with the type and severity of the injuries (19% in stab wounds, 49% in gunshot wounds and 55% in blunt trauma) as well as with the number of associated injuries.
Conclusions: The management of complex liver injuries often requires advanced surgical techniques. This is especially the case in our setting where there is limited access to interventional radiology thus increasing the need for definitive surgical management of these patients. Surgical management of complex liver injuries is feasible in our setting and demonstrates a unique challenge with a unique solution.

[ABST-0125]

Laparoscopic versus open anatomical liver resection for hepatocellular carcinoma: A systematic review and meta-analysis

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Background: To compare the short- and long-term outcomes of laparoscopic anatomical liver resection (LALR) and open anatomical liver resection (OALR) for hepatocellular carcinoma (HCC). OALR has been accepted as an effective and oncologically safe treatment for HCC, but more studies on LALR are required.
Methods: Electronic databases were searched from January 2000 to September 2021. Pooled risk ratios (RRs), weighted mean differences (WMDs), and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using the fixed- or random-effects model.
Results: Eighteen retrospective studies comprising 1750 patients (LALR 741, OALR 1009) were included. Regarding short-term outcomes, LALR had a longer operation time (WMD 64.14, 95% CI [30.70, 97.57], p = 0.0002) but less blood loss (WMD -143.46, 95% CI [-229.34, -57.57], p = 0.001), overall morbidity (RR 0.58, 95% CI [0.49, 0.69], p < 0.00001), severe morbidity (RR 0.50, 95% CI [0.31, 0.79], p = 0.003), and hospital stay (WMD -3.25, 95% CI [-4.73, -1.77], p < 0.0001) than OALR. There were no significant differences between the two groups in transfusion, tumor size, resection margin, and R0 resection rate. For long-term outcomes, LALR had better 3-year overall survival (OS) (HR 0.68, 95% CI [0.49, 0.95], p = 0.03), 5-year OS (HR 0.74, 95% CI [0.57, 0.95], p = 0.02), 3-year disease-free survival (DFS) (HR 0.82, 95% CI [0.69, 0.98], p = 0.03), and 5-year DFS (HR 0.81, 95% CI [0.67, 0.96], p = 0.04) than OALR but without significant differences in 1-year OS and DFS.
Conclusions: LALR seems feasible for the treatment of HCC considering the clinical advantages regarding short- and long-term outcomes.

[ABST-0265]

The learning curve of the laparoscopic liver resection according to the previous surgical experience

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Background: Liver resection is a difficult operation due to anatomical complexity or unexpected bleeding. Among them, laparoscopic liver resection is an operation that requires a very high level of technique. We tried to analyze the learning curve of liver resection according to the previous surgical experience.
Methods: All consecutive cases of laparoscopic liver resection between July 2007 and July 2019 in a tertiary referral hospital were enrolled in this retrospective cohort study. One surgeon performed all surgical procedures. The total number of cases was 1000, and the learning curve was analyzed by dividing them by surgical type using a cumulative sum control chart of the operative time.
Results: The first laparoscopic liver resection was left lateral sectionectomy, and its cutoff value of the learning curve was 50. The second one was left hemihepatectomy, and its cutoff value of the learning curve was 45. Laparoscopic right hemihepatectomy was performed for the first time in case 14, and its cutoff value of the learning curve was 35. Laparoscopic donor right hemihepatectomy was performed for the first time in case 390, and its cutoff value of the learning curve was 5.
Conclusions: For the simplest anatomical liver resection, left lateral sectionectomy, the cutoff value of the learning curve for the laparoscopic liver resection was 50, and for complex donor right hemihepatectomy, the cutoff value of learning curve for the laparoscopic liver resection was 5. As a result of these analyses, we found that the learning curve of laparoscopic liver resection is greatly affected by the previous surgical experience.

[ABST-0276]

Development and validation of a safety and efficacy-associated risk calculator for hepatocellular carcinoma in the elderly after resection (SEARCHER): An international multicenter study

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Background: Increased life expectancy and improved perioperative management have resulted in increased utilization of hepatectomy for hepatocellular carcinoma (HCC) among elderly patients. However, individualized model for predicting the surgical safety and efficacy is lacking. The present study aimed to develop a Safety and Efficacy-Associated Risk Calculator for HCC in the Elderly after Resection (SEARCHER).
Methods: From an international multicenter database, elderly patients who underwent curative-intent hepatectomy for HCC were stratified by patient age: 65–69 years, 70–74 years, 75–79 years, and ≥ 80 years. Short- and long-term outcomes among the 4 groups were compared. Univariate and multivariate analyses of risk factors of postoperative major morbidity, cancer-specific survival (CSS), and overall survival (OS) were performed in the training cohort. A nomogram-based online calculator was then constructed and validated in the validation cohort.
Results: With increasing age, the risk of postoperative major morbidity and worse OS increased (P = 0.001 and 0.020), but not postoperative mortality and CSS (P = 0.577 and 0.890) among patients across the 4 groups. Based on three nomograms to predict major morbidity, CSS and OS, the SEARCHER model was constructed and made available at https://elderlyhcc.shinyapps.io/SEARCHER. The model demonstrated excellent calibration and optimal performance in both the training and validation cohorts, and performed better than the several commonly-used conventional scoring and staging systems of HCC.
Conclusions: With higher potential postoperative major morbidity and worse OS as patients age, the decision whether to perform a hepatectomy for HCC needs to be comprehensively considered in the elderly. The proposed SEARCHER model demonstrated good performance to individually predict safety and efficacy of hepatectomy in elderly patients with HCC.

[ABST-0277]

Association of adjuvant radiotherapy with long-term overall and recurrence-free survival following hepatectomy for hepatocellular carcinoma: A multicenter propensity-matched study

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Background: R0 resection with wide margins is the gold standard for hepatocellular carcinoma (HCC), yet R0 resection with narrow-margin and even R1 resection is not uncommon in real-world clinical practice. We sought to characterize the efficacy of adjuvant radiotherapy on long-term oncological survival following hepatectomy for HCC with close/positive surgical margins using propensity-matched analysis.
Methods: Using a multi-institutional database, patients with HCC who underwent hepatectomy with close margins (0.1 $\sim$ 1.0 cm) or pathologically positive margins were analyzed. Using propensity score matching (PSM) and multivariate Cox-regression analysis, the effect of adjuvant radiotherapy on long-term overall survival (OS) and recurrence-free survival (RFS) was evaluated.
Results: Among 683 patients who met inclusion criteria, 82 patients received adjuvant radiotherapy within 10 weeks after surgery. Radiotherapy-related major toxicity was minimal among patients receiving adjuvant radiotherapy. PSM analysis created 78 matched pairs of patients. In the PSM cohort, median OS and RFS among patients treated with adjuvant radiotherapy were more favorable than individuals who were not treated (72.5 and 37.3 months vs. 52.5 and 24.0 months, both $P < 0.05$). After adjustment for other confounding factors on multivariate analyses, adjuvant radiotherapy remained independently associated with favorable OS and RFS following hepatectomy with close/positive margins for HCC (HRs: 0.821 and 0.827, respectively).
Conclusions: Despite the lack of consensus on the role of adjuvant radiotherapy following HCC resection, this PSM analysis suggested improved OS and RFS with adjuvant radiotherapy following hepatectomy with close/positive margins for HCC. Future randomized controlled trials are needed to further define the survival benefit of adjuvant radiotherapy for patients with HCC.

[ABST-0299]

Reappraisal of clinical significance of microvascular invasion in single hepatocellular carcinoma up to 2 cm

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Background: In AJCC 8th edition, solitary hepatocellular carcinoma (HCC) $\leq$ 2 cm belongs to T1a irrespective of microvascular invasion (MVI) because MVI does not affects long-term survival in this stage. However, the effect of MVI on postoperative recurrence has not fully investigated in patients with HCC up to 2 cm.
Methods: From January 2000 to December 2020, 243 patients with the distinct type of HCC $\leq$ 2 cm who underwent curative resection were included for this study. All patients were divided into the two groups: MVI (+) (n = 87) and MVI (-) (n = 156) groups. Propensity score matching (PSM) was conducted to match patients with a ratio of 1:1 based on clinical and liver function-related variables. A total of 66 patients were matched. Disease-free survival (DFS) and overall survival (OS) were compared before and after PSM. In addition, we investigated predictive factors for MVI.
Results: MVI (+) group showed younger age, more B viral etiology and less severe fibrosis score before propensity score matching (PSM). Low platelet count (< 100,000) (HR: 2.054, p = 0.009) and blood loss more than 150 cc (HR: 1.883, p = 0.028) were significant poor prognostic factor and B viral etiology was positive prognostic factor (HR: 0.392, p = 0.028) for DFS in multivariate analysis. Low platelet count (< 100,000) was the only poor prognostic factor for OS (HR: 2.388, p = 0.046). After PSM, MVI (+) group showed significantly poor DFS than MVI (-) group (p = 0.007), however OS did not show statistical difference (p = 0.084). Invasive gross type and poorly differentiation ($p < 0.01$ for all) were found to be predictive factors for MVI.
Conclusions: In patients with HCC up to 2 cm, underlying liver function was the dominant prognostic factor for long-term survival, however MVI was found to have a strong effect on postoperative recurrence after matching the liver function status. Therefore, MVI should be considered to predict prognosis and postoperative surveillance in T1a HCC.

[ABST-0309]

Robotic single plus one right hepatectomy for donation

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Background: Most important concern in living donor liver transplantation is donor safety. At the same time, minimal invasive approach has become widely performed in major hepatectomy. Nowadays, pure laparoscopic or robotic donor hepatectomy has been increased with development of surgical technique. This is first case of successful robot donor hepatectomy using minimized port number.
Methods: Donor is 32 years old male. There is no anomaly in liver anatomy. Mid hepatic vein has two branches from right liver. MRCP show normal confluence of bile duct. According this finding, Robotic

donor hepatectomy was performed using the Da Vinci Xi single-site© surgical platform (DVSSP) and additional one port. Additional robotic 12 mm-port was placed left side of patient and 3rd arm was used this site.
Results: After the pathologist confirmed that there was no fatty liver in the liver biopsy, full right lobe mobilization was performed, and hilar dissection was done. right hepatic artery was isolated carefully. Right portal vein was completely exposed and isolated under retracting right hepatic artery laterally. Liver parenchymal transection line was drawn after transient clamping of the right hepatic artery and right portal vein using bulldog clamp. Transection plane was straightly exposed using rubber band retraction technique. After liver parenchymal resection was performed, hilar plate was isolated carefully. After The caudate lobe parenchyma was divided, and parenchyma transaction was completed. After suprapubic transverse incision was made for liver delivery, right bile duct, right hepatic artery, right portal vein was divided. Right hepatic vein also ligated and divided using endo GIA.
Conclusions: The donor was discharged on the 5th postoperative day after confirming that there was no complication on postoperative CT scan. donor and recipient live well without complication.

[ABST-0325]

Effect of postoperative administration of nafamostat mesilate on posthepatectomy liver failure: A propensity score match analysis

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Background: Ischemia/reperfusion (I/R) injury caused by massive bleeding is a major risk factor for posthepatectomy liver failure (PHLF). Nafamostat mesilate (NM), a synthetic protease inhibitor, decreased the risk of I/R injury in observational studies. The aim of this study is to investigated whether the administration of NM reduces the risk of PHLF in patients undergoing hepatectomy for hepatocellular carcinoma (HCC).
Methods: We retrospectively reviewed the medical records of 1114 consecutive patients who underwent hepatectomy for HCC between 2004 and 2020. NM was selectively administered to patients undergoing major hepatectomy with an estimated blood loss of > 500 mL. NM group was administered via intravenous infusion of 20 mg of NM from immediately after surgery until postoperative day 4. We performed 1:1 propensity score matching and included 56 patients in each group. PHLF was defined according to the criteria of the International Study Group of Liver Surgery (ISGLS), and only grade B or C patients were considered to have PHLF.
Results: The incidence of PHLF was lower in the NM group than in the control group (4 vs. 9 patients, $P = 0.018$). The mean peak total bilirubin (2.5 ± 4.7 vs. 3.7 ± 2.4, $P = 0.006$), aspartate transaminase (241.4 ± 174.6 vs. 502.5 ± 683.3 IU/L, $P = 0.01$), and alanine aminotransferase (333.2 ± 362.3 vs. 507.4 ± 795.1 IU/L, $P = 0.01$) levels postoperatively were significantly lower in the NM group. The mean hospital stay (13.2 ± 11.8 vs. 23.1 ± 26.8 days, $P = 0.01$) and major complication rate (38.6% vs. 44.6%, $P = 0.02$) were also significantly lower in the NM group.
Conclusions: Prophylactic administration of NM reduced the risks of complications and PHLF, and facilitated recovery in patients who underwent major hepatectomy with massive blood loss.

[ABST-0335]

A prospective study of somatostatin as pharmacologic portal modulation for post-hepatectomy liver failure: A pilot study

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Background: Liver resection has been established as a curative treatment for various hepatic tumors. However, severe post-hepatectomy liver failure (PHLF) is a major cause of mortality and factor in choosing non-surgical palliative treatment. Postoperative excessive portal pressure could cause shear stress to the small remnant liver after extensive liver resection as contributing factor for developing the PHLF. This study aimed to report a prospective clinical trial to evaluate somatostatin's effect as pharmacologic portal modulation for severe PHLF.
Methods: This prospective study enrolled 20 patients who received somatostatin for the treatment of PHLF between 2016 and 2021. When the patients fulfilled the 50–50 criteria (serum bilirubin > 2.9 mg/dL and prothrombin time $< 50\%$) on or before postoperative day 5, somatostatin (3.5 ug/kg/h) was administered by continuous infusion. The discontinuation criteria were as follows: serum bilirubin < 2 mg/dL and prothrombin time $\geq 50\%$. Prospectively collected clinical characteristics, laboratory tests, postoperative morbidity, and mortality were evaluated.
Results: Among the study cohort, 17 (85.0%) patients underwent major liver resection with the extent above right hemihepatectomy, and 3 (15.0%) underwent preoperative right portal vein embolization. The median ICG-R15 was 13.0 (range 6.8–56.1), and the MELD score was 10 (6–24). After the operation, somatostatin was started on a postoperative day 1 (1–19) and was administered for 9 (2–29) days. There were no obvious side effects related to the somatostatin. The median hospital stay was 33 (8–249) days. The 30-day and 90-day mortality were both 10.0%, and 17 (85.0%) patients recovered from severe PHLF.
Conclusions: Administration of somatostatin in the early postoperative period is considered safe and effective for the treatment of PHLF. Further large-scale comparative clinical trials are needed to validate this finding.

[ABST-0373]

Minimally invasive versus open liver resection for intrahepatic cholangiocarcinoma: A multi center propensity score matched study

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Background: Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver cancer and its incidence has increased in recent reports. Surgical resection is the only known option for curative treatment. However, there have been few studies about the feasibility and safe of minimally invasive liver resection for ICC. This study aimed to compare short- and long term oncologic outcomes between minimally invasive and open liver resection in patients with ICC.
Methods: This study retrospectively reviewed minimally invasive (laparoscopic and robotic) (N = 74) and open liver resection (N = 157) cases for ICC from 2010 to 2021 from four institutes in Korea. A multivariable logistic model based on factors related to the patient, tumor and surgical procedure were then used to estimate a propensity score. Before and after matching, short and long-term outcomes were compared between the two groups.
Results: There was no statistical difference in operative time, postoperative complication rate, transfusion rate, re-admission rate and R0 resection rate, however, the minimally invasive group provided less blood loss (median 365 cc vs 588 cc, P = 0.004) and shorter hospital stay (median 10.55 days vs. 13.24 days, p = 0.032) than the open approach. There were 5 open conversion cases in minimally invasive group. After propensity score matching, no significant difference was found in overall (P = 0.171) and disease free survival (0.317) between the two groups. 5-year survival rate was 69.6% in minimally invasive group and 65.5% in open group. Lymph node dissection was more frequently performed in the open group (37.84% vs. 65.61%, P < 0.001) and there was higher tendency of lymph node dissection in the robotic approach than laparoscopic group (63.64% vs 33.33%, p = 0.09).
Conclusions: Minimally invasive liver resection provided less blood loss and shorter hospital stay and comparable long term oncologic outcomes compared with open resection in patients with ICC. Therefore, laparoscopic or robotic surgery should be considered one of the options for surgical resection of ICC in well-selected patients.

[ABST-0442]

Clinicopathological profile, surgical indication and management of liver hemangioma: A 10 year experience of tertiary care centre

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Background: Hemangioma is the commonest benign liver tumor.- Most of the hemangiomas are asymptomatic and are usually discovered incidentally. Giant hepatic hemangioma, which may cause a variety of symptoms or complications including abdominal pain, early satiety, nausea, vomiting, jaundice, fever, dyspnoea, and spontaneous or traumatic rupture. Surgical treatment includes enucleation and resection whenever indicated.
Methods: Retrospective analysis of 10 years of prospectively collected data of patients who were treated surgically for hemangiomas between 2011 to 2011. Cases in which biopsy not correlating with hemangioma were excluded.
Results: During the 10 year period, we analyse 23 patients of liver hemangiomas who underwent surgical treatment and postoperative biopsy correlating with liver hemangiomas. Out of 23 patients,20 were female and 3 were male. The mean age of patients were 43.8 years with a range from (22-71 year).Most common symptoms were pain abdomen (n = 18),lump abdomen (n = 2),dyspnoea (n = 1),early satiety (n = 2).The most common location of the hemangioma was in the right lobe (n = 14) in segment 6. Out 0f 23,13 were multiple and 10 were solitary. hepatomegaly was present in 13 patients out of 23. and on endoscopy 8 patients had extraneous impressions over the duodenum or stomach. Out of 23,15 underwent enucleation and 8 resection, there was no mortality overall, no morbidity in the enucleation group while in the resection group one patient develop post-operative hemorrhage and one developed chyle leak, both managed conservatively.
Conclusions: Hemangiomas may present with a variety of symptoms such as pain abdomen, lump abdomen, early satiety, and dyspnea. Most lesions are found in women (female: male ratio = 7:1) and are detected between the third and fifth decades. Enucleation and resection were the surgical modalities with enucleation having overall fewer complications.

[ABST-0443]

Emergency right hepatectomy for atypical presentation of hepatic adenoma

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Background: Hepatic adenoma is a benign solid liver tumor. They are rare, tumors of epithelial origin and occur in less than 0.007–0.012% of the population. Hepatic adenomas are usually asymptomatic, about 25–50% may present with pain abdomen. Large adenomas have a tendency to rupture and bleed massively inside the abdomen. Whenever indicated surgical resection is a definitive treatment modality.
Methods: We present a unique case of a 65-year female who presented with progressive and deteriorating breathlessness for the last six months with hepatic adenoma compressing right lung, Inferior Vena Cava, and right ventricle for which emergency right hepatectomy was done with a right thoracoabdominal incision.
Results: The patient was kept on mechanical ventilation postoperatively for 48 h, and electively extubated on POD -3. In the postoperative period patient showed immediate improvement in symptoms and the patient was able to lie down in a supine position comfortably.and peripheral edema was reduced subsequently. The postoperative period was uneventful except for chylous ascitis, which was improved with conservative management and the patient was discharged in stable and satisfactory condition on Postoperative day 14.
Conclusions: Timely surgical intervention is needed to alleviate sypmtoms in such rare presentations of hepatic adenoma.

[ABST-0489]

Single versus multiple port laparoscopic left lateral sectionectomy for hepatocellular carcinoma: A retrospective comparative study

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Background: Single port laparoscopic surgery has been applied in the hepato-biliary-pancreas (HBP) field. We aimed to describe our experience with single port laparoscopic left lateral sectionectomy (SLLS) and to compare the feasibility of this technique with those of conventional multi-port laparoscopic left lateral sectionectomy (MLLS) in the treatment of hepatocellular carcinoma (HCC).
Methods: A total of 65 consecutive patients who underwent SLLS (n = 22) and MLLS (n = 33) for HCC were enrolled. The operative parameters of safety and feasibility and the short-term oncological outcomes were compared.
Results: The length of postoperative hospital stay (PHS) was significantly shorter in the SLLS group than in the MLLS group (3.42 vs. 4.15 days, P = 0.023). No significant difference between the two groups was found in the operation time (62.38 vs. 69.24 min in the SLLS group and MLLS group, respectively, P = 0.583). The 1-year recurrence-free survival rate was 76.8% in the SLLS group and 74.6% in the MLLS group (P = 0.82). Subgroup analysis showed that for patients without cirrhosis (METAVIR fibrosis more than F2), the PHS was shorter in the SLLS group than in the MLLS group (P = 0.023), while for patients with cirrhosis, the PHS was not significantly different between the two groups (P = 0.326), although it was shorter in the SLLS group.
Conclusions: SLLS was a feasible and safe surgical approach for treating HCC on the left lateral section.

[ABST-0508]

Safety and feasibility of laparoscopic liver resection for hepatocellular carcinoma located in posterosuperior segments compared to anterolateral segments

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Background: Laparoscopic liver resection has become a standard procedure for hepatocellular carcinoma (HCC) in many centers. Nevertheless, laparoscopic liver resection for HCC located in posterosuperior segments is demanding procedure even experienced hepatobiliary surgeons. We compared the outcomes between laparoscopic liver resection for HCC located in posterosuperior segments (S7, S8) and anterolateral segments (S5, S6).
Methods: We performed a retrospective analysis for 279 patients who received laparoscopic liver resection (except left hepatectomy) for HCC from September 2014 to December 2021 in Kyungpook National University Hospital. Patients were classified two groups, posterosuperior group (n = 170) and anterolateral group (n = 109).
Results: There were no differences in preoperative patients characteristics between two groups. Distribution of resection type (anatomical vs non-anatomical resection) was no significant differences between two groups. Operation time and intraoperative transfusion were greater in posterolateral group. Postoperative complication rate, hospital stay and oncologic outcomes (pathologic report, overall survival and disease free survival) were not significantly different between two groups. We had no open conversion case in posterolateral group.
Conclusions: With increased experience for major hepatectomy and the advance of laparoscopic instruments, laparoscopic liver resection for HCC located in posterosuperior segments is safe and feasible surgical procedure compared to anterolateral segments resection. Tumor status and anatomical variation of liver must be considered for oncologic safety.

[ABST-0512]

The usefulness of platelet based predictors in liver fibrosis assessment

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Background: Liver fibrosis is conventionally diagnosed with liver biopsy. Surrogate markers, various prediction models, and scoring systems have been proposed for predicting liver fibrosis. This study aimed to validate known predictors in liver fibrosis assessment.
Methods: We enrolled 101 patients who underwent liver biopsy or liver resection prospectively between November 2015 and July 2019. We scored liver tissue for the degree of fibrosis according to Metavir score system (0 to 4). We evaluated the correlation between the degree of fibrosis and various predicting values; total serum bilirubin, platelet count, AST to Platelet Ratio Index (APRI), Albumin-bilirubin (ALBI) score, Model For End-Stage Liver Disease (MELD) score, FIB-4 score, serum Mac-2 binding protein glycosylation isomer (M2BPGi).
Results: The histological stage of liver fibrosis was F0 in 36 patients, F1 in 6 patients, F2 in 10 patients, F3 in 14 patients, F4 in 35 patients. Predictors showed statistical significance for diagnosis of liver fibrosis as follows; Serum total bilirubin ($P < 0.001$), platelet count ($P < 0.001$), AST to Platelet Ratio Index (APRI, $P < 0.001$), Albumin-bilirubin (ALBI, P = 0.007) score, Model for End-Stage Liver Disease (MELD, p = 0.021) score, FIB-4 score ($P < 0.001$), serum Mac-2 binding protein glycosylation isomer (M2BPGi, P = 0.040). Among them, platelet count (0.792) revealed the highest AUC values, followed by Fib-4 (0.727) in ROC curves.
Conclusions: Although scores and markers for predicting liver fibrosis have been developed, platelet count has still been one of the most powerful predictors. However, the sample size of our study is small, so it is necessary to verify more various markers in more large patients.

Biliary and Pancreatic Disease

[OP-0918]

Integrated bile lipidome and meta-proteome analysis classifies lipid species and microbial peptides predictive of Carcinoma of Gall bladder

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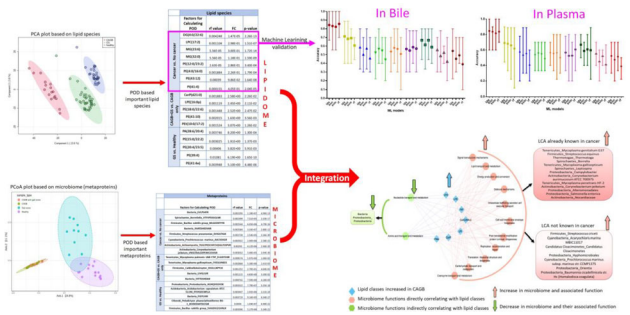
Objectives: Histopathological examination is gold standard for detection of gall-stone (GS) or gall bladder carcinoma (CAGB). Bile

concentrated in the gall bladder, is expected to recapitulate metagenomics/molecular changes associated to development of CAGB.
Materials and Methods: Bile samples were screened for lipidomics and metaproteome (microbiome) signatures capable of early detection of cancer. Analysis of training cohort (n = 87) showed that metastability of bile was reduced in CAGB patients ($p < 0.05$).
Results: Our results showed that CAGB was associated with the alteration of bile lipidome and microbiome as indicated by multivariate PLS-regression analysis and alpha, beta diversity indexes. Significant reduction of lipid species and increase in bacterial taxa were found associated to development of CAGB with gallstone and without Gallstone ($p < 0.05$, Log FC > 1.5). Multimodular correlation network (MMCN) created using weighted lipid/ Meta-proteomic correlation network analysis (W [L/MP] CNA) showed striking associations between lipid modules and meta-proteomic functionality. A significant and direct correlation of Meta-proteomic modules/ functionality and inversely correlation of lipid modules and species with the clinical parameters and bile acid profile was observed in CAGB patients ($p < 0.05$). Signifcant increase in bacterial taxa; Leptospira, Salmonella enterica, Mycoplasma gallisepticum and their functionality showed direct correlation with lipid classes; Lysophosphatidylinositol, Ceramide 1-phosphates, Lysophosphatidylethanolamine, others and development of CAGB ($r^2 > 0.85$). Lipid/metaproteomic signature based probability for CAGB was > 90% whereas probability for gall-stone was > 80% ($p < 0.05$). Finally, we identified 8 lipid species of diagnostic capability for CAGB and cross-validated, using 4 machine learning approaches in two separate test cohorts (n = 38; bile (T1) and paired plasma (T2) cohort, which jointly showed highest accuracy (99%), sensitivity (98%) and specificity (100%) with random forest model for CAGB detection.
Conclusion: Deep and integrated analysis of bile lipidome and metaproteome identify a panel of lipid species /meta-proteome capable of segregating patients predisposed to carcinogenesis of the gall bladder.



Pediatric Hepatology

[OP-0586]

Variceal bleeding in toddlers: Is the endoscopic outcome in extrahepatic portal hypertension worse than liver disease?

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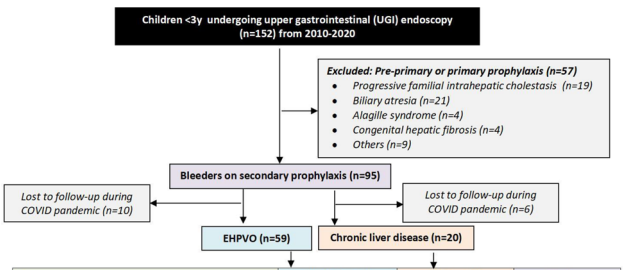
Objectives: Children < 3 years with portal hypertension may have life-threatening variceal bleeding due to higher portal pressures as compared to older patients. We aimed to evaluate the role of secondary prophylaxis and the endoscopic outcome of bleeding toddlers.
Materials and Methods: Toddlers with extrahepatic portal venous obstruction (EHPVO) were compared with chronic liver disease (CLD). As a standard protocol, all bleeders underwent endoscopic sclerotherapy at 2–3 weekly sessions till primary eradication of esophageal varices (EV) followed by 3–6 monthly sessions for endoscopic surveillance. Final outcome was noted at follow-up.
Results: Of the 151 patients, 79 (n = 59 EHPVO,n = 20 CLD) underwent secondary prophylaxis. The etiology of CLD was operated biliary atresia (n = 15), sclerosing cholangitis (n = 3) and congenital hepatic fibrosis (n = 2). Figure 1 shows the study flow and compares the differences in the endoscopic outcomes of the two groups. As compared to CLD, EHPVO had earlier onset of bleeding, more hypersplenism, endoscopic sessions,total volume of sclerosant, recurrence of EV and portal hypertensive gastropathy (PHG). 6% had sclerotherapy complications (bleeding ulcers and stricture). Duration of follow-up was 36 (12–120) months. 22% EHPVO required secondary eradication of EV. Overall interval bleeding from varices during primary eradication occurred in 20% within 11 (7–16) days from last endoscopic session. None of the patients developed bleeding from gastric varices or PHG. Beta-blockers were given in 67% (EHPVO,n = 26; CLD,n = 4) for 22 (19–36) months. Using multivariate analysis, the independent predictors of recurrence of EV and secondary eradication were age of onset < 9mo (OR:4.8, 95%CI:2.6–13.3, $p < 0.01$), hypersplenism (OR:3.6, 95%CI:1.6–15.9, $p < 0.01$) and primary gastric varices (OR:5.4, 95%CI:4.5–8.8, $p = 0.03$). Non-favourable vascular anatomy for portosystemic shunting was observed (100% for Meso-Rex bypass; 64% for non-selective shunts) in EHPVO. 38% BA were referred for liver transplantation.
Conclusion: Toddlers with EHPVO have a greater degree of portal hypertension as compared to CLD. Endoscopic therapy is the mainstay since the majority may not have favourable anatomy for portosystemic shunting.



Parameters	EHPVO (n=59)	CLD (n=20)	P value
Age at first UGI bleed/mo	8 (4-36)	20 (8-30)	**0.01**
Age at presentation/mo	13 (6-36)	24 (10-30)	**0.01**
Hypersplenism[f], n (%)	36 (61)	5(25)	**0.007**
Post-bleed ascites, n (%)	23 (38)	8 (40)	0.9
Addition of beta-blockers, n (%)	36 (61)	5 (25)	**0.007**
Large EV at onset, n (%)	59 (100)	18 (90)	0.9
Total No of endoscopic sessions	9(4-15)	5 (4-8)	**0.03**
Achievement of first eradication of EV, n (%)	56 (94)	16 (80)	0.05
No of sessions till first eradication	6 (4-10)	4 (2-11)	**0.04**
Volume of sclerosant[a] till first eradication/ml	17.5 (8-53)	10 (4-63)	**0.03**
Interval bleeding, n (%)	13 (22)	3 (15)	0.8
Recurrence of esophageal varices[i] n (%)	20 (34)	3 (15)	**0.04**
No. requiring second eradication[ij] n (%)	7 (22)	0	-
Sessions required for second eradication	4 (1-5)	Not applicable	-
Volume of sclerosant[a] till second eradication/ml	12 (4-26)	Not applicable	-
Gastric varices at onset, n (%)	23 (39)	11 (55)	0.6
Location of Gastric Vx at onset [g] (LC/GC/F)	20/2/1	8/0/3	-
Gastric varices at last endoscopy, n (%)	15 (29)	4 (20)	0.6
Location of Gastric Vx at last endoscopy (LC/GC/F)	10/3/2	3/0/1	-
PHG[c] at onset, n (%)	12 (20)	9 (45)	**0.03**
PHG at last endoscopy, n (%)	28 (47)	8 (40)	0.5

EHPVO: extrahepatic portal venous obstruction; BA: biliary atresia; UGI: upper gastrointestinal; RCS: red colour signs; PHG: portal hypertensive gastropathy; GOV: gastroesophageal varices; IGV: isolated fundal gastric varices. [a]Sclerosant: 1% polidocanol; Classification systems: [g] Paquet; [k] Sarin, [v]Taor; [c]Hypersplenism defined as total leucocyte count <3500/mm^3 and Platelets <80,000/mm^3 evaluated 3 months post-variceal bleeding. [ij] Primary eradication: Eradication of naive varix till no varix is persisting or till tag± neovascualrisation formation; [ij]Secondary eradication: : Eradication of recurrence of varix (≥Grade II with RCS) till no varix is persisting or till tag formation. [i]Recurrence: appearance of ≥ grade I esophageal varices. LC: lesser curvature, GC: greater curvature, F: fundus

[OP-0590]

Application value of serum HBV RNA, HBcrAg and HBsAg for safely antiviral therapy cessation in children with chronic hepatitis B

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Objectives: To explore the related factors for safely stopping antiviral therapy in children with chronic hepatitis B (CHB) patients.
Materials and Methods: 125 children with CHB received IFN combination with nucleoside analogues (NAs) or NAs monotherapy was studied. The primary end point was meeting the stopping criteria (HBeAg seroconversion, HBV DNA undetectable for at least four consecutive times, ALT normal). HBV RNA levels were measured using real-time fluorescence quantitative PCR. The level of serum HBcrAg was detected using chemiluminescence enzyme immunoassay. The dynamic changes of HBV RNA, HBV DNA and HBeAg and the correlation of HBV RNA with other HBV markers were investigated and followed up every 3 months until meeting the stopping criteria.
Results: Baseline HBV RNA levels was positively correlated with serum HBsAg levels ($r = 0.688$, $p < 0.0001$), HBV DNA ($r = 0.521$, $p < 0.0001$) and HBcrAg levels ($r = 0.472$, $p < 0.0001$). The cumulative rates of HBsAg loss was 49.4% at end of treatment. Patients with double negative HBV RNA and HBsAg at the end of treatment had high HBsAg seroclearce rate (100%), can be considered stopping antiviral treatment. EOT positive HBV RNA and HBsAg were found had higher the risk of virological recurrence rates (62.5%).
Conclusion: NAs cessation is suitable only for double negative HBV RNA and HBsAg.

[OP-0976]

Plasma metabolomics and machine learning characterises metabolite signature capable of segregating patients with poor outcome in paediatric cirrhosis

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Objectives: Pediatric cirrhosis is a life-threatening illness with high mortality up to 40%. Primary causes of cirrhosis in children are biliary atresia, genetic-metabolic diseases, autoimmune hepatitis, Wilson's disease and others. Development of cirrhosis in children's predisposes them to early development of sepsis and/or poor outcome. Early diagnosis of cirrhosis, sepsis and/or poor outcome in such patients may increase survival rate; therefore, development of new diagnostic methods is crucial. We investigated whether metabolomics and machine learning (ML) approaches could segregate patients with poor outcome (sepsis/mortality) in paediatric cirrhosis at baseline.
Materials and Methods: Plasma metabolomics was studied using ultra-high-performance liquid chromatography and high-resolution mass-spectrometry to identify patients with poor outcome (sepsis/mortality) in paediatric cirrhosis at baseline. Altogether, 154 paediatric patients were analysed of them, 54 in derivative[40Cirrhotics (C) and 14Non-cirrhotics (NC)] and 100 in validation cohort[75C, 25NC]. Differentially expressed metabolites (DEM) with highest AUC and lowest mean decrease in accuracy were identified in cirrhotics, sepsis and were correlated with the severity (PELD score) and outcome (mortality) in pediatric patients.
Results: Of the 762 annotated features (metabolomic/biochemical/spectral databases), at baseline 120 plasma metabolites (Up-109, Downregulated-11) discriminated Cirrhotics from Non-Cirrhotics in paediatric patients ($FC > 1.5$, $p < 0.05$). Cirrhotics documented significant increase in Tryptophan metabolism, steroid hormone biosynthesis, purine metabolism and others ($p < 0.05$). Most importantly high L-Formylkynurenine (546 Folds), 3-Hydroxy-1H-quinolin-4-one (20 Folds), 12-Hydroxydodecanoic acid (12 Folds), L-Isoleucine (11 Folds), Cortisone (8 Fold), Hypoglycine-A (5 folds), Aminopropylcadaverine (5 Folds), 2,3,4,5-Tetrahydrodipicolinate (3 Folds) and others segregated Cirrhosis from Non-Cirrhosis ($p < 0.05$). Additionally, plasma L-Formylkynurenine, 3-Hydroxy-1H-quinolin-4-one, 12-Hydroxydodecanoic acid, L-Isoleucine and Cortisone segregated sepsis and non-survivors ($FC > 2$, $p < 0.05$, $AUC > 0.8$). In validation cohort, baseline plasma L-Formylkynurenine; hazard-ratio (HR) of 3.5 (1.2–5.6), and Cortisone; HR:3 (1.5–5.2) showed high reliability[$AUC > 0.95$ (0.91–0.97)] for predicting non-survivors and correlated with PELD score ($r^2 > 0.5$, $p < 0.05$). L-Formylkynurenine (4FC), and Cortisone (3.5FC) cut-off reliably segregated non-survivors (log-rank $p < 0.01$) and showed $< 96\%$ accuracy, $< 95\%$ sensitivity and $< 95\%$ specificity using Random Forest-based Machine-Learning model.
Conclusion: Conclusion: Plasma metabolite L-Formylkynurenine (> 4FC), and Cortisone (> 3.5FC) can reliably predict cirrhosis, sepsis and poor outcome in paediatric patients.

Other

[OP-0179]

Urinary microbiome-based metagenomic signature for non-invasive diagnosis of hepatocellular carcinoma

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Objectives: Gut microbial dysbiosis plays an important role in the progression of chronic liver disease and hepatocellular carcinoma (HCC), but the role of microbiomes from different body sites, especially urinary tract, has not been studied. This study evaluated whether disease-specific changes of urinary microbiome are present in patients with HCC, and their potential as diagnostic biomarkers.
Materials and Methods: We performed cross-sectional analyses of urine samples from 471 HCC patients and 397 healthy controls, and

validated in an independent cohort of 170 HCC patients and 170 controls. Urinary microbiomes were analyzed by 16S rRNA gene sequencing. Urinary m-crobial diversity was significantly reduced in HCC, compared with control.
Results: There were significant differences in the relative abundances of several bacterial taxa that correlate with the presence of HCC, thus defining a specific urinary microbiome-derived metagenomic signature of HCC. We identified 14 microbial markers-based model which had a robust diagnostic accuracy (AUC, 0.94; balanced accuracy, 86.3%). In the validation, this model distinguished HCC with an AUC of 0.86 and an accuracy of 80.9%.
Conclusion: This study provides preliminary evidence for a urinary microbiome-based metagenomics signature to detect HCC.

Poster Exhibition

Basic Research

[OP-0009]

Liver enzyme changes following Covid-19 in patients with underlying liver diseases

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Objectives: In the recent 2 years,a novel Covid-19 virus played a crucial role in development of severe respiratory and multiple organ failure, including liver.The aim of the study is determine liver injury in patients with underlying liver diseases and evaluate the effect of treatment.
Materials and Methods: 137 patients (51% males, 49% females, mean age 34 years ± 6.5 with known liver diseases were admitted to our department for post-COVID control (median time post-infection 34 days ± 1.4). Previously, HBV was diagnoses in 18 (13.5%),mean ALT 31 (52.4–12.6),mean AST 24.8 (52.4–12.6), HCV in 43 (32% mean ALT 57 (195.1–16.9)mean AST 31.3 (61.9–17)), NAFLD/NASH in 74 ((54.5%)mean ALT 152.4 (1186 -19.7)mean AST 57.9 (70–19.4)). 22 (32.8%) have received antibiotic prophylaxis only, 25 (37% antiviral treatment (40% favipiravir,60% remdesivir)),9 (13.4%) had both antibiotics and antiviral treatment).
Results: Median Elevation of ALT/AST was mostly observed in NASH/NAFLD group with pre-COVID high liver enzymes (median ALT value 42 IU/ml vs 98 IU/ml $p < 0.005$; AST 26 IU/ml vs 84 $p < 0.005$).Mixed treatment with both antibiotics (azithromycin) and Favipirovir was associated with higher elevation of liver enzyme in all groups. NASH/NAFLD patients had the highest elevation of liver enzymes following COVID among chronic liver disease groups.
Conclusion: All Post-Covid patients, especially those with NASH/NAFLD, regardless of the presence or absence of concurrent chronic liver disease, regardless of receiving antibiotics, require monitoring of liver function tests from the beginning of the disease.

[PP-0025]

Role of aqueous suspension of Ocimum sanctum on liver biomarkers and lipid profile in alloxan monohydrate induced Diabetic rats

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Objectives: The present study was undertaken to evaluate the insulin secretion and anti-oxidative potential of Ocimum sanctum extract in diabetic rats.
Materials and Methods: alloxan monohydrate 70 mg/kg BW and Ocimum sanctum leaves 2.5 mg/kg BW.The biochemical parameters evaluated were serum lipid profiles and liver biomarkers using diagnostics kit.
Results: Diabetes increase blood glucose level and oral administration of Ocimum sanctum extracts daily for 14 days, to the diabetic rats caused 32.7% decrease on 7^{th} day and 56% decrease in the blood glucose level on 14 days of the start of treatmet. The levels of SGOT, SGPT, ALP, bilirubin, total Cholesterol, triglyceride and creatinine were significantly increased in alloxan induced diabetic rats. These adverse changes were reversed to near normal values in extracts of OS treated. In the present study indicates the increase in the levels of SGOT, SGPT, ALP, bilirubin, total Cholesterol, triglyceride and creatinine in serum when compared with control rat serum. The levels of SGOT, SGPT, ALP and bilirubin were increase 146%, 213%, 500%, 190.1%, 78.5%, 136.3% and 186% increase in alloxan induced diabetic rat serum as compared with control rats. Oral administration of Ocimum sanctum extracts for 14 days showed antidiabetic potential against alloxan diabetes induced alterations in the level of SGOT, SGPT, ALP and bilirubin. The levels of SGOT, SGPT, ALP and bilirubin were decreased by 38.6%, 42%, 78%, 46%, 35.3%, 44.4% and 51% in diabetic rats given OS extracts treatment compared with diabetic control rats.
Conclusion: Ocimum sanctum extracts increase insulin activity and reduced oxidative stress complication in diabetic rats.

[PP-0084]

Low-dose versus high-dose ursodeoxycholic acid co-administration with rosuvastatin/ezetimibe in a nonalcoholic fatty liver disease mouse model

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Objectives: Ursodeoxycholic acid (UDCA), statins, and ezetimibe have beneficial effects in nonalcoholic fatty liver disease (NAFLD). We investigated the efficacy of UDCA and rosuvastatin/ezetimibe co-administration in NAFLD therapy.
Materials and Methods: NAFLD mouse models were obtained through thioacetamide (TAA) injection and by fasting-refeeding with high-carbohydrate, high-fat diet (HFD), and choline-deficient L-amino acid-defined high-fat diet (CDAHFD). Low-dose UDCA (15 mg/kg) or high-dose UDCA (30 mg/kg) with rosuvastatin/ezetimibe (5: 10) (1 mg/kg) was administered.
Results: Rosuvastatin/ezetimibe co-administration with both low-dose (L-URE) and high-dose UDCA (H-URE) significantly decreased the serum alanine aminotransferase (ALT) levels (all $P < 0.01$) compared with the vehicle group; H-URE significantly decreased smooth muscle actin (SMA), collagen type 1 alpha 1 (Col1a1), and actin alpha 2 (ACTA2) mRNA levels compared with the vehicle and L-URE treatments in TAA-treated mice (all $P < 0.01$). In addition, in the group fasted and re-fed with high-carbohydrate, L- and H-URE treatments decreased the serum ALT levels and apoptotic cell

numbers compared with the vehicle group (all $P < 0.05$). Subsequently, H-URE decreased the number of ballooned hepatocytes and stearoyl-CoA desaturase 1 mRNA levels ($P < 0.05$) in the liver of HFD-fed mice compared with the vehicle group. In the CDAHFD-fed mouse model, L- and H-URE significantly attenuated collagen accumulation, SMA protein levels, and SMA, Col1a1, and transforming growth factor-beta mRNA levels compared with the vehicle group (all $P < 0.05$).
Conclusion: The hepatoprotective effects of the combination therapy with high-dose UDCA and rosuvastatin/ezetimibe were superior to those obtained with low-dose UDCA in a NAFLD mouse model.

[OP-0134]

Epidemiology of HCC in patients with viral hepatitis

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Objectives: Hepatocellular carcinoma is the most common cancer in the worldwide, representing more than 5% of all cancers. Liver cirrhosis, age, sex, smoking and drinking, and metabolic risk factors will increase the risk of cancer in HBV/HCV/HDV patients. Viral load, FIB-4, and stiffness of the liver can predict the risk of HCC in patients with viral infection. Moreover, effective prevention strategies are needed to reduce the risk of HCC. Secondary prevention includes effective antiviral treatment for HBV/HCV/HDV to prevent disease progression to HCC.
Materials and Methods: During period since January 2019 to September 2021, 4413 patients (57% males, 43% females, mean age 34 years ± 6.5) were included to our study, while 1421 (32%) with Hepatitis B, 2992 (67,7%) Hepatitis C and 181 (4%) with Viral Hepatitis B and D.
Results: Totally HCC was diagnosed in 117 patients (2,6%), with Hepatitis C 69 (2,3%), with Hepatitis B 41 (2,8%) and also with Hepatitis B + D—7 (3,8%) patients.
Conclusion: Chronic Viral Hepatitis are most important causes of HCC. Among viral hepatitis HCC often determined in B + D viral hepatitis group. Eliminating the route of transmission and vaccination against Hepatitis B will lead to a decrease in the incidence of HCC.

[OP-0203]

Combinatorial effect of ezetimibe and empagliflozin in nonalcoholic fatty liver disease in a mouse model and liver organoid for disease modeling of hepatic steatosis

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Objectives: Sodium-glucose cotransporter 2 inhibitor (SGLT2i) and ezetimibe, a cholesterol-lowering drug by targeting NPC1L1, have shown therapeutic potential for non-alcoholic fatty liver disease (NAFLD). SGLT2i and ezetimibe have different pharmacological mechanism, we hypothesized the combination of empagliflozin (selective SGLT2i) and ezetimibe could improve NAFLD additively.
Materials and Methods: We used the choline-deficient high fat diet (CD-HFD)-induced murine model of NAFLD that has key features of human metabolic syndrome. 6-week-old C57BL/6 J mice were fed a CD-HFD for 8 weeks. Then these mice were divided into four groups: vehicle, ezetimibe (10 mg/kg), empagliflozin (10 mg/kg), and ezetimibe (10 mg/kg) + empagliflozin (10 mg/kg). After 8 weeks, mice were sacrificed and subjected to blood measurements, and tissues for RNA isolation, lipid measurements and histology.
Results: CD-HFD-fed mice group exhibited liver weight gain with lipid accumulation and increased serum alanine aminotransferase (ALT). Ezetimibe, empagliflozin, and combination therapy significantly reduced liver steatosis. However, the histological NAFLD activity score (NAS) was most improved in the ezetimibe/empagliflozin group (0.667) than in the ezetimibe group (2.0, $P = 0.032$) or empagliflozin group (3.33, $P = 0.043$). Hepatic lipid contents were also significantly lower in the ezetimibe/empagliflozin group compared to other groups. Hepatic expression of lipogenesis genes such as ACC1 (Acetyl-CoA carboxylase 1) was significantly decreased in the ezetimibe/empagliflozin group. For in vitro studies of ezetimibe and empagliflozin, we established a long-term mouse liver organoids which were provided with fatty acid for inducing hepatic steatosis. Lipid accumulation was well observed in mouse organoids with fatty acid compared with control organoids. Then these liver organoids with fatty acid were also treated with ezetimibe and empagliflozin. Similarly, lipid accumulation was most diminished in the ezetimibe/empagliflozin group by fluorescence intensity.
Conclusion: Our data suggested that combined administration of empagliflozin and ezetimibe can additively improve NAFLD by decreasing lipogenesis. These results provide new insight into pathogenesis and strategies for treatment of the NAFLD.

[PP-0305]

Knowledge attitude and practices on hepatitis B and C among students in Kaski District, Nepal

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Objectives: The purpose of this study was to assess knowledge, attitude and practices of Bachelor level students, regarding hepatitis B and C.
Materials and Methods: The data were collected from bachelor level student of Prithivi Narayan campus, Kaski. The data were collected from January to June 2021. Purposive sampling method was used to collect the data. Descriptive statistics was applied for the data analysis.
Results: Of total 200 students 25.5% were male and remaining were female among them 5% were married. Regarding the religion 90% were hindu. All the students' knowledge regarding mode of transmission from unsterilized syringe and contaminated blood was found 100%. Likewise, 73.5% and 69.5% knows that tattooing and ear/nose piercing respectively can be the modes of transmission. Similarly, only 75.5% and 42% were known about the vaccine availability of hepatitis B &C. Likewise, 72% and 41% of students knows the treatment availability. Regarding the practice, 100% were found using sterilized syringe when required and get blood screened before transfusion. Only 87% were found asking barber to use new blades for

shaving or haircut. Regarding the attitude of students toward hepatitis B and C, 77.5% were liked to get themselves screened for hepatitis B and C. Similarly, Only 66% were liked to get further investigation or treatment if found positive for hepatitis B and C without symptoms.
Conclusion: The study shows the satisfactory level of knowledge attitude and Practices of students regarding Hepatitis B and C.

[OP-0350]

Pharmacovigilance studies of combination antihypertensive medications in liver disorders based on WHO causality assessment scale at tertiary care hospital, Hyderabad, Pakistan

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Objectives: Pharmacovigilance is a key part of rationale therapy. The objectives of current therapy was to assess the ADRs of combination antihypertensive therapy based on WHO causality assessment scale in different liver disorders.
Materials and Methods: A descriptive, non-interventional study was conducted at tertiary care hospital of Hyderabad, Pakistan. The duration of study was 01 year. A total of 674 patients were enrolled who atleast taken one combination antihypertensive therapy. A series of questions were asked to assess the ADRs based on WHO guidelines.
Results: Out of 674 patients, 73.88 were from male gender and 26.12 from female. Maximum patients age range from 55 to 65 years of age. More than 50% of patients had positive family history of hypertension. Telmisartan in combination with hydrochlorothiazide was the most frequently prescribed combination. Most common adrs were from valsartan with amlodipine. Based on WHO, maximum ADRs were classified in category of possible followed by probable. The p value is less than 0.05.
Conclusion: The study revealed that combination dual therapy has ADR reporting hence it should prescribed with great care. Pharmacovigilance studies is an ongoing process for assessment so proper education may also be provided to the health care professional for their importance.

[PP-0356]

Statin ameliorates hepatic inflammation and macrophage activation in CCL4 induced liver injury

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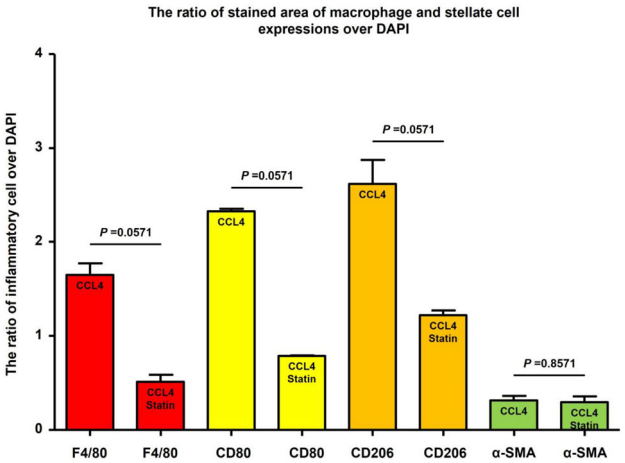
Objectives: The main cause of liver diseases including cirrhosis and cancer is the presence of hepatic inflammation. Recently, statin has been studied in chronic liver disease, and revealed the beneficial effects on the primary and secondary prevention of liver cirrhosis and cancer. In this study, we tried to reveal the underlying mechanism of statin to protect the hepatic disease progression focused on ameliorating hepatic inflammation and macrophage activation.
Materials and Methods: Eleven mice were divided into four groups as follows: the control group (n = 2); the Carbon Tetrachloride (CCL4) alone group (n = 4); CCL4 with statin group (n = 3); and statin alone group (n = 2). CCL4 was administered via oral route three times a week for 16 weeks. Atorvastatin administered via oral route twice a week for 16 weeks. Statin was administered on the day of not administering CCL4. Immunohistochemical staining of macrophage and stellate cell was performed in liver tissues and the ratio of staining area over DAPI was analyzed.
Results: Administration of CCL4 with statin decreased the expressions of F4/80, CD80 and CD206 in hepatic macrophage compared with CCL4 alone group. On the contrary, the expression of α-SMA in hepatic stellate cell was not changed between CCL4 alone group and CCL4 with statin group. The quantitative analysis of macrophage expression showed the tendency of decrease in CCL4 with statin group compared with CCL4 alone group. However, there was no statistical significance in F4/80 (P = 0.0571), CD80 (P = 0.0571) and CD206 (P = 0.0571), respectively. The α-SMA expression was not changed by CCL4 alone or CCL4 with statin or statin alone compared with control group. (P = 0.1025).
Conclusion: Statins can alleviate hepatic macrophage activation and polarization. However, statin does not affect the activation of hepatic stellate cells. Therefore, it is thought that the anti-inflammatory effect of statins appears through the amelioration of hepatic macrophage activity.



[PP-0437]

Role of plasmapheresis in liver failure management

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Objectives: Acute liver failure as a result of liver cirrhosis and HCC is still remaining one of the challenging and one the most discussed agenda in hepatology. We have been conducting a number of basic researches in this area and would like to share our results and conclusions with other collegues. The aim of this research is to assess plasmopheresis effect on liver failure.
Materials and Methods: Group 1 patients consisted of 120 patients with liver failure underwent therapeutic membranous plasmapheresis, 67 male and 53 female patients. Mean age of patients was 38 y.o. we have been using therapeutic membranous plasmapheresis without initial heparinization. Citrate and isotonic solutions were replaced

with neutral anolit. We have invention patent for this method #IAP 03,988 from 20.7.2009. Group 2 patients (Control group) consisted of 120 liver failure patients who were managed according standart protocol without plasmapheresis.
Results: In group 1 we have observed moderate to remarkable devrease of bile acids, ALT, AST, CRP, mean molecular peptides, alkaline phosphotase after 3rd session of plasmapheresis, meanwhile in Group 2, all above mentioned parameters were still elevated. Follow up imaging (US, CT scan, MRI) also showed better regressive ocourse at Group 1, meanwhile at Group 2 we have recorded more stationary course and even progressive course at some patients.
Conclusion: Therapeutic plasmapheresis with neutral anolit results in better detoxication effect, which is presented by free radicals process recuperation and improvement of clinical, laboratory and imaging features of liver failure patients. This result has been achieved due to efferent and oxidase technologies, which in its turn approve feasibility of this method.

[PP-0439]

Laser effect on adenocarcinoma 755

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Objectives: Nowadays cancer treatment is still remaining one of the most challenging problems of modern medicine. Many treatment protocols, as well as many new approaches are being tested now to treat the cancer. However, in the data, we could not find sufficient reviews on laser beam influence on cancer cells. We conducted laboratory research of low intense laser radiation (LILR) on tumor cells.
Materials and Methods: Adenocarcinoma 755 tissue was implanted to 20 Vistar rats. Group 1 consisted of 10 animals, which were not exposed to radiation Group 2 consisted of 10 animals, which were exposed to 10 sessions of laser therapy. Mean mass of tumor in Group 1 was 1,8 g at the beginning of study and 2,75 g at the end of research. Mean mass of tumor in Group 2 was 1,75 g at the beginning and 1,15 after 10 sessions of radiation.
Results: Thus, tumor mass growth indicates a remarkable decrease after LILR exposure. After 5 sessions of LILR tumor mass decreased more than 3 times comparing to control group. Morphological studies showed tumor cell decreased to 1/3 in nucleus, as well as incresed of intercelullar space, tumor cells became more polymorphic. it is essential to note the dramatical increase in neutrophylic number in tumor stroma. The number of tumor cell mitosis decreased significantly, as well as number of nucleus including 3H thymidine.
Conclusion: In this regard, we think that LILR with IR range slow down adenocarcinoma 755 growth, which was presented by proliferation and mitosis decrease.

[PP-0449]

Liver function tests in recovered COVID-19 patients with acute heart failure and associated outcomes

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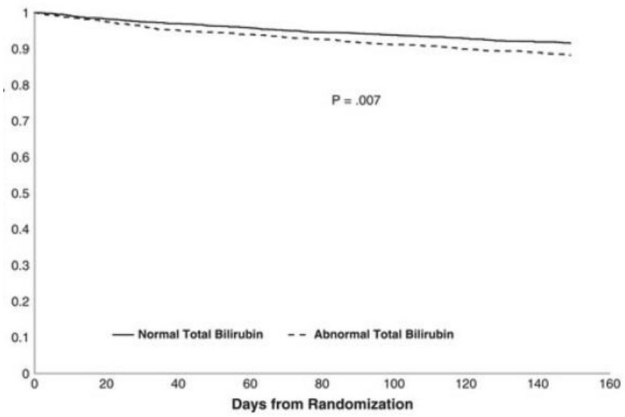
Objectives: The objective of this study characterize abnormal liver function test after recovered coronavirus in patients with heart failure (HF) as they are commonly encountered yet poorly defined.
Materials and Methods: This study is a Clinical Effectiveness of nesiritide in decompensated Heart Failure use data from SCEND-HF to characterize associations with baseline liver function tests (LFTs). each LFT was analysed as both a continuous and dichotomous variable [normal vs. abnormal; bilirubin > 1.0 mg/dL; aspartate aminotransferase (AST) and alanine aminotransferase ALT > 35 mmol/L.
Results: Mean Logistic regression assessed the association of LFTs and 30-day all-cause mortality and HF rehospitalization, and Cox proportional hazards assessed the association with 180-day all-cause mortality among patients alive at a 30-day landmark. In SCEND-HF, 2128 (48%) had complete admission LFT data. Of these, 39% had abnormal bilirubin, 22% had abnormal ALT, and 29% had abnormal AST. Patients with abnormal LFTs were younger, had lower body mass index, and lower left ventricular ejection fraction. In multivariable models, increased total bilirubin was associated with increased 30-day mortality or HF rehospitalization [hazard ratio (HR) 1.17 per 1 mg/dL increase 85% confidence interval (CI) 1.04, 1.32; P = 0.012], but not with an increase in 180-day mortality (HR 1.10, 95% CI 0.97, 1.25; P = 0.13) per 1 mg/dl increase. Compared with normal bilirubin levels, abnormal bilirubin was associated with increased 30-day mortality or HF rehospitalization (HR 1.24, 95% CI 1.00, 1.54; P = 0.048) and 180-day mortality (HR 1.32, 95% CI 1.08, 1.62; P = 0.007). We found no association with AST or ALT and outcomes.
Conclusion: More than 40% of patients Hospitalized with acute HF had abnormal LFTS.After multivariable regulation, only High bilirubin was independently related with worse clinical outcomes and may represent an important prognostic variable.



[OP-0455]

RIG-I induced reactive oxygen species drive metabolic changes that modulate the antiviral immune response in human hepatocytes

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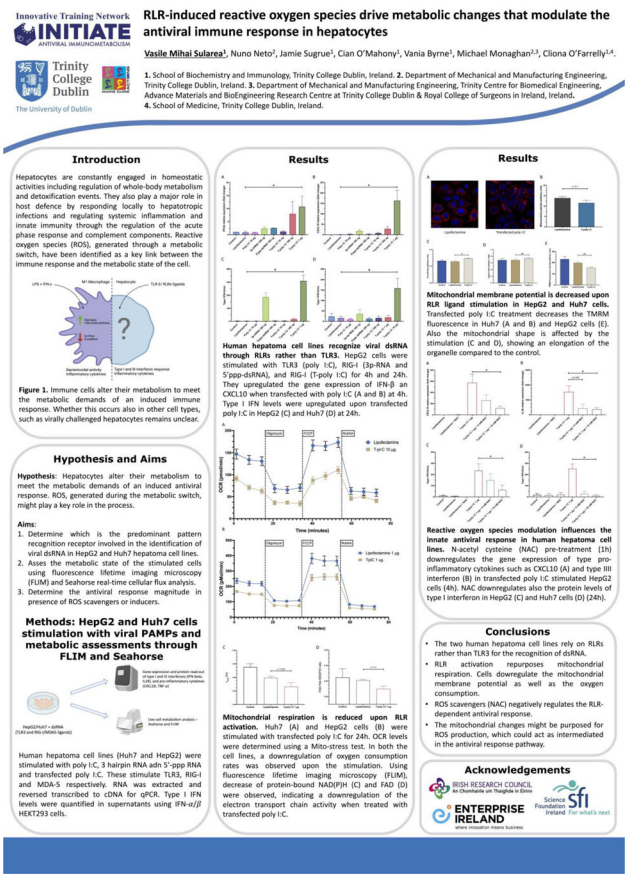
Objectives: Hepatocytes mediate diverse activities including processing of gut-derived products, regulation of whole body metabolism and detoxification events. They also play a major role in host defence by mediating systemic inflammation and innate immunity through the production of acute phase proteins and complement components, and responding locally to infection by hepatotropic viruses via pattern recognition receptor activation, such as RIG-I and TLR3. Immune cells alter their metabolism to meet the metabolic demands of an induced immune response and reactive oxygen species (ROS), generated through a metabolic switch, have been identified as a key link between the immune response and the metabolic state of the cell. We sought to determine whether hepatocytes also use this process to mediate anti-viral immunity.
Materials and Methods: We used two hepatoma cell lines (HepG2 and Huh7), treated with polyI:C, a viral analogue, to explore the link between the metabolic state of hepatocytes and their innate antiviral immune activity.
Results: Following polyI:C treatment, we saw increased CXCL10 and IFN-b gene expression and protein production. To assess the metabolic activity of hepatocytes, we used fluorescence lifetime imaging microscopy (FLIM) and Seahorse real-time cellular flux analysis and demonstrated reduced oxygen consumption following polyI:C treatment. Using Mito SOX as ROS-fluorescent probe, we found that ROS levels increased after treatment with polyI:C. Modulating ROS levels through scavengers (N-acetyl cysteine) and oxidants (Rotenone), regulated the amplitude of the antiviral response, reducing or enhancing the response respectively.
Conclusion: Our results indicate a role for ROS in shaping the antiviral immune responsiveness of human hepatocytes.



[PP-0493]

Evogliptin attenuates liver fibrosis by preventing hepatic stellate cell activation and decreasing connetive tissue growth factor

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Objectives: Evogliptin, a dipeptidyl peptidase 4 inhibitor, is an antidiabetic drug. Several studies have reported the anti-fibrotic effects of DPP-4 inhibitors in various organ systems including heart, lungs, liver and kidneys. However, there are few reports of the effect of evogliptin on liver fibrosis. Therefore, in this study, we investigated whether evogliptin reduces liver fibrosis in primary hepatic stellate cells and primary hepatocytes.
Materials and Methods: We isolated primary hepatic stellate cells and primary hepatocyte from C57BL/6 mice and primary hepatocyte from hepatocyte-specific ATG7 knockout (ATG7$^{f/f}$-Cre^{+})t mice. The expression levels of αSMA, CTGF, collagen, LC3 and Samd3 were evaluated by western blot analysis. LC3 puncta was observed with a fluorescence staining microscope.
Results: Evogliptin reduced the expression of αSMA and collagen in primary hepatic stellate cells, confirming that hepatic stellate cell activation was inhibited. Evogliptin inhibited TGF-β-induced CTGF and phospho-Smad3 in primary hepatocytes. Evogliptin increased LC3 II conversion, LC3 puncta formation and autophagy flux, but did not decrease CTGF expression in primary hepatocyte of ATG7$^{f/f}$-Cre^{+} mice. Therefore, it was confirmed that an increase in autophagy of evogliptin was associated with a decrease in the expression of CTGF.
Conclusion: In our study, evogliptin attenuates liver fibrosis by preventing hepatic stellate cell activation. In addition, evogliptin induces autophagy in hepatocytes, thereby reducing CTGF expression. These results suggest that evogliptin could be a new drug to treat liver fibrosis.

[PP-0494]

Autophagy regulates CTGF expression by ERK phosphorylation in hepatocyte

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Objectives: Autophagy is an intracellular lysosomal degradation process that performs important cell functions in the liver. Several studies have shown that hepatocyte-specific ATG7 or ATG5 knockout mice have increased liver injury, including liver fibrosis. However, the relationship between autophagy and liver injury and fibrosis has not been clarified so far. In this study, we investigated the genes associated with autophagy inhibition and hepatic fibrosis.

Materials and Methods: Hepatocyte-specific ATG7 knockout mice were generated by crossing ATG7 Flox/Flox mice with albumin Cre mice. We isolated and cultured ATG7 K/O mouse primary hepatocyte, mouse hepatocyte and human hepatic stellate cell line (AML12, LX2). We used bafilomycin A or chloroquine as an autophagy inhibitors and PD98059 or U0126 as an ERK inhibitors. ATG7, CTGF, collagen, αSMA and PAI-1 mRNA expression were measured by Real Time RT-PCR analysis. The expression levels of CTGF, LC3, p62 and ERK were evaluated by western blot analysis.
Results: Primary hepatocyte isolated from hepatocyte-specific ATG7 knockout mice showed increased fibrosis related genes, CTGF and phospho-ERK. Furthermore, treatment with autophagy inhibitors (BFM or CQ) increased CTGF and phospho-ERK expression in AML12 and LX2 cells without altering CTGF mRNA. In addition, increased CTGF expression by BFM or CQ was decreased by ERK inhibitor.
Conclusion: These results suggest that inhibition of autophagy increased the expression of CTGF and phospho-ERK, and increase of CTGF by inhibition of autophagy was mediated by upregulation of ERK phosphorylation.

[PP-0497]

Hybrid detoxication effect on multiorgan failure

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Objectives: Multiorgan failure syndrome (MOFS) often develops after surgical complications through releasing of aggressive inflammation mediators and more than in 70% of cases leads to lethal outcomes. Endotoxemia development results in significant pathological changes and fast decompensation of detoxication resources which leads to multiorgan failure. Traditional detoxication methods showed insufficient effect and poor outcomes at patients with MOFS. One of the solution to increase detoxication effecacy is to cange sorbents' physical and chemical features. In this aspect, oxidizing sorbents development and their use at MOFS is perspective. Our study was conducted to evaluate efficacy of modified hemosorbent application at MOFS.
Materials and Methods: We have conducted animal study at 20 not purebred dogs. The acute liver failure was modelled by bandaging of distal CBD. After pathological process developed and was confirmed with laboratory blood tests, 2 methods of detoxication were used. Group 1 animals underwent detoxication with hemosrbent SKN-2 K. Group 2 animals underwent oxidizing detoxication method, which was developed n our laboratory.
Results: Our study results showed that Group 2 patterns health condition improvement was much faster than Goupr 1 ones. Both group laboratory blood results confirmed positive effect of detoxication, with stopping of progressive course of pathological changes to stationary. meanwhile in that Group 2 patterns blood results normilized and showed even regressive course of MOFS.
Conclusion: Our study showed that modified oxidizung detoxication method is effective and feasible. Currently we have been conducting research using this method at MOFS patients.

[PP-0499]

Argininosuccinate synthase1 and L-arginine enhances apoptosis by alteration of anti-apoptotic pathway in hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma is one of the most common malignant cancers worldwide, and liver cancer has increased in mortality due to liver cancer because of its late diagnosis and therapeutic limitation. We aim to examine the new possible way for HCC therapy.
Materials and Methods: We examined cytotoxic effect of argininosuccinate synthase 1 (ASS1) expression and its end-product, L-arginie using HCC cell lines and hepatocellular patients-derived primary cells. We investigated the clinical value of ASS1 in Korean paitnets with HCC. ASS1-mediated improvement of chemotherapy efficiency was observed using high content screening. The mechanism underlying L-arginine-mediated cytotoxicity was observed by examination of altered signaling pathways. ASS1 overexpression and L-arginine-mediated modification of metastatic potential was studied by wound healing assay and colony forming assay.
Results: Studies of tumor tissue from Korean HCC patients showed that high levels of ASS1 were associated with favorable overall survival of patients. We found that ASS1 and L-arginine has cytotoxic effect and also can improve chemotherapy efficiency. ASS1 overexpression modify glycolysis and nitric oxide synthetic pathway and effectively induced cell death. L-arginine itself has cytotoxic effect and can increase more the sensitivity of chemotherapy with ASS1 expression. The expression alteration of glycolysis enzyme is one of the mechanisms for L-arginine cytotoxic effect. As well as ASS1 overexpression, L-arginine can inhibit metastatic potential but not dependent on the status of ASS1.
Conclusion: These results demonstrated that ASS1 and its end-product, L-arginine, has tumor supprossor activity in HCC and suggest that L-arginine in HCC is a potential strategy in HCC with low ASS1 expression.

[PP-0552]

Risk of renal function and mortality in cured COVID-19 patients with kidney biomarkers and acute heart failure

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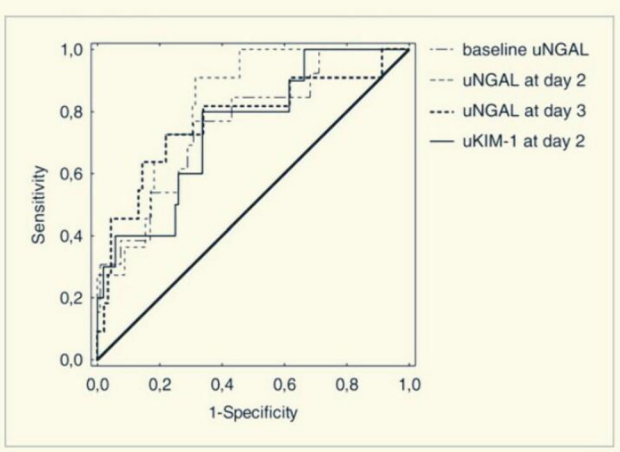
Objectives: Recent studies indicate the need to redefine renal function (RF) in acute heart failure (AHF) linking a rise in creatinine with clinical status to identify patients who develop evaluated the usefulness of serial assessment of urinary levels of neutrophil gelatinase-associated lipocalin kidney injury molecule-1 (KIM-1).
Materials and Methods: In 96 patients with AHF, uNGAL, uKIM-1, and uCysC were measured using a highly sensitive immunoassay based on a single-molecule counting technology (Singulex, Alameda, CA, USA) at baseline, day 2, and day 3. Patients who developed WRF

($a \geq 0.3$ mg/dL increase in serum creatinine or a $> 25\%$ decrease in the estimated glomerular filtration rate from the baseline value).
Results: were differentiated into those presence of deterioration/no improvement in clinical status during hospitalization vs. 'pseudo-WRF' (uneventful clinical course). occurred in 12 (10%), 'pseudo-WRF' in 14 (11%), whereas the remaining 104 (79%) patients did not develop WRF. Patients with 'true WRF' were more often females, had higher levels of NT-proBNP, creatinine, and urea on admission, higher urine albumin to creatinine ratio at day 2, higher uNGAL at baseline, day 2, and day 3, and higher KIM-1 at day 2 (vs. pseudo-WRF vs. without WRF, all $P < 0.05$). Patients with pseudo-WRF did not differ from those without WRF. In the multivariable model, elevated uNGAL at all time points and KIM-1 at day 2 remained independent predictors.
Conclusion: identify patients at high risk of death. Larger studies with more frequent biomarker assessments in the early stages of hospitalization are needed to portray the dynamics of these patients in a realistic way, to better demonstrate the usefulness of biomarkers.



[OP-0566]

Diagnostic accuracy of GPR score versus fibroscan in detecting fibrosis in patients with chronic hepatitis B and C

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Objectives: To determine the diagnostic accuracy of GPR (Gamma Glutamyl transferase to platelet ratio) in diagnosis of fibrosis in chronic viral hepatitis patients taking fibroscan as a reference standard.
Materials and Methods: This is a cross-Sectional Validation Study. This study was conducted at National Institute of Liver and GI Diseases (NILGID), Dow University Hospital, Karachi, Pakistan. Six months after the approval of synopsis from June 30, 2020 to December 29, 2020. after approval from institutional review board. All patients who fulfilled the inclusion criteria and visited to national institute of liver and GI diseases (NILGID), Dow university of hospital (DUH) Karachi were included in the study. Informed consent was taken after explaining the procedure, risks and benefits of the study. All blood samples were investigated from same hospital biochemical laboratory. The value of GPR in diagnosing liver fibrosis was evaluated according to test results. All the collected data were entered into the proforma attached at the end and used electronically for research purpose.
Results: The Mean $\pm$ SD of age was 37.84 ± 12.67 years. In distribution of gender, 119 (70%) patients were male while 51 (30%) were female patients. Diagnostic accuracy of GPR score was noted as 67.65% in diagnosis of liver fibrosis with sensitivity 56.64%, specificity 89.47% PPV 91.43% and NPV 51% by using fibro scan as gold standard.
Conclusion: It is to be concluded in this study that fibroscan is better non invasive modality in detecting fibrosis as compared to GPR score. In evaluation of fibrosis in chronic viral hepatitis patients GPR did not prove helpful and comparable with fibroscan in our patients. Further large scale studies needed to validate this.

TABLE # 8
DIAGNOSTIC ACCURACY OF GPR SCORE BY USING FIBROSCAN AS GOLD STANDARD
n=170

GPR SCORE	FIBROSCAN (GOLD STANDARD)	
	POSITIVE	NEGATIVE
POSITIVE	True positive(a) 64	False positive(b) 6
NEGATIVE	False negative(c) 49	True negative (d) 51
Total	a + c 113	b + d 57

				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.5664	**56.64**	0.4750	0.6577
Specificity	d/ (b + d)	0.8947	**89.47**	0.8151	0.9744
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.6647	**66.47**	0.5937	0.7357
Positive Predictive value	a/ (a +b)	0.9143	**91.43**	0.8487	0.9799
Negative Predictive value	d/ (c+ d)	0.5100	**51.00**	0.4120	0.6080
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6765	**67.65**	0.6061	0.7468

[PP-0649]

MicroRNA-101-3p is a dual function regulator in the therapeutic potential of human bone marrow-derived mesenchymal stem cells on liver fibrosis

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Objectives: Although bone marrow-derived mesenchymal stem cells (BM-MSC) are still unclear, BM-MSCs play key therapeutic roles in liver fibrosis. Furthermore, microRNAs (miRNAs) are regulators in hepatic differentiation and liver fibrosis. miR-101-3p is upregulated during hepatic trans-differentiation, whereas miR-101-3p is down-regulated in a stage of liver fibrosis. The purpose of this study is to investigate miR-101-3p's roles in the hepatic differentiation of human BM-MSC (hBM-MSCs) and hepatic stellate cell (HSC) activation.
Materials and Methods: miRTarBase and miRDB were used to predict targets EZH2 of miR-101-3p selected next-generation sequencing. hBM-MSC was treated with miR-101-3p mimic, inhibitor, or EZH2 siRNA during the hepatic differentiation. hHSC LX2 was treated with TGF-β1 and with or without miR mimic and siRNA. BM-MSCs and PRL-1 (+) BM-MSCs were injected into the tail vein in the BDL rat model. The role of miR-101-3p was identified through the change of liver-specific genes, EMT markers, and fibrosis genes using quantitative real-time PCR and western blotting.
Results: miR-101-3p showed a higher expression level in the PRL-1 (+) BM-MSCs transplantation group than the BDL group and in differentiated hepatocyte-like cells than hBM-MSC but lower expression level in fibrosis than the normal liver. miR-101-3p caused the increase in the liver-specific genes in hBM-MSC, while mesenchymal markers, fibrosis markers, and apoptosis inhibitor genes decreased in LX2. At this time, the expression of EZH2 has reduced, and the same result as miR-101-3p overexpression was obtained by knockdown of EZH2. As a result, miR-101-3p mimic promoted the hepatic differentiation of hBM-MSC and inhibited the TGF-β1 mediated LX2 activation via regulating EZH2.
Conclusion: In this study, we identified miR-101-3p that can regulate the hepatic differentiation of hBM-MSC and hepatic fibrosis. Our results demonstrate that miR-101-3p may be a biomarker, monitoring the response to therapeutic effect by BM-MSC in liver fibrosis.

[OP-0698]

Basing on network pharmacology and transcriptomics analysis to discover the effective components in FZHY and the corresponding key targets in macrophages by which FZHY against liver fibrosis

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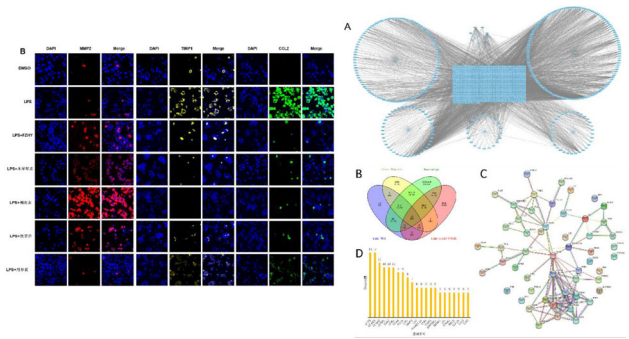
Objectives: FZHY may play an anti-liver fibrosis role by regulating the polarization of intrahepatic macrophages, but the key targets and effective components of FZHY based on macrophages are still unclear.
Materials and Methods: The potential anti-liver fibrosis targets set of FZHY based on macrophages was obtained by network pharmacological analysis, and the differentially expressed genes set of FZHY for the prevention and treatment of mouse liver fibrosis was obtained through RNA-Seq transcriptome sequencing. The potential core targets of FZHY against liver fibrosis based on macrophages were obtained by Degree value analysis of the intersecting target proteins of the above two sets. Then, through the retrieval and analysis of PubMed medical literature database, the potential key targets of FZHY against liver fibrosis based on macrophages were determined. After that, the effective components in FZHY corresponding to key targets were obtained by reverse pharmacological analysis. Finally, experimental verification of these effective components on the key target genes expression regulation was carried out by the LPS-induced M1 type THP-1 human monocyte-macrophages.
Results: The data analysis showed that FZHY might play an anti-liver fibrosis role by regulating the expression of CCL2, TIMP1 and MMP2 genes in macrophages. The results in vivo Showed that FZHY could significantly inhibit the expression of CCL2 and TIMP1 genes and promote the expression of MMP2 genes in liver tissues of liver fibrosis mice. The results in vitro showed that FZHY and its four effective components: Luteolin, Ursolic Acid, Quercetin, and Danshensu, could significantly inhibit the expression of CCL2 and TIMP1 genes in M1 THP-1 cells. In addition, Luteolin, Ursolic Acid, and Quercetin could promote but Danshensu inhibit MMP2 gene expression.
Conclusion: FZHY could inhibit the expression of CCL2 and TIMP1 genes in M1 macrophages by four effective components: Luteolin, Ursolic Acid, Quercetin and Danshensu, so as to achieve its anti-inflammatory and anti-liver fibrosis effect.



[OP-0700]

Findings of liver histopathology among the samples retrieved by minimally invasive tissue sampling

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Objectives: The study was conducted with objective of exploring the liver pathologies among deceased adults of Gandaki province of Nepal.
Materials and Methods: This s a quantitative cross-sectional observational study conducted at three health facilities of Gandaki Province of Nepal. The cases were deceased adults either in hospital or else. The minimally invasive autopsy was done to determine the cause of death and in this paper, we are presenting the liver pathology among the studied cases. We performed a puncture with the Bard Monopty 16G 100 mm needle to obtain histopathological samples from the liver. The tissue specimens collected for histological analysis

were fixed with 10% neutral buffered formalin for four hours and then passed into a tissue processor for eight hours, embedded in paraffin, and cut into four-micron sections, which were then stained with hematoxylin and eosin (H&E) as per standard procedures. All the cylinders of tissues collected in each block were carefully evaluated, recording all the organs present under a microscope Olympus CX 23, in 4x, 10x, 40 × and 100 × magnification.
Results: In total, 100 cases were enrolled into the study period, among which 76 (76%) were males and 24 (24%) females. The mean age of the cases was 50.8 years (range: 18 to 84, standard deviation: 15.9). Steatosis was diagnosed from the liver tissues in 33 (33%) cases. Liver cirrhosis was diagnosed in four (4%) and hepatocellular carcinoma in two (2%) cases.
Conclusion: The minimally invasive tissue sampling can be useful to detect liver pathology among the deceased and it can suffice to add to cause of determination of death without significant disfigurement of the body and delay as caused by complete diagnostic autopsy.

[PP-0709]

Inhibitory effect of the clusterin on LPS-induced liver inflammation

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Objectives: Lipopolysaccharide (LPS) contribute to the pathogenesis of fatty liver and hepatitis, and is one of the important mechanisms inducing liver inflammation. Clusterin is a glycoprotein involved in inflammation proliferation, cell death, Alzheimer disease and aging. However, it is not known whether clusterin is effective for liver inflammation. Here, we investigated the anti-inflammatory effects of clusterin on liver inflammation.
Materials and Methods: To study the liver inflammation effect of clusterin, we used a mouse (C57BL/6 or Clusterin knockout) primary kupffer cell, primary hepatocyte and co-culture (1:4) model. To investigate the effect of clusterin on pro-inflammatory cytokines mRNA expression, expression was measured by real-time RT-PCR analysis. Liver inflammation was induced by LPS-injection for 3 h in Clusterin knockout mice.
Results: Clusterin significantly decrease LPS-stimulated TNFα, IL1α and IL1β mRNA expression in C57BL/6 primary kupffer cells, primary hepatocyte and co-culture. On the other hand, LPS-induced inflammatiory cytokine mRNA expression was further increased in primary kupffer cells of clusterin KO mice. In addition, loss of clusterin accelerate liver inflammation after LPS injection.
Conclusion: This study shows that clusterin inhibits LPS-induced pro-inflammatory cytokine mRNA expression in primary hepatocyte and primay kupffer cells, and that loss of clusterin promotes liver inflammation in animals. This suggests that clusterin has anti-inflammation effect in liver inflammation.

[PP-0719]

Angelica keiskei attenuates bile duct ligation-induced liver injury in mice

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Objectives: Although multiple studies have shown that Angelica keiskei of Umbelliferae family has potent anti-inflammatory and anti-oxidative activities and that it reduces the serum bile acids in humans, whether Angelica keiskei has protective role on cholestasis-induced liver injury has until now remained unexplored.
Materials and Methods: This study tests the hypothesis that Angelica keiskei root extract (AKE) alleviates the liver injury, inflammation and fibrosis induced by bile duct ligation (BDL) in mice.
Results: Oral administration of AKE (200 or 500 mg/kg) attenuated hepatocellular necrosis and significantly reduced serum levels of bile acids and bilirubin in BDL mice. The critical enzyme of bile acid synthesis, CYP7A1, was repressed by AKE, suggesting that reduced bile acid production may contribute to liver protection. Moreover, we determined through gene expression, cytokine analysis and histological examination that AKE treatment reduced liver inflammation, oxidative stress, and fibrosis. AKE also suppressed the NF-κB pathway, suggesting this as a possible mediator of its anti-inflammatory effect.
Conclusion: Our findings substantiate that AKE may work well as a new therapeutic option for the treatment of cholestatic liver diseases.

[OP-0723]

Effects of human embryonic stem cell-derived mesenchymal stem cells on mitochondrial oxidative dysfunction in non-alcoholic fatty liver disease

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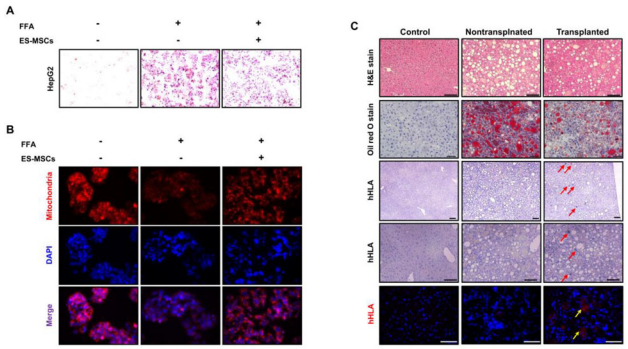
Objectives: Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases worldwide, but its pathophysiology is not fully understood and pharmacological therapy for NAFLD is not yet. We investigated therapeutic potential of embryonic stem cell-derived mesenchymal stem cells (ES-MSCs) on hepatic steatosis and mitochondrial oxidative function.
Materials and Methods: HepG2 cells were treated with free fatty acids (FFA) and then co-cultured with ES-MSCs. Intracellular lipid accumulation was measured by Oil-red-O staining. The mitochondrial oxidative function was assessed by quantifying mitochondrial mass and measuring reactive oxygen species (ROS) and activity of antioxidant enzymes. C57BL/6 mice were chronically fed with choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD). At week 20, mice were injected with either phosphate-buffered saline (nontransplanted) or ES-MSCs (transplanted). Four weeks later, liver histology and function were assessed.
Results: FFA-induced intracellular lipid accumulation was attenuated when co-cultured with ES-MSCs (Fig. 1_A). The functional

mitochondrial mass was reduced by FFA treatment and then was restored following co-culture with ES-MSCs (Fig. 1_B). Increased cellular ROS production by FFA treatment was attenuated after co-culture with ES-MSCs. The activity of superoxide dismutases (SODs) and the ratio of reduced/oxidized glutathione were decreased by FFA treatment and were restored by co-culture with ES-MSCs. After infusion of ES-MSCs, a successful engraftment of transplanted stem cell was confirmed, leading to amelioration of severe hepatic steatosis in CDAHFD-fed mice (Fig. 1_C). Decreased mitochondrial DNA content in CDAHFD-fed mice was reinstated to near-control level after transplantation of ES-MSCs. Augmented hepatic ROS accumulation caused by CDAHFD was attenuated after transplantation of ES-MSCs with dynamic changes in the activity of SODs and the ratio of glutathione.

Conclusion: Hepatic steatosis and mitochondrial oxidative dysfunction in NAFLD can be ameliorated by transplantation of ES-MSCs. Our study findings suggest the therapeutic potential of ES-MSCs in NAFLD and help understanding alterations in hepatic lipid metabolism, which may be restored by ES-MSC transplantation.



[OP-0727]

The effect of mesenchymal stem cells on intrahepatic B cells in acute liver injury

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Objectives: Acute liver injury (ALI) can be accompanied by liver immune dysfunction and immune cells infiltration, which further causes complications such as multiple system failure, severe metabolic disorders. The immunoregulation ability of mesenchymal stromal cells (MSCs) opens the path for their use in acute liver injury. In this study, we focused on exploring the therapeutic effects of MSCs on acute liver injury and characterization of intrahepatic B cells in the response and repair of liver injury.

Materials and Methods: Compact bone-derived MSCs were isolated from C57BL/6 mice and injected intravenously into ALI mice induced by carbon tetrachloride (CCl4) administration. Potential efficacy of MSCs was determined by survival rate, biochemical and histopathological changes. Intrahepatic B cells were characterized at different timepoints by flow cytometry and single-cell RNA sequencing (scRNA-Seq). The expression of B cell activation-related genes were further validated in isolated intrahepatic B cells using reverse transcription-polymerase chain reaction.

Results: MSCs treatment significantly reduced the symptoms of ALI induced by CCl4, as indicated by the decrease in serum liver enzyme levels, the improvement in histopathology and survival rate. Flow cytometry analysis showed that frequencies of CD19 + B cell in the CD45 + fraction of liver cells decreased in MSCs group with respect to ALI group. Based on our scRNA-Seq results, the differentially expressed genes (DEGs) in intrahepatic B cells in both the control group and ALI group were involved in B cell activation. Moreover, the DEGs regulated by MSCs were enriched in B cell activation, B cell proliferation, and B cell differentiation. MSCs treatment significantly reduced B cell infiltration and inhibited the expression of B cell activation-related genes.

Conclusion: Mesenchymal stem cells can effectively alleviate acute liver injury, and can effectively inhibit B cell activation and proliferation in vivo.

[OP-0749]

The impact on clinical outcome of nutrition on severity and mortality among patients with covid-19 infection

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Objectives: It is the objective of the study to assess the impact of nutrition on the clinical outcome of Covid-19 infection and its correlation with mortality.

Materials and Methods: Among patients who were admitted for Covid 19 infection, nutritional parameters were evaluated at baseline and correlated with severity of Covid 19 infection and clinical outcome. This is a retrospective correlational study conducted in Fatima University Medical Center from March 2020 to October 2021 in adult patients admitted due to COVID-19 infection.

Results: Among the two hundred and one patient were evaluated, 137 patients were malnourished (68%) with about 11 (8%) underweight, 33 (24%) overweight, Obese I 69 (50%) and Obese II 24 (18%). Among patients with abnormal BMI, hospital stay is significantly longer (14 days) than those with normal weight 11 days. Patients with abnormal BMI progressed to severe and critical cases (p-value 0.00010), while normal BMI are more likely to have mild cases. Mortality is significantly higher among those with abnormal BMI (29.2% vs 12.5%) p value of 0.0002.

Conclusion: Patients with abnormal baseline weight showed a more progressive Covid 19 infection with direct correlation with hospital stay and mortality. Baseline nutrition is thus a predictor factor for mortality and suggest that prompt nutrition care or intervention and monitoring be performed.

	Underweight	Normal	Overweight	Obese I	Obese II	p
Days of Hospital stay [All Patients]						
Mean	22.0	10.7	13.4	13.6	12.7	0.0010*
SD	12.8	4.9	6.6	10.3	7.5	
Days of Hospital stay [All Survivors]						
Mean	28.2	10.9	13.4	15.1	15.2	0.0010*
SD	13.6	4.8	5.9	10.1	7.2	
Mortality						
Expired	6 (54.5)	8 (12.5)	3 (9.1)	20 (29.0)	11 (45.8)	0.0002*
Alive	5 (45.5)	56 (87.5)	30 (90.9)	49 (71.0)	13 (54.2)	
COVID Severity, n, %						
Mild	0 (0.0)	32 (50.0)	12 (36.4)	7 (10.1)	1 (4.2)	0.0001*
Moderate	0 (0.0)	18 (28.1)	11 (33.3)	18 (26.1)	6 (25.0)	
Severe	3 (27.3)	7 (10.9)	5 (15.2)	19 (27.5)	4 (16.7)	
Critical	8 (72.7)	7 (10.9)	5 (15.2)	25 (36.2)	13 (54.2)	

*Significant, ns not significant

[PP-0760]

Effects of proton pump inhibitors (Esomeprazole) on TLR4/NF-κB pathway in hepatic ischemia reperfusion injury

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Objectives: Recent studies have shown that proton pump inhibitors (PPIs) have a protective effect on an experimental ischemia/reperfusion (I/R) models of various organ, but little is known about its effect on hepatic I/R injury. The aim of this study was to evaluate the beneficial effects of a PPI, esomeprazole in an experimental model of hepatic I/R injury, focusing on TLR4-mediated signaling, which has been implicated in the development and progression of hepatic I/R injury.
Materials and Methods: Twenty-four male wild-type (C57BL/6) mice were randomized into four groups: saline + sham, saline + I/R, PPI + sham, and PPI + I/R. Esomeprazole was intraperitoneally injected 30 min prior to surgery. The animals were subjected to 60 min of partial warm ischemia (70%), followed by reperfusion for 6 h on the same day. The ischemic lobe of the liver and blood were collected for molecular biochemical analyses and histopathological analyses. The ischemic lobe of the liver was harvested for hematoxylin and eosin (H&E) stain, western blot and immunohistochemical analyses. Blood was collected and levels of alanine aminotransferase (ALT), tumor necrosis factor (TNF)-α, interleukin (IL)-6, and high mobility group box 1 (HMGB1) were measured.
Results: Pretreatment with esomeprazole attenuates hepatocellular injury after hepatic I/R. Pretreatment with esomeprazole reduced the levels of circulating inflammatory mediators, such as IL-6 and TNF-α in serum. Pretreatment with esomeprazole suppressed HMGB1 expression in serum and ischemic liver after hepatic I/R. Esomeprazole markedly down-regulated the expression of TLR4 and NF-κB in ischemic liver.
Conclusion: Proton pump inhibitor, esomeprazole attenuates hepatic I/R injury by down-regulation of the TLR4/NF-κB signaling pathway. Esomeprazole can be considered as new therapeutic agent for hepatic I/R injury.

[PP-0769]

Study of IL4Rα and IL13Rα1 expression in gallbladder cancer

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Objectives: Gallbladder cancer is commonly associated with inflammation. Therefore, inflammation related cytokines and cytokine receptors might be related to the progression of gallbladder cancers. Recently, it has been reported that IL4Rα and IL13Rα1, constituents o f type II IL4 receptors, are involved in the progression of human cancers through activation of the JAK2 pathway. However, studies on IL4Rα and IL13Rα1 in gallbladder cancers have been limited. Therefore, this work investigated the expression of IL4Rα and IL13Rα1 in 122 gallbladder carcinomas and the effect ofi nhibition of JAK2 in SNU308 gallbladder cancer cells.
Materials and Methods: To evaluate the clinicopathological significance of the expression of IL4Rα and IL13Rα1 in human gallbladder cancers, 122 cases of gallbladder carcinomas treated between January 2000 and December 2009 were evaluated. In human gallbladder carcinomas, the expression of IL4Rα and IL13Rα1 were evaluated with immunohistochemical staining in tissue microarray sections. we checked expression level of phosphorylated JAK2 and also, evaluated proliferation and apoptosis level after the treatment of AZD1480, a JAK2 inhibitor.
Results: Immunohistochemical expression of IL4Rα was significantly associated with the expression of IL13Rα1 in human carcinoma tissue. Additionally, in univariate analysis, nuclear expression of IL4Rα, cytoplasmic expression of IL4Rα, nuclear expression of IL13Rα1, and cytoplasmic expression of.
IL13Rα1 were significantly associated with overall shorter survival and shorter relapse free survival. The treatment of AZD1480, a JAK2 inhibitor, inhibited proliferation and increased apoptosis of SNU308 cells.
Conclusion: In conclusion, this study showed that the expression of IL4Rα and IL13Rα1, especially nuclear expression of IL 4Rα, was a potential prognostic indicator of gallbladder carcinomas. Furthermore, suppression of the IL4R pathway with the treatment of JAK2 inhibitor might be an effective.
therapeutic approach to gallbladder carcinomas.

[OP-0776]

Vaccine breakthrough Infection among COVID19 vaccinated patients: The real world data

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Objectives: To present the real-life report of relationship between vaccine breakthrough infection and the last dose of COVID-19 Vaccine. The occurrence COVID-19-related symptoms from the time the patient received the last dose of covid-19 vaccine, comparing the different brands of COVID-19 vaccine were correlated with interval of occurrence of illness, level of severity and the effect among elderly and patients with comorbidities.
Materials and Methods: A descriptive retrospective study investigating the interval between Vaccine Breakthrough Infection and Last dose of COVID-19 Vaccine among admitted patients in Tertiary Hospital year 2021. Descriptive statistical analyses of age, sex, comorbidity, severity of COVID-19, onset of illness with mean, standard deviation, frequency, and percentage were performed using

SPSS version 25.0. Statistical differences of factors included in the study were treated using Independent T-Test. Statistical tests were two-sided and p value < 0.05 was considered statistically significant.
Results: Among patients vaccinated with Sinovac (69%), 20.29% of them had Vaccine Breakthrough Infection from 99 to 112 days after 2nd dose of Sinovac Vaccine (p value of 0.001). While patients vaccinated with Astra Zeneca had Vaccine Breakthrough Infection 85–98 days after the 2nd dose of Astra Zeneca Vaccine, (p value of 0.001). Elderly People who are elderly with Sinovac and Astra Zeneca mostly developed moderate symptoms.
Conclusion: Vaccines do lessen the severity of COVID-19 infection, although Vaccine Breakthrough Infection may occur which directly correlates with severity of the disease. Patients vaccinated with Sinovac appear to develop Vaccine Breakthrough infection more than 100 days after their 2nd dose of Vaccine. While Patients vaccinated with Astra Zeneca, develop Vaccine Breakthrough Infection 70 days after their 2nd dose of vaccine. Presence of Comorbidity, nor elderly patients do not correlate with level of severity of Vaccine Breakthrough Infection. These data may suggest the need for a booster dose especially among elderly patients or those with comorbidities.

[PP-0809]

Iron oxide-based nanoparticles for staging of liver fibrosis by magnetic resonance imaging

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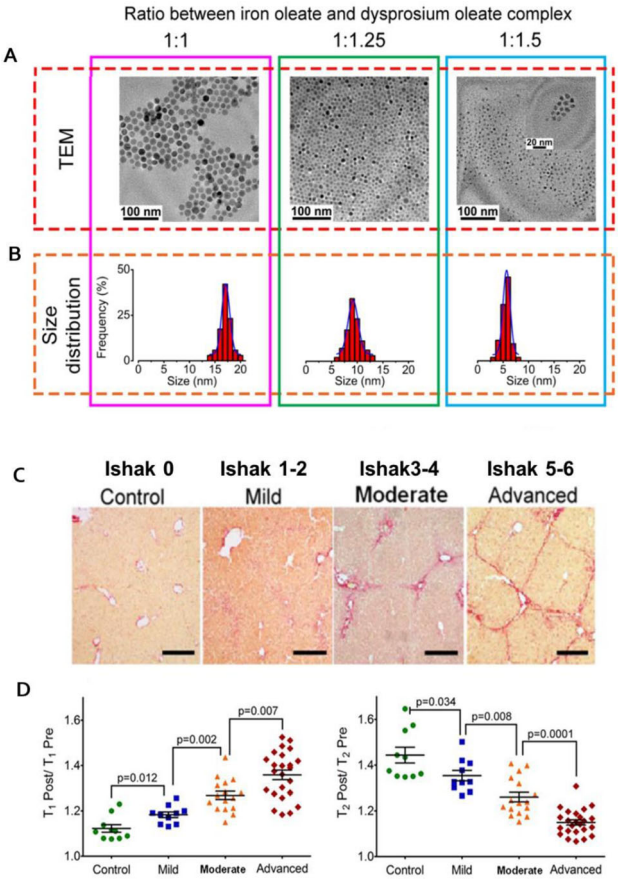
Objectives: Liver fibrosis has become a severe public health issue worldwide. So far, precisely diagnosing the progress of liver fibrosis by a non-invasive way still suffers big challenges. The purpose of this study is to develop iron Oxide-based nanoparticles as a contrast agent to precisely diagnose liver fibrosis in vivo.
Materials and Methods: Heterogeneous iron oxide /dysprosium oxide nanoparticles (IO-DyO NPs) were synthesized using iron oxide and rare earth metal dysprosium oxide through high temperature decomposition method. Then the surface of nanoparticles was modified with poly (acrylic acid) (PAA). The physical characterizations of IO-DyO nanoparticles were obtained by transmission electron microscopy (TEM) and dynamic light scattering instrument. Liver fibrosis mice models were constructed via intraperitoneal injecting 10% carbon tetrachloride (CCl4) twice each week for 12 weeks. At time intervals of 0, 1–2, 6–8 and 9–12 weeks, 10 mice were randomly selected for T_1 and T_2 MRI analysis at a high field magnetic field (7.0 Tesla) and biopsy analysis. The stages of the fibrosis are determined via Ishak scoring 1–2 (mild fibrosis stage), 3–4 (moderate fibrosis stage) and 5–6 (advanced fibrosis stage). The MR results are compared with the biopsy result and graph is plotted by their respective Ishak scoring.
Results: IO-DyO NPs with different size were synthesized and the IO-DyO NPs with 4 nm were used in the further MRI as a contrast agent. The IO-DyO NPs can target liver and differentiate stages of fibrosis, and there is a significant difference between no fibrosis/mild fibrosis, mild fibrosis/moderate and moderate/advanced fibrosis stages.
Conclusion: IO-DyO NPs can precisely distinguish the mild, moderate and advanced stage of liver fibrosis. This work illustrates an advanced contrast agent used in MRI for the precise diagnosis of liver fibrosis via a non-invasion means.



[OP-0907]

Assessment of COVID-19 response on hepatitis B virus and hepatitis C virus prevention and treatment from nationwide survey in Japan

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Objectives: Elimination of Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) require continuous interventions. This study aimed to assess the response and impact of COVID-19 on Hepatitis prevention and treatment in Japan. This international joint research was conducted by three research groups of Ministry of Health, Labour and

Welfare (MHLW) in Japan with The Task Force for Global Health and in cooperation with Japan Society of Hepatology (JSH).
Materials and Methods: We have conducted this cross-sectional study by questionnaire survey both in Japanese and English language on online Microsoft forms platform from 24 August to 03 October 2021. The questionnaire was designed to address the impact of COVID-19 on hepatitis treatment, testing, screening; mitigation strategies; response to COVID-19; and perceived benefits of COVID-19.
Results: Total 196 medical doctors have participated from 35 prefectures among them 49.5% are in administrative positions. 55.6% of participants responded about no interruption while 11.7% reported supply chain disruptions during the survey period. 1–25% decrease in HBV screening, testing was reported by 38.8% and 43.9% participants, respectively. Decease of 1–25% in HCV screening, testing and were reported by 39.8% and 43.4% participants, respectively. However, no decline to initiate HBV and HCV treatment was reported by 53.6% and 45.4%, respectively. But extend of hospital visits was reported by 65.3%. The survey response illustrated the decrease in patients' imaging (65.8%), lab testing (68.4%), HCC screening (55.1%), gastrointestinal endoscopy (87.2%), and liver biopsy (43.4%). Patient anxiety and fear (67.4%), loss of staff to COVID-19 response (49.0%), and limited availability of staff (46.4%) are responded as challenges to resume services to pre-COVID-19 level.
Conclusion: A greater decrease has been noticed in HBV and HCV testing, screening, and other associated liver diseases than treatment initiation in Japan. However, anxiety and fear of patients, lack of staff and facilities are major challenges to overcome such situation.

[OP-0957]

Sexual function deterioration among donor and recipients of living donor liver transplantation (LDLT): A systematic review

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Objectives: Although sexual functioning is an essential facet of living donor QoL, risk factors for hypogonadism and erectile dysfunction after liver transplantation (LT) are largely unknown in recipients and donors.
Materials and Methods: An integrative literature review from an electronic database was conducted to determine the incidence of sexual dysfunction before and after LT both in recipients and donors. Inclusion criteria include 1) patients and donor LDLT aged 18 or over; and 2) using Female Sexual Function Index (FSFI) and International Index of Erectile Function (IIEF).
Results: Sexual dysfunction is characterized by disturbances in sexual desire and the psychophysiological changes associated with the sexual response cycle in men and women. QoL LDLT patients remain similar to the general population except had lower mental health scores. The result also shows that sex hormone disturbances are highly prevalent in patients after LT, even though the rate is higher in men. It indicates that mental health problems after LT are related to sexual function deterioration. On the Donor side, sexual functioning was lower at the evaluation phase and three months than at one-year post-donation: difficulty reaching orgasm, lower sexual desire, dissatisfaction with sexual life. However, there has been an improvement in sex hormone levels after LT in some instances, namely, normalization of estradiol levels and lowering prolactin and progesterone levels.
Conclusion: LT has been shown to increase the QoL of liver patients. However, it is vital to assess QoL level after LT in patients and donors to know their satisfaction to cope with the situation. Mainly including the topic of sexuality in the routine of care. Finally, it is crucial to maintain high therapeutic adherence, thus ensuring a good outcome of the care received before and after the transplantation process. It aims to prepare them for the early recovery phase may improve recovery and reduce distress regarding sexual functioning.

[PP-1028]

Methods for the diagnosis and surgical treatment of liver hemangiomas

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Objectives: To evaluate the results of diagnostics and surgical treatment of patients with liver hemangiomas.
Materials and Methods: The work is based on the analysis of the results of liver resections of 31 patients, 23 women (74.1%) and 8 men (25.8%), ratio 3: 1, age ranged from 25 to 66 years.. All patients underwent ultrasound (29 patients) and CT (21 patients) of the liver, and several patients with giant liver hemangiomas underwent MSCT (8 patients) to detect compression of the vessels and bile ducts of the liver.
Results: As a result of the study, the right lobe of the liver was affected in 20 patients which is 64.5%, the left lobe was affected in 8 patients—25.8% and a giant hemangioma in 3 patients—9.6%, 3 or more affected segments were revealed in 12 -38.7% patients, lesion of 2 segments in 13 -41.9% patients and lesion of 1 segment in 6 -19.3% patients. 5 (16.1%) patients underwent right-sided hemihepatectomy (PHGE), left-sided hemihepatectomy (LHGE) was performed in 2 (6.4%) patients, 20 (64.5%) patients underwent atypical liver resection (AR), including in itself a lobectomy and 2 (6.4%) patients underwent explorative laparotomy. The maximum blood loss was about 1.5 L, the minimum blood loss was 200 ml, 30 (96.7%) patients had Tachocomb hemostatic sponges glued to the resected liver lobes. 8 (25.8%) patients underwent simultaneous operations. The result of the histological report confirmed cavernous hemangioma in 24 (77.4%) patients. 3 (9.6%) patients had concomitant diseases and capillary hemangioma in 1 (3.2%) patient.
Conclusion: Thus, liver resection is an effective and affordable method for treating liver hemangiomas. Ultrasound, CT and MSCT of the liver allows in the preoperative period to determine the volume of the proposed operation.

[PP-1037]

Effect of combined treatment with statins and ezetimibe in NASH model: Anti-inflammatory and antifibrotic effects of statins and improvement of steatosis of ezetimibe

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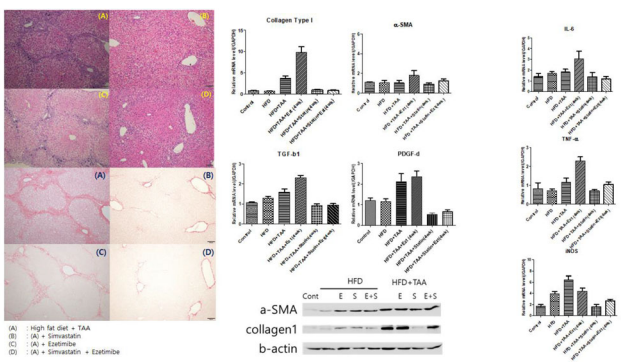
Objectives: Simvastatin exerts pleiotropic effects on the cardiovascular system. The beneficial effects of statins in cirrhosis have been reported in various experimental results. Statin-Ezetimibe combination therapy is widely used as a treatment of hyperlipidemia. Clinically, there are limited options for treatment for NASH-related cirrhosis. We aimed to evaluate the effects of ezetimibe-statin combination therapy in NASH-related liver fibrosis both in vivo and in vitro.
Materials and Methods: A High-fat diet and Thioacetamide (300 mg/kg, intraperitoneal injection twice a week for 8 weeks) was given to establish mice models with non-alcoholic steatohepatitis (NASH) related cirrhosis mice model. Human hepatic stellate cell (HSC) line Lx-2 cells were cultured in an adipogenic differentiating mixture (ADM) and induced quiescent form. Both activated and quiescent forms of HSC were treated with transforming growth factor b1 (TGF-b1), served as a positive control, simvastatin, TGF-b1 plus simvastatin, ezetimibe, simvastatin plus ezetimibe, TGF-b1 plus simvastatin and ezetimibe, respectively. The expressions of Collagen I and a-smooth muscle actin, fibronectin was measured by real-time reverse transcriptase-polymerase chain reaction (qRT-PCR) and Western blot in liver tissue.
Results: Statin ameliorated hepatic fibrosis and inflammation in the NASH model. In vivo, with the progress of NASH-related fibrosis, mRNA and protein expressions of a-SMA, TGF-b1, and collagen I increased in the liver. Statin ameliorated the expression of collagen type 1, a-SMA, and TGF-b1. Statin treatment suppresses hepatic fibrosis by suppression of HSC activation via downregulating TNF-a, IL-6 and this causes anti-fibrosis effects as TGF-b and PDGF down-regulation. Ezetimibe administration showed only improvement in steatosis, not inflammation and fibrosis. It also showed similar results when administered in combination with statins.
Conclusion: Statins showed anti-inflammatory action through TNF-a inhibition in the NASH-cirrhosis model and improvement of fibrosis through suppression of HSC activation. Ezetimibe showed improvement in steatosis, but the anti-inflammatory and fibrosis improvement effects were insignificant.



[PP-1066]

Liver profile test among non-pregnant and pregnant women attending tertiary care hospital in Western Nepal

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Objectives: Deviation of liver profile associated with pregnancy are mostly physiological and rarely pathological specifically in "Acute fatty liver of pregnancy". So we aim to study the physiological adaptation to normal pregnancy over pattern of changes in liver function at third trimester attending tertiary care Hospital in western Nepal.
Materials and Methods: Cross sectional study conducted at tertiary care hospital in Pokhara, Nepal over a period of one year among age matched 50 pregnant women at their third trimester (24.8 ± 3.5 years) and 50 nonpregnant women (25.2 ± 2.6 years) not receiving oral contraceptives without past history of jaundice, chronic alcoholism and seropositivity for hepatitis B. Serum total and direct bilirubin, alanine transaminase (ALT) activity, aspartate transaminase (AST) activity, alkaline phosphatase (ALP), total protein, albumin concentration was measured by the standard operating procedure and principle provided in the literature of each of test reagents from "Randox India". Results were expressed as mean ± SE.
Results: Total, direct bilirubin and albumin concentrations in serum were significantly lower in third trimester compared to nonpregnant respectively as 0.94 ± 0.32 and 0.50 ± 0.56 mg/dl, 0.43 ± 0.10 and 0.16 ± 0.05 mg/dl, 4.65 ± 0.43 and 3.07 ± 0.57 gm/dl with p value < 0.005. Albumin/Globulin ratio was significantly decreased from 1.68 ± 0.54 to 0.96 ± 0.37 U/L with $p < 0.005$.Serum ALT as 20.66 ± 4.40 and 32.25 ± 15.57 U/L and AST activity as 18.88 ± 5.54 and 33.42 ± 22.64 U/L was at the level of high normal but significantly increased in third trimester compared to nonpregnant. ALP was significantly increased far above the normal range as 140.45 ± 34.5 and 399.1 ± 125.65 U/L with $p < 0.0001$.
Conclusion: Proper interpretation of liver function tests (LFTs) can lead to proper diagnosis, avoidance from misinterpretation and timely management of diseases and may reduce complications in both mother and fetus.

[OP-1069]

Presence of gastrointestinal manifestations is not a predictor for mortality among patients with COVID 19: A retrospective study

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Objectives: The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS – COV 2) has become a major health crisis in the Philippines, affecting about 2.8 million Filipinos with case fatality rate of about 2%. This infection is mainly manifested as fever, cough, difficulty of breathing and body malaisehowever, there are evidences showing that gastrointestinal (GI) symptoms are also manifesting symptoms of COVID-19 patients. The pathophysiology is centered on the presence of angiotensin converting enzyme (ACE 2) receptors found primarily in the respiratory tract, but are also present in the gastrointestinal tract. It is our objective to determine whether the presence of a GI manifestation of COVID -19 infection is a predictor for severity and mortality.
Materials and Methods: This study is a single-center, retrospective observational study conducted at a tertiary center hospital in San Juan, Philippines, which included a total of 542 confirmed COVID-19

patients who had gastrointestinal symptoms as the presenting symptoms of COVID-19 from January to May 2021.
Results: Among the 542 COVID-19 confirmed patients admitted at Cardinal Santos Medical Center, we identified 26 patients who initially presented with gastrointestinal symptoms – 11 (42%) with diarrhea, 6 (23%) with abdominal pain, 6 (23%) with anorexia and 2 (7%) with gastrointestinal bleeding and 1 (4%) jaundice. None of these patients developed acute hepatitis. One patient who had a history of Gilbert's disease presented with jaundice, and apparently this patient survived and did not present with critical COVID. Furthermore, among these patients, 5 (19%) succumbed due to acute respiratory failure and bacterial superinfection. In our study, patients who presented with gastrointestinal symptoms were not associated with poorer outcomes.
Conclusion: The presence of gastrointestinal manifestations is uncommon among patients with COVID-19 with a prevalence of 4.7%. Furthermore, GI manifestations is not a direct factor for severity and mortality.

[OP-1089]

Transient Elastography as a diagnostic criteria in advanced liver injury

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Objectives: Transient elastography (FibroScan)is a non-invasive method in used in the diagnosis of liver diseases. It provides early diagnosis achieves successful results in the treatment.Among the non-invasive tests, FibroScan, with controlled attenuation parameter (CAP) has demonstrated good accuracy in stratifying the levels of liver diseases and the fibrosis, the factors associated with disease progression. The method is fast, reliable, and reproducible, with good intra- and interobserver levels of agreement, thus allowing for population-wide screening and disease follow-up. Fibroscan with CAP is a practical alternative to ultrasonography, both as an initial assessment and during follow-up of patients with liver diseases. Its' ability to exclude patients with advanced fibrosis may be used to identify liver diseases patients in whom liver biopsy is not needed, therefore reducing the financial costs and the risk of complications.
Materials and Methods: Since June 2018 to October 2021, liver patients were scanned with the Fibroscan 502. In addition, liver biochemistry blood tests were performed to all patients.
Results: Among 1022 patients—252 patients with F4 (24.7%), 129 patients with F3 (12.6%), 168 patients with F2 (16.4%) and 473 patients with F0-F1 (46.3%) were seen. Viral hepatitis (179 patients – 47%), alcoholic hepatitis (41 patients – 10.7%), autoimmune diseases (22 patients – 5.8%), NAFLD (93 patients – 24.4%) and metabolic diseases (46 patients – 12.1%) were investigated in patients with fibrosis F3-F4 (381 patients).
Conclusion: Viral hepatitis is the most common among patients with advanced fibrosis. Considering that fibrosis values ??are high in patients with viral hepatitis in all scans, extensive Fibroscan screening should be performed in Azerbaijan.

[PP-1156]

Descriptive study of the relationship between mental health, lifestyle

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Objectives: Liver disease is one of the diseases that the world is very concerned about, including Indonesia. This study analyzed the percentage of gender, smoking behavior, and happiness factors in liver patients.
Materials and Methods: The method used is a simple tabulation using IFLS 5 data. with 351 liver respondents and 30,871 respondents not. The variables used are gender, smoking behavior and happiness.
Results: The results showed that 190 patients were male and the remaining 125 patients were female who suffered from liver disease. As many as 266 people have ideal body weight (BMI), while 49 do not. As many as 242 respondents feel happy, only 34 people are not happy. As many as 189 people smoke the rest as many as 126 people do not smoke. So it can be seen that people who smoke and are male have a lot of liver disease in Indonesia. So it needs special attention for men in particular and who smoke.
Conclusion: So it can be seen that people who smoke and are male have a lot of liver disease in Indonesia. So it needs special attention for men in particular and who smoke.

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. tab liver bmism
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liver	bmism 0	1	Total
0	5,473	25,398	30,871
1	49	266	315
Total	5,522	25,664	31,186

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. tab liver  sex
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liver	sex 0	1	Total
0	16,510	14,361	30,871
1	125	190	315
Total	16,635	14,551	31,186

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. tab liver smoke
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liver	smoke 0	1	Total
0	21,262	9,609	30,871
1	189	126	315
Total	21,451	9,735	31,186

[PP-1181]

Assessment of liver function parameters in thyroid dysfunction patient attending tertiary care hospital: A case control study from Nepal

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Objectives: To assess liver function parameters in thyroid dysfunction patient attending tertiary care hospital.
Materials and Methods: A total of 105 subjects (35 hyperthyroid, 35 hypothyroid and 35 euthyroid) aged from 20 to 70 years were studied in the Department of Biochemistry, Manmohan Memorial Teaching Hospital. Thyroid hormone profile including Free T3 (FT3), Free T4 (FT4), Thyroid Stimulating Hormone (TSH), and liver function profile covering Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Total Protein (TP) and albumin were estimated in the serum of participants using standard protocol. Data were analyzed using SPSS version 20 and Microsoft Excel 2013. Student's t-test was used to analyze differences in liver parameter of case and control where p- value < 0.05 was taken statistically significant.
Results: AST and ALT level were increased in 24 (68.5%) and 15 (42.8%) of hyperthyroid subjects respectively. Similarly AST and ALT level were increased in 17 (48.5%) and 10 (28.5%) of hypothyroid subjects respectively. Level of AST and ALT both increased significantly in hyperthyroid subjects whereas only AST level increased significantly (P-value < 0.05) in hypothyroid subjects. Total protein and albumin were found to be decreased significantly (P-value < 0.05) in both the study subjects as compared to euthyroid group. Increase in level of ALP was not significant in both the subjects.
Conclusion: Potentially adverse changes in liver function parameter such as increase in enzyme activity and decrease in protein and albumin in the subjects with thyroid disorder suggest the possible liver injury in near future. Hence, it is essential to screen liver function in every thyroid disorder patients.

[L-OP-1323]

Therapeutic efficacy of an oncolytic influenza virus carrying an antibody against programmed cell death 1 in hepatocellular carcinoma

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Objectives: Oncolytic virus (OV) therapy is a promising novel immunotherapy.
Materials and Methods: In this report, we engineered a novel oncolytic influenza virus carrying an anti-human programmed cell death 1 (PD-1) monoclonal antibody utilizing reverse genetics.
Results: A reassortant chimeric influenza virus, named rFlu-huPD1, was synthesized as follows: the heavy chain of the PD-1 antibody was encoded on the PB1 fragment, and the light chain of the PD-1 antibody was encoded on the PA fragment. rFlu-huPD1 antibodies were produced in infected ovalantoic eggs and could replicate to high titers. Moreover, selective cytotoxicity of rFlu-huPD1 was upregulated in multiple hepatocellular carcinoma (HCC) cancer cell lines compared to a control, as determined by a 3- (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Furthermore, the activation of T cells in the spleen of tumor-bearing BALB/c mice treated with rFlu-huPD1 was observed, especially cytotoxic CD8 + T cell activation in vivo. Additionally, in a patient-derived xenograft (PDX) liver cancer mouse model, tumor growth was reduced and the overall survival of the mice was increased by intratumoral injections with rFlu-huPD1 compared with wild-type PR8 virus.
Conclusion: Taken together, these findings provide evidence for the utility of a combination of oncolytic influenza viruses expressing PD-1 inhibitors for use in HCC virotherapy.

[L-OP-1329]

Handgrip strength as a measure of Sarcopenia and its utility in predicting outcomes in cirrhosis of liver

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Objectives: Role of sarcopenia measured by handgrip strength, in complications of cirrhosis. To correlate sarcopenia with MELD score. To investigate whether a combined MELD score with sarcopenia can be a better predictor of mortality.
Materials and Methods: A total of 72 patients between December 2019 and June 2021 diagnosed with liver cirrhosis on the basis of imaging were included in our study. Hand grip strength was measured by hand grip dynamometer in the non-dominant hand in sitting position with semi-flexed arm. Mean of three values was taken as final reading. Cutoffs of < 26 kg for men and < 18 kg for women were taken from Asian Working Group for Sarcopenia 2014 consensus. Patients were followed up for a period of 6 months.
Results: In our study, the prevalence of sarcopenia was 83.3%. The mean MELD-Na score was 20. Presence of sarcopenia correlated with complications like bleeding esophageal varices ($p = 0.01$), Hepatic Encephalopathy (HE) ($p = 0.002$) and Hepatorenal Syndrome (HRS) ($p = 0.006$). On univariate analysis, when MELD-Na was > 20.5, sarcopenia was significantly associated with HE [Odd's Ratio (OR), 9.33; 95% confidence interval (CI), 1.86—46.68; $p = 0.007$], bleeding esophageal varices [OR, 4.29; 95% CI, 1.35—13.58; $p = 0.01$] and HRS [OR, 12.43; 95% CI, 1.46 -105.74; $p = 0.02$]. The MELD-Na score of more than 20.5 with sarcopenia predicted mortality with sensitivity 100%, specificity 65% and $p = 0.038$. The estimated survival of sarcopenics at 6 months with MELD-Na > 20.5 was 83.3%.
Conclusion: Hand grip strength is a simple, non-expensive test to diagnose sarcopenia. As a measure of sarcopenia, it shows a statistically significant association with decompensation events of cirrhosis. In resource limited countries, it can be used instead of CT scan measured SMI.

[L-OP-1339]

Modulation of hedgehog signaling by quercetin against thioacetamide induced hepatotoxicity in Rattus norvegicus

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Objectives: Hedgehog (Hh) signaling pathway act as a morphogenetic signaling cascade. Its dysregulation has been implicated in the initiation of chronic and acute liver injuries. The precise mechanism for quercetin modulation of Hedgehog signaling had not previously elucidated herein we study the quercetin curative effect to regulate hedgehog signaling pathway against thioacetamide induced hepatotoxicity in Wistar rats.
Materials and Methods: Total of forty healthy male Wistar rats were equally divided into four groups. First control group remaining three treated with thioacetamide (200 mg/kg/ i.p.) twice a week for 6 weeks, two groups followed by quercetin treatment (50 mg/kg/day) and silymarin (50 mg/kg/day) oral dose for the next 4 weeks.
Results: Serological analysis showed statistically improved cholesterol H.D.L-Cholesterol and lower L.D.L-Cholesterol in treated groups as compared to the hepatotoxic rats. Hedgehog signaling genes (Ihh, Shh, Hhip, Smo, Ptch-3, and Gli-3) expressions were significantly downregulated in the quercetin and silymarin treated as compared to the thioacetamide induced hepatotoxicity group. Histological studies using Sudan Black B staining showed pronounced black patches of lipids and steatosis of liver cells were packed as droplets of fats in hepatotoxic group meanwhile treatment with quercetin and silymarin improved lipid contents as shown by a clear hepatic region devoid of triglycerides cysts, reduced number of lipid droplets and hepatocytes necrosis.
Conclusion: Our findings show that quercetin could ameliorate hepatic toxicity by antagonizing the hedgehog pathway and also suggest hedgehog pathway as a potential therapeutic target for the treatment of hepatic toxicity.

[ABST-0038]

Engineering calreticulin-targeting monobodies to detect immunogenic cell death in cancer chemotherapy

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Background: Cancer cell surface–exposed calreticulin (ecto-CRT) is the primitive form of signal during immunogenic cell death (ICD). It is a well-known candidate to allow "eat-me" signal from dying cells, which further contributes to their perception in directing the immune system. Various forms of anticancer agents and ionizing radiation can facilitate the ICD via ecto-CRT exposure. Ecto-CRT is an immunogenic signal induced in response to treatment with chemotherapeutic agents such as doxorubicin (DOX) and mitoxantrone (MTX), and two peptides (KLGFFKR (Integrin-α) and GQPMYGQPMY (CRT binding peptide 1, Hep-I)) are known to specifically bind CRT.
Methods: To engineer CRT-specific monobodies as agents to detect immunogenic cell death (ICD), we fused these peptide sequences at the binding loops (BC and FG) of human fibronectin domain III (FN3). CRT-specific monobodies were purified from E. coli by affinity chromatography. Using these monobodies, ecto-CRT was evaluated in vitro, in cultured cancer cell lines (CT-26, MC-38, HeLa, and MDA-MB-231), or in mice after anticancer drug treatment.
Results: Monobodies with both peptide sequences (CRT3 and CRT4) showed higher binding to ecto-CRT than those with a single peptide sequence. The binding affinity of the Rluc8 fusion protein–engineered monobodies (CRT3-Rluc8 and CRT4-Rluc8) to CRT was about 8 nM, and the half-life in serum and tumor tissue was about 12 h. By flow cytometry and confocal immunofluorescence of cancer cell lines, and by in vivo optical bioluminescence imaging of tumor-bearing mice, CRT3-Rluc8 and CRT4-Rluc8 bound specifically to ecto-CRT and effectively detected pre-apoptotic cells after treatment with ICD-inducing agents (DOX and MTX) but not a non-ICD-inducing agent (gemcitabine).
Conclusions: Taken together, our data clearly demonstrate the functional properties of engineered CRT-targeting monobodies to detect ICD during cancer chemotherapy. This strategy of engineering novel monobodies using peptides may simplify the process required to generate high-affinity biomolecules for inaccessible or challenging targets.

[ABST-0080]

Disruption of collagen alignment by an MMP2-responsive nanosystem to enhance penetration of chemotherapeutic agents in pancreatic ductal adenocarcinoma

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Background: Collagen is one of the most important stromal components of pancreatic ductal adenocarcinoma (PDAC), and studies have revealed its double-edged role in the progression of PDAC. On the one hand, collagen can physically limit the rapid growth of tumor cells. On the other hand, the linear arrangement of collagen promotes the differentiation of tumor cells and inhibits the infiltration of chemotherapy drugs. Therefore, disrupting the linear arrangement of collagen while preserving the limiting effect of collagen on tumor cell growth is of great significance for promoting the treatment of pancreatic cancer.
Methods: Second-harmonic generation (SHG) and Scanning electron microscope was used to analyze the architecture of collagen fibers. Immunohistochemistry was used to evaluate the expression of LOXL2 in PDAC tissues. DDR1 inhibitor was first incorporated into PEG-PLGA nanoparticles using a modified double emulsion method. And then the nanoparticles were encapsulated into liposomes with the LOXL2 inhibitor to construct the MMP2-responsive nanosystem LOXL2-DDR1@MLP. Transmission electron microscope (TEM) was used to observe the morphology and dynamic light scattering (DLS) was used to analyze the size distribution of LOXL2-DDR1@MLP. Orthotopic PDAC model characterized with abundant tumor stroma was used to evaluate the anticancer efficacy of the nanosystem combined with nab-paclitaxel (Nab-p) in vivo.
Results: We confirmed that collagen fibers in PDAC tissues showed a significant linearized arrangement, and the degree of collagen fiber alignment was positively associated with the expression level of LOXL2. The LOXL2-DDR1@MLP nanoparticles encapsulated LOXL2 and DDR1 inhibitors and responded to the MMP2 enzyme effectively. The LOXL2-DDR1@MLP successfully disrupted the

alignment of collagen and maintained the stable content of collagen in vitro and in vivo. In orthotopic PDAC models, the nanosystem enhanced the treatment of nab-paclitaxel (Nab-p) significantly.
Conclusions: We have successfully devised an MMP2-responsive nanosystem for delivering LOXL2 and DDR inhibitors. The nanosystem disrupted collagen alignment and enhanced penetration of chemotherapeutic drugs effectively, which provided a new therapeutic strategy in desmoplastic pancreatic cancers.

[ABST-0093]

Concept of gastro-intestinal system in ayurveda

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Background: What gastroenterology means Gastroenterology is the study of the normal function and diseases of the esophagus, stomach, small intestine, colon and rectum, pancreas, gallbladder, bile ducts and liver. Abstract Concept of gastrointestinal tract is very much elaborated by the Ayurvedic Saamhitas. A consistent, clear and precise anatomical description for the most part of the gastro-intestinal tract has been furnished by Atreya Samhita which has been quoted by Vaidyaka-Sabda Sindhu. The gastrointestinal tract is described by various terms like Mahsrotas, Annavaha srotas and Kostha etc. Srotasa are channel system for transportation and transformation of sharirbhava and dhatu. The term Annavaha Srotas points out the functions performed by this channel means the transportation of the food. Annavahasrotas is associated with digestion and flow of food material which later forms.
Methods: Four Samhita and eleven different Nighantu were reviewed. The obtained data have been analyzed and being presented in a precise manner with regards to their various reported activity on gastrointestinal diseases. Components of Annvah Srotas Amashaya (Stomach) Acharya Charak described location of amashaya in between nabhi (umbilicus) and stana (nipples). It perform the function of pachan (digestion) of all type offood material Stomach is a muscular bag forming widest and most distensible part of digestive tube. Amashaya is divided into two parts, Urdhva and AdhoAmashya is considered as Kshudrantantra, pacyamanasaya and agnyasaya.
Results: Analysis of the compiled data reveals that out of 324 plants, described under Shakavarga, 58 vegetables are indicated in the diseases related to gastrointestinal tract like Ajirna (Dyspepsia), Arshas (Hemorrhoids), Grahani (Malabsorption syndrome) etc. Among them, botanical identity of 57 classical plants has been established and maximum number of vegetables belongs to the family Cucurbitaceae & Solanaceae. Different parts of the plants like leaves, fruits, rhizome/tuber, stem, owners are recommended as vegetables in gastrointestinal diseases. Some of these vegetables are also reported for their effect in the management of peptic ulcer, chronic in'amatory bowel disease etc.
Conclusions: The observed results may be helpful in planning further scientific studies about the affiance of these plants on prevention as well as management of gastrointestinal diseases.

[ABST-0181]

Analysis of DNAs in normal and tumor tissues of hepatocellular carcinoma using whole genome sequencing

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Background: Primary liver cancer is the second leading cause of cancer-related deaths in Korea. Hepatocellular carcinoma (HCC) is one of the most common types of primary liver cancer, and infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) is one of the important causes of the development of HCC. However, the mechanisms of the development of HBV and HCV-infected related HCC are not clear. The aim of this study is to examine the genes involved in the development of HBV and HCV-infected related HCC.
Methods: 4 HBV-infected HCC and adjacent normal liver tissue and 2 HCV-infected hepatocellular carcinoma and adjacent normal liver tissue were included in this study. Single point mutation (single nucleotide polymorphisms, SNP) and insertion/deletion (indel) mutations were analyzed using whole genome sequencing.
Results: Indel mutation of DNMT3A gene was commonly observed in 4 samples. Single point mutations of SIRT1, ZDHHC8P1, FGF18-SMIM23, and KRT73-KRT2 were observed in common in 3 samples. rs148398571 SNP of DPP9 gene was found only in HCV samples, and rs140405310 of ANGPTL6 was found only in recurred sample.
Conclusions: The mutations between HCC and adjacent normal liver tissue were not consistent in all samples. However, indel mutations in the DNMT3A gene and SNPs of SIRT1, ZDHHC8P1, FGF18-SMIM23, and KRT73-KRT2 might contribute to the development of HCC. These results could provide evidence for the development of diagnostic and therapeutic tools for HCC.

[ABST-0195]

Factors influencing alcohol consumption in adolescents in Indonesia: A literature study

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Background: Although it has been stated in the Minister of Trade Regulation No. 20/M-Dag/Per/4/2014 Article 15 which contains rules that the age limit for being allowed to drink alcoholic beverages (according to the dose) is above > 21 years, there are still many teenagers under 21 years old participate in alcohol consumption. In addition to endangering the period of brain development that occurs during adolescence, namely 15–19 years, alcohol consumption can also damage the liver. For those this study aims to find out the factors that influence alcohol consumption in adolescents in Indonesia.
Methods: This research study is a literature review by extracting research with relevant topics for the last six years (2016–2021), and involving adolescents 18 years as the object of research.
Results: The results of the analysis show that the factors that influence alcohol consumption are the habit of drinking alcohol ($p = 0.004$), availability of alcoholic beverages ($p = 0.002$), how to get alcoholic beverages ($p = 0.001$), peers who consume alcohol ($p = 0.010$), lack of self-confidence ($p = 0.000$), want to try ($p = 0.000$), run away from problems ($p = 0.000$), living environment ($p = 0.002$), family ($p = 0.000$). Factors that influence alcohol consumption found in qualitative research are the behavior of consuming

alcoholic beverages from outside and within adolescents such as the environment in which they live, social environment, ridicule, trends or traditions, stress, solidarity and curiosity.
Conclusions: this study expect various stakeholders to carry out supervision and education on alcohol consumption among Indonesian youth.

[ABST-0329]

Risk of renal function and mortality in cured COVID-19 patients with kidney biomarkers and acute heart failure

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Background: Recent studies indicate the need to redefine renal function (RF) in acute heart failure (AHF) linking a rise in creatinine with clinical status to identify patients who develop evaluated the usefulness of serial assessment of urinary levels of neutrophil gelatinase-associated lipocalin kidney injury molecule-1 (KIM-1).
Methods: In 96 patients with AHF, uNGAL, uKIM-1, and uCysC were measured using a highly sensitive immunoassay based on a single-molecule counting technology (Singulex, Alameda, CA, USA) at baseline, day 2, and day 3. Patients who developed WRF (a $\geq$ 0.3 mg/dL increase in serum creatinine or a $>$ 25% decrease in the estimated glomerular filtration rate from the baseline value.
Results: were differentiated into those presence of deterioration/no improvement in clinical status during hospitalization vs. 'pseudo-WRF' (uneventful clinical course). occurred in 12 (10%), 'pseudo-WRF' in 14 (11%), whereas the remaining 104 (79%) patients did not develop WRF. Patients with 'true WRF' were more often females, had higher levels of NT-proBNP, creatinine, and urea on admission, higher urine albumin to creatinine ratio at day 2, higher uNGAL at baseline, day 2, and day 3, and higher KIM-1 at day 2 (vs. pseudo-WRF vs. without WRF, all $P < 0.05$). Patients with pseudo-WRF did not differ from those without WRF. In the multivariable model, elevated uNGAL at all time points and KIM-1 at day 2 remained independent predictors.
Conclusions: identify patients at high risk of death. Larger studies with more frequent biomarker assessments in the early stages of hospitalization are needed to portray the dynamics of these patients in a realistic way, to better demonstrate the usefulness of biomarkers.

[ABST-0232]

Engineering technology in hepatology

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Background: This is the era of integration of Engineering Technology monitoring of a person's health and its management. I am highlighting currently available digital health technologies.
Methods: Digital health is presently in a nascent stage, so I am trying to analyze Literature reviews.
Results: Wearable health technology, Fitness bands: It is used to monitor health. It has sensors that measure their heart rate, blood pressure, and temperature, sleeping patterns, etc. Smart piezoelectric necklaces: It uses artificial Intelligence. It detects the swallowing of medications. During swallowing its piezoelectric sensor converts neck movements into electrical signals for transmission into a smartphone apparatus to be read. Implantable and ingestible sensors: Advancements in microelectronics, data processing, and wireless communication have resulted in devices that can be implanted under the skin or ingested. It allows continuous and unobtrusive monitoring of key vital signs, like heart rate. It can also alert patients and caregivers if a problem is detected. Wearable therapeutic devices: Optune system, wearable overhead is used to treat glioblastoma. It delivers electric signals to stop cell division & cancer growth. Pain-relief in neuro-technology: Quell, a band that is wrapped around the calf uses electricity to block pain signals. Automated home-based monitoring: Pain can be managed with telecare. Scheduled telephone calls may be placed for necessary advice. Home blood tests: A remote monitoring device is under research to test a drop of blood at home to measure white cells count, hemoglobin.
Conclusions: Digital technology has created innovative models of healthcare delivery that empower people living with chronic diseases. It is also being widely accepted.

Hepatitis B—Basic

[OP-0071]

A case control study on HCV in HIV infected and non-infected individuals

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Objectives: A case–control study was designed to examine the HCV infection in HIV infected individuals as the case and non-HIV infected individuals as healthy controls.
Materials and Methods: A Case–control study was carried out in 244 participants including 122 HIV infected and 122 HIV non-infected (healthy) individuals for the comparison of HCV infection using the RDT method. The samples for the case were taken from HIV infected and for control, samples were taken from Pokhara valley through counseling and Questionnaires.
Results: Among the 122 HIV-infected participants 16 individuals had HCV infection 13.11% positive prevalence rate. Among the healthy 122 participants only 2 participants, had HCV infection 1.63% of positive prevalence rate. This showed the significance level of P-value of 0.001 and OR = 9.057 with nine-fold higher in the case and control. Male participants were found to have higher levels of HCV infection, among 16 HCV positive, 9 (7.4%) were male and 7 (5.7%) were female. In control, the equal prevalence of positive HCV-infection was sheen between male and female i.e. 1 (0.8%). The sex-wise distribution showed no significance with the HCV infection. In the case 3 (2.5%), 4 (3.3%), 1 (0.8%) of the participants were HCV positive in the age group $<$ 20, 20–40, 40–60, $>$ 60 years respectively.
Conclusion: The highest, HCV positive was among the case in our study which might be due to the defect in the immune system of HIV-infected individuals than of non-infected (healthy control) individuals. HIV-infected persons are highly prone to any infection which increases the chances of HCV infection.

[OP-0239]

The Chinese herbal XiaoChaiHu decoction inhibits HBV-related hepatoma cell proliferation via regulating the HBx-YAP-NR4A1 axis

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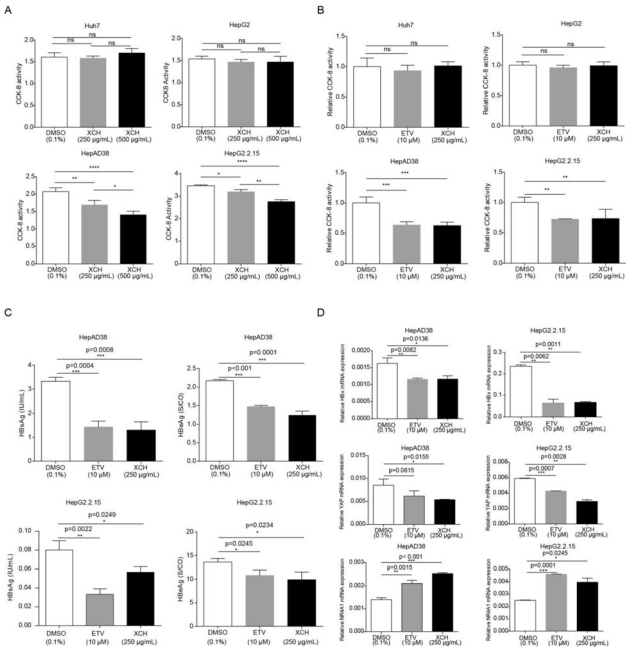
Objectives: The Chinese herbal XiaoChaiHu decoction (XCH) has been applied to treat hepatocellular carcinoma (HCC) and hepatitis B virus (HBV) infection in the clinic. However, it is unclear about its function on HBV-related HCC. The hepatitis B virus X (HBx) expression and yes-associated protein (YAP)-nuclear receptor NR4A1 axis play an important role during HBV-related hepatocarcinogenesis. Here we aimed to explore the functions of XCH on HBV-related hepatoma cell proliferation via regulating the HBx-YAP-NR4A1 axis.
Materials and Methods: The HBV-replicated HepAD38 and HepG2.2.15 cell lines, and No-HBV HepG2 and Huh7 cells were maintained in DMEM supplemented with 10% fetal bovine serum. For HepAD38 and HepG2.2.15 cells, the media were additionally supplemented with 400 μg/mL G418 sulfate. XCH granules were dissolved in dimethyl sulfoxide and added to the cell culture with 250 and 500 μg/mL final concentrations. After treatment, the cell viability was detected by CCK-8 kit, the levels of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) in the cell culture supernatant were detected by the quantitative determination kits. The mRNA expression of HBx, YAP, and NR4A1 was detected - by qRT-PCR.
Results: The CCK-8 results showed that the XCH could suppress proliferation of HBV replicating cells, including HepAD38 and HepG2.2.15 in a dose-dependent manner, but it had no comparable inhibitory effect on No-HBV replicating hepatoma cells, including HepG2 and Huh7. After treatment, the levels of HBsAg and HBeAg were downregulated significantly in the XCH group compared to the control in HepAD38 and HepG2.2.15 cells. Moreover, the expression levels of HBx and YAP were lower expressed in the XCH group, while NR4A1 was upregulated in both HepAD38 and HepG2.2.15 cells.
Conclusion: XCH's anti-HCC effect depended on its anti-HBV functions at the cell level. The inhibitory effect of XCH on HBV-related hepatoma cell proliferation may achieve by downregulating the HBx-YAP-NR4A1 axis.



[PP-0307]

Hepatitis B surface antibody in relation to all-cause mortality in the serum HBsAg-negative and HBcAb-positive patients: Prospective cohort study

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Objectives: Effect of hepatitis B surface antibody (HBsAb) on the long-term prognosis of hepatitis B infected patients who have achieved HBsAg (Hepatitis B surface antigen) clearance is still unknown. For patients who have achieved HBsAg clearance, is it necessary to pursue HBsAg seroconversion (HBsAg negative and anti-HBsAg positive)? Herein, we investigated the association between hepatitis B surface antibody and all-cause mortality in the serum HBsAg-negative and HBcAb-positive patients.
Materials and Methods: This is a prospective cohort study. Data come from US National Health and Nutrition Examination Survey (NHANES) 1999–2014. 2718 patients with serum HBsAg-negative and HBcAb-positive were enrolled in this study. Main outcome measures were all cause mortality from baseline until 31 December 2015.
Results: Out of 82,091 NHANES examinees, 59,866 were tested for HBsAg, HBcAb and HBsAb, of whom 2718 met the inclusion criteria (serum HBsAg-negative and HBcAb-positive). HBsAb-negative participants had higher self-reported liver condition ($p < 0.001$), percentage of anti-HCV-positive ($p < 0.001$), FIB-4 score ($p < 0.001$) and APRI score ($p = 0.001$), compared with HBsAb-positive participants. During a mean follow-up of 7.58 years, 497 deaths occurred. Compared with participants with serum HBsAb-positive, HBsAb-negative participants had a 43.6% (hazard ratio 1.436, 95% confidence interval 1.183 to 1.744, P = 0.000) higher risk of all-cause mortality.

Conclusion: HBsAb-negative were associated with increased risks of mortality in serum HBsAg-negative and HBcAb-positive patients. These data highlight HBsAb may be a potential prognostic biomarker for patients who have achieved HBsAg clearance. Compared to HBsAg clearance, HBsAg seroconversion may be a better endpoint for hepatitis B infected populations.

[OP-0484]

HBV Haplotype number at baseline predicts treatment outcome in HBeAg-positive chronic hepatitis B

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Objectives: We have investigated associations between hepatitis B virus (HBV) genome-length haplotype number (HN) at baseline in chronic HBV subjects, and the likelihood of achieving functional cure during therapy.
Materials and Methods: A test cohort (Gilead trial GS-US-174–0103 "G103 cohort") of 161 HBeAg positive baseline samples from HBV genotype A to D patients enrolled in a chronic hepatitis B (CHB) Phase III tenofovir disoproxil fumarate (TDF) clinical trial were analysed to determine if HN was a predictive biomarker of HBsAg loss or remaining HBsAg positive on long term therapy. Findings were validated in two independent clinical trials utilising TDF or tenofovir alafenamide (TAF) therapy, from HBeAg positive CHB (n = 654 "G110 cohort") and HBeAg negative (n = 304, "G108 cohort") CHB.
Results: In the G103 and G110 HBeAg positive cohort, we identified significantly lower HN in HBsAg negative patients for the Caucasian genotypes A & D ($p < 0.0001$). No significant differences were observed for the Asian genotypes B & C. In HBeAg positive A & D genotype patients, HN ≤ 2 was statistically associated with predicting functional cure (HBsAg loss) at baseline, prior to therapy with an odds ratio of 41 (95% CI 15–204) and 23 (95%CI 10–143) for the G103 and G110 cohorts, respectively. The positive predictive value to predict HBsAg loss if HN ≤ 2 was 64% & 60%, and the negative predictive value to predict non HBsAg loss if HN > 2 was even higher with 92% & 98% respectively, for the G103 and G110 cohorts. Baseline HN was a stronger predictor of functional cure than the presence of HBV BCP mutations, previously shown to be associated with reduced likelihood of progression to functional cure.
Conclusion: Here, we report for the first time, that HN ≤ 2 across the complete HBV genome predicts, at baseline, which patients will progress to functional cure on long term antiviral therapy.

[OP-0560]

The Chinese herbal JiGuCao capsule inhibits the replication of hepatitis B virus and related disease via integrating cell and animal experiment verification

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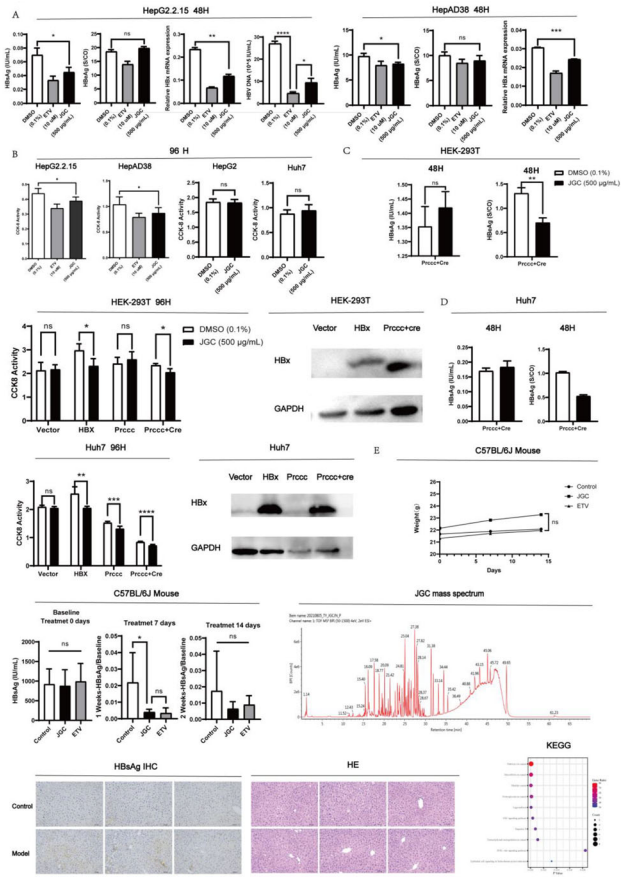
Objectives: The Chinese herbal JiGuCao capsule (JGC) has been proven effective for acute hepatitis B in clinical trials. Here we aimed to explore the function and mechanism of JGC on hepatitis B virus (HBV)-related disease.
Materials and Methods: The cells were maintained in DMEM supplemented with 10% fetal bovine serum. Plasmids were transfected into the cell by lipofection and into the mice's liver by hydrodynamic injection via the tail vein. The cell viability was detected by the CCK-8 kit. The cells were treated with 500 μg/mL JGC and the mice were treated with JGC by intragastric administration. The levels of HBV surface antigen (HBsAg) and HBV e antigen (HBeAg) were detected by the quantitative determination kits. The HBV X (HBX) gene' expression was examined by qRT-PCR and western blotting. The effective components of JGC were detected by mass spectrometry (MS). The related pathway was analyzed by network pharmacology.
Results: After JGC treatment, the levels of HBsAg and HBeAg in culture supernatant were decreased, and the expression of intracellular HBx was also downregulated in HepAD38 and HepG2.2.15 cells. The CCK-8 results showed that the JGC could suppress proliferation of cells with HBV replicating and HBx expressing but had no inhibitory effect on none-HBV/HBx hepatoma cells. In the HBV mice model, compared to the control group, the HBsAg level was lower in the JGC-treated group on the 7th day which showed a faster clearance of HBV. The MS analysis suggested there were about one hundred components of JGC. And the network pharmacology analysis indicated that the effect of JGC on HBV was related to the TNF signaling pathway.
Conclusion: JGC exerted functions of anti-HBV and inhibiting HBV-related hepatoma cells' proliferation relied on its active components and regulation on key targets and pathways. The current study provided a basis for further clinical applications.



[PP-0584]

Evaluating the efficacy and safety of switching from tenofovir disoproxil fumarate to besifovir dipivoxil maleate in virologically suppressed chronic hepatitis B patient

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Objectives: Besifovir dipivoxil maleate (BSV) shows comparable antiviral activity to tenofovir disoproxil fumarate (TDF), and a better safety profile in the phase 3 trial. Herein, we report 48-week data of the phase 4 trial in chronic hepatitis B (CHB) patients who switched to BSV from TDF.

Materials and Methods: This is a randomized, active-controlled, open-label, multicenter study to evaluate the 48-week safety and non-inferior efficacy of BSV switched from TDF in virologically suppressed CHB patients. The primary efficacy endpoint was the proportion of patients with HBV DNA level < 20 IU/mL at week 48. Efficacy analyses included virologic, biochemical, and serologic responses, and safety assessments included changes in bone mineral density (BMD), bone turnover markers and renal outcomes.

Results: A total of 130 patients were included for the Per protocol analysis (BSV group, n = 64; TDF group, n = 66). At week 48, 100.0% of patients who received BSV and 98.5% of patients who received TDF met the primary efficacy endpoint, indicating the non-inferiority of BSV to TDF (95% CI -0.01 to 0.04; p = 1.000). Only one participant in the BSV group showed HBsAg seroconversion at week 48. The rates of HBeAg seroconversion were 14.8% and 10.7% in the BSV and TDF groups, respectively (p = 0.7049). A significantly higher decline in alanine aminotransferase (ALT) was observed in patients receiving BSV compared with patients receiving TDF (p = 0.0267), and ALT normal were shown 90.6% and 86.4% in the BSV and TDF groups, respectively (p = 0.4471). The mean % changes of eGFR was persistently higher in the BSV group (repeated measures ANOVA: p = 0.0096). All bone turnover biomarkers were statistically significantly improved in the BSV group compared to the TDF group; similarly, hip and spine BMD increased in the BSV group.

Conclusion: In patients with virologically suppressed CHB, BSV was non-inferior to TDF, and had improved safety.

[PP-0853]

Distinctive HBV replication capacity and susceptibility to tenofovir induced by a polymerase point mutation in hepatoma cell lines and primary human hepatocytes

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Objectives: Tenofovir disoproxil fumarate (TDF) has been regarded as the most potent drug for treating patients with chronic hepatitis B (CHB). However recently, viral mutations associated with tenofovir have been reported. Here, we found a CHB patient with suboptimal response after more than 4 years of TDF treatment.
Materials and Methods: HBV DNA was extracted from the serum of a CHB patient with suboptimal response to TDF therapy. Mutational profile was analyzed by specifically amplifiying the reverse transcriptase (RT) of HBV polymerase. Then, we constructed the HBV mutant replicons harboring artificially substituted or patient-derived RT domains by site-directed mutagenesis. Using these clones, drug susceptibility test was examined by several experiments, including southern and northern blot analysis, quantitative real-time PCR, and ELISA.
Results: Clonal analysis of hepatitis B virus (HBV) isolated from sequential sera of this patient identified the seven previously reported TDF-resistant mutations (CYELMVI). Interestingly, a threonine to alanine mutation at the 301 amino acid position of the reverse-transcriptase (RT) domain (rtT301A), was commonly accompanied with CYELMVI at a high rate (72.7%). Since the rtT301A mutation has not been reported yet, we investigated the role of this naturally occurring mutation on the viral replication and susceptibility to tenofovir in various liver cells (hepatoma cells as well as primary human hepatocytes). A cell-based phenotypic assay revealed that the rtT301A mutation dramatically impaired the replication ability with meaningful reduction in sensitivity to tenofovir in hepatoma cell lines. However, attenuated viral replication by the rtT301A mutation was significantly restored in primary human hepatocytes (PHHs).
Conclusion: Our findings suggest that the replication capability and drug sensitivity of HBV is different between hepatoma cell lines and PHHs. Therefore, our study.
emphasizes that validation studies should be performed not only in the liver cancer cell lines but also in the PHHs to understand the exact viral fitness under antiviral pressure in patients.

[OP-0904]

Prevalence and genotype distribution of hepatitis B among pregnant women in Siem Reap province, Cambodia

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Objectives: Since Cambodia has not yet established HBsAg screening program in pregnant women, this study aimed to estimate HBsAg prevalence among pregnant women and then to examine their genomic structure and the mutation pattern.
Materials and Methods: This study is a part of the ongoing longitudinal study aiming to estimate HBV transmission rate from mother to child. Total 1565 pregnant women who visited three hospitals in Siem Reap for antenatal care from Feb-Sep 2020 participated in this study. The sero-markers such as HBsAg, HBsAb, HBcAb, HBeAg and HBeAb were detected from their blood samples using chemiluminescent enzyme linked. Viral titer was measured by real-time PCR. Full HBV genomes were amplified by direct sequencing.
Results: The age of pregnant women ranged from 15 to 47 years old with the mean age of 28.3 ± 5.6 years old. The prevalence of HBsAg, HBsAb, and HBcAb were 4.28%, 38.53%, 23.13%, respectively. Among the HBsAg positives, the prevalence of HBeAg and HBeAb were 41.79% and 55.22%, respectively. The overall mean viral titer was 2.22×10^6 copies/ml, where 5.30×10^6 copy/ml for $HBeAg^+$ and 5.58×10^3 copy/ml for $HBeAb^+$. Thirty-nine samples were able to perform full-genome sequencing. HBV genotype C1 was predominant (71.79%), followed by B4 (15.38%) and B2 (12.82%). All HBV genotype B were found to be recombinant B/C. By full genome analysis on 39 HBV isolates, mutation at a determinant region of surface protein was 23.1%. Additionally, the combination mutation was found in 2.25% and double mutation in 28.20% and V149I mutation at core region in 3%, all of which were highly associated to hepatocellular carcinoma occurrence.
Conclusion: The results from our study illustrated the level of HBV infection endemicity, genotype distribution and mutation pattern among pregnant women in Siem Reap. These findings contribute to the establishment of HBV screening program and the management of HBsAg positive for pregnant women in Cambodia.

[OP-0905]

Genotype distribution and mutation pattern linked to liver disease progression among chronic hepatitis B carriers in Goto Islands, Japan

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Objectives: Hepatitis B virus surface antigen (HBsAg) screening has been conducted in all residents of the Goto Islands of Nagasaki Prefecture in Japan since 1977, and HBsAg prevalence was 4.3% in 2017. This study aimed to examine the genomic characteristics of circulating Hepatitis B Virus (HBV) in Goto Islands and explore the relation between each genotype and liver disease progression among chronic HBV carriers.
Materials and Methods: A total of 916 stored samples from a cohort of HBsAg-positive patients during 1980–2017 underwent serologic (HBeAg and HBeAb) and genomic analyses. Partial or full HBV genomes were amplified by direct sequencing using an in-house developed primer set. Phylogenetic tree was performed by the neighbor-joining method. This study was approved by our institutional ethics committee.
Results: This cohort includes 57.4% males, and the average age was 45.5 ± 17.3 years, with a median follow-up duration of 14.6 ± 9.2 years. At entry, 61% were asymptomatic carriers, but a 172% increment of hepatocellular carcinoma was found at the end of follow-up. The average viral titer was 2.0×10^4 copies/ml, and

HBeAg and HBeAb prevalence were 26.5% and 71.2%, respectively. HBV genotype C2 was predominant (96.2%) followed by genotype B (3.4%) and A (0.6%). Three main clusters of cases were found having 95.6%-99.0% homology, and each cluster was closely related to HBV isolates from China and Japan. Full genome analysis of 92 isolates (10% of total) found combination mutation (C1653T and A1762T/G1764A or T1753C and A1762T/G1764A) in 29.4%, double mutation (A1762T/G1764A) in 73.5%, and V149I mutation in the core region in 26.9% of the isolates.
Conclusion: Genotype C2 is the predominant circulating genotype in Goto Islands, suggesting a large influence from East Asia. In addition, notable mutations related to hepatocellular carcinoma occurrence were found. Improvement of countermeasures and genomic surveillance are essential to reduce HBV burden in Goto Islands.

[L-PP-1263]

Clinical Characteristics of COVID-19 Patients With Chronic Hepatitis B From Kocaeli, Turkey

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Objectives: The outbreak of coronavirus disease 2019 (COVID-19) has been declared a pandemic on 11 March, 2020 by WHO. Turkey is a middle endemic country regarding chronic hepatitis B. Because of that, co-infection of chronic hepatitis B and COVID-19 is common as well. Although COVID-19 is caused by infection in the respiratory tract, extrapulmonary manifestations have also been observed. In this article, we aimed to study the impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and HBV coinfection in patients.
Materials and Methods: Diagnosis of COVID-19 was conducted using real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) to detect SARS-CoV-2 RNA in nasopharyngeal swab specimens. The diagnosis of chronic hepatitis B was made according to the APASL 2016 Hepatitis B guideline.
Results: A total of 28 patients with chronic hepatitis B were included in this study. 21 of these patients were male. All individuals' nasopharyngeal swab specimens tested positive by SARS-Cov-2 PCR. The current HBV DNA levels of 13 patients is negative. 6 patients needed oxygen treatment and 3 of them had followed in the intensive care unit. The HBV DNA levels of these patients were negative, however patients had comorbidities of prostate cancer, hepatocellular cancer and diabetes mellitus, respectively. Among these 3 patients, 2 of them have died due to COVID 19.
Conclusion: SARS-CoV-2 and HBV coinfection does not significantly affect the outcome of COVID-19. Although there were a small number of patients in our study, it can be said that comorbid conditions other than hepatitis B are associated with more severe outcomes.

[L-OP-1327]

Preliminary study of S antigen mutation in the pathogenesis of occult hepatitis B infection through the UPR-ERAD pathway of endoplasmic reticulum stress

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Objectives: More and more studies have shown that the mutations of hepatitis B surface antigen can lead to the occurrence of occult hepatitis B virus infection, especially the amino acid (AA) substitutions in small hepatitis B surface proteins (SHBs), but the mechanism is still not clear. The purpose of this study was to investigate the potential impact and mechanisms of OBI-related SHBs mutations on serum HBsAg.
Materials and Methods: Huh7 and HepG2 cells were transfected with OBI-related SHBs mutations and wild type plasmid. The level of HBsAg in cell culture supernatant was detected by chemical luminescence, and the level of HBsAg and endoplasmic reticulum stress-related protein in cell lysate were detected by western blotting, then immunofluorescence assays were used to observe the intracellular localization of HBsAg.
Results: The HBsAg levels of cell supernatant and cell lysate were lower in the OBI-related SHBs mutated plasmid transfected groups than that in wild type plasmid transfected group. It was found that both the intracellular and extracellular expression level of HBsAg in the OBI-related SHBs mutated plasmid transfected groups was relatively higher than that in the wild type plasmid transfected group, and there was a certain intracellular accumulation. It was also found that HBsAg accumulated in the endoplasmic reticulum by immunofluorescence analysis. The levels of endoplasmic reticulum stress-related proteins were significantly higher in the mutated plasmid transfected groups than that in wild-type plasmid transfected group.
Conclusion: The OBI-related mutated protein may accumulate in the endoplasmic reticulum to trigger endoplasmic reticulum stress and reduce the transcription and translation levels of HBsAg by activating the unfolded protein response, and activate the endoplasmic reticulum associated protein degradation pathway (ERAD). Finally, the assembly and secretion of HBV particles in the endoplasmic reticulum are reduced.

[L-PP-1350]

Oral combination vaccine against hepatitis B & Anthrax

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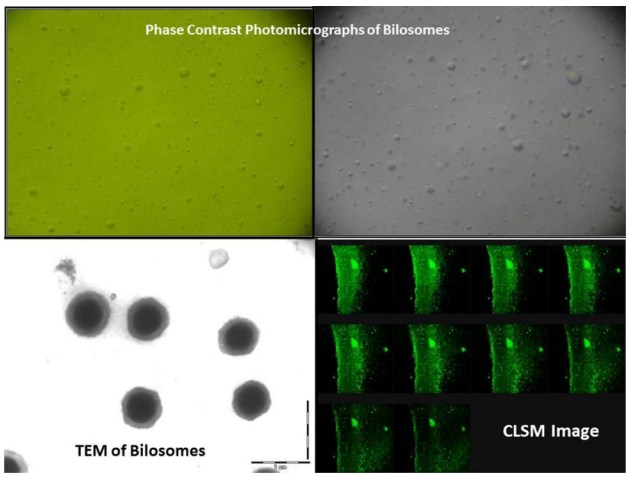
Objectives: Vaccination has not only become vital but a lot of revolutionary changes are being observable in the field of vaccine delivery. Vaccine antigens administered by the oral route are often degraded during gastrointestinal transit. Bile salt stabilized vesicles i.e. bilosomes are found to be effective in preventing antigen degradation and enhance mucosal penetration. The aim of the present work was to prepare a combination vaccine system against hepatitis-B (HBsAg) and anthrax (rPA). Oral immunization induces both mucosal and systemic immune responses, whereas mucosal responses are not generally observed following systemic immunization. Bilosomes provide needle free, painless approach for immunization, thereby increasing patient compliance and consequently increasing vaccination coverage.

Materials and Methods: Bilosomes containing HBsAg and rPA were prepared by a lipid cast film method. Antigen loaded bilosomes were characterized in-vitro for their shape, size, percent antigen entrapment and stability. Fluorescence microscopy was carried out to confirm the uptake of bilosomes. The in-vivo study comprised of estimation of IgG response in serum and sIgA in various body secretions using specific ELISA.
Results: Bilosomes formed were multilamellar and were stable in gastric and intestinal fluids. Fluorescence microscopy suggested that bilosomes were taken up by the gut associated lymphoid tissues. In-vivo data demonstrates that bilosomes produced both systemic as well as mucosal antibody responses upon oral administration at higher dose levels as compared to intramuscular immunization but fail to produce any synergistic effect.
Conclusion: Thus, HBsAg potentiates the production anti-rPA antibody. Also measurable sIgA in mucosal secretions were observed. Thus, the bilosomes are a promising carrier for oral combination vaccines. This approach could be adapted for human use because the mucosal surfaces are the initial sites of infection and it therefore seems logical to attempt to develop vaccination strategies that evoke appropriate localized responses to counteract the early events of pathogenesis.



Hepatitis B—Clinical

[PP-0017]

Switching from tenofovir-based combination therapy to tenofovir monotherapy in multi-drugexperienced chronic hepatitis B patients: A 5-year experience at two centers

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Objectives: Patients with chronic hepatitis B (CHB) administered tenofovir disoproxil fumarate (TDF)-based combination therapy after receiving multiple drugs are frequently switched to TDF monotherapy in South Korea. We evaluated the efficacy and safety of switching to TDF monotherapy from TDF-based combination therapy over a 5-year period.
Materials and Methods: This was a retrospective study of multi-drug–experienced CHB patients switched from TDF-based combination therapy to TDF monotherapy after achieving a virologic response (VR; < 20 IU/mL) at Konkuk University Hospital and Sanggye Paik Hospital. Each patient was assessed from the date of switching to TDF monotherapy to the date of the last follow-up over a 5-year period.
Results: A total of 39 patients who received at least one antiviral therapy before TDF-based combination therapy were analyzed. The median duration of VR before switching to TDF monotherapy was 18 months and the median duration of TDF monotherapy was 55 months. In this study, with the exception of one patient who had poor compliance, all patients maintained a VR. Three patients had a temporarily increased HBV DNA level and 91.2% of the patients showed a biochemical response.
Conclusion: In conclusion, switching multi-drug–experienced patients to TDF monotherapy is generally safe and effective.

Table 1. Efficacy of switching to TDF monotherapy at 60 months.

	6M	12M	24M	36M	48M	60M
Virologic response[1]	35/39 (89.7%)	36/37* (97.3%)	35/35* (100%)	36/37* (97.3%)	34/36* (94.4%)	33/34* (97.1%)
Virologic breakthrough[2]	2/39 (5.13%)	0/37 (0.00%)	0/35 (0.00%)	1/37 (2.70%)	1/36 (2.78%)	0/34 (0.00%)
Biochemical response[3]	35/39 (89.7%)	37/37 (100%)	33/35 (94.3%)	34/37 (91.9%)	35/36 (97.2%)	31/34 (91.2%)

* The total number of patients was different because of missing data or loss to follow-up. One patient converted to TDF-based combination therapy because of VBT at 3 months; after 6 months, their data were excluded from the analysis.

[1] Virologic response is defined as a serum HBV DNA level of < 20 IU/mL by real time PCR.

[2] Virologic breakthrough is defined as an increase in HBV DNA level of > 1 $\log_{10}$ IU/mL from nadir or a change in status from undetectable to detectable.

[3] Biochemical response is defined as normalization of the serum alanine aminotransferase (ALT) level after treatment.

[PP-0045]

The Clinical and histologic features of chronic hepatitis B patients with mildly elevated alanine aminotransferase

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Objectives: Well understanding the histology severity of CHB patients with significant viremia and mildly elevated ALT is important. This study aimed to evaluate the histologic features of CHB patients with 1–2 folds of ULN of ALT.
Materials and Methods: Methods: Naïve chronic HBV infected patients with absence of cirrhosis, HBV DNA $>$ 2000 IU/mL in HBeAg negative or HBV DNA $>$ 20,000 IU/mL in HBeAg positive, and ALT of 1–2 folds of ULN participated in a phase IV study (NCT04674423) were enrolled. Liver histology was evaluated by a single pathologist who was blinded to clinical information and scored for histology activity index (HAI) by Knodell system and fibrosis stage by Metavir system. Liver stiffness measurement (LSM) by FibroScan at same day of liver biopsy was performed.

Results: Results: Of the 19 patients received liver biopsy, mean HAI score was 3.9 ± 1.8 and mean Metavir fibrosis stage was 2.0 ± 0.9. HAI score ^{3} 4 was found in 16 patients (84.2%). The distribution of fibrosis was 1 patient of stage 0 (5.3%), 8 patients of stage 1 (42.1%), 3 patients of stage 2 (15.8%), and 8 patients of stage 3 (42.1%). LSM (r = 0.498, p = 0.030), AST (r = 0.581, p = 0.009), and ALT (r = 0.486, p = 0.035) were moderately correlated with fibrosis stage, while only AST (r = 0.504, p = 0.023) correlated with HAI.
Conclusion: Conclusion: A significant proportion of CHB patients with viremic and mildly elevated ALT exhibit significant necroinflammation and fibrosis (Metavir fibrosis 2 or 3) implies that this kind of CHB patients may need antiviral treatment to halt liver disease progression.

[OP-0054]

Risk factors for very low-level viremia in patients with chronic hepatitis B virus infection

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Objectives: To explore the risk factors of very low-level viremia (VLLV, HBV DNA 9–12 IU/mL) in patients receiving nucelos (t)ide analogues treatment for more than one year.
Materials and Methods: This retrospective study used a 1:1 ratio propensity score matching test and finally 139 patients were enrolled in each of the VLLV group and MVR group (maintained virological response, HBV DNA undetectable) group between 2016–2020.
Results: HBeAg positive (OR, 5.14; 95%CI, 2.53–10.42), no drug replacement (OR, 7.84; 95%CI, 3.35–18.38), higher mean HBsAg (OR, 2.12; 95%CI, 1.44–3.12) had an increased risk of VLLV significantly. In a subgroup of patients stratified by HBeAg status, both in HBeAg positive and negative patients, mean HBsAg (OR, 6.84; 95%CI, 1.76–26.63 vs OR, 1.93; 95%CI, 1.28–2.90) and no drug replacement (OR, 48.76; 95%CI, 7.60–312.66; vs OR, 4.42; 95%CI, 1.65–11.86) were significantly related to development of VLLV. In a subgroup of patients stratified by age, both less than 40 years old and greater than or equal to 40 years old, HBeAg positive (OR, 9.16; 95%CI, 3.11–27.03 vs OR, 3.60; 95%CI, 1.20–10.79), mean HBsAg levels (OR, 2.63; 95%CI, 1.37–5.03 vs OR, 1.80; 95%CI, 1.09–2.97) and no drug replacement (OR, 15.23; 95%CI, 3.92–59.20 vs OR, 5.22; 95CI%, 1.67–16.27) were significantly associated with development of VLLV.
Conclusion: HBeAg positive, HBsAg levels and no drug replacement are risk factors for VLLV in patients with CHB. If HBV DNA could not decrease efficiently after preferred therapy, it is important to conduct resistance testing and replace the drug with another preferred therapy.

[OP-0056]

Efficacy and safety of tenofovir alafenamide fumarate in the treatment of patients with chronic hepatitis B complicated with non-alcoholic fatty liver disease

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Objectives: The incidence of CHB complicated with NAFLD is increasing. We aimed to explore the efficacy and safety of TAF in patients with CHB complicated with NAFLD.
Materials and Methods: A total of 86 patients with CHB and NAFLD were enrolled between 2019–2020. They were divided into 22 cases in the treatment-naïve group and 64 cases in the treatment-experienced group. Two groups were compared baseline and after 48 weeks treatment.
Results: By weeks 48, in treatment-naive group, the ratio of undetected rate and 9-20 IU/mL of HBV DNA (50% vs. 0%, 22.7% vs. 0%, resp) were statistically higher than baseline. By weeks 48, in treatment-experienced group, the undetected rate of HBV DNA was higher than the baseline, the rate of 9-20 IU/mL of HBV DNA was statistically lower than the baseline (64.1% vs. 39.1%, 12.5% vs. 35.9%, resp). TCH (median 4.7 mmol/L vs 4.0 mmol/L, TG (median 2.2 mmol/L vs 2.0 mmol/L), HDL-C (median 1.7 mmol/L vs 1.0 mmol/L) were statistically higher than baseline and LDL-C (median 2.6 mmol/L vs 3.0 mmol/L) were statistically lower than the baseline. Comparing weeks 48 with baseline, differences of blood creatinine and blood phosphorus in two group did not statistically significant.
Conclusion: TAF can obtain higher virological responses in patients with CHB complicated with NAFLD both in treatment-naive and treatment-experienced group and has little effect on renal function, but it may increase TCH, TG and HDL-C.

[OP-0074]

Long-term outcome of peginterferon-α2a treatment in patients with chronic hepatitis B: A single-center, real world study in Japan

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Objectives: Peginterferon-α2a (PegIFNα2a) has been available for treatment of chronic hepatitis B for ≥ 10 years. In this study, we determined the rate of HBsAg seroclearance in a long-term after PegIFNα2a treatment and clarified the characteristics of patients who achieved HBsAg seroclearance.
Materials and Methods: 50 patients with chronic hepatitis B (30 men/20 women; median age, 36 years; 22 HBeAg-positive/28 HBeAg-negative; 44 with genotype C) were included. 19 received PegIFNα2a monotherapy and 31 received combination with nucleos (t)ide analog. A short-term response was defined as normal ALT, negative HBeAg and HBV DNA < 3.3 log IU/mL at 1 year post-treatment, and long-term response was defined as HBsAg seroclearance.
Results: In the monotherapy group (n = 19), 6 (32%) achieved the short-term response. 10 (52%) started nucleos (t)ide treatment at 2.1 ± 1.5 years posttreatment; 9 (48%) remained drug-free at 4.5 ± 2.4 years posttreatment. HBsAg decreased by 0.20 log/year during follow-up of 5.5 ± 2.4 years, and became negative in 2 (11%) patients (annual incidence, 2.0%). In the combination group (n = 31), 9 (29%) achieved the short-term response. 15 (48%) started nucleos

(t)ide treatment at 2.1 ± 1.5 years posttreatment; 16 (52%) remained drug-free at 3.5 ± 2.7 years posttreatment. HBsAg decreased by 0.10 log/year during follow-up of 5.3 ± 3.0 years, and became negative in 5 (16%) patients (annual incidence, 3.0%). Multivariate analysis showed baseline HBsAg ≤ 2.89 log IU/mL (p = 0.019; OR 16.39) and HBsAg decrease at week 24 ≥ 0.45 log (p = 0.025; OR 26.06) were independent predictors of HBsAg seroclearance.
Conclusion: Patients with low baseline HBsAg levels and high HBsAg decrease at week 24 are more likely to have the long-term HBsAg seroclearance (annual incidence, 2.0–3.0%).

[OP-0088]

Fibrotic burden in patients with hepatitis B virus-related cirrhosis is independently associated with adverse kidney outcomes

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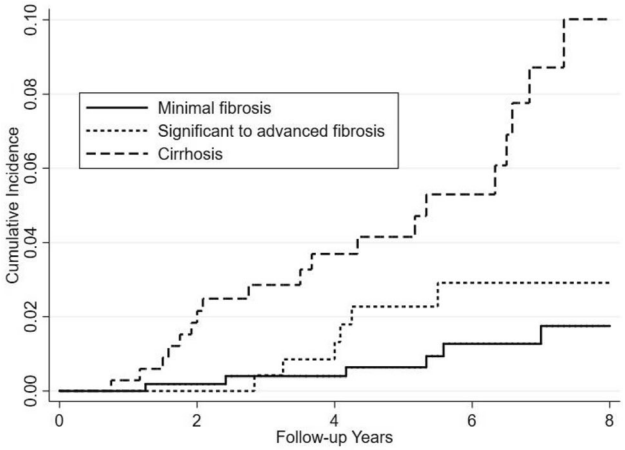
Objectives: Liver cirrhosis and chronic kidney disease (CKD) are progressive chronic conditions that share important cardiometabolic risk factors and pathogenic mechanisms. We investigated whether differences in remaining fibrotic burdens, assessed using transient elastography (TE), were independently associated with adverse kidney outcomes in patients with hepatitis B virus (HBV)-related cirrhosis.
Materials and Methods: A total of 1,204 patients with HBV-related cirrhosis but without baseline CKD who underwent TE between March 2012 and August 2018 were selected. The study outcome was the composite of development of incident CKD, defined as the occurrence of estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73m^2 or proteinuria (≥ 1 + on dipstick test) on two consecutive measurements during follow-up, 50% decline in eGFR or onset of end-stage kidney disease (initiation of chronic dialysis), or all-cause mortality.
Results: The mean age was 53.3 years and 711 (59.1%) patients were male. During 6,312 person-years of follow-up (median follow-up of 5.5 years), 32 patients (2.7%) developed adverse kidney outcomes. When stratified into TE-defined remaining fibrotic burden, multivariable Cox models revealed that risk of adverse kidney events was 4.58-fold (95% CI, 1.51–13.96, P < 0.001) higher in patients with cirrhosis (≥ 11.7 kPa), compared to patients with minimal liver fibrosis (< 7.9 kPa). These associations remained significant even after adjustment for potential confounding factors, including comorbidities of hypertension and diabetes, history of acute kidney injury, and use of potentially nephrotoxic antiviral agents.
Conclusion: Higher remaining fibrotic burden assessed using TE was independently associated with unfavorable long-term kidney outcomes in patients with HBV-related cirrhosis.



[OP-0095]

HBsAg seroclearance is associated with a lower risk of recurrence of hepatitis B virus-related hepatocellular carcinoma after surgical resection

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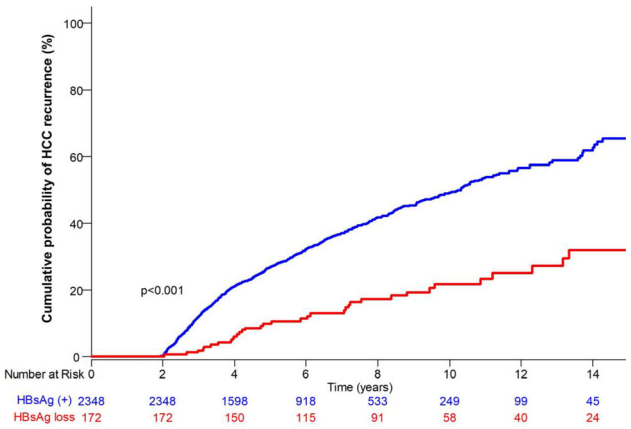
Objectives: It is unknown whether HBsAg seroclearance affects the risk of hepatocellular carcinoma (HCC) recurrence after liver resection. We aimed to investigate the impact of HBsAg seroclearance on the recurrence of HCC after curative liver resection, with a focus on late recurrence.
Materials and Methods: This study comprised 2,520 consecutive patients who received curative-intent liver resection for HBV-related HCC of Barcelona Clinic Liver Cancer stage 0 or A in Korea between 2000 and 2017. To focus on late recurrence, patients with recurrence or a follow-up duration less than 2 years were excluded. The impact of HBsAg seroclearance on HCC recurrence was assessed by landmark analysis (2-and 5-year after liver resection), time-dependent Cox, propensity score (PS) matching, and multistate modeling.
Results: The mean patient age was 54.4 years and 75.7% were men. A total of 891 (35.4%) patients developed HCC recurrence at rates of 11.2%, 25.5%, and 46.8% at 3, 5, and 10 years after resection. HBsAg seroclearance was achieved in 172 (6.8%) patients during a median follow-up of 6.9 years after resection. HBsAg seroclearance, compared with persistent HBsAg positivity, was associated with a lower risk of HCC recurrence by 2-year and 5-year landmark analysis (p < 0.001 and p = 0.02, respectively), time-dependent multivariable Cox modeling (adjusted hazard ratio [AHR], 0.62; p = 0.01) and PS matching (AHR, 0.64; p = 0.02). Based on a three-state unidirectional illness–death model, patients without HBsAg seroclearance transitioned to HCC recurrence more rapidly than patients who experienced HBsAg seroclearance.
Conclusion: Achievement of HBsAg seroclearance is associated with lower risk of HBV-related HCC recurrence after curative liver resection.



[PP-0098]

A machine learning model for predicting hepatocellular carcinoma risk in patients with chronic hepatitis B

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Objectives: Machine learning (ML) algorithms can be used to overcome the prognostic performance limitations of conventional hepatocellular carcinoma (HCC) risk models. We established and validated an ML-based HCC predictive model optimized for patients with chronic hepatitis B (CHB) infections receiving antiviral therapy (AVT).
Materials and Methods: Treatment-naïve CHB patients who were started entecavir (ETV) or tenofovir disoproxil fumarate (TDF) were enrolled. We used a training cohort (n = 960) to develop a novel ML model that predicted HCC development with 5 years, and validated the model using an independent external cohort (n = 1,937). ML algorithms consider all potential interactions and do not use predefined hypotheses. The prognostic performance of our model was compared to current models, including the modified PAGE-B (mPAGE-B) and CAMD models.
Results: The mean age of the patients in the training cohort was 48 years and males predominated. During follow-up, 69 (7.2%) patients developed HCC. Our ML-based HCC risk prediction model had an area under the receiver operating characteristic curve (AUC) of 0.930, which was better than those of the mPAGE-B (AUC = 0.773) and CAMD (AUC = 0.801) models (both $P < 0.05$). The better performance of our model was maintained (AUC = 0.946 vs. 0.663 for mPAGE-B and 0.674 for CAMD) in the validation cohort. Using cut-off probabilities of 0.3 and 0.5, the cumulative incidence of HCC development was differed significantly among the three risk groups.
Conclusion: Our new ML model performed better than models in terms of predicting the risk of HCC development in CHB patients receiving AVT.

[PP-0100]

Tenofovir alafenamide for multiple drug-resistant chronic hepatitis B: A 3-year clinical trial

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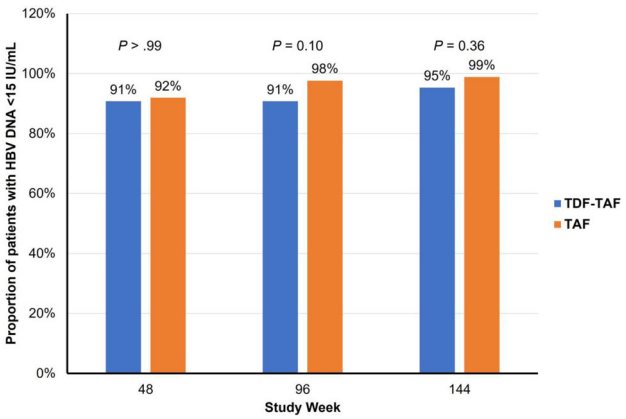
Objectives: We recently demonstrated that monotherapy with tenofovir alafenamide (TAF) for 48 weeks showed non-inferior efficacy to tenofovir disoproxil fumarate (TDF) in patients with multiple drug-resistant chronic hepatitis B (CHB). However, the long-term efficacy and safety of prolonged TAF monotherapy in these special population is to be defined.
Materials and Methods: 174 patients with hepatitis B virus (HBV) resistant to multiple drugs (lamivudine, entecavir, and/or adefovir) under TDF monotherapy for ≥ 96 weeks were randomized 1:1 to switch to TAF (n = 87) or continue TDF (n = 87) for 48 weeks. And then, 172 patients continued TAF (TAF-TAF; n = 87) or switched to TAF (TDF-TAF; n = 85), and completed the 144-week study.
Results: In the full analysis set, the proportion of patients with serum HBV DNA < 60 IU/mL at week 144 was 98.9% (86/87) in TAF-TAF group and 95.4% (85/87) in TDF-TAF group (P = 0.99). Three patients who failed to achieve virological response showed very low level of HBV DNA at week 144 (180, 86, and 149 IU/mL, respectively). No significant difference was observed from baseline in estimated glomerular filtration rate between the two groups at week 144 (0.9% vs -0.9%; P = 0.33). Compared with baseline, both TAF-TAF and TDF-TAF groups showed increase in spine bone mineral density at week 144 (3.0 vs 2.1; P = 0.21). Total, LDL, and HDL cholesterol levels increased significantly at 24 weeks after switching TDF to TAF in both groups ($P < 0.001$ for all), however, the levels did not increase further during up to 144 weeks of TAF treatment.
Conclusion: TAF monotherapy was efficacious and safe for up to 144 weeks, providing sustained virological response in heavily pretreated patients with multidrug-resistant HBV.



[OP-0103]

Global prevalence and risk factors of depression among Hepatitis B virus infection

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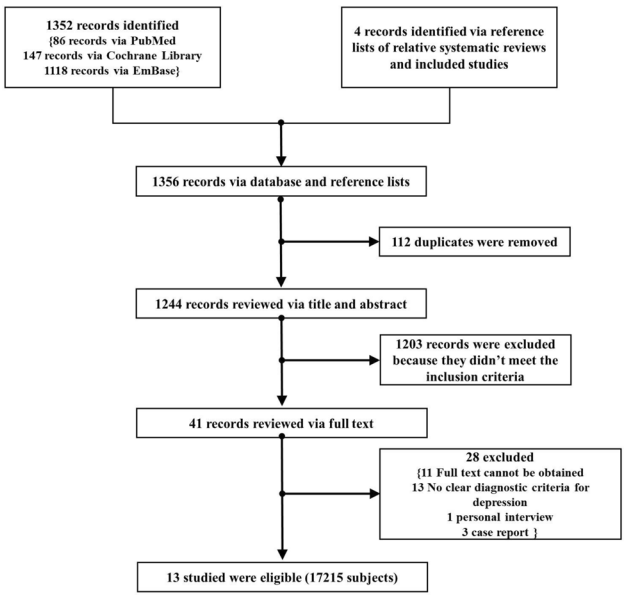
Objectives: To provide a complete screen of the prevalence and risk factors of depression in patients with HBV.
Materials and Methods: The electronic database of PubMed, Embase and Cochrane Library were searched without language and year restrictions. The research about depression of patients with chronic viral hepatitis B was included from the establishment of the database to February,11,2021. Two independent researchers screened the literatures and extract the data according to the inclusion and exclusion criteria. According to the results of heterogeneity test, STATA16.0 statistical software was applied for the random effects model data analysis.
Results: Thirteen studies were included in the analysis with a combined total of 17,215 HBV patients. The combined value of depression detection rate was 4.24%. The incidence of mild depression in CHB patients was 29.61%, and the incidence of major depression was 0.94%. The prevalence of depression in HBV carriers is 14.00%, Child–Pugh A is 25.00%, Child–Pugh B is 34.69%, Child–Pugh C is 50%. The incidence of depression in CHB patients in China is 2.98%, and that in hepatitis B patients in other countries is 37.18%. The incidence of depression was 31.05% in CHB patients whose average onset age $\leq$ 45 years old, and 2.82% in CHB patients whose average onset age $>$ 45 years old.
Conclusion: An accurate proportion of patients with hepatitis B were experiencing depressive disorders. The findings of this study may facilitated to assess method to mitigate mental health risks and to make patient-focused interventions.



[OP-0110]

Comparison of on-treatment ALT or FIB-4 as an on-treatment biomarker of hepatitis B treatment for liver cirrhosis patients

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Objectives: It is unclear whether 'normalization of ALT' can be endpoint of antiviral therapy for hepatitis B virus (HBV)-related cirrhosis patients. We tested on-treatment ALT and several other potential on-treatment biomarkers that can be clinical surrogate of antiviral therapy.
Materials and Methods: A total of 911 HBV-related liver cirrhosis patients who started entecavir or tenofovir were analyzed. We tested 'ALT normalization', 'undetectable serum HBV DNA', 'fibrosis-4 (FIB-4) index improvement', and 'serum HBeAg loss' at 1 year as a potential biomarker for HCC development.
Results: During 6.6 (3.8–10.2) years of follow-up, 222 patients newly developed HCC. Among 747 patients with elevated ALT levels, ALT normalization was observed in 49.5% at one year. HCC incidence rate was not different between those with and without ALT normalization. The risk of HCC was significantly lower in those with complete virological response (adjusted hazard ratio (HR) 0.66, 95% CI 0.50–0.87) in 911 patients. FIB-4 improvement (FIB-4 $<$ 3.25) was observed (34.1%) among 478 patients with elevated FIB-4 index (FIB-4 $\geq$ 3.25). HCC incidence rate was lower for those with FIB-4 improvement than those without, and was associated with lower risk of HCC (adjusted HR 0.59, 95% CI 0.55–0.82). HCC incidence rate was not different between those with and without HBeAg seroconversion (19.7% vs. 20.1% at 5-years, p = 0.55).
Conclusion: Among HBV-related liver cirrhosis patients who started antiviral therapy, complete virological response and improvement of FIB-4 at one-year was independently associated with future HCC risk. This indicate HBV DNA and FIB-4 index can be better on-treatment endpoints of antiviral therapy for cirrhotic patients.

TABLE Association between on-treatment biomarkers and future HCC risk

Endpoint	Number at risk	Proportion achieved endpoint at one year	Un-adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Normalization of ALT	747	370 (49.5)	1.13 (0.84-1.51)	0.39	1.21 (0.90-1.62)	0.19
Undetectable HBV DNA levels	911	667 (73.2)	0.66 (0.50-0.87)	0.004	0.66 (0.50-0.87)	0.004
Improvement of FIB-4(<3.25)	478	163 (34.1)	0.59 (0.40-0.86)	0.007	0.55 (0.38-0.82)	0.003
HBeAg loss/seroconversion	367	55 (15.0)	1.16 (0.70-1.93)	0.55	1.17 (0.70-1.94)	0.53

[PP-0116]

Sarcopenia in treatment naive chronic hepatitis B patients with liver cirrhosis

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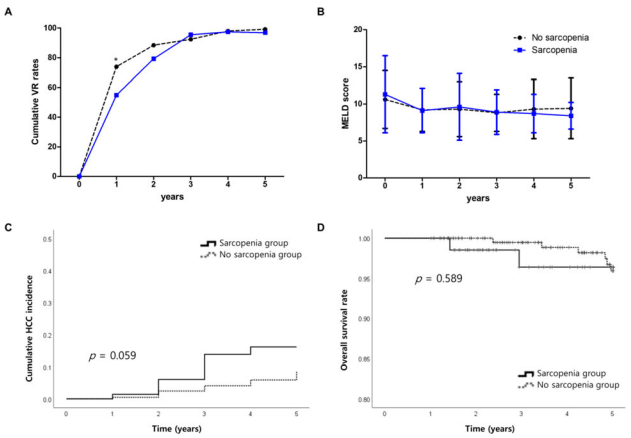
Objectives: To investigate the clinical significance of sarcopenia on treatment naïve chronic hepatitis B patients with liver cirrhosis.
Materials and Methods: We retrospectively reviewed data from treatment-naïve chronic hepatitis B patients who had started antiviral therapy from 2007 to 2018 at Jeonbuk national university hospital. Eligible patients were diagnosed with liver cirrhosis and maintained antiviral therapy for more than a year. L3 skeletal muscle index (L3SMI) was calculated by computed tomography (CT) and classified by gender quartile method. The cut-off value of sarcopenia was 46.0 cm^2/m^2 for male and 35.37 cm^2/m^2 for female.
Results: A total of 283 patients (sarcopenic group 71, non-sarcopenic group 212) was enrolled in this study. The average age of the patients was 54.5 ± 10.3 years, while the men were 181 (64.0%). The group of sarcopenia had a high alcohol drinking history and a low incidence of dyslipidemia. The mean initial HBV NDA levels and MELD scores were not different between the groups. The cumulative virological response (VR) rates were analyzed and the VR of the first year was significantly lower in the sarcopenic group. However, lower VR rate was restored by continuous administering antiviral agents. There was no difference between the initial and subsequent MELD scores, regardless of sarcopenia. We additionally compared the cumulative HCC incidence and overall survival rate using a life table method and Kaplan–Meier analysis, respectively, and there was no significant difference due to sarcopenia.
Conclusion: Sarcopenic patients with chronic hepatitis B and liver cirrhosis tend to delay VR achievement after initiating antiviral treatment. There was no difference in MELD score alteration, HCC incidence, and overall survival according to sarcopenia.



[PP-0130]

Reduction in the liver stiffness value is associated with HBeAg loss in chronic hepatitis B patients receiving antiviral therapy

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Objectives: Long term antiviral therapy with nucleoside or nucleotide analogs in chronic hepatitis B patients has been reported to improve liver fibrosis. Also it has been demonstrated that non-invasive liver stiffness measurement is associated with fibrosis stage. Therefore we analyzed the association between the liver stiffness value by Fibroscan and hepatitis B viral markers in chronic hepatitis B patients treated with oral antiviral drugs.
Materials and Methods: A total of two hundred and ninety six chronic hepatitis B patients who have received oral antiviral therapy and underwent at least two liver stiffness measurements by Fibroscan were analyzed. The differences in the liver stiffness values were compared with liver function tests and hepatitis B virus related markers.
Results: The mean age (213 men and 83 women) was 45.6 years. During the median follow-up periods of 20 months (5 – 47.7 months), the median improvement in the liver stiffness was 1.3 kPa (-34.1 – 58.9 kPa) and the median decrease in the HBV DNA was 8.73 $log10^3$ copies/ml. HBsAg loss developed in 3 patients (1.0%) and HBeAg loss in 28/296 patients (9.5%). In multivariate analysis, the decrease of 2 kPa in fibroscan was identified to be significantly associated with HBeAg loss ($p = 0.004$).
Conclusion: Liver stiffness improved with antiviral therapy in chronic hepatitis B patients and the only significant factor associated with HBeAg loss was the improvement in liver stiffness value by more than 2 kPa. Therefore it can be concluded that the measurements of liver stiffness with Fibroscan at regular intervals in chronic hepatitis B patients may be a useful tool in predicting HBeAg loss noninvasively.

[PP-0131]

Delayed serologic response in multi-drug resistant CHB patients with tenofovir and entecavir combination therapy in real practice

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Objectives: Current guidelines suggest tenofovir (TDF) based combination therapy for CHB patients with multi-drug resistance (MDR) although TDF monotherapy is recently considered as a sufficient option. We evaluated the virologic and serologic responses of MDR patients under entecavir (ETV) 1 mg and TDF combination therapy and compared the results with the treatment-naïve patients who received TDF or ETV monotherapy.
Materials and Methods: 754 patients were enrolled and 621 patients (treatment-naïve patients under either ETV 0.5 mg or TDF monotherapy n = 579, MDR n = 42) who were treated for more than 24 weeks were analyzed. Quantitative serum levels of HBsAg, HBeAg, HBV DNA were serially assessed at 4–12 week intervals.
Results: Baseline characteristics of the patients showed that there were more patients with younger age, male, lower HBV DNA levels, HBeAg-positive, and better liver function in the MDR group. 88.1% of the patients in the MDR group were HBeAg + . In the subanalysis of the HBeAg-positive patients, baseline characteristics showed that more patients in the MDR group were male, had lower HBV DNA, lower ALT levels and better liver function. There was no significant

difference in the VR between the two groups. In terms of serologic response, 27.1% vs. 20% of the patients in the naïve group and MDR group respectively achieved HBeAg loss by week 96 (P = 0.550). However no patient in the MDR group achieved HBe seroconversion while 7.2% of the patients in the naïve group achieved HBe seroconversion by week 96. There was no difference in the quantitative HBsAg and HBeAg titer reduction rates between the two groups.

Conclusion: Our results suggest that entecavir and tenofovir combination therapy in MDR patients can provide a high rate of viral suppression but with relatively slower serologic response.

[OP-0154]

Changes in blood lipids in patients with chronic hepatitis B after 48 weeks of tenofovir alafenamide treatment: A prospective real-world clinical study

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Objectives: Tenofovir alafenamide (TAF) is a new anti-hepatitis B virus nucleotide analogue. It can cause dyslipidaemia in AIDS patients, but the effect of TAF on blood lipids in patients with chronic hepatitis B (CHB) is not known. we conducted this prospective, real-world, observational clinical study to evaluate the effect of TAF on blood lipid levels in patients with CHB.

Materials and Methods: Eighty-three patients with CHB were enrolled, including 49 treatment-naïve patients who received TAF as the initial treatment and 34 patients with nucleoside/nucleotide analogue experience before TAF treatment. All patients were followed up regularly for 48 weeks. The total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels and the incidence of dyslipidaemia before and after TAF treatment were compared.

Results: After 48 weeks of TAF treatment, the TC concentration did not notably change from baseline, and the LDL-C level decreased slightly but not significantly, the TG level was significantly higher than that at baseline. The incidence of dyslipidaemia did not change significantly. The proportion of patients with TC abnormalities increased from 22.9% at baseline to 26.5% at week 48 (an increase of 3.6%), LDL-C abnormalities decreased from 50.6% at baseline to 41.0% (a change of -9.6%), and TG abnormalities increased from 12.0% at baseline to 19.3% (an increase of 7.3%). Abnormalities in TC, LDL-C, and TG occurred in eight patients, five patients, and nine patients with normal blood lipid levels at baseline, and the abnormal rates were 12.5% and 12.2% and 12.3%, respectively. While the TC, LDL-C, and TG levels returned to normal in five patients, 13 patients, and three patients with dyslipidaemia at baseline, the normalization rate were 26.3%, 31.0% and 30.0%, respectively.

Conclusion: TAF treatment mainly affects the TG level in patients with CHB but has little effect on TC or LDL-C.

Table 1 Changes in blood lipid levels after TAF treatment (mmol/L, median [IQR])

	Baseline	week 48	Change from baseline	*P*
Treatment naïve				
TC	5.14 (4.53,5.76)	5.00 (4.68,5.67)	0.14 (-0.30,0.53)	0.346
LDL-C	3.44 (2.69,3.96)	3.16 (2.77,3.99)	-0.01 (-0.49,0.41)	0.680
TG	1.05 (0.83,1.43)	1.09 (0.83,1.75)	0.11 (-0.05,0.36)	0.023
HDL-C/TC	0.26 (0.21,0.30)	0.23 (0.18,0.28)	-0.02 (-0.05,0.01)	0.009
Nas experienced				
TC	4.59 (3.99,5.14)	4.59 (4.16,5.61)	0.24 (-0.31,0.54)	0.136
LDL-C	2.90 (2.61,3.45)	3.01 (2.55,3.34)	-0.04 (-0.29,0.21)	0.614
TG	1.11 (0.77.29)	1.15 (0.90,1.85)	0.20 (-0.08,0.49)	0.012
HDL-C/TC	0.24 (0.20,0.27)	0.22 (0.19,0.26)	-0.01 (-0.04,0.02)	0.305
Total				
TC	4.80 (4.25.5.62)	4.89 (4.40,5.67)	0.23 (-0.30,0.53)	0.098
LDL-C	3.22 (2.66,3.74)	3.08 (2.60,3.62)	-0.01 (-0.30,0.30)	0.580
TG	1.06 (0.81,1.39)	1.12 (0.88,1.80)	0.13 (-0.05,0.41)	0.001
HDL-C/TC	0.25 (0.21,0.29)	0.23 (0.19,0.27)	-0.02 (-0.05,0.02)	0.005

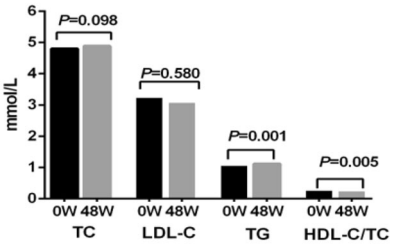

Figure 1 Changes in blood lipids of all patients before and after TAF treatment

[PP-0159]

Clinical outcomes of hepatitis B virus related hepatocellular carcinoma patients with undetectable serum HBV DNA levels

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Objectives: Some hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) patients show undetectable serum HBV DNA levels at HCC diagnosis. The risk of HBV reactivation and its impact on clinical outcomes are not well-unknown.

Materials and Methods: This retrospective cohort study included a total of 985 HBV-related HCC patients with undetectable serum HBV DNA levels (< 12 IU/mL) at HCC diagnosis (112 were antiviral treatment (AVT)-naïve; 873 were receiving AVT). Incidence and risk factors for HBV reactivation (re-detection of HBV DNA in serum) during follow-up, as well as its association to overall survival, were assessed.

Results: During a median of 33.4 months of follow-up (range: 0.2–124.2 months), HBV reactivation was observed in 279 patients. HBV reactivation rate was significantly lower for patients receiving AVT than AVT-naïve patients (three-year cumulative incidence rate: 27.3% vs. 56.0%; P < 0.001). In multivariable-adjusted analysis, the risk of HBV reactivation was lower for those receiving AVT compared to AVT-naïve patients (adjusted hazard ratio: 0.39, 95% confidence interval: 0.29–0.54). Overall survival was significantly lower for those experiencing HBV reactivation than those who did not (71.5% and 85.7% at five-year) and was associated with a higher risk of overall mortality (adjusted hazard ratio: 5.15, 95% confidence interval: 3.60–7.38).

Conclusion: More than half of AVT-naïve patients experienced HBV reactivation within three years, which was associated with an

increased risk of overall mortality. The risk of HBV reactivation was lower for those receiving AVT, suggesting that prompt AVT needs to be considered for AVT naïve HBV-related HCC patients with undetectable HBV DNA levels.

[PP-0167]

Sero-prevalence of hepatitis B virus infection in the general population of Kaski District, Nepal

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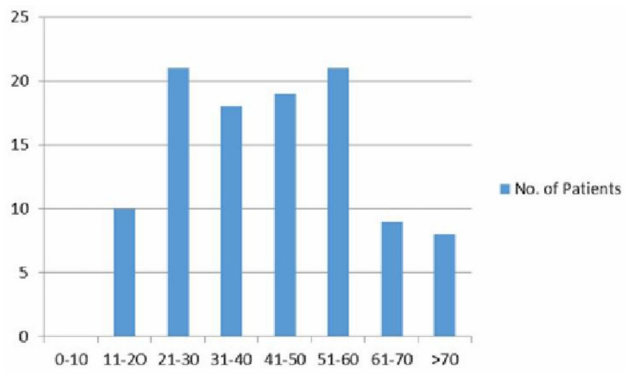
Objectives: a) General Objective: To find the distribution of hepatitis B infected patients in Kaski district of Nepal. Specific Objectives: To determine the various age groups and ethnicity of infected hepatitis B patients.
Materials and Methods: This was a cross-sectional type of study. The research was conducted in Microbiology lab. of Pokhara University,Pokhara, Nepal. 300 Samples of different age group ethnicity were taken.Among 300 samples 106 (35.3%) were positive for HBsAg. The basic criteria for this study were separated as Inclusion criteria and Exclusion criteria. The Inclusion criteria was all the age groups and all the ethinicity was taken. And, the Exclusion criteria other than kaski district people.
Results: This study was conducted at Microbiology laboratory, Pokhara University, Pokhara, Nepal. A total of 300 serum samples were collected from people, in between June 2018 to November 2019. The hepatitis B surface antigen (HBsAg) was studied from serum sample obtained from people using the diagnostic HBsAg- ELISA Kit. Written consent was taken from each patient before sample collection. The data obtained were analysed using the SPSS version-24. Out of 106 positive patients 68 (64.15%) were males and 38 (38.10%) were females. Age of the enrolled patients was from 13 to 78 years. The highly infected patients were the age group of 21–30 and 51–60. The ethnic group, Gurung was found to be predominantly infected.
Conclusion: Out of 300 samples, 106 were positive our findings explore that hepatitis B infection has been gradually increasing and has been seen predominantly among Gurung ethnicity.Implemenation of newborn and HBV- vaccination, as well as social awareness and health campaigns, are required.



[PP-0186]

Efficacy and safety of switching to tenofovir alafenamide for decompensated hepatitis B cirrhotic patients with poor response to nucleos(t)ide analogs therapy/low-level viremia

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Objectives: Tenofovir alafenamide (TAF) significantly increases complete virological response (CVR) and demonstrates good safety in patients with chronic hepatitis B and compensated liver cirrhosis. Real-world data on the efficacy and safety of switching to TAF for decompensated hepatitis B cirrhosis patients with poor response to nucleos (t)ide analogs (NAs) therapy/LLV are unclear. The purpose of this study was to investigate efficacy and safety of TAF for them.
Materials and Methods: This prospective cohort study included 56 patients with decompensated hepatitis B cirrhosis who switched to TAF monotherapy due to poor response to NAs therapy/LLV for at least 6 months. These patients were followed up every 12 weeks.
Results: The rate of CVR at 48 weeks for them who switched to TAF was significantly higher than that at 12 weeks (80.00% vs 32.14%, $P < 0.05$). According to the baseline HBV DNA level, the patients were divided into LLV group (HBV DNA < 2000 IU/mL) and poor response group (HBV DNA ≥ 2000 IU/mL). Subgroup analysis showed that LLV group achieved higher CVR rate at 12 weeks, which was 61.54% compared with that of 6.67% in the other group. Additionally, mean changes of the HBsAg and HBV DNA level at 48 weeks were -0.44 and -3.38 logIU/mL, respectively ($P < 0.05$). The rate of ALT normalization at 48 weeks was 95.00%, which was significantly higher than the baseline which was 66.07% ($P < 0.05$). The mean Child–Pugh score and the proportion of Child A at 48 weeks was 5.45 ± 0.76 and 85%, which were significantly improved than 8.66 ± 2.30 and 21.43% at the baseline, respectively ($P < 0.05$). During the 48 weeks treatment period, there were no remarkable changes in serum creatinine, phosphorus, eGFR. The median urinary β2-microglobulin at 24 weeks was 0.98, compared to 1.14 at the baseline ($P > 0.05$).
Conclusion: Switching to TAF monotherapy for patients with decompensated hepatitis B cirrhosis, is effective regarding both CVR and the liver function benefits. TAF has good renal safety for them.

[PP-0236]

Reactivation of hepatitis B in patient with COVID-19

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Objectives: Reactivation of hepatitis B is defined as dramatic increase in hepatitis B virus (HBV) replication in a patient with inactive or resolved hepatitis B. Reactivation can occur spontaneously but typically is triggered by immunosuppressive therapy or discontinuation of antiviral treatment. Some cases with COVID-19 progress into severe or critical disease requiring immunosuppressive therapy.

Materials and Methods: We report the case of hepatitis B virus reactivation in a young adult with COVID-19.
Results: 40-year-old male presented on day 7 of disease with sustaining fever and weakness. Chest CT scan revealed ground glass opacity. Nasopharyngeal mucus sample showed positive for SARS-Cov-2 PCR. Oxygen saturation (SpO2) was over 93% on room air. 10 years ago patient was diagnosed with HBV infection HBeAg + and high viral concentration, thus tenofovir was initiated. After 3 year of AVT seroconversion of HBeAg was achieved, after 5 years of AVT HBV PCR was negative. As treatment for COVID-19 high doses of methylprednisolone was administered and titrated during a month. Patient refused AVT, and it was terminated. COVID-19 resolved but after 2 months blood analysis revealed following: ALT‘ 357 U/L, AST‘ 147 U/L, GGT‘ 110U/l, ALP‘ 67 U/L, PCR HBsAg‘ 11.000 U/L, HBeAg‘ positive, PCR HBV‘ positive. HBV reactivation was diagnosed and ATV was restarted. After 1 week of ATV HBsAg lowered to 9000, HBeAg became negative, ALT- 1400 U/L, AST- 375 U/L, GGT- 191U/L, ALP- 164U/L. 1 month later HBsAg was 76 U/L, HBeAg- negative and ALT- 90 U/L, AST- 46 U/L, GGT- 116 U/L, ALP- 72 U/L. After 2 months HBsAg became negative, without AntiHBsAg, ATV was continued.
Conclusion: This case is a vivid example of the association of HBV reactivation and immunosuppressive treatment with discontinuation of AVT during COVID-19 and illustrates the importance of AVT maintenance and careful consideration of high doses of steroids in patients with HBV infection.

[OP-0241]

Effect of nucleotide analogue on HBeAg-positive chronic hepatitis B patients with normal ALT and high HBV DNA level

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Objectives: To investigate the effect of nucleotide analogues on HBeAg-positive chronic hepatitis B patients with normal ALT and high HBV DNA level.
Materials and Methods: The naïve chronic hepatitis B patients who were treated and followed up in the infectious disease center of West China Hospital of Sichuan University from January 2019 to January 2020 were selected. The demographic characteristics, laboratory examination results before treatment and one year after treatment of the patients were retrospectively collected. The patients were divided into TDF group and TAF group according to the type of medication. The changes of serum HBVDNA level, HBeAg seroconversion and HBsAg quantitative level were analyzed and compared between two groups.
Results: A total of 38 patients were enrolled, including 16 patients in TDF group and 22 patients in TAF group. After one year of antiviral treatment, 60.5% (23/38)of the patients achieved virological response. Higher undetectable rate of serum HBV DNA was achieved in the TAF group than in the TDF group [68.2% (15/22) vs. 50.0% (8/16), $p = 0.258$] and similar result was also observed in HBeAg seroconversion [18.2% (4/22) vs. 6.3% (1/16), $p = 0.374$], but these differences were not statistically significant. In addition, the incidence of ALT elevation in the TAF group was lower than that in the TDF group. Multivariate logistic regression analysis showed that age was an independent predictor of virological response to antiviral therapy.
Conclusion: HBeAg-positive CHB patients with persistent normal ALT and high HBVDNA level can get better curative effect from TDF and TAF treatment.

[OP-0243]

Dynamics of serum pregenome RNA in chronic hepatitis B patients receiving 96-month nucleos(t)ide analogue therapy

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Objectives: Tissue covalently closed circular DNA (cccDNA) can reflect the activity of HBV replication. However, it is impractical to assess intrahepatic cccDNA in every outpatient. Serum pregenome RNA (pgRNA) is transcribed from intrahepatic cccDNA and may reflect the activity of intrahepatic cccDNA. The aim of the study was to explore whether serum pgRNA is a strong biomarker to monitor the antiviral efficacy in patients receiving long-term NAs treatment.
Materials and Methods: Serum pgRNA, HBV DNA, HBsAg, HBeAg and ALT levels were quantified, and the relationships between serum pgRNA and these common clinical indicators before and after the treatment were investigated.
Results: Serum pgRNA showed dynamic change during the 96-month NAs therapy, and serum pgRNA levels were positive and detectable in 19 patients with undetectable serum HBV DNA. Serum pgRNA showed strong and positive correlation with serum HBV DNA ($r = 0.693$, $p < 0.001$) and serum HBsAg levels ($r = 0.621$, $p < 0.001$) at baseline. Patients with HBeAg seroconversion had lower baseline serum pgRNA levels ($p = 0.002$). The area under the curve (AUC) of baseline serum pgRNA for predicting HBeAg seroconversion was 0.742 (95% CI: 0.606–0.850) with 63.16% sensitivity and 80.56% specificity. The cumulative HBeAg seroconversion rate was higher in patients with low serum pgRNA ($p = 0.001$).
Conclusion: Serum pgRNA of low level at baseline or great decline at month 6 may independently predict the high incidence of undetectable serum pgRNA at year 4 following NAs therapy, and the baseline serum pgRNA may serve as a novel predictor for HBeAg seroconversion during NAs therapy.

[OP-0247]

Efficacy of a combination of HBV RNA and HBsAg in predicting HBsAg seroconversion in children with chronic hepatitis B

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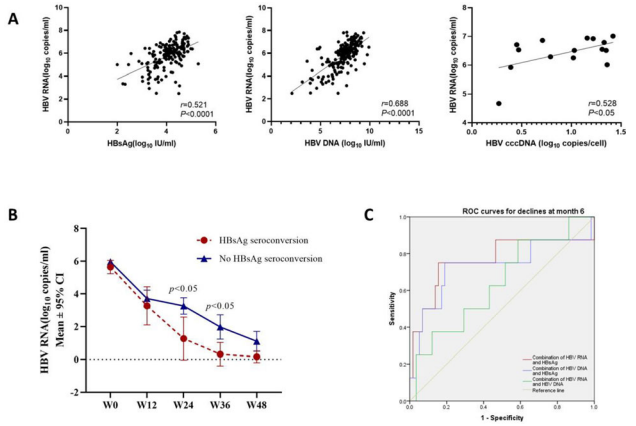
Objectives: To explore the role of HBV RNA predict HBsAg seroconversion in children with chronic hepatitis B (CHB) treated with interferon alfa (IFN).

Materials and Methods: 198 children with CHB received 48 weeks IFN monotherapy or IFN combination with lamivudine was studied. The primary end point was HBsAg seroconversion at week 48 after IFN discontinuation. Ability of biomarkers to predict HBsAg seroconversion at treatment week 24 was evaluated using receiver operating characteristics (ROC) analyses. HBV RNA levels were measured using real-time fluorescence quantitative PCR. Intrahepatic cccDNA was detected using rolling ring expansion add cross gap real-time fluorescence quantitative PCR. The dynamic changes of HBV RNA and the correlation of HBV RNA with other HBV markers were investigated.
Results: HBV RNA was positively correlated with HBV DNA, HBsAg and HBV cccDNA. The HBV RNA levels decreased more rapidly in patients with HBsAg seroconversion than those without HBsAg seroconversion. The area under the receiver operating characteristic (AUROC) of HBV RNA decreased levels compared to HBV DNA and HBsAg at week 24 was 0.634 vs 0.608 vs0.732, respectively. The AUROC of HBV RNA and HBsAg decreased levels combination was significantly higher than that of HBV RNA and HBV DNA as well as HBsAg plus HBV DNA decreased levels combination (0.767 vs 0.640 vs 0.731). HBV RNA decreased levels above 2.42 $\log_{10}$ copies/ml and HBsAg decreased levels above 2.14 $\log_{10}$ copies/ml at treatment week 24 showed the positive predictive value (PPV) and negative predictive value (NPV) for HBsAg loss were 63.6% and 97.1%, respectively, with a sensitivity of 75% and specificity of 84.5%.
Conclusion: The level of HBV RNA decreased levels at treatment week 24 was a powerful predictor of HBsAg seroconversion in children with CHB, while the combination of HBV RNA and HBsAg decreased levels was superior to HBV RNA and HBsAg alone in predicting HBsAg seroconversion.



[OP-0248]

Hepatitis B virus basal core promoter/precore mutants inhabit the HBsAg seroclearance in children with chronic hepatitis B

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Objectives: To investigate the impact of HBV basal core promoter (BCP) and precore (PC) mutants on HBsAg seroclearance in children with chronic hepatitis B (CHB).

Materials and Methods: A total of 140 HBeAg-positive children aged 2–17 with CHB treated by IFN alone or IFN combinated with lamivudine for 82.62 ± 65.97 weeks was studied. Serum levels of HBV RNA, HBV DNA, and HBsAg were measured according to routine laboratory methods, HBV PC/BCP mutants was measured by HBV DNA sequencing experiment.
Results: 37.1% (52/140) of patients exhibited HBsAg seroclearance after IFN discontinuation, 62.9% (88/140) of patients without HBsAg loss. Patients with HBsAg seroclearance showed a significantly lower HBV PC/BCP mutant rate in comparison to those without HBsAg seroclearance ($p < 0.05$). In the non HBsAg seroclearance group, 71.6% (63/88) of the patients had HBV mutations, of which 50.0% (44/88) was HBV BCP + /PC- mutations, 12.5% (11/88) was BCP-/PC + mutations, and 9.1% (8/88) was BCP + /PC + mutations, these mutations were associated with the absence of HBsAg loss during IFN therapy. Patients with WT had higher HBsAg seroclearance rate than patients with non-WT patients. The baseline HBV DNA level in HBsAg seroclearance group was higher than that non HBsAg seroclearance group, the difference was statistically significant ($p = 0.029$), but there was no significant difference in baseline HBsAg levels between two groups.
Conclusion: Patients with HBV PC and/or BCP mutants have a lower HBsAg seroclearance rate and should be less optimal candidates for IFN therapy in children with CHB.

[OP-0259]

Tenofovir alafenamide for treatment-nave and nucleos(t)ide-experienced patients with hepatitis B virus infection-interim analysis of a real-world study (TRUE)

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Objectives: Tenofovir alafenamide (TAF) has been approved for the treatment of chronic hepatitis B (CHB). We aimed to assess the effectiveness and safety of TAF-based therapy in treatment naïve (TN) or experienced (TE) CHB patients.
Materials and Methods: This multicenter, prospective, real-word study included 500 CHB patients treated with TAF monotherapy or combining with entecavir (ETV) for 144 weeks. Virological and biochemical responses and safety were evaluated (clinicaltrial.gov: NCT03752658).
Results: 320 patients (TN, 102; TE, 218) with available data were included in this interim analysis. 16.3% had cirrhosis, and 64.0% were HBeAg positive at baseline. All TN patients and 134 TE patients received TAF alone, and 84 TE patients received TAF plus ETV. Of TN patients, 61.1% and 79.7% achieved virological response (HBV DNA < 20 IU/mL) at week 24 and 48, respectively. 68.1% and 78.9% achieved biochemical response (ALT < 40U/L) at week 24

and 48, respectively. Among TE patients switching to TAF, virological response rate was significantly increased, from 73.9% at baseline to 85.9% at week 24 and 88.5% at week 48 ($P < 0.01$). Biochemical response rate was 81.9% at baseline 77.7% at week 24, and 83.7% at week 48. Of TE patients receiving TAF + ETV, virological response rate was significantly increased from 39.3% at baseline to 81.5% at week 24, and 80.0% at week 48 ($P < 0.001$). Biochemical response rate was significantly increased from 79.5% at baseline to 90.9% at week 24, and 92.3% at week 48 ($P < 0.05$). Of patients with estimated glomerular filtration rate (eGFR) below 90 mL/min/1.73m^2 at baseline, eGFR was significantly improved ($P < 0.01$), and creatinine level tended to decrease ($P = 0.07$) at week 48. TAF-based therapy was well-tolerated.
Conclusion: TAF-based therapy was effective for HBV suppression and ALT normalization in both TN and TE CHB patients. The renal glomerular function was improved after 48-week treatment in patients with prior impaired renal function.

[PP-0273]

Family history and the risk of hepatocellular carcinoma in immune tolerant chronic hepatitis B patients

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Objectives: The definition and long-term prognosis of immune tolerant (IT) phase patients remain unclear. We investigated IT-to-immune active (IA) phase transitions and assessed the cumulative incidence rate and risk factors of hepatocellular carcinoma (HCC) in IT patients and antiviral-treated immune active HBeAg-positive (AVT-IA) patients.
Materials and Methods: We recruited 1,064 (IT, 516; AVT-IA, 548) patients. IT group inclusion criteria were HBeAg-positive, HBV DNA $> 10^6$ IU/mL, no cirrhosis, and alanine aminotransferase (ALT) < 80 U/L. AVT-IA differed from IT only in ALT > 80 U/L and leading to AVT. Prognostic variables for HCC and phase transition were used to develop new criteria for IT patients.
Results: Fifteen patients (seven IT patients, eight AVT-IA patients) developed HCC during a median of 7.3 years follow-up. Cumulative HCC incidences in the IT group were lower than the AVT-IA group (5-year, 0.3% vs 0.9%; 10-year, 1.7% vs 2.7%, respectively). Family history of HCC was the only independent predictor for IT patients developing HCC ($p = 0.036$). Cumulative 5-, 10-, and 15-year IT-to-IA transition rates were 37.6%, 68.7%, and 87.0%, respectively. Female patients aged < 35 years, ALT < 25 U/L, HBV DNA > 8 log IU/mL, and no family HCC history were predictive of favourable long-term outcome of IT phase. Patients meeting these criteria had the lowest risk of IT-to-IA transition ($\sim 50\%$) and/or HCC development (0%) at 10 years.
Conclusion: Most IT patients underwent IT-to-IA transition but showed very low cumulative HCC rates. Family HCC history was the only independent risk factor for HCC in IT patients. A strict combination of young, female, no family HCC history, high HBV DNA, and low ALT identified true progression-free IT patients.

[OP-0276]

Safety and efficacy of 2 mg Bulevirtide in patients with chronic HBV/HDV Co-Infection. First real-world results (French Early Access Program)

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Objectives: Bulevirtide (BLV) is a first-in-class entry inhibitor to treat HBV/HDV co-infected patients. BLV monotherapy as well as combination with PEG-interferon α 2a (PEG-IFNα) for 48 weeks induced serum and intrahepatic HDV RNA declines in two phase 2 trials (MYR202/203). The aim of this study was to evaluate 12-month results of the French early access program on HBV/HDV patients receiving 2 mg BLV with or without PEG-IFNa 2a (real-life study).
Materials and Methods: 152 patients with chronic HBV/HDV co-infection, with cirrhosis or moderate fibrosis and elevated ALT levels, without liver decompensation, were included. Patients received 2 mg BLV q.d./day s.c. alone in combination with PEG-IFNα once weekly for 12 months, according to physician's choice. Seven patients with undetectable HDV-RNA at inclusion were excluded from this per-protocol analysis.
Results: Characteristics of the 145 patients were: 99 (68.3%) males, 41 years, cirrhosis N = 91/108 (62.8%), median viral load of 6.2 $\log_{10}$IU/ml. Safety: BLV was well tolerated during 12 months. Mild side-effects were headache, asthenia. Severe side effects were: ascites, HCC, rectal cancer, ovarian cancer, variceal bleeding, asthenia, neutropenia. Twelve patients receiving BLV + PEG-IFN were excluded from the per-protocol analysis because they stopped PEG-IFN before month 12. In the BLV and in the BLV + PEG-IFN groups, 7 and 14 patients stopped early BLV, respectively. Efficacy: Main results are indicated in Table. At month 12, in the BLV

monotherapy and in the BLV + PEG-IFN group, the median decrease of HDV-RNA was -3,64 et -5,56 log10IU/ml, respectively. Moreover, at month 12, HDV-RNA was undetectable in 39% and 85% of patients treated with BLV monotherapy and BLV + PEG-IFN group, respectively.

Conclusion: In this first real-world cohort, daily BLV 2 mg monotherapy is safe and well tolerated during 12 months. Strong antiviral responses against HDV in real-life confirmed previous trial results. Final results (month 12) will be presented during the meeting.

Month	Mean HDV viral load (log_{10} IU/ml)		HDV-RNA decrease > 2 log_{10} or undetectable and normal ALT level (< 40 IU/L)	
	BLV (N=77)	BLV + PEG-IFN (N=56)	BLV (N=77)	BLV + PEG-IFN (N=56)
Day 0	6.26	6.21	NA	NA
M1	5.85	4.96	1/73	0/53
M3	4.78	2.97	11/73 (15.1%)	10/51 (19.6%)
M6	3.76	1.66	15/65 (23.1%)	15/46 (32.6%)
M9	3.25	1.12	19/50 (38%)	15/38 (39.5%)
M12	2.62	0.65	16/41 (39%)	10/33 (30.3%)

[OP-0291]

A more comprehensive multistate approach for evaluating outcomes of HBV-related compensated cirrhotic patients on antiviral therapy

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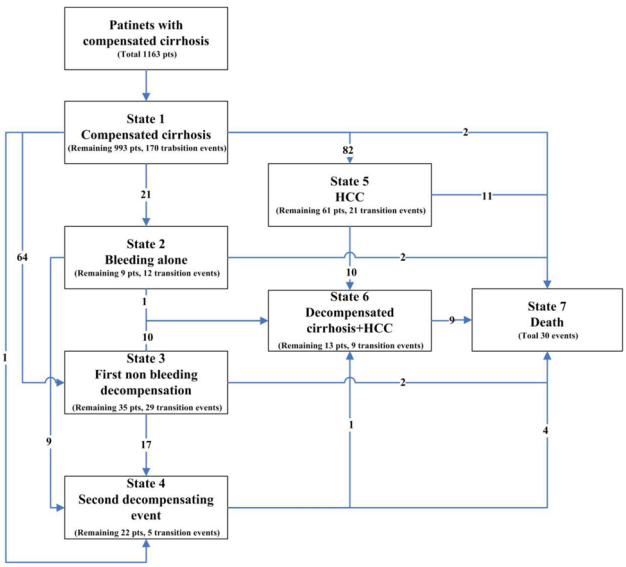
Objectives: We proposed a more comprehensive clinical endpoint system for evaluating the natural history of a large cohort of treated HBV cirrhosis and to describe the patients who are still at risk for decompensate and/or HCC.

Materials and Methods: The current study was based the prospective cohorts of CHB patients with compensated cirrhotic (CC) enrolled from March 2012 to October 2015 in two clinical studies (ClincialTrials.gov number NCT01943617, NCT01720238, NCT03366571, NCT02849132). The transition of individuals through a series of distinct states was describe with the multistate model, and the state transition probability (STP) and state occupation probabilities (SOP) were calculated.

Results: 1. Totally 246 transition events occurred in 170 of the 1,163 (14.6%) CHB patients with CC, resulting in an overall disease progression probability of 19.72% during the 7-year treatment time. The hierarchical sequence of first clinical events occurring in those patients were HCC (10.18%), nonbleeding decompensation (7.52%), bleeding (2.23%), death (0.18%), and second decompensation (0.09%). 2. HCC development accounted for 50% of all liver-related events in NA-treated CHB patients with CC; moreover, a significantly higher cumulative incidence of HCC occurred in DC stage. 3. The STP from compensated cirrhosis to decompensated cirrhosis (any decompensating state) was similar to the transition probability to HCC. Furthermore, we found a higher transition probability from CC to nonbleeding decompensation state than to bleeding state. Bleeding had a higher probability of developing second decompensation; in contrast, nonbleeding decompensation had a higher transition probability to HCC. 4. SOP analysis showed that over 80% CHB patients with CC could stay at CC state during 7-year treatment time. 5. By using multivariate transition-specific Cox model, we identified several predictive factors with different impact on the transitions from CC.

Conclusion: Overall, treated CHB patients still decompensate and/or develop HCC. Our multistate approach could portray the panorama of the clinical course of CHB-related CC.



[OP-0293]

Situation and factors related to hepatitis B virus infection among patients in Cam Khe 103 Clinic

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Objectives: Hepatitis B infection is among the most common public health concerns globally, particularly in poor countries. Aims: To describe the situation and factors related to hepatitis B virus infection among patients in Cam Khe 103 Clinic.

Materials and Methods: Cross-sectional study design. The study included patients aged 18 years and older in Cam Khe 103 Clinic from May 2018 to April 2020. We analyzed the data to examine factors associated with hepatitis B virus infection using binary and multivariable logistic regression models.

Results: The overall prevalence of hepatitis B virus (HBV) infection among the study participants was 12.6%. The majority (47.9%) of the study participants infected by hepatitis B were in the age group 40–49 years. Males had higher rate of HBV infection than females (OR = 1.29, 95%CI = 1.03–1.71). Farmers had higher rate of HBV infection than the others (OR = 1.45; 95%CI = 1.05–2.05). Those who have relatives living with liver disease had higher rate of HBV infection than the others (OR = 2.11; 95%CI = 1.41–3.17). Those who experienced the kidney dialysis had higher rate of HBV infection than ones who did not experience this procedure (OR = 3.70; 95%CI = 1.09–13.21). Having history of abortion (OR = 0.13; 95%

CI: 0.04–0.48) and having history of tattooing [OR = 0.20; 95%CI: 0.07–0.63) were found to be statistically significantly associated with the prevalence of hepatitis B virus infection among patients. The vaccinated group had a lower rate of HBV infection than the unvaccinated group (OR = 0.43; 95%CI = 0.36–0.65). Those who had good knowledge and good behaviors had lower rates of HBV infection than the ones with poor knowledge (OR = 0.70; 95%CI = 0.51–0.96) and poor behaviors (OR = 0.33; 95%CI = 0.18–0.49).
Conclusion: Some factors increased the risk of HBV infection, such as: gender; occupation; relatives living with liver diseases, kidney dialysis experience; having history of abortion; having history of tattooing. Some factors reduced the risk of HBV infection, such as: hepatitis B vaccination; knowledge and behaviors.

[OP-0306]

Comparison of antiviral efficacy of different ALT levels in patients with HBeAg positive chronic hepatitis B during 336 weeks follow-up

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Objectives: To evaluate the differences in antiviral outcomes between different alanine aminotransferase (ALT) levels in patients with HBeAg-positive chronic hepatitis B (CHB).
Materials and Methods: Retrospective studies were adopted to compare the antiviral outcomes of HBeAg-positive CHB patients with normal ALT levels, mildly elevated (1 $\sim$ 2 upper limit of normal (ULN)) ALT and moderately elevated ($\geq$ 2 ULN) ALT levels; the appropriateness of antiviral treatment was confirmed by liver biopsy.
Results: In total, 145 patients were recruited to the study and followed up 336 weeks. The patients with normal ALT had significant necroinflammation ($\geq$ G2) (84.2%, 32/38) and fibrosis ($\geq$ S2) (68.4%, 26/38). 28.9% (11/38) of patients in the normal ALT group were in the stage 4 fibrosis. The virological response rate in the normal ALT group at 24 weeks was lower than those in the elevated ALT groups (26.3% versus 30.9% versus 36.9%, respectively, P = 0.022); however, up to 336 weeks, there were no significant differences among the groups. The serological negativity rate of HBeAg increased as time passed, but there was no significant difference in the rates among the groups.
Conclusion: For patients with HBeAg-positive chronic hepatitis B infection, even if ALT level is normal, we recommend initiating antivirus therapy and it may achieve a better viral response rate in the first 24 weeks.

[PP-0331]

Total antioxidant activity as biomarker on liver fibrosis in HBV patients: A pilot study

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Objectives: In hepatitis B virus (HBV) carriers, oxidative stress is a major cuase contributing heaptic fibrosis. Although many studies have reported that oxidative stress can mediate hepatic fibrosis, it is still unclear whether hepatic fibrosis/cirrhosis can be evaluated using serum redox biomarkers in HBV carriers.
Materials and Methods: We invastigated hepatofibrotic severity (5.5 $\leq$ liver stiffness measurement (LSM) score $\leq$ 16.0 kPa) and oxidative/antioxidative capacity (total eight kinds) in fifty-four HBV carriers, and analyzed mild to moderate/severe levels of hepatic fibrosis in accordance with oxidative/antioxidative levels.
Results: Serum total anti-oxidant (TAC, 73.91%) and the aspartate transaminase platelet ratio index (APRI, 56.52%) correlated with the LSM scores in HBV carriers. In two groups (LSM $\leq$ 8.5 kPa versus 8.5 kPa $<$ LSM), TAC was dominantly decrased in 8.5 kPa $<$ LSM group compared to LSM $\leq$ 8.5 kPa group. While APRI was increased in 8.5 kPa $<$ LSM group compared to LSM $\leq$ 8.5 kPa group. Superoxide dismutase (SOD), catalase, glutathione (GSH) glutathione peroxidase (GPx) and glutathione reductase (GRd) in serum showed tendency of reduction in the LSM $>$ 8.5 kPa group, while reactive oxigen species (ROS) and malondialdehyde (MDA) - did not reveal any change.
Conclusion: TAC might become a valuable indicator of the progression of liver fibrosis in HBV carriers, at least in males. As a simple alternative predictor, TAC can assist us to evaluate the extent of liver fibrosis in patients with chronic HBV, along with LSM and biopsies.

[OP-0335]

Effect of liver steatosis on liver stiffness measurement in chronic hepatitis B patients with normal serum alanine aminotransferase levels: A multicenter cohort study

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Objectives: Liver steatosis is becoming increasingly common in patients with chronic hepatitis B (CHB), and its effect on liver stiffness measurement (LSM), as assessed by transient elastography, remains controversial. We examined whether the histological degree of liver steatosis affects the accuracy of transient elastography-assessed LSM in these patients.
Materials and Methods: Seven hundred and fifty-five patients with CHB and normal serum alanine aminotransferase levels, who underwent vibration-controlled transient elastography and liver biopsy, were included in the study.

Results: Among the 755 CHB patients included in the study, 286 (37.9%) had liver steatosis, of whom 156 had grade S1, 74 had grade S2, and 56 had grade S3 on histology. Presence of liver steatosis was independently associated with greater body mass index (BMI, adjusted-odds ratio [OR] = 5.786, 95%CI: 3.998–8.373, P = 0.018), and higher serum total cholesterol (adjusted-OR = 7.944, 95%CI: 4.731–13.339, $P < 0.001$) and triglyceride levels (adjusted-OR = 2.777, 95%CI: 2.050–3.761, $P < 0.001$). There was no significant association between liver steatosis and fibrosis stage (OR = 1.016, 95%CI: 0.905–1.140, P = 0.790). Age (B-coefficient = 0.020, 95%CI: 0.001–0.040, P = 0.044), BMI (B-coefficient = 0.060, 95%CI: 0.011–0.127, P = 0.019), serum gamma-glutamyl-transpeptidase (GGT, B-coefficient = 0.015, 95%CI: 0.001–0.029, P = 0.032), positivity for HBeAg (B-coefficient = -0.816, 95%CI:—1.568 ~ -0.064, P = 0.034), as well as liver fibrosis stage (B-coefficient = 2.796, 95%CI: 2.501–3.090, $P < 0.001$), and inflammation activity grade (B-coefficient = 0.648, 95%CI: 0.162–1.135, P = 0.009) were all independently associated with higher LSM, while no significant association was found between degree of liver steatosis and LSM. Among patients with the same histologic fibrosis stage, LSM values did not show any significant difference among patients with absent, mild, moderate, or severe steatosis.
Conclusion: Liver steatosis has no significant effect on transient elastography-measured LSM in CHB patients with normal serum alanine aminotransferase levels.

[PP-0340]

Exploring the patient voice in hepatitis B care, education, and cure research

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Objectives: As patient input into drug development increases in importance, the Food and Drug Administration has provided guidance on various methods of patient engagement to ensure incorporation of the patient voice into drug development. One strategy is hosting patient focused drug development (PFDD) meetings. In June 2020, the Hepatitis B Foundation (HBF) led a PFDD meeting, "The Voice of the Patient: Living with Chronic Hepatitis B" and identified gaps in our knowledge and understanding of patient needs. In order to ensure drug development plans take patient needs into account, we hosted a hepatitis B virus (HBV) virtual meeting with patients. The objective was to obtain feedback on patient care, education, and drug development for HBV cure.
Materials and Methods: In partnership with the HBF, we developed a patient advisory program to gain understanding of patient perspectives related to hepatocellular carcinoma risk associated with HBV, educational needs, preferences for a cure regimen, clinical trial participation, and patient reported outcomes. HBF co-developed the content, facilitated recruitment of participants, and co-moderated the meeting. The two-day meeting took place virtually where the team gave short presentations on the selected topics followed by discussion to elicit feedback from the participants.
Results: Seven participants represented diverse geographies and demographics across the U.S. Table 1 presents key insights and tactical strategies to address. Patient engagement best practice principles were utilized throughout the process. This initial advisory provides a roadmap for future meetings across the globe that may provide a diverse view of patient perspectives. Lastly, this meeting has served as a basis to broaden and prioritize patient advocacy throughout the company.
Conclusion: Patient engagement will require ongoing collaboration with advocacy organizations and patients. It is imperative that patients are engaged early and often throughout the drug development process. Patients provide valuable input on drug development strategies that can benefit the field at large.

Table 1. Key Takeaways

Topic	Select Feedback from Participants	Opportunities for Patient Engagement
Chronic Hepatitis B and Liver Cancer	Broader community not aware of HCC risk reduction with antiviral treatment.	Increase liver cancer awareness through educational programs in partnership with advocacy groups.
Unmet Educational Needs	Educational resources should minimize confusion, be transparent, accessible to all patients, and available in different languages.	Create patient-oriented resources for patients and peer to peer education.
Clinical Trial Participation	Factors that may affect clinical trial participation include safety, out of pocket costs, travel required, and time away from home.	Simplify clinical trial participation and make it easier for patients.
Preferences for a Cure Regimen	The most important features include affordability, cure rate, safety, and impact on quality of life.	Use patient insights to further develop meaningful and preferred HBV cure specific regimens and patient focused outcomes.

[PP-0341]

A risk scoring system to predict clinical events in chronic hepatitis B virus infection: A nationwide cohort study

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Objectives: Many patients with chronic hepatitis B do not receive adequate follow-up. This study aimed to develop a risk score to predict clinical events in patients with chronic hepatitis B virus (HBV) infection at the population level for identifying patients at high-risk to warrant regular follow-up.
Materials and Methods: This study analyzed population-based data from the nationwide claims database of South Korea obtained between 2005 and 2015. We identified 507,239 non-cirrhotic patients with chronic HBV infection who are not under antiviral treatment. A risk score for predicting clinical events (hepatocellular carcinoma, death, or liver transplantation) was developed based on multivariable Cox proportional hazard model in a development cohort (n = 401,745) and validated in a validation cohort (n = 105,494).
Results: The cumulative incidence rates of clinical events at 5 years were 2.56% and 2.44% in the development and validation cohorts, respectively. Clinical events in Asymptomatic Patients with chronic HBV infection (CAP-B) score ranging from 0 to 7.5 points based on age, sex, socioeconomic status, chronic hepatitis C co-infection, diabetes mellitus, statin or antiplatelet exposure, smoking, alcohol consumption, alanine aminotransferase, and gamma-glutamyltransferase had good discriminatory accuracy in both the development and

validation cohorts (c-indices for 3-, 5-, 10-year risk prediction: all 0.786). The predicted and observed probabilities of clinical events were calibrated in both cohorts. A score of > 3.5 points identified subjects at distinctly high risk.
Conclusion: The CAP-B score using easily accessible variables can predict clinical events and may allow selection of patients with chronic HBV infection for priority of regular follow-up.

[PP-0351]

Plasma bile acid profiles are associated with the presence of fibrosis in patients with concomitant nonalcoholic fatty liver diseases and chronic hepatitis B infection

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Objectives: The concomitance of nonalcoholic fatty liver disease (NAFLD) and chronic hepatitis B (CHB) is more common nowadays and more studies are warranted. Bile acids (BA) are known mediators of hepatic inflammation, with their altered metabolism implicated in both diseases. This study investigated the relationship between BA profiles and liver fibrosis, one of the most important predictors of mortality and liver?related events, in both chronic liver diseases.
Materials and Methods: We prospectively recruited CHB patients with concomitant NAFLD. Liver steatosis and stiffness were assessed by vibration-controlled transient elastography (Fibroscan, Echosens, Paris). Steatosis and severe steatosis were defined as controlled attenuation parameter $\geq$ 248 dB/m & $\geq$ 280 dB/m respectively, while advanced fibrosis was defined as $\geq$ 9 kPa in patients with normal alanine aminotransferase. Bile acid profiles including 28 different BAs were quantified by liquid chromatography-tandem mass spectrometry.
Results: Among 61 patients (68.9% male, median age 61.6 years), 48 (78.7%) were treated with nucleoside analogues for a median duration of 72 (54–115) months. 61 (100%) and 34 (55.8%) had steatosis and advanced fibrosis respectively. Increasing total serum BA and the proportion of primary conjugated BA were associated with a significantly increased risk of significant fibrosis (LSM $\geq$ 9 kPa) in a multivariable-adjusted model for age, sex, presence of obesity and type-2-diabetes (Odd ratio: 1.319 [1.038–1.793], P = 0.049 and OR: 1.038 [1.005–1.077], P = 0.034 respectively). Conversely, increasing proportion of total unconjugated BA and proportion of secondary unconjugated BA were associated with a decreased risk of significant fibrosis after adjusted for age, sex, presence of obesity and type-2-diabetes (OR: 0.966 [0.931–0.996], P = 0.038 and OR: 0.945 [0.897–0.988], P = 0.034 respectively).
Conclusion: Altered BA metabolism is associated with fibrosis in patients with concomitant NAFLD and CHB. BA profiling could be a potential noninvasive biomarker for the severity of liver diseases or progression to liver fibrosis.

Table 1. Cohort characteristics and differences in selected bile acid profiles when comparing fibrotic and non-fibrotic patients with concomitant

	Total (n=61) Median (IQR)	**Steatosis Only** (n=27) Median (IQR)	**Steatosis & Fibrosis** (n=34) Median (IQR)	*p* value
Age (years)	61.63 (56.87 - 66.02)	60.18 (53.82 - 64.96)	61.75 (57.03 - 67.66)	0.35
Gender, male (%)	42/61 (68.85)	19/27 (70.4)	23/34 (67.6)	1
On nucleoside analogues treatment (%)	48/61 (78.69)	18/27 (66.7)	30/34 (88.2)	0.08
HBV treatment duration (months)	72 (54 - 115)	90.5 (69.5 - 116)	62 (32 - 112)	0.24
Aspartate transaminase (U/L)	30 (23 - 39)	24 (20.5 - 32)	35.5 (28 - 41.75)	0.00 **
Alanine transaminase (U/L)	33 (25 - 53)	29 (22.5 - 43.5)	46 (26.25 - 54.75)	0.16
Alkaline phosphatase (U/L)	71 (60 - 80)	71 (57.5 - 82)	70 (60.25 - 80)	0.86
Albumin (g/dL)	46 (45 - 48)	47 (46 - 47.5)	46 (45 - 47.75)	0.25
Body Mass Index (kg/m^2)	27.5 (24.83 - 29.81)	27.03 (24.19 - 28.43)	29.11 (25.28 - 31.58)	0.10
Fasting blood glucose (mmol/L)	6.9 (5.6 - 7.7)	5.8 (5.35 - 7.45)	7.15 (6.53 - 8.3)	0.01 *
Hemoglobin A1c	6.6 (5.7 - 7.3)	6 (5.6 - 6.8)	6.9 (6.12 - 7.3)	0.09
Total cholesterol (mmol/L)	4.2 (3.7 - 4.9)	4.6 (3.65 - 4.95)	3.95 (3.7 - 4.85)	0.41
HDL-cholesterol (mmol/L)	1.2 (1 - 1.4)	1.2 (1 - 1.3)	1.2 (1 - 1.4)	0.76
LDL-cholesterol (mmol/L)	2.4 (1.8 - 2.9)	2.6 (2.05 - 3.1)	2.15 (1.72 - 2.75)	0.18
Triglycerides (mmol/L)	1.3 (1 - 1.6)	1.3 (1 - 1.5)	1.3 (1 - 1.78)	0.9
Chest circumference (cm)	95 (91.25 - 101.25)	95 (88.25 - 100)	95.25 (93 - 103)	0.25
Waist circumference (cm)	96.5 (91.88 - 104)	95 (92 - 99.5)	98 (91.5 - 105)	0.11
Hip circumference (cm)	98 (95 - 105)	99 (96.75 - 101.75)	98 (95 - 107)	0.94
Total Bile Acid (nM)	2945.97 (1749.62 - 4962.19)	2055.42 (1313.56 - 4116.71)	3630.9 (2776.75 - 5726.46)	0.01 *
Total Primary BA (nM)	2107.77 (1010.09 - 3695.61)	1356.49 (738.06 - 2442.47)	2491.28 (1704.31 - 3982.41)	0.005 **
Total Secondary BA (nM)	957.22 (560.23 - 1599.37)	776.46 (502.27 - 1470.43)	1169.94 (708.8 - 1697.38)	0.24
Total Secondary BA (%)	31.08 (25.75 - 45.41)	35.25 (27.38 - 51.47)	30.59 (22.39 - 35.9)	0.06
Total ConjugatedBA (nM)	1885.41 (938.75 - 3198.46)	967.87 (680.83 - 2151.27)	2524.01 (1207.79 - 4004.82)	0.003 **
Total Unconjugated BA (nM)	1100.28 (640.88 - 1767.43)	859.02 (677.83 - 1722.4)	1256.1 (591.4 - 1796.56)	0.57
Total Unconjugated BA (%)	38.07 (26.32 - 52.83)	48.89 (31.92 - 59.59)	35.41 (21.72 - 47.13)	0.02 *
Total Primary Conjugated BA (nM)	1268.35 (734.28 - 2530.14)	816.42 (373.59 - 1440.68)	1917.83 (1033.6 - 3131.24)	0.002 **
Total Primary Conjugated BA (%)	36.12 (24.14 - 45.36)	32.96 (19.18 - 42.79)	38.31 (32.34 - 51.76)	0.03 *
Total Primary Unconjugated BA (nM)	455.82 (169.9 - 978.68)	395.72 (169.28 - 896.77)	692.76 (184.64 - 1023.88)	0.35
Total Primary Unconjugated BA (%)	16.97 (8.93 - 28.01)	17.24 (8.68 - 28.87)	16.35 (9.19 - 24.16)	0.64
Total Secondary Conjugated BA (nM)	410.92 (184.58 - 781.01)	288.51 (123.95 - 581.78)	451.63 (224.85 - 864.31)	0.07
Total Secondary Conjugated BA (%)	13.17 (9.26 - 17.44)	13.17 (9.49 - 16.19)	13.17 (9.17 - 18.08)	1
Total Secondary Unconjugated BA (nM	469.95 (331.16 - 897.71)	457.5 (316.64 - 881.91)	503.13 (331.68 - 882.15)	0.86
Total Secondary Unconjugated BA (%)	18.83 (11.22 - 26.69)	23.59 (15.46 - 38.94)	16.37 (7.51 - 22.63)	0.004 **
Controlled Attenuation Parameter (dB/r	313 (296 - 340)	315 (288 - 336.5)	312.5 (298 - 340.75)	0.50
Liver Stiffness (kPa)	9.4 (5.3 - 14.2)	5 (4.6 - 5.55)	12.35 (10.72 - 15.33)	0.000 **

* p<0.05, ** p<0.01 between fibrosis and non-fibrosis
Steatosis defined as controlled attenuation parameter >=248dB/m; fibrosis defined as liver stiffness >=9kPa

[PP-0377]

HBcrAg; Useful biomarker to predict HBeAg seroconversion in chronic hepatitis B patients treated with antivirals

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Objectives: HBeAg seroconversion is an important treatment endpoint for HBeAg-positive patients and is a pre-requisite for HBsAg loss or functional cure. We aimed to identify predictors of seroconversion using serum highly-sensitive HBsAg and hepatitis B core-related antigen (HBcrAg), in HBeAg-positive patients treated with nucleos (t)ide analogues (NAs).
Materials and Methods: Data and samples from 70 HBeAg-positive patients started on entecavir or tenofovir between Jan 2007 and Dec. 2017 were retrospectively analysed. The mean follow-up duration was 11 years. Cumulative incidence of HBeAg seroconversion according to HBcrAg level at baseline and 2 years after antiviral therapy. The predictive power of HBcrAg at baseline and 2 years after antiviral therapy was determined using receiver operating curve (ROC) analysis and cut-off values determined by maximized Youden's index.
Results: Twenty-one patients (30%) achieved HBeAg seroconversion at a mean of 28 months (12–84 months) after antiviral treatment. HBcrAg and highly-sensitive HBsAg levels were lower in the patients achieving HBeAg seroconversion; the median baseline HBcrAg and highly-sensitive HBsAg levels were 6.35 ± 0.77 vs. 5.86 ± 0.61, (P = 0.006), 4.75 ± 0.45 vs. 4.50 ± 0.53 (P = 0.044) in the non-seroconverters and seroconverters, respectively. In multivariate analysis, serum HBcrAg levels at baseline and 2 years after antiviral therapy were predictive factors for HBeAg seroconversion. (HR, 0.326, CI, 0.111–0.958, P = 0.042 and HR, 0.4555, CI, 0.211–0.984, P = 0.045) The HBcrAg level $\leq$ 6.5 log10U/mL at baseline and $\leq$ 5.3 log10 U/mL at 2 years after antiviral therapy had a sensitivity of 53.1%, 69.8%, specificity of 95.2%, 70.6%, positive predictive value of 82.6%, 50.0% and negative predictive value of 82.6%, 84.5%, with AUROC of 0.712 (0.596, 0.830; 95%CI) and 0.745 (0.599, 0.891; 95%CI) to predict HBeAg seroconversion.

Conclusion: In chronic hepatitis B patients achieved entecavir or tenofovir induced HBeAg seroconversion, HBcrAg level $\leq$ 6.5 log10U/mL at baseline and HBcrAg level $\leq$ 5.3 log10U/mL at 2 years after antiviral therapy were useful predictive factors of HBeAg seroconversion.

[PP-0380]

HBcrAg and highly-sensitive HBsAg: Useful biomarker to detect the presence of hepatitis B virus proteins before rituximab treatment

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Objectives: Rituximab can lead to HBV reactivation in patients with occult HBV infection as well as in HBV carriers. To prevent HBV reactivation-related hepatitis, when HBsAg-negative and anti-HBc-positive patients treated with rituximab, HBV prophylactic antiviral treatment is being performed regardless of HBV DNA detection or HBsAg seroconversion. This study aimed to investigate whether hepatitis B core-related antigen (HBcrAg) and highly-sensitive HBsAg are more effective than conventional HBsAg test in assessing the presence of HBV proteins before rituximab treatment.
Materials and Methods: From June 2014 through October 2020, autoimmune bullous disease patients with HBsAg-/HBcAb + who received rituximab were included. Medical records including hepatitis B serology (conventional HBsAg, anti-HBc, anti-HBs) and HBV-DNA titer, alanine-aminotransferase (ALT), aspartate-aminotransferase (AST) levels were reviewed. Using stored sample, HBcrAg, and highly-sensitive HBsAg titer were checked at baseline before Rituximab therapy.
Results: In our study, all 16 autoimmune bullous disease patients who treated with Rituximab were HBsAg-/HBcAb + . At baseline, Among the 16 patients, 12.5% (2/16) of the patients were 6% (1/16) was seropositive for HBcrAg, seropositive using the highly-sensitive HBsAg assay. Based on this result, at least 3 patients were confirmed to have HBV proteins in serum that were not detected by conventional HBsAg test.
Conclusion: HBcrAg and highly-sensitive HBsAg assay are useful biomarkers to detect the presence of hepatitis B virus proteins before rituximab treatment. It might be considered that all HBsAg-/anti-HBc + patients are not unnecessarily given prophylactic antiviral treatment, but only in the case of seropositive for HBcrAg or highly-sensitive HBsAg.

[PP-0383]

Liver fibrosis scores and risk of liver-related mortality in young adults with chronic hepatitis B

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Objectives: The predictive role of noninvasive liver fibrosis scores on liver-related mortality in patients with chronic hepatitis B below 40 years of age remains unclarified. We examined the association of liver fibrosis scores with liver-related mortality in young (< 40 years) and older adults with hepatitis B virus (HBV) infection.
Materials and Methods: A cohort study was performed in 21,360 HBsAg-positive Korean adults without liver cirrhosis or liver cancer at baseline who were followed up for up to 18 years. The liver fibrosis scores were determined using the fibrosis-4 score (FIB-4) and aspartate transaminase to platelet ratio index (APRI). Patients' vital status and cause of death were ascertained through the National Death Records.
Results: During a median follow-up of 10.2 years, 283 liver-related deaths were identified (liver-related mortality, $127.4/10^5$ person-years). The liver fibrosis scores were significantly associated with increased risks of liver-related mortality; this association did not differ by age group (< 40 vs. $\geq$ 40 years). The multivariable-adjusted HRs with 95% CIs for liver-related mortality comparing intermediate and high to low FIB-4 scores were 4.23 (1.99–9.00), and 15.16 (5.18–44.38), respectively, among individuals under 40, and 4.46 (3.03–6.56) and 22.47 (15.11–33.41), respectively, among older individuals. These associations were similar in analyses using APRI.
Conclusion: In this cohort of HBsAg-positive individuals, the liver fibrosis scores were associated with increased risks of liver-related mortality in young and older adults. The liver fibrosis scores have a role in predicting liver mortality, even in young adults with HBV.

[PP-0384]

HBcrAg, highly-sensitive HBsAg: Useful biomarker to discriminate chronic infection and chronic hepatitis in treatment naive patients with HBeAg positive

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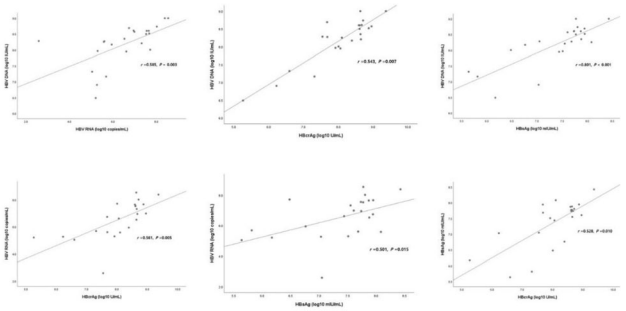
Objectives: The correlation between serum HBcrAg, HBV RNA, highly-sensitive HBsAg and serum HBV DNA is rarely reported in patients with chronic hepatitis B infection. This study aimed to assess the correlation of HBcrAg, HBV RNA, highly-sensitive HBsAg, and HBV DNA, and investigate whether serum HBcrAg, HBV RNA and highly-sensitive HBsAg is useful biomarker to discriminate chronic infection and chronic hepatitis in treatment naïve patients with HBeAg positive.
Materials and Methods: Treatment naïve HBeAg positive 23 patients from January 2018 to December 2019 were included. Patients were classified into 2 clinical phases according to ALT levels. (1) HBeAg positive chronic infection (EPI) group consisted of patients with HBeAg positive and normal ALT (KASL guideline, ALT $\leq$ 34 IU/L in men and ALT $\leq$ 30 IU/L in women) (2) HBeAg positive hepatitis (EPH) group consisted of HBeAg positive patients with elevated ALT levels. serum HBcrAg, HBV RNA and highly-sensitive HBsAg titer were measured at baseline.
Results: HBcrAg was correlated positively with highly-sensitive HBsAg ($r = 0.651$, $P = 0.01$), and HBV RNA ($r = 0.759$, $P < 0.001$), and HBV DNA ($r = 0.726$, $P < 0.001$). Highly-sensitive HBsAg was correlated positively with HBV RNA ($r = 0.544$, $P = 0.007$), and HBV DNA ($r = 0.785$, $P < 0.001$). In EPI group, HBcrAg, and

highly-sensitive HBsAg titer were significantly higher than those in EPH group (HBcrAg, 8.5 ± 0.4 vs. 7.7 ± 1.2 $\log_{10}$ U/mL, P = 0.047; HBsAg, 7.8 ± 0.2 vs. 7.0 ± 0.8 $\log_{10}$ mIU/mL, P = 0.007). However, HBV RNA level is similar between two groups (7.0 ± 0.9 vs. 6.1 ± 1.7 $\log_{10}$ copies/mL, P = 0.143).
Conclusion: HBcrAg, HBV RNA and highly-sensitive HBsAg were correlated with serum HBV DNA at baseline in treatment naïve HBeAg positive patients (Figure). HBcrAg and highly-sensitive HBsAg assay are useful biomarkers to discriminate EPI and EPH group.



[PP-0385]

Performance evaluation of highly-sensitive hepatitis B surface antigen and core-related antigen in the clinical practice

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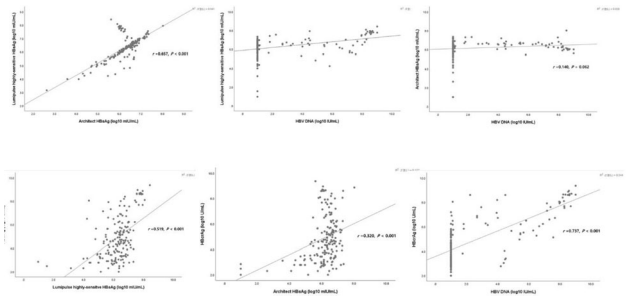
Objectives: Both serum hepatitis B virus core–related antigen (HBcrAg) and highly-sensitive hepatitis B surface antigen (HBsAg) are emerging markers for diagnosis, monitoring and prognosis in patients with CHB. We evaluated the linearity of highly-sensitive HBsAg assay and conventional HBsAg assay and the correlation of highly-sensitive HBsAg, HBcrAg and HBV DNA levels.
Materials and Methods: A total of 178 serum samples from patients with chronic hepatitis B were tested. Conventional HBsAg levels were determined by using the Architect (Abbott Laboratories, Abbott Park, IL), and highly-sensitive HBsAg level was measured by a two-step sandwich immunoassay method on the LUMIPULSE G1200 (Fujirebio, Tokyo, Japan). HBcrAg was measured by chemiluminescence immunoassay on the Lumipulse G12000 automated analyzer (Fujirebio, Tokyo, Japan).
Results: Both conventional HBsAg and highly-sensitive HBsAg assays showed linearity from 2.7 to 8.0 $\log_{10}$ mIU/mL and correlated well (r = 0.657, $P < 0.001$). HBV DNA level was more correlated with Highly-sensitive HBsAg levels (r = 0.397, $P < 0.001$) than that of conventional HBsAg levels (r = 0.140, P = 0.062). HBcrAg was more correlated with Highly-sensitive HBsAg levels (r = 0.519, $P < 0.001$) than that of conventional HBsAg levels (r = 0.320, $P < 0.001$). HBcrAg was also correlated with HBV DNA (r = 0.737; $P < 0.001$).
Conclusion: HBcrAg, and highly-sensitive HBsAg assays provide the possibility for further research to validate the clinical usefulness in real-world practice.



[PP-0401]

Incidence of viral hepatitis in Mongolia in the last decades

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Objectives: to estimate new incidence of viral hepatitis and investigate policy documents of fighting viral hepatitis.
Materials and Methods: desk review study, analyzed policy and strategic documents and statistics issued by governmental organizations.
Results: Mongolia is implementing the following key policy documents to reduce the incidence of viral hepatitis: National Program of Prevention and Control of Infectious Diseases, Whole liver program (Hepatitis Prevention, Control and Elimination Program). In 2020, a total of 353 new cases or 1.1 per 10 000 population of viral hepatitis were registered at the national level, which accounts for 1.1% of all communicable diseases. The incidence decreased by 174 cases or 0.6 /per 10 000 pop/ as compared to the previous year. Viral hepatitis registered nationwide in the last ten years was the highest in 2011 at 54.8 per 10,000 population, and since 2012, the incidence has been steadily declining. Nationally, the incidence of viral hepatitis for over the last decade it is seen that the highest rate (peaks) was observed in December 2007, 2010 and in November 2011. Since 2012, the incidence rate has decreased steadily. Out of all viral infections, 22.4% was viral hepatitis A, 40.5% was viral hepatitis B, 21.2% was viral hepatitis C and 15.9% was other viral hepatitis.
Conclusion: Last decades, Mongolia has been reducing the incidence of new infections through HPCE programs, public awareness campaigns, and new antiviral medicines have been introduced into chronic viral hepatitis treatment.

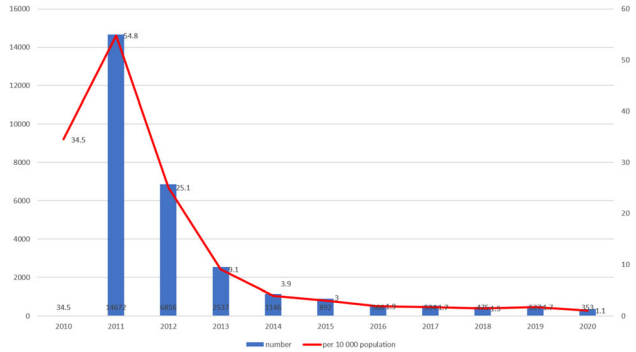

Figure 1. The incidence of viral hepatitis, 2010-2020

[PP-0403]

Effectiveness and renal safety of tenofovir alafenamide compared to tenofovir disoproxil fumarate among patients with chronic hepatitis B in Mongolia

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Objectives: To provide compare of the efficacy and safety tenofovir alafenamide (TAF) to tenofovir disoproxil fumarate (TDF) in patients with HBeAg-negative and HBeAg-positive chronic hepatitis B.
Materials and Methods: We performed a randomized, unblinded, non-inferiority study in which patients with compensated cirrhosis (Child–Pugh A and B stage) between 18–70 years old with a positive chronic hepatitis B test were randomized to receive either TAF, TDF, or were switched from TDF to TAF. The primary efficacy endpoint was the proportion of patients with HBV-DNA < 29 IU/ml at week 48.
Results: The efficacy endpoint, an HBV-DNA < 29 IU/ ml at weeks 48, was achieved by 251 (79.9%) of 314 patients receiving TAF, which was not significantly different from the 113 (74.8%) of 151 patients receiving TDF. After 48 weeks of treatment, patients receiving TAF had significantly smaller bone mineral density reductions than patients receiving TDF. At week 48, the median decrease in eGFR was significantly less in the TAF recipients than the TDF recipients.
Conclusion: TAF treatment has the same efficacy as TDF treatment. However, TAF treatment had a better safety profile than TDF. Patients receiving TAF had a significantly smaller median decrease in the eGFR by the Cockcroft-Gault equation than patients receiving TDF.

Table 1. Renal and bone safety at 48 weeks of treatment with TAF or TDF

Variable	TAF 25mg Mean ± SD	TDF 300mg Mean ± SD	TDF-TAF Mean ± SD	*p-value
HBeAg-negative				
T-s core (%)	-0.11 ± 0.68[d]	-1.61 ± 1.37[d]	-1.1 ± 1.05	0.000
Z-s core (%)	-0.43 ± 0.94[e]	-2.20 ± 1.66	-1.6 ± 1.18[e]	0.000
eGFR (ml/min)	-0.6 ± 0.97[f]	-5.3 ± 2.80[f]	-2.4 ± 1.23	0.000
Serum creatinine (mmol/l)	0.8 ± 1.01	2.6 ± 1.97g	1.5 ± 1.11g	0.021
HBeAg-positive				
T-score (%)	0.28 ± 0.10a	-2.11 ± 1.53a	-1.51 ± 1.09	0.000
Z-score (%)	-0.89 ± 0.11b	-2.25 ± 1.60	-1.90 ± 1.23b	0.000
eGFR (ml/min)	1.6 ± 0.35	4.6 ± 2.97c	2.0 ± 1.16	0.004
Serum creatinine (mmol/l)	0.8 ± 0.76	1.7 ± 1.59	1.2 ± 1.06	0.321

[PP-0404]

Incidence of acute hepatitis B in Mongolia between 2010–2019

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Objectives: To define situation of acute hepatitis B infection.
Materials and Methods: Desk review study, reviewed documents from governmental organization.
Results: Hepatitis B incidence per 100 000 population Decrease the spread of infectious diseases through prevention, early detection, and preparedness to treat infectious diseases, by improving the rapid response capacity of health services, and by ensuring access to priority vaccines for everyone. Under this objective by 2020, reduce the prevalence of hepatitis in 100,000 populations to 3. As of 2019, a total of 219 cases of viral hepatitis B were reported nationwide; the case rate was 6.9 per 100 000 population, which decreased by 1.6 cases compared to the previous year. Looking by age group, the incidence rates were high among people aged 20–34 years, in 2019 and the majority diagnosed in the female. The incidence was 35 per 100 000 population. In 2000, it was to 6.9 per 100 000 population in 2019, decreased by 27 per 100 000 people, compared to 2000.
Conclusion: There is a tendency that the incidence rate has decreased in recent years. But not completed mission. The incidence rates of acute HBV infection were high among people aged 20–34 years, majority diagnosed in the female.

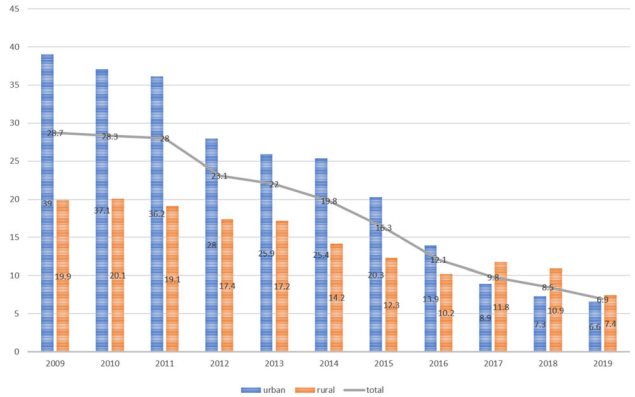

Figure 1. Hepatitis B incidence per 100 000 population, 2010-2019

[PP-0405]

Self-reported survey on HBV vaccination status of healthcare workers in Mongolia

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Objectives: To investigate hepatitis B (HepB) vaccine coverage among health care workers.
Materials and Methods: We conducted a cross-sectional survey of health care workers' vaccination status in 36 hospitals in Mongolia. Vaccination histories were obtained through self-administered questionnaires.
Results: All 1135 participants reported about their vaccination status and 77.8% (883) of them said that they have received HBV vaccination while 22.2% (252) of the participants reported that they're not vaccinated. In terms of vaccination coverage, physicians (81.0%), nurses (80.8%) and nursing assistant (66.7%) were vaccinated. Among unvaccinated HCWs, comparably high percentage of nursing assistants (29.4%) and other HCWs such as clerical and laundry staff (27.6%) were not vaccinated in compare to other occupations. Among 883 HCWs who reported that they are vaccinated, 60.9% (538) of them received the full 3 doses of HBV vaccine while 29.1% (257) were received 2 doses of vaccine and 10% (88) were received 1 dose of vaccine. The average dose of HBV vaccine administered by all HCWs was reported as 1.95 ± 1.20, and the highest dose by type of hospital was 2.27 ± 1.07 in HCWs of soum and family health centers. The dose of HBV vaccine administered by private HCWs was 1.25 ± 1.17 ($p < 0.001$).
Conclusion: Hepatitis B vaccination coverage rate among HCWs in Mongolia is adequately, and coverage is different from occupation, health care facilities and locations.

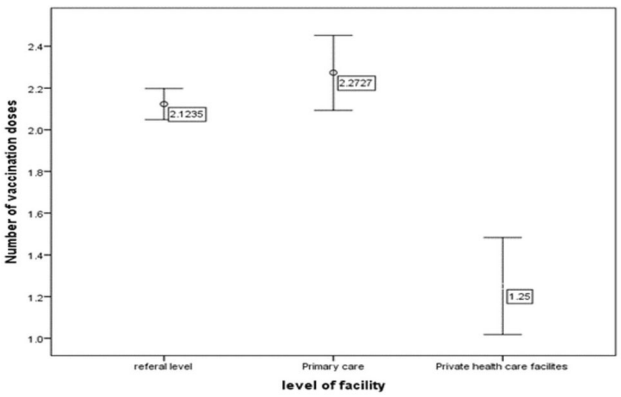

Figure 1. Average number of vaccination dose against HBV in participants, by level of healthcare

[PP-0406]

Prevalence of chronic HBV infection among health care workers in Mongolia

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Objectives: To determine prevalence of chronic HBV infection among health care workers.
Materials and Methods: Cross-sectional study, the survey conducted 1135 health care workers at 36 health care facilities in 2 urban and 4 rural areas of Mongolia, used a multi-stage sampling to ensure for inclusion of study population from all geographical and socio-economic regions of the country. Blood samples from the subjects were tested for HBsAg in the NCCD's Laboratory of Viral Hepatitis and Enterovirus using the Enzyme-linked Immunosorbent Assay (ELISA).
Results: Most of the participants were nurses (28.0%) and medical doctors (29.1%). 13.5% (153) were service staff. In terms of location, 753 HCWs from urban areas and 382 were rural provinces. HBsAg was positive in 4.6%. Out of HBsAg positive participants, 84.9% were women (45/53) and 15.1% were men (8/53). 84.9% were those born before 1992 (45) while 15.1% were born after 1992 (8). In terms of level of health care facilities, 84.9% (45/53) of HCWs from referral level and 15.1% (8/53) were from primary health care facilities. 20.7% (11/53) were physician, 39.6% (21/53) were with experience of working more than 11 years. There is statistically significant difference between age groups ($?2 = 14.76$, $p = 0.001$) and years of service ($?2 = 40.31$, $p < 0.001$).
Conclusion: The prevalence of participants who was born before the start of hepatitis B virus vaccination (1992), works at referral level and working experience more than 11 years was high.

[OP-0410]

Macrotrabecular-massive feature in tumor tissues is associated with a higher risk of the recurrence of hepatocellular carcinoma

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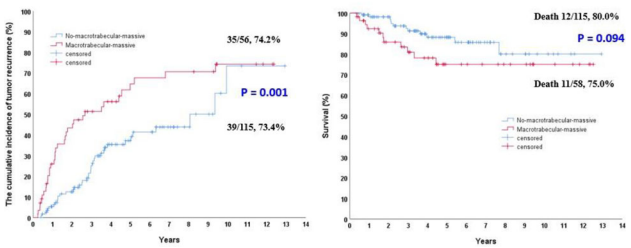
Objectives: Hepatocellular carcinoma (HCC) with a macrotrabecular-massive feature (MTM) have been reported to be associated with frequent recurrence and poor disease-specific survival in resected HCCs. We aim to investigate the clinical significance of MTM feature to predict the recurrence of HCC.
Materials and Methods: Data and samples from 171 patients with HCC treated by surgical resection between Jan 2007 and Dec. 2017 were retrospectively analyzed. By pathological review, the prognostic significance of MTM feature was evaluated in a series of 171 patients with HCC treated by surgical resection in Gangnam Severance Hospital.
Results: Among the 171 patients (136 males, mean age 63.1 ± 10.0 years) who underwent surgical resection, the median clinical follow-up was 6.2 (2.5–13.5) years. The median duration of the recurrence of HCC was 4.1 (1.0–12.9) years. Among them, 74 patients (43.3%) experienced HCC recurrence. The MTM feature was identified in 32.7% of the whole cohort (n = 35, 47.3% in recurrence group vs. n = 21, 21.6% in no-recurrence group, P < 0.001). The recurrence of HCC after curative resection was associated with age, maximal tumor size, and MTM feature (HR, 1.036, P = 0.028, HR, 1.132, P = 0.032, and HR, 3.248, P = 0.001, respectively) in univariate analysis. Multivariate analysis showed that the independent predictor of HCC recurrence was only MTM feature (hazard ratio, 1.881; 95% confidence interval, 1.143–3.095; P = 0.013). The cumulative incidence of HCC recurrence showed significant difference according to the presence of MTM feature (35/56, 74.2% vs. 39/115, 73.4%, p = 0.001). The overall survival rates did not show significant difference according to the presence of MTM feature (11/58, 75.0% vs. 12/115, 80%, p = 0.094).
Conclusion: We have shown that MTM feature in tumor tissues is associated with a higher risk of the recurrence of HCC in retrospective cohorts of patients with HCC treated by surgical resection.

Figure 1. Cumulative incidence of tumor recurrence and survival rates according to macrotrabecular-massive subtype



[OP-0447]

Tenofovir alafenamide after switching from entecavir or nucleos (t)ide combination therapy for patients with chronic hepatitis B

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Objectives: Tenofovir alafenamide (TAF) has been newly approved for the treatment of chronic hepatitis B (CHB). We aimed to assess the effectiveness and renal safety of switching from entecavir (ETV) or nucleos (t)ide analogue (NA) combination therapy to TAF.
Materials and Methods: This multicenter, retrospective, cohort study included 313 consecutive CHB patients who switched to TAF monotherapy after treatment with ETV or a nucleoside-nucleotide analog (NA) combination for over two years. Virological/laboratory responses were evaluated for the 48 weeks after switchover. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m2. Differences in longitudinal parameters were compared by the generalized estimating equation method. In the prior ETV group (n = 191), the HBV DNA suppression rate at week 48 was significantly increased, from 75.9% to 96.9% (P < 0.001). Additionally, mean changes in the HBsAg level at week 48 in HBsAg ≥ 3.0 logIU/mL and < 3.0 logIU/mL groups were -0.09 and -0.13 logIU/mL, respectively.
Results: In the prior NA combination group (n = 122), the mean changes in HBsAg level at week 48 in the HBsAg ≥ 3.0 logIU/mL and < 3.0 logIU/mL groups were -0.08 and -0.11 logIU/mL, respectively. For patients with CKD, the eGFR at week 48 was significantly improved compared to those with non-CKD (adjusted slope coefficient difference: 2.75 mL/min/1.73m2/48 weeks; P = 0.001).
Conclusion: Switching from ETV or an NA combination to TAF was effective for HBV suppression and continued HBsAg reduction. Moreover, the renal glomerular function of patients in the prior NA combination group with CKD was significantly improved compared to those with non-CKD.

[PP-0453]

Pharmacokinetics and safety of the siRNA JNJ-73763989, an RNA interference therapy for hepatitis B virus, in moderately hepatically impaired participants

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Objectives: JNJ-73763989 comprises hepatitis B virus (HBV)-specific short interfering RNA (siRNA) triggers, JNJ-73763976 and JNJ-73763924, which silence HBV RNA transcripts from host-integrated HBV and episomal DNA. Pharmacokinetics and safety/tolerability of JNJ-73763989 in participants with moderate hepatic impairment (Child–Pugh B) without HBV were compared to healthy participants with normal liver function.
Materials and Methods: In this Phase 1 single-dose, open-label, parallel study, 8 Child–Pugh B participants and 8 healthy participants matching for sex, age, and body weight received one 200 mg subcutaneous dose of JNJ-73763989. Plasma and urine concentrations of JNJ-73763976 and JNJ-73763924 were collected over 72 h and analyzed using liquid chromatography-fluorescence hybridization and liquid chromatography-mass spectrometry, respectively.

Pharmacokinetic parameters were estimated using non-compartmental analysis (Phoenix). Safety/tolerability were assessed throughout.
Results: Pharmacokinetic parameters are summarized (table). JNJ-73763976 geometric mean ratio for C_{max} and AUC was 1.3–1.4-fold higher in Child–Pugh B participants; for JNJ-73763924, 2.0–2.2-fold higher. Half-life and amount of drug renally excreted were slightly higher for both analytes in Child–Pugh B participants. There were no deaths, serious adverse events (AEs) or discontinuations. Overall, 2 participants (1 per group), reported $\geq$ 1 mild/moderate treatment-emergent AE not related to JNJ-73763989. All treatment-emergent laboratory abnormalities were mild/moderate, except for transient platelet reductions (grade 2 at screening, grade 3 in 2 Child–Pugh B participants). There were no relevant cardiovascular findings.
Conclusion: JNJ-73763976 and JNJ-73763924 exposures were higher in participants with moderate hepatic impairment. A single JNJ-73763989 200 mg dose was well tolerated in participants without and with moderate hepatic impairment.

	JNJ-73763976		JNJ-73763924	
Liver status	Child-Pugh B	Healthy participants	Child-Pugh B	Healthy participants
N	8	8	8	8
C_{max} (ng/mL)	1,640 (1,087)	1,068 (565)	444 (355)	190 (75)
t_{max} (h)	7.00 (0.25–12.00)	9.00 (4.00–12.00)	6.00 (0.25–12.00)	8.00 (0.50–12.00)
AUC_{last} (ng.h/mL)	26,569 (13,132)	18,237 (6,192)	6,410 (3,605)	2,862 (694)
AUC_{∞} (ng.h/mL)	26,711 (13,085)	18,273 (6,194)	6,335 (4,172), [n=6]	3,023 (634), [n=7]
$t_{1/2}$ (h)	6.93 (3.76)	5.39 (1.75)	7.11 (5.74), [n=6]	4.34 (1.55), [n=7]
Ae (% dose)	34.4 (14.1)	26.6 (7.47)	29.1 (13.6)	21.2 (5.83)

C_{max}, maximum plasma concentration; t_{max}, time to reach C_{max}; AUC, area under the plasma concentration-time curve from time 0 to the time of the last measured concentration (AUC_{last}) or extrapolated to infinity (AUC_{∞}); $t_{\frac{1}{2}}$, half-life; Ae, amount of drug excreted.
Mean (SD) except for t_{max}, median (range).

[PP-0457]

Experience and impact of chronic hepatitis B and content validity of the hepatitis B quality of life instrument: A qualitative study

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Objectives: To develop a patient-focused measurement strategy, we 1) explored the patient experience and impact of chronic hepatitis B (CHB), and 2) evaluated the content validity of the Hepatitis B Quality of Life Instrument (HBQOL) in line with the FDA PRO Guidance for Industry.
Materials and Methods: Patients with CHB recruited in the United Kingdom participated in a 60–90 min semi-structured telephone interview. Interviews included: 1) concept elicitation (CE) to explore patient's experiences and impacts of living with CHB, and 2) cognitive debriefing (CD) of the HBQOL.
Results: Twenty-four patients with CHB participated (mean age 39 years; n = 11 [46%] females; and n = 10 [42%] Asian). CE identified fatigue (n = 16, 67%; feeling tired, weak, and lacking energy) as the most commonly reported symptom. The predominant impacts were on emotional/psychological wellbeing, including self-stigmatization. Impacts on social functioning, family relationships, and difficulty dating/starting relationships were also experienced. CD exploration confirmed the conceptual relevance of the HBQOL items; all items were endorsed as relevant by most participants. Most patients expressed that recall periods of seven days, two weeks, 24 h, or one month could be easily used to report their experiences with CHB. The item wording and response scale/options were considered appropriate for answering the items.
Conclusion: Patients with CHB experience emotional and psychological impacts, fatigue, relationship issues, and self-stigmatization. Results support the content validity of the HBQOL in this population, including its conceptual relevance, item wording, and response options. A recall period is needed to capture meaningful longitudinal data.

[PP-0461]

The state of the mucous membrane of the oral cavity and periodontium in patients with HBV

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Objectives: Recently, there has been a tendency to an increase in the number of patients with chronic liver diseases, which may be due to an increase in the incidence of viral hepatitis, taking toxic and medicinal drugs, and unhealthy style of life.
Materials and Methods: A total of 95 patients with HBV were examined: 24 (25.3%) women, 71 (74.7%) men who were admitted to the Nork Hospital in Yerevan in 2018–2019. The average age of the patients was 40.17 $\pm$ 13.48 (mean $\pm$ SD).
Results: External examination of the lips in 2.1% (2) patients with HBV revealed erosion on the lips ($p > 0.614$). The frequency of detecting cracks in the corners of the mouth in patients with HBV was 52.6% (50), which significantly and reliably exceeded the latter in the control group ($p < 0.001$). Hemorrhages on the buccal mucosa and hard palate were detected in 91.6% (87) ($p < 0.001$). Telangiectasias were found on the buccal mucosa in 26.3% (25) cases ($p < 0.001$). An objective examination of the oral cavity revealed a number of pathological changes in the gums. In patients with HBV, hyperemia and edema of the gums were detected in 66.3% (63) of cases, which is statistically significantly higher than in the control group ($p < 0.001$).
Conclusion: The most characteristic symptoms of lesion of various parts of the MMM In patiets with HBV are disorders of the MMM relief (93.7%), the presence of hemorrhages (91.6%). The most common symptom is bleeding of the gums (74.7%). The detection rate of periodontal disease in the examined patients with HBV patients was 100%.

[OP-0471]

Safety, pharmacokinetics (PK), and antiviral activity of the capsid assembly modulator (CAM) ALG-000184 in Asian and non-Asian subjects with chronic hepatitis B (CHB)

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Objectives: The safety and PK profile of ALG-000184 in Asian and non-Asian healthy subjects was previously shown to be favorable and similar. We sought to investigate the profile in Asian and non Asian CHB subjects.
Materials and Methods: An ongoing three-part, double-blind, randomized, placebo-controlled study is evaluating cohorts (N = 10/cohort; 8 active:2 placebo) of currently not treated (CNT)/treatment naïve (TN) HBeAg-negative or positive CHB subjects receiving 28 daily oral doses of ALG-000184/placebo. We report here preliminary blinded safety and PK data in Asian and non-Asian CHB subjects. Antiviral data will be included at the conference.
Results: Twenty one Asian and 15 non-Asian CHB subjects have received 10, 50, or 100 mg of ALG-000184/placebo. Most subjects were male (56%), with a mean age of 40 years. Asian and non-Asian subjects were similar except Asians had a lower BMI (22.4 kg/m^2 vs. 27.7 kg/m^2), and different baseline viral characteristics: a higher prevalence of HBeAg positivity (47.6% vs 0%), a higher HBV DNA (mean 6.2 $\log_{10}$ IU/mL vs 4.3 $\log_{10}$ IU/mL) and a different predominant HBV genotype (B vs D). ALG-000184 was generally well tolerated. One unrelated SAE occurred in an Asian subject who was hospitalized for management of pre-existing back pain. There were no TEAEs leading to premature discontinuation. All TEAEs were Grade 1 or Grade 2 in severity except for a Grade 3 post-treatment ALT elevation in a non-Asian subject. Grade 1 TEAEs were more frequent among Asians (71% vs. 40%), while Grade 2 TEAEs were more frequent among non-Asians (33% vs. 10%). Plasma exposures increased proportionally between 50 and 100 mg dose levels, with low variability, minimal accumulation, and no clinically relevant differences observed between Asians and non-Asians.
Conclusion: ALG-000184 at doses up to 100 mg for 28 days is associated with a favourable safety and PK profile in both Asian and non-Asian TN/CNT CHB subjects.

[OP-0474]

Changes of liver fibrosis in chronic hepatitis B patients receiving tenofovir alafenamide with different body mass index

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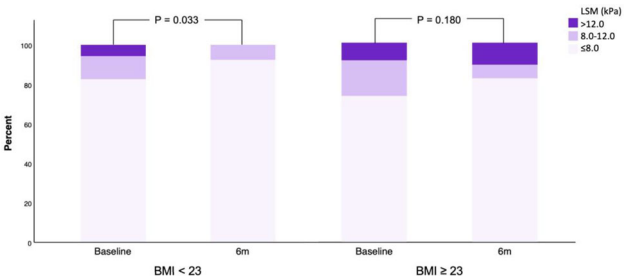
Objectives: Tenofovir alafenamide (TAF) is a prodrug of tenofovir and is recommended as first-line antiviral treatment for chronic hepatitis B (CHB) infection. Previous studies found TAF is associated with unfavourable metabolic changes including weight gain. We aimed to evaluate the impact of baseline body mass index (BMI) on the liver fibrosis of CHB patients receiving TAF.
Materials and Methods: This is a prospective territory-wide cohort study of CHB patients who have been receiving TAF therapy. Baseline was defined as the start date of receiving TAF. Weight, height and liver stiffness measurement (LSM) were collected at baseline and 6 months later.
Results: Among 97 patients included, 57 (58.8%) were males and their mean age was 61.6 ± 11.1 years. BMI increased from 22.4 ± 3.2 kg/m^2 at baseline to 22.8 ± 3.2 kg/m^2 at 6 months later (P = 0.007). Number of patients with LSM ≤ 8.0 kPa, 8.0 – 12.0 kPa and > 12.0 kPa were 76 (78.4%), 14 (14.4%), 7 (7.2%) at baseline and 85 (87.6%), 7 (7.2%), 5 (5.2%) at 6 months later (P = 0.012). For 52 patents with BMI < 23 kg/m^2 at baseline, number of patients with LSM ≤ 8.0 kPa, 8.0 – 12.0 kPa and > 12.0 kPa were 43 (82.7%), 6 (11.5%), 3 (5.8%) at baseline and 48 (92.3%), 4 (7.7%), 0 at 6 months later (P = 0.033). Their BMI increased from 20.1 ± 1.8 kg/m^2 to 20.6 ± 1.8 kg/m^2 (P = 0.002). For 45 CHB patients with BMI ≥ 23 kg/m^2 at baseline, neither LSM levels nor BMI changed significantly (P = 0.180 for LSM; P = 0.466 for BMI). (Figure).
Conclusion: TAF therapy is associated with liver fibrosis improvement and BMI increase in CHB patients with BMI < 23 kg/m^2 but not in those with BMI ≥ 23 kg/m^2.



[OP-0475]

The CAGE-B and SAGE-B models better predict the development of hepatitis B virus-related hepatocellular carcinoma after 5 years of entecavir treatment than the PAGE-B model

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Objectives: The PAGE-B model uses variables at initiation of antiviral therapy (AVT), whereas the SAGE-B and CAGE-B models use variables at 5 years of AVT. We compared the predictive accuracy of the CAGE-B, SAGE-B, and PAGE-B models in patients with chronic hepatitis B (CHB).
Materials and Methods: This study enrolled 1,335 patients who were treated with entecavir and followed up for more than 5 years without hepatocellular carcinoma (HCC) development between 2006 and 2011.
Results: The median age was 49 years and males predominated (n = 901, 67.5%). At AVT initiation, the median liver stiffness (LS) value and PAGE-B model score were 11.6 kPa and 14, respectively. At 5 years of AVT, the median SAGE-B and CAGE-B scores were 6 and 6, respectively. After 5 years of AVT, 93 (7.0%) patients experienced HCC development. In multivariate Cox regression analysis, the PAGE-B (hazard ratio [HR] = 1.151; 95% confidence interval [CI], 1.087–1.219), SAGE-B (HR = 1.340; 95% CI, 1.228–1.463), and CAGE-B (HR = 1.327; 95% CI, 1.223–1.440) models independently predicted HCC development (all $P < 0.001$). Irrespective of risk prediction model, patients in the high-risk group showed a significantly higher risk for HCC development than patients in the medium- and low-risk groups (all $P < 0.05$). The area under the receiver operating characteristic curves of the SAGE-B (0.772–0.844) and CAGE-B (0.785–0.838) models were significantly higher than that of the PAGE-B model (0.696–0.745) from 6 to 10 years of AVT for predicting HCC development (all $P < 0.05$).
Conclusion: The CAGE-B and SAGE-B models were superior to the PAGE-B model for predicting HCC development after 5 years of AVT in patients with CHB.

[PP-0477]

Efficacy of entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide in treatment-naive hepatitis B patients

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Objectives: Antiviral agents for chronic hepatitis B (CHB) reduced the risk of hepatocellular carcinoma (HCC) development. The outcomes of entecavir (ETV), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) were compared in patients with CHB.
Materials and Methods: Between 2017 and 2019, treatment-naïve patients with CHB treated with ETV, TDF, and TAF were recruited from three Korean tertiary institutes. The cumulative incidences of HCC and orthotopic liver transplantation (OLT) or mortality were calculated and compared using Kaplan–Meier analysis before and after trimatch.
Results: Among recruited 2,082 patients, 43 patients developed HCC, whereas 66 developed OLT or mortality. Before trimatch, the cumulative incidence of HCC was statistically similar among patients treated with three antiviral agents ($P = 0.340$). However, the cumulative probability of OLT or mortality development in patients treated with ETV or TDF was significantly higher than that of patients with TAF before trimatch (all $P < 0.05$). On multivariate analysis, male sex [hazard ratio (HR) = 2.990] and older age (HR = 1.044) were independently associated with an increased risk of HCC development, whereas higher platelet count (HR = 0.993) was independently associated with a decreased risk (all $P < 0.05$). The type of antiviral agents did not significantly influence the risk of HCC and OLT or mortality development (all $P > 0.05$). After trimatch, no significant difference in the cumulative probability for HCC and OLT or mortality according to antiviral agents was found (all $P > 0.05$).
Conclusion: The outcomes of ETV, TDF, and TAF on the risk of HCC and OLT or mortality were statistically similar in treatment-naïve patients with CHB.

[OP-0481]

Mechanism of matrine combined with entecavir intervening multidrug resistant hepatitis B virus

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Objectives: To explore the effect of matrine combined with entecavir intervening multidrug resistant hepatitis B virus (HBV).
Materials and Methods: Taking multidrug resistant hepatitis B virus replication cell line as the model, effects of matrine and entecavir alone or combination for HBsAg secretion, HBV DNA replication, IL-17 and p38 protein expression levels in multidrug resistant HBV cells were measured by enzyme-linked immunosorbent assay, real-time fluorescence quantitative polymerase chain reaction and western blot.
Results: Compared to the matrine or entecavir alone, the secretion levels of HBsAg and the replication levels of HBV DNA decreased significantly after the combination of matrine and entecavir in 60 h. At the same time, the expression levels of IL-17 and p38 protein decreased significantly in combination group of matrine and entecavir. The combination of matrine and entecavir can significantly inhibit the secretion of HBsAg and replication of HBV DNA.
Conclusion: Matrine combined with entecavir may achieve antiviral effect by down regulating the expression of IL-17 and inhibiting the phosphorylation of p38 protein. The combination of matrine and entecavir can significantly enhance the effect of against multidrug resistant HBV virus.

[PP-0547]

Development and content validation of a new self-stigma patient reported outcome instrument for chronic hepatitis B: A concept elicitation and cognitive debriefing study in Asia, Europe, and US

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Objectives: A qualitative study was conducted to explore the experience of self-stigma in people with chronic hepatitis B (CHB) and to establish the content validity of a new patient-reported outcome (PRO) instrument to measure CHB self-stigma.
Materials and Methods: People diagnosed with CHB in China, Germany, Italy, Japan, and the US participated individually in a 90-min semi-structured interview (face-to-face/remote) in local language. The interviews included 1) concept elicitation (CE) to understand the experience of self-stigma to build a measurement framework and 2) cognitive debriefing (CD) of draft PRO items to evaluate content validity using methods in line with the US FDA PRO Guidance. The interviews also explored whether a curative CHB treatment would change self-stigma related thoughts. Thematic and framework analyses were used. Ethics approvals were obtained.
Results: Sixty-three people (12 each from China, Germany, Italy, and Japan, and 15 from the US) diagnosed with CHB participated. Ages ranged 25–71, 39 were female. CE revealed that concealment, devaluation, shame, marginalization, and social withdrawal were relevant aspects for the measurement framework for CHB self-stigma. Some PRO items were rephrased, combined, or removed for relevance or conceptual equivalence following CD. Participants were able to self-report the frequency (5-point scale) with which they had experienced each aspect of self-stigma over the past four weeks (recall period). Participants also reported that a curative CHB treatment would reduce their self-stigma.
Conclusion: The results support the content validity of the new self-stigma PRO instrument including its conceptual relevance, suitability of the items, response options, and recall period.

[PP-0548]

Total healthcare resource utilization and costs among chronic hepatitis B patients in Japan

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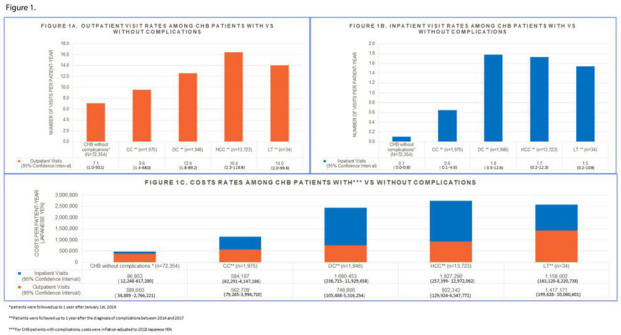
Objectives: To describe total Healthcare Resource Utilization (HCRU) and costs among Chronic Hepatitis B (CHB) patients. This included CHB patients without and with CHB-related complications (Compensated and Decompensated Cirrhosis (CC, DC), Hepatocellular Carcinoma (HCC), or Liver Transplant (LT)).
Materials and Methods: A retrospective database study describing total HCRU and costs rates per patient-year among CHB patients between 2013 and 2019 was conducted using a hospital-based administrative and medical claims database managed and provided by Medical Data Vision (MDV) Co., Ltd. (Tokyo, Japan). Outpatient (Physician visits, procedures, medications) and inpatient (hospitalizations, emergency visits, procedures, medications) visits per patient-year were reported.
Results: Among CHB patients without and with complications, the mean ages were 62.9 (± 14.3) and 66.7 (± 12.2), and 49.3% and 38.4% of the patients were women. Prior history of Nucleos (t)ide analogues therapy was seen among 4.1% and 4.3% of those without and with complications. HCRU rates per patient-year among those without complications for outpatient and inpatient visits were 7.1 (95%CI:1.0–50.1) and 0.1 (95%CI:0.0- 0.8), while HCRU rates per patient-year among those with complications ranged from 9.6 (CC,95%CI:1.4–68.0) to 16.4 (HCC,95%CI:2.3–116.8) and 0.6 (CC,95%CI: 0.1- 4.6) to 1.8 (DC,95%CI: 0.3–12.6) for outpatient and inpatient visits (Fig. 1A/B). Costs rates (Japanese Yen) per patient-year among those without complications for outpatient and inpatient visits were 389,660 (95%CI:54,889–2,766,221) and 86,952 (95%CI:12,248–617,280), while costs rates (Japanese Yen) per patient-year among those with complications ranged from 562,709 (CC,95%CI:79,265–3,994,710) to 1,417,171 (LT,95%CI: 199,628–10,060,601) and 584,187 (CC,95%CI:82,291–4,147,186) to 1,827,290 (HCC,95%CI:257,399–12,972,062) for outpatient and inpatient visits (Fig. 1C).
Conclusion: CHB patients with complications showed higher HCRU and costs compared to those without complications.
Funding: GlaxoSmithKline (Study 213927).

Figure 1.



[OP-0554]

Clinical, biochemical, virological and liver fibrosis level responses in patients with HBV-related cirrhosis treated with TDF

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Objectives: Background: Many studies have demonstrated that HBV antiviral treatment will help to reduce the level of liver fibrosis, prevent complications. Aims: to evaluate the efficacy of TDF in patients with HBV-related cirrhosis and using acoustic radiation force impulse (ARFI) to monitor liver fibrosis during antiviral treatment.
Materials and Methods: This study was conducted in 126 patients with HBV-related cirrhosis who had the indication of antiviral therapy at 103 Cam Khe Clinic from May 2019 to September 2021. All patients with HBV-related cirrhosis treated with TDF during 18 months. Liver fibrosis stages was appreciated by ARFI before and after 18 months treatment.
Results: The average age of patients was 48 years, with men accounted for 92.1% of the total. Having improvement of clinical symptoms, a significant reduction in Child–Pugh scores, suppressing HBV replication to undetectable levels after treatment. Serum albumin and total bilirubin concentrations in the Child A group had a higher rate and improved earlier in comparison to the Child B, C group. 59% of patients had reduced level of liver fibrosis from F4 to $\leq$ F3 post—treatment. The Child B, C cirrhotic group had 29.6% improved liver fibrosis level significantly. Four factors to predict the level of liver fibrosis: albumin concentration > 31.9 g/l (OR 6.29; 95% CI 1.01—36.01; $p < 0.05$), HBV DNA load > 14.167 IU/mL (OR 8.19; 95% CI 1.81—37.02; $p < 0.01$), Child–Pugh scores < 7 (OR 14.68; 95%CI 1.61—139.68; $p < 0.05$) and SWV $\leq$ 1.96 m/s (OR 5.41; 95% CI 1.51—18.96; $p < 0.01$).
Conclusion: TDF was effective for patients with HBV-related cirrhosis after treatment. Albumin concentration, HBV DNA load, Child–Pugh scores and SWV were four independent factors to predict improvement of the level of liver fibrosis a long-term antiviral treatment.

[PP-0559]

B-Clear: Design of a phase 2b multi-center randomized, participant-blinded, parallel cohort study to assess the efficacy and safety of bepirovirsen in patients with chronic hepatitis B virus infection

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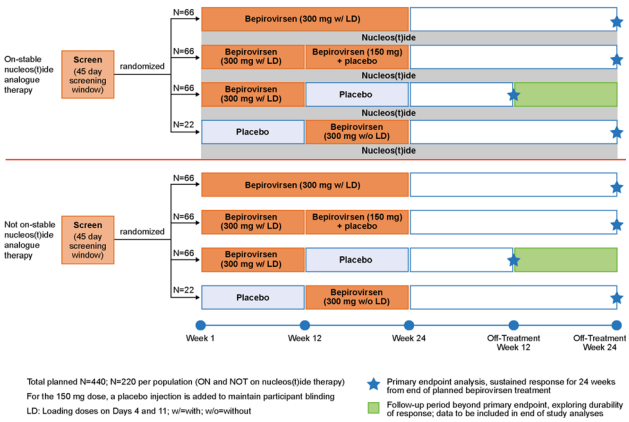
Objectives: To assess the efficacy and safety of bepirovirsen (GSK3228836) in adult patients with chronic hepatitis B virus (HBV) infection in the presence or absence of nucleos (t)ide analogue (NA) therapy (NCT04449029).
Materials and Methods: On-NA and not on-NA participants were randomized to one of four treatment arms (Fig. 1). Key inclusion criteria: chronic HBV infection $\geq$ 6 months prior to screening; either not on-NA or on stable NA $\geq$ 6 months before screening (on-NA); hepatitis B surface antigen (HBsAg) > 100 IU/mL; HBV DNA < 90 IU/mL and alanine aminotransferase (ALT) $\leq$ 2 X ULN (on-NA); HBV DNA > 2000 IU/mL and ALT < 3 X ULN (not on-NA). Exclusion criteria included: co-infection (hepatitis C/hepatitis D/HIV); cirrhosis; hepatocellular carcinoma. Analyses will be conducted separately for the on-NA and not on-NA populations. Primary endpoint: proportion of patients achieving sustained virologic response (HBsAg < lower limit of quantification [LLOQ] and HBV DNA < LLOQ sustained for 24 weeks after last planned bepirovirsen dose). Secondary endpoints include: proportion of patients with HBsAg/HBV DNA < LLOQ at end-of-treatment; ALT normalization; pharmacokinetics. Safety is assessed via adverse event monitoring.
Results: Unavailable (study ongoing).
Conclusion: The novel study design allows evaluation of different bepirovirsen dosing regimens, the effect of a loading dose, and sustained virologic response data beyond 24 weeks in a broad population of patients with chronic HBV infection. The placebo-first arm also enables assessment of safety/efficacy in the first 12 weeks. Enrolment has ended, and the last patient visit is expected March 2022.
Funding: GlaxoSmithKline (209,668).

Figure 1. B-Clear study design for the on- and not on-stable nucleos(t)ide analogue therapy populations



[PP-0562]

Immunogenetic diversity predicts viral control in chronic HBV (CHB) patients after discontinuation of direct antiviral treatment

Marianne Tuefferd[1], Chau-Ting Yeh[2], Marjolein Crabbe[1], Tsung-Hui Hu[3], Chi-Yi Chen[4], Rong-Nan Chien[5], Kuo-Liang Wei[6], Cheng-Yuan Peng[7], Wan-Long Chuang[8], Wei-Wen Su[9], Kung-Hao Liang[10,2], Anna Shen[1], Yu-Shuang Lin[1], Alessandro Di Cara[11], Jacques Bollekens[1], Kurt Spittaels[1], Jeroen Aerssens[1]

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Objectives: Specific human leukocyte antigen (HLA) genotypes are risk factors for many disease-related traits. Higher HLA genetic diversity may positively influence cancer immunotherapy efficacy and HIV-1 control. Here we studied whether genetic build-up of the HLA region in chronic hepatitis B patients (CHB) may predict viral control after discontinuation of direct antiviral (DA) treatment.
Materials and Methods: A multi-center, prospective study enrolled 186 CHB patients in their last year of DA treatment, with $\geq$ 2 year follow-up after treatment discontinuation. Virological relapse (VR) was defined as HBV DNA $\geq$ 2000 IU/mL, clinical relapse (CR) as VR with serum ALT $\geq$ 80 IU/L, and sustained clinical response (SCR) as absence of VR during the follow-up period. DNA samples were collected for HLA-typing. Beside allelic association, HLA evolutionary divergence (HED) score was derived.
Results: 161 patients experienced VR of whom 110 also had a CR, 6 experienced hepatic flare without VR, and 23 were considered as SCR. HLA-B*51, HLA-C*07 and HLA-C*15 alleles were predictive for onset of VR and SCR; none were associated with onset of CR. High HED score in classes I and II regions were protective against early onset of VR and CR and predictive for SCR. Regression model performance was improved when adding immunogenetic composite markers to established clinical covariates.
Conclusion: The significance of HLA class I and of high HLA evolutionary diversity for long term viral control in CHB patients is here demonstrated for the first time. Host immunogenetic markers are major contributors in predicting patient outcome when considering cessation of DA treatment.

[PP-0565]

Short interfering RNA JNJ-3989 combination therapy in chronic hepatitis B (CHB) shows potent reduction of all viral markers but no correlate was identified for HBsAg reduction and baseline factors

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Objectives: siRNA therapy with JNJ-3989 includes 2 triggers which silence all HBV RNA transcripts. In AROHBV1001 (phase 2a; NCT03365947), JNJ-3989 (3 monthly doses 25–400 mg) + nucleos (t)ide analogue (NA) demonstrated antiviral activity in patients with CHB. Here we assessed baseline factors associated with HBsAg reduction and compared the effect of JNJ-3989 against viral markers (HBsAg, HBeAg, HBcrAg, HBV RNA).
Materials and Methods: NA experienced or naïve, HBeAg $\pm$ ve CHB patients received 3 s.c. doses of JNJ-3989 100 (n = 8), 200 (n = 8), 300 (n = 16) or 400 mg (n = 8) Q4W. Patients started/continued with an NA from Day 1–392. Viral markers were assessed using standard assays.
Results: Treatment with JNJ-3989 + NA resulted in mean (range) HBsAg reductions from baseline at nadir of 1.93 (0.73, 3.84) $\log_{10}$IU/mL with 39/40 patients achieving $> 1\log_{10}$IU/mL reduction. Baseline HBsAg, treatment status (naïve vs NA suppressed), BMI, and HBV genotype had no impact on HBsAg reduction. Greater reduction in HBsAg was seen in HBeAg + ve vs HBeAg -ve patients, driven by HBeAg + ve females (n = 4) who showed the greatest HBsAg response. Pronounced reductions in HBeAg, HBcrAg and HBV RNA were observed; HBeAg and HBcrAg reductions were generally smaller than HBsAg. Reductions of different markers generally correlated within patients.
Conclusion: JNJ-3989 achieved potent reduction of all viral markers, with more pronounced reductions in HBsAg than other markers; HBsAg reduction was greater in HBeAg + ve compared to HBeAg -ve patients. Reductions in HBeAg, HBcrAg and HBV RNA generally correlated with HBsAg reductions. Findings are being validated in larger Phase 2b studies.

[PP-0575]

Efficacy and safety of tenofovir disoproxil orotate in chronic hepatitis B patients previously treated with tenofovir disoproxil fumarate: Multi-center, open label, prospective study

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Objectives: We aimed to demonstrate the efficacy and safety of tenofovir disoproxil (tenofovir disoproxil orotate, TDO) compared with that of tenofovir disoproxil fumarate (TDF) in patients with chronic hepatitis B.
Materials and Methods: This multicenter, open-label, prospective clinical trial (KCT0004185) was conducted to evaluate the efficacy and safety of TDO on switching from TDF for 24 weeks in virologically suppressed chronic hepatitis B patients. The primary efficacy endpoint was the maintenance of virologic response. Safety was assessed by evaluating major adverse events, changes in renal function, and occurrence of hepatocellular carcinoma (HCC).
Results: TDO treatment was not inferior in terms of virological response when compared with that on TDF treatment, with a non-inferiority margin of -10% (risk difference, -3.17%; 95% confidence interval, -7.5%–1.15%). The biological response of TDO was also comparable to that of TDF, with no significant difference in the proportion of patients with normalized alanine transaminase levels. After 24 weeks of treatment, hepatitis B core-related antigen (HBcrAg) significantly decreased to a mean titer of 3.91 log U/mL from 4.15 log U/mL at baseline (P = 0.01). There were no cases of

grade 3 or higher adverse events and HCC. The mean estimated glomerular filtration rate increased from 91.09 mL/min to 93.34 mL/min (P = 0.056), and the mean serum level of phosphorus increased from 3.33 mg/dL to 3.44 mg/dL (P = 0.045), suggesting improvement in renal function with TDO treatment.
Conclusion: In patients with chronic hepatitis B, the efficacy of TDO was non-inferior to that of TDF, with a significant decrease in the HBcrAg titer and improved renal function.

[PP-0596]

Epidemiology, clinical features and outcome of acute hepatitis B and Delta in Mongolia

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Objectives: To investigate the clinical and laboratory features and the rate of development to chronic infection in patients with acute hepatitis B and delta in adult patients.To investigate the clinical and laboratory features and the rate of development to chronic infection in patients with acute hepatitis B and delta in adult patients.
Materials and Methods: A total of 182 patients with acute hepatitis B (AHB) and acute hepatitis Delta (AHD) were enrolled and followed-up 12 months in this study. They admitted to the acute viral hepatitis unit at National Center for Communicable Diseases between January 2016 and January 2018. All laboratory tests were performed using standardized laboratory procedures at the Department of Laboratory of NCCD.
Results: A total of 182 participants (108 male, 74 female) enrolled, 59.3% were male. 105 patients were diagnosed with acute hepatitis B (AHB), five patients were diagnosed with HBV/HDV co-infection, and 72 patients were diagnosed with acute HBV/HDV super-infection on chronic hepatitis B. Mean age was 25.2 ± 6.1 years in AHB group, 30 ± 7.6 years in HBV/HDV super-infection group and 28.4 ± 2.2 years in HBV/HDV co-infection (p = 0.0001). In patients with AHB and HBV/HDV co-infection, the clinical symptoms completely disappeared and liver function tests returned to normal. HBV/HDV super-infection patients' recovery of clinical symptoms was 95.8%. Although, changes in liver function test findings were statistically significantly different comparing to other groups ALT (85.5 ± 125.8; 18.2 ± 36 vs 13.8 ± 6.5; p = 0.0001), AST (63.4 ± 67.1; 18.9 ± 19.2 vs 19.7 ± 9.6; p = 0.0001) by final follow-up. The chronicity rate was significantly higher in HBV/HDV super-infection patients than in AHB and HBV/HDV co-infection patients.
Conclusion: 6.7% of patients with acute hepatitis B virus infection, 40% of patients with HBV/HDV co-infection and 93.3% of patients with HBV/HDV super-infection developed chronic infection. In patients with AHB and HBV/HDV co-infection, the clinical symptoms and liver function tests were completely cleared.

[PP-0598]

The efficacy and safety of tenofovir alafenamide fumarate in Nucleos(t)ide analogue experienced chronic hepatitis B patient with sub-optimal response and LLV

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Objectives: To investigate the efficacy and safety of tenofovir alafenamide Fumarate (TAF) in Nucleos (t)ide Analogue (NA) experienced chronic hepatitis B (CHB) patients with sub-optimal response or low-level viremia (LLV).
Materials and Methods: This was a single-center, retrospective, real world study. 24 CHB patients with sub-optimal response (HBV DNA > 2000 IU/mL) and 67 patients with LLV (20 IU/mL.
Results: The complete virologic response (HBV DNA < 20 IU/mL) rate in sub-optimal response group were 29.1% and 75.0% after 24 weeks and 48 weeks, the CVR rates in LLV group were 76.1% and 88.1%, respectively. The patients in sub-optimal response group have experienced 17.7% and 41.0% decline of HBeAg level from baseline after switch to TAF in 24 weeks and 48 weeks; the decline of HBeAg level in LLV group were 41.0% and 47.3%, respectively. The patients in sub-optimal response group have experienced 9.0% and 5.0% decline of HBsAg level from baseline after switch to TAF in 24 weeks and 48 weeks, and the decline of HBsAg level in LLV group were 2.1% and 3.6%, respectively. The ALT normalization rate increased 24.2% after switch to TAF in 48 weeks compared to baseline level. There were no events of serious adverse reactions (SAE) or deaths due to AE.
Conclusion: The real-world study demonstrated that for NA experienced patients with sub-optimal response and LLV, switch to TAF is safe enough and has promising virologic and biochemical response rate.

[PP-0606]

Clinical usefulness of non-invasive fibrosis indices for predicting hepatocellular carcinoma in treatment-nave patients with chronic hepatitis B following entecavir therapy

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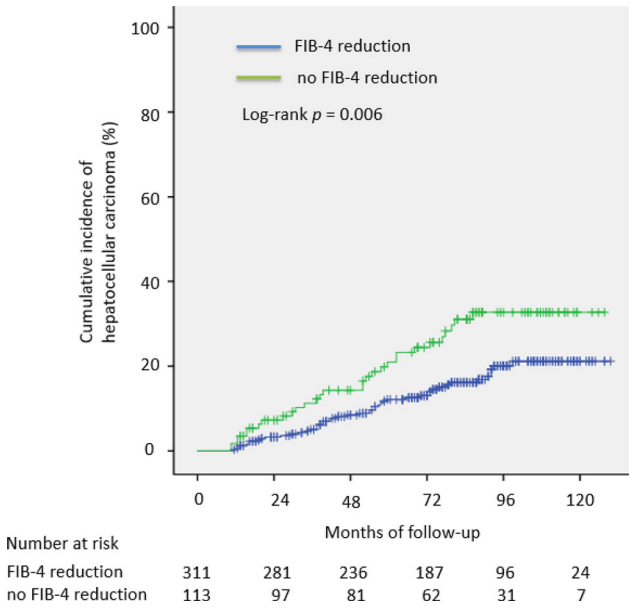
Objectives: This study aimed to evaluate the clinical usefulness of the aminotransferase to platelet ratio index (APRI), fibrosis-4 (FIB-4) and modified FIB-4 (m FIB-4) indices in predicting hepatocellular carcinoma (HCC) in patients receiving entecavir (ETV) treatment.
Materials and Methods: Among 1955 patients treated with ETV, a total of 857 treatment-naive CHB patients (liver cirrhosis [LC] 424, non-cirrhosis 433) treated with ETV for > 1 year were analyzed.
Results: Of the 857 patients, 85 (9.9%) patients (77 in LC group and 8 in non-LC group) developed HCC during the follow-up period. The median observation period was 6.9 years. Multivariate regression analysis of HCC incidence revealed that the initial mFIB-4 index (Hazard ratio [HR] 1.058, 95% confidence interval [C.I.] 1.007 –

1.112, P = 0.027) and the improvement in the FIB-4 index after 1-year of ETV treatment (HR 0.531, 95% C.I. 0.339 – 0.831, P = 0.006) were independent prognostic factors in the entire cohort. In the LC group, the improvement of the FIB-4 index following ETV treatment (HR 0.491, 95% CI 0.280 – 0.861, P = 0.013) was negatively correlated with incidence of HCC. However, in the non-LC group, none of the invasive fibrosis indices could not predict HCC incidence. The cumulative incidence of HCC for 3, 5, 7-years was 2.5%, 5.4% and 7.0%, respectively, for patients with a reduced FIB-4 index; 5.7%, 10.0%, and 14.3%, respectively, for patients with no reduction in their FIB-4 index.
Conclusion: The specific cut-off value of the FIB-4 index was not suitable for predicting HCC. However, the improvement in the FIB-4 index after 1-year of ETV therapy could be a predictor of HCC development in cirrhotic patients.



[PP-0611]

The effects of tenofovir alafenamide on the lipid profile in a cohort of CHB patients; Comparison with healthy control subjects using propensity score-matching

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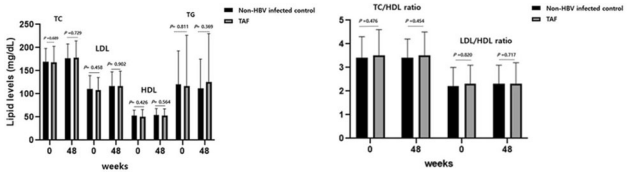
Objectives: Tenofovir alafenamide (TAF) has a less favorable effect on lipids in clinical trials. However, data regarding these outcomes in patients with chronic hepatitis B (CHB) in real-life practice are scarce. The effect of TAF on lipid profile in patients with CHB, compared with general health check-up individuals was investigated.
Materials and Methods: This study is to evaluate the effects of TAF on the lipids of 237 CHB patients, compared with 3853 non-HBV infected healthy control groups, using propensity score-matching (PSM).
Results: Following 1: 4 PSM, an analysis was conducted on cohorts with matching of 140:560 (TAF: non-HBV infected healthy control). The mean ± SD of the TC level at 48 weeks in the healthy control and TAF groups was 172.6 ± 31.2 and 173.4 ± 33.2, respectively (P = 0.805). Upon comparison of changes of TC level at 48 weeks, there was no significant difference between groups. (3.99 ± 26.48, 4.72 ± 25.70, P = 0.768). In the healthy control-matched cohort, 45 TAF and 180 healthy control subjects had detailed lipid profiles. Upon comparing TC, LDL-C, HDL-C, TC/HDL-C ratio, and LDL-C/HDL-C ratio between two groups at 48 weeks, no significant differences were observed between the healthy control and the TAF groups.
Conclusion: TAF might not worsen lipid profiles in real practice, comparing with non-HBV infected healthy control.



[PP-0614]

Comparison of lipid changes in TAF-treated patients and inactive CHB patients; A propensity score-matched analysis

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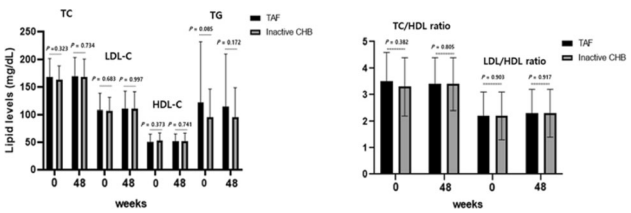
Objectives: To date, no study has assessed lipid profile changes by TAF therapy in patients with CHB in real-life practice. In order to clarify the effect of TAF on the lipid profile, it may be more suitable for comparing with inactive CHB subjects, rather than simply comparing with matched-healthy group.
Materials and Methods: This study is to evaluate the effects of TAF on the lipids of 237 CHB patients, compared with 150 inactive CHB group, using propensity score-matching (PSM).
Results: Following 1:1 PSM, we compared TC at baseline and 48 weeks for TAF and inactive CHB groups. The mean ± SD of the TC level at baseline in the TAF (n = 89) and inactive CHB groups (n = 89) was not significantly different between groups at 48 weeks. Upon comparison of the changes in TC levels at 48 weeks, no significant differences were observed between groups. Among the 1:1 PS-matched cohort, 56 patients each in the TAF and inactive CHB groups had detailed lipid profiles. Upon comparing TC, LDL-C, HDL-C, TC/HDL-C ratio, and LDL-C/HDL-C ratio between two groups at 48 weeks, no significant differences were observed between the TAF and inactive CHB groups (P = 0.734, 0.997, 0.741, 0.172, 0.805, and 0.917, respectively).
Conclusion: Upon comparison with the inactive CHB subjects who were not treated with anti-viral therapy, TAF might not worsen the lipid profiles in real clinical practice.



[PP-0617]

Epidemiology and prevalence of HBV and HCV in the 40–64 age population of Mongolia

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Objectives: The aim of our study is to determine the prevalence of hepatitis B and C among the 40–64 years of age population, including the capital city and countryside, assessing liver function by measuring AST and ALT, and identifying liver fibrosis M2BPGI marker levels in all participants.
Materials and Methods: We identified HBV and HCV by using a high-sensitivity CLEIA method, covering 3196 people aged 40–64 which is the innovation of our research. In order to reflect the administrative and geographical features of Mongolia, the sampling was done at three levels: urban, province center, and rural. Immunological test was measured by chemiluminescence enzyme immunoassay (CLEIA). The statistical package for the social sciences (SPSS) version 25 was used for the statistical analyses.
Results: The survey covered 3196 people. 71.8% of the patients surveyed had anegativeinhepatitis test.10.1% had a positive HBsAgtest. 17% had a positive anti-HCVtest. 1.1% had both a positive both HBsAg and anti-HCV (< 0.0001). AST and ALT increased more frequently duringco-infection. M2BPGI protein average level in thenon-infected group was 1.00 C.O.I, in the HBsAg positive group 1.65 C.O.I, in theanti-HCV positive group 1.83 C.O.I, and in thecoinfection group 1.87 C.O.I (< 0.0001).
Conclusion: 10.1% of 40–64 year-olds in Mongolia were infected with hepatitis B virus, and 17% had Hepatitis C virus and 1.1% had hepatitis B and C virus co-infections. Serum M2BPGi is increasing in hepatitis C virus infection and in co-infection.

[PP-0618]

Comparison of lipid changes in the tenofovir disoproxil fumarate (TDF)-treated patients and non-HBV infected healthy control group

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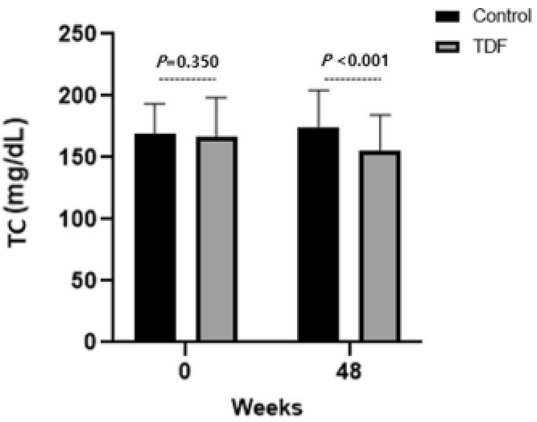
Objectives: Previous studies regarding human immunodeficiency virus (HIV) treatment have shown that the HIV treatment regimen, including TDF, has consistently been associated with lower lipids compared to the healthy volunteers. However, data regarding these outcomes in patients with chronic hepatitis B (CHB) are scarce.
Materials and Methods: This study is to evaluate the effects of TDF on the lipids of 884 CHB patients, compared with 3698 non-HBV infected healthy control group, using propensity score-matching (PSM).
Results: Following 1:4 PSM, we compared the TC level at baseline and 48 weeks of TDF and non-HBV infected healthy control groups. The mean ± SD of the TC level at baseline in the non-HBV infected healthy control (n = 1472) and TDF groups (n = 368) was 169.1 ± 24.6 and 167.5 ± 24.6, respectively (P = 0.292); the mean ± SD of the TC level at 48 weeks in the healthy control and TDF groups was 175.0 ± 29.5 and 156.2 ± 28.3, respectively (P < 0.001). Upon comparison of the changes in TC levels at 48 weeks, there was a significant difference between groups (5.8 ± 23.4, − 11·3 ± 27.3, P < 0.001). At baseline, the number of patients with TC > 240 mg/dL in the control and TDF groups was nine (0.6%) and three (0.8%), respectively (P = 1.000). However, at 48 weeks, the number of patients with TC > 240 mg/dL in the control and TDF groups were 24 (1.6%) and one (0.3%), respectively (P = 0.043).
Conclusion: TDF-treated patients had a significantly lower TC level than the non-HBV infected healthy control group.



[PP-0619]

The effects of tenofovir alafenamide on the lipid profile in a cohort of CHB patients; Comparison with tenofovir disoproxil fumarate (TDF)-treated patients using propensity score-matching

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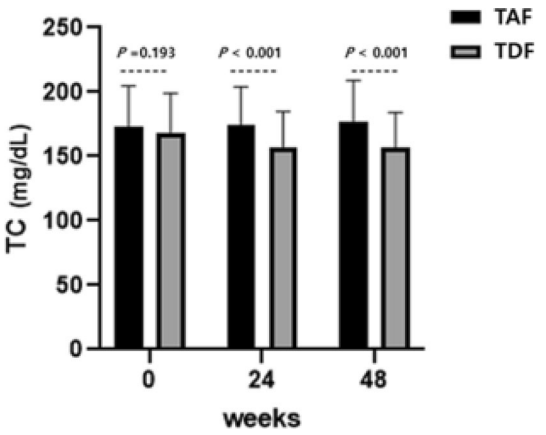
Objectives: Tenofovir alafenamide (TAF) has a less favorable effect on lipids compared to TDF (Tenofovir disoproxil fumarate) in clinical trials. However, data regarding these outcomes in patients with chronic hepatitis B (CHB) are scarce.
Materials and Methods: This study is to evaluate the effects of TAF on the lipids of 237 CHB patients, compared with 884 TDF, using propensity score-matching (PSM).
Results: Following 1:2 PSM, we compared TC at baseline and 48 weeks for TAF and TDF groups. The mean ± SD of the TC level at baseline in the TAF (n = 70) and TDF groups (n = 140) was not significantly different between groups at baseline (P = 0.193); however, there was a significant difference at 48 weeks between groups

($P < 0.01$) (Table 4; S Fig. 1C). Upon comparison of the changes in TC levels at 48 weeks, significant differences were observed between groups (-11.9 ± 26.5, 2.88 ± 25.2, $P < 0.001$). Notably, the TAF group had a higher proportion of patients with ALT normalization and VR12 than did the TDF group at 48 weeks; however, it did not show any statistical significance between groups (76.7% vs 85.9%, P = 0.086; 81.5% vs 89.5%, P = 0.069, respectively).
Conclusion: TDF-treated patients seemed to have a lipid lowering effect compared with TAF-treated patients.



[OP-0635]

Perception of disease, well-being and financial burden in self-reported assessment of patients with chronic hepatitis B

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Objectives: Though prevalence of hepatitis B in Asia has reduced with universal vaccination, it remains a cause of concern in the older population. This study aims to look at patients' perspectives, well-being and financial burden of patients with chronic hepatitis B.
Materials and Methods: A self-reported questionnaire was administered to 520 hepatitis B patients on follow-up at Singapore General Hospital Department of Gastroenterology and Hepatology, a tertiary care center. The questionnaire collated demographics, perception, burden of disease in terms of financial, emotional and loss of productivity in patients and their caregivers.
Results: Amongst 520 patients surveyed, 194 patients were on treatment (OT) and 326 were not on treatment (N-OT) for hepatitis B. Mean age was 56.8 ± 12.6 years. 77.5% of patients rated regular blood tests as very important, however many were unsure of the exact indications and implications of the results. 22.4% and 16.0% of respondents rated their general and emotional health respectively as fair/ poor. Self-reported financial difficulty is higher in the OT group than the N-OT group (38.7% vs 19.4%, $p < 0.001$), with greatest financial impact of treatment felt on the lower educational groups. 14.3% of the patients reported the need for a caregiver to accompany them for hospital appointments, higher in the OT group than the N-OT group (20.2% vs 10.7%, $p < 0.001$).
Conclusion: From a patient's perspective, hepatitis B has impacts on their financial, general and emotional wellbeing. Financially, patients with lower education are affected more than those with higher education. Also, awareness of purpose of blood tests and follow-up has to be improved.

[PP-0644]

Clinical and epidemiological characteristics of chronic hepatitis D in Kazakhstan

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Objectives: The aim of this study was to characterize the clinical profile of patients with chronic hepatitis D (CHD) and the response to standard antiviral therapy (AVT) in the Republic of Kazakhstan within the National Roadmap on prevention, diagnostics treatment of parenteral viral hepatitis.
Materials and Methods: These were National epidemiological cohort and retrospective descriptive study in 139 patients with CHD (2015–2020). Routine clinical data, biochemical, serologic, virologic profile, instrumental examination (ultrasound, transient elastography) as well as response to AVT with Pegylated interferon alpha-2a (Peg-IFN alpha-2a) were analyzed.
Results: 2,389 patients with CHD were listed in the National Registry, of which 1,413 (59.1%) were men, 976 (40.9%) were women, mainly the residents of Southern regions (Kyzylorda, Turkestan, Almaty). Among the 139 patients studied, the average age was 47.55 ± 11.87 years. With the use of transient elastography, severe fibrosis or liver cirrhosis were diagnosed in most of them (56.7%). Out of 55 patients received standard AVT with Peg-IFN alpha-2a, 14 (25.5%) achieved an undetectable level of HDV RNA at the end of therapy and 6 of them relapsed within a year after completion of therapy. In total, only 8 out of 55 patients (14%) maintained virologic response one year after AVT.
Conclusion: In the Republic of Kazakhstan, CHD is predominantly diagnosed in young and middle-aged patients (men and women alike) and characterized by the prevalence of severe disease (severe fibrosis and liver cirrhosis) with low response to AVT and high risk of early and late relapse.

[OP-0668]

Evaluating hepatitis delta virus testing patterns and disease prevalence among a large cohort of veterans with chronic hepatitis B infection in the United States

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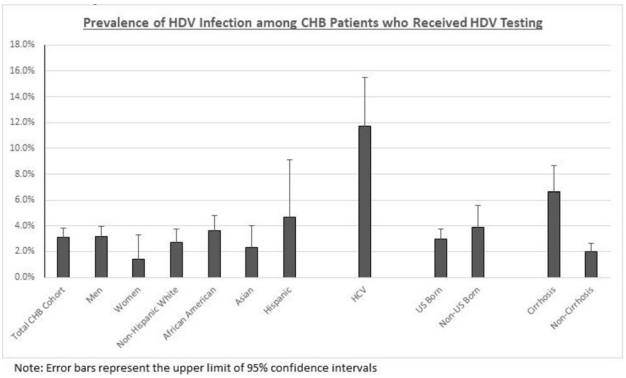
Objectives: Hepatitis Delta virus (HDV) infection in patients with chronic hepatitis B (CHB) is associated with significantly greater risk of cirrhosis and hepatocellular carcinoma. We aim to evaluate HDV testing patterns and disease prevalence among a national cohort of U.S. veterans with CHB.
Materials and Methods: Using the Veterans Affairs (VA) Corporate Data Warehouse, comprehensive national data on U.S. veterans receiving healthcare within VA health systems was evaluated from 2010 to 2020 to identify adults with CHB using combination of laboratory results and ICD-9/10 diagnosis coding. HDV prevalence among CHB patients was assessed with anti-HDV antibody, HDV antigen, and HDV RNA. HDV testing patterns and disease prevalence among CHB patients were stratified by age, sex, race/ethnicity, country of birth, presence of cirrhosis, and concurrent HIV or HCV. Comparison of HDV testing and HDV prevalence between groups used chi-square testing.
Results: Among 12,002 adults with CHB (6.1% female, 64.5% age > 60y, 39.1% non-Hispanic white (NHW), 41.7% African American, 10.4% Asian, 2.3% HIV, 15.0% HCV, 14.0% non-U.S. born), 29.5% had cirrhosis. Overall, 19.7% (95% CI 19.0–20.4) of CHB patients received testing for HDV infection, among which HDV prevalence was 3.1% (95% CI 2.4–3.8). HDV testing was similar by sex, but was significantly higher in Hispanics (39.4% vs. 19.6% in NHW, $p < 0.001$), Asians (24.1% vs. 19.6% in NHW, $p < 0.001$), non-U.S.-born (28.6% vs. 18.4% in U.S.-born, $p < 0.001$), and in patients with cirrhosis (20.8% vs. 15.8% in non-cirrhosis, $p < 0.001$). The highest prevalence of HDV infection in CHB patients was observed in Hispanics (4.7%), patients co-infected with chronic HCV (11.7%), and patients with underlying cirrhosis (6.6%) (Figure).
Conclusion:.Among a large cohort of U.S. Veterans, only 19.7% of CHB patients received any form of HDV testing. Among those tested for HDV, overall prevalence was 3.1%, but was noted to be significantly higher in patients with underlying cirrhosis and chronic HCV co-infection.



Note: Error bars represent the upper limit of 95% confidence intervals

[OP-0671]

The prevalence of hepatitis B, hepatitis D and associated risk factors in American

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Objectives: To estimate the prevalence of hepatitis B, Hepatitis D and associations with relevant risk factors in American.
Materials and Methods: A cross-sectional study was undertaken using a nationally representative sample of U.S. population. Serum samples were processed, stored, and shipped to the Centers for Disease Control and Prevention for analysis. Data on risk factors were collected by blood tests and questionnaire found on the NHANES website. Associations between risk factors and the prevalence were estimated using multivariable logistic regression.
Results: During 1999–2018, 0.4% (95% CI 0.4–0.5%) of noninstitutionalized civilian adults in the United States, approximately 1.2 million persons, were reported for hepatitis B surface antigen (HBsAg) positive, and 4.2% with hepatitis B core antibody (HBcAb) positive, and an estimated 28.2% Hepatitis B surface antibody (HBsAb) positive persons, while 0.1% (95%CI 0.1–0.1%) of all adults, approximately 0.3 million persons, was present in hepatitis delta virus antibodies (anti-HDV) positive. The prevalence of HBsAg-positive were significantly increased in Americans of 0.3% from 1999 to 2008 compared to 0.5% from 2009 to 2018 (OR 2.09). In comparison to HBV infection alone, HBV/HDV coinfection is associated with serologic evidence among Americans with a history of marijuana or hashish, cocaine, heroin, and methamphetamine, as well as intravenous use of these and other drugs (OR 2.29).
Conclusion: A high prevalence of Hepatitis B and Hepatitis D were observed among Americans, while the. Drug-using history was the most consistent risk factor for Americans.

Table 1: Prevalence of Hepatitis B and Hepatitis D in American

Year	Number of patients aged 6 years or above (n)	Number of patients detected the presence of HBsAg(n)	Number of patients with HBsAg-positive(n)	Weighted prevalence (%)	(95%CI)	Number of patients detected the presence of HBcAb(n)	Number of patients with HBcAb-positive(n)	Weighted prevalence (%)	(95%CI)	Number of patients detected the presence of HBsAb(n)	Number of patients with HBsAb-positive(n)	Weighted prevalence(%)	(95%CI)	Number of patients detected the presence of anti-HDV(n)	Number of patients with anti-HDV-positive (n)	Weighted diagnosis rate(%)	(95%CI)
1999-2008	42773	37259	95	0.3	(0.2 - 0.3)	37259	1732	4.5	(4.5 - 4.6)	37243	11826	26.2	(26.1 - 26.2)	37259	5	0.00	(0.0 - 0.0)
2009-2018	41792	23456	175	0.5	(0.4 - 0.5)	36525	2126	4	(4.0 - 4.0)	36471	10560	27.5	(27.4 - 27.5)	23454	49	0.1	(0.1 -0.2)
1999-2018	84565	60715	270	0.4	(0.4 - 0.4)	73784	3858	4.2	(4.1 - 4.3)	73714	22386	26.9	(26.8 - 26.9)	60713	54	0.1	(0.1 - 0.2)

Note：Prevalence rates of HBsAg-positive、HBcAb-positive、HBsAb-positive and anti-HDV-positive in people aged 6 years or above

[OP-0672]

Electronic medical records-based big-data analyses of higher ALT elevation in patients with or without HBV infection

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Objectives: Hepatitis B virus (HBV) infection is one of the serious health problems in the world as HBV infection causes acute hepatitis, chronic hepatitis, cirrhosis and hepatocellular carcinoma. Acute liver failure is also caused by HBV infection and could lead to fatal

outcomes. In patients with resolved HBV infection using immunosuppression and anticancer drugs, HBV reactivation has occasionally occurred and could also lead to fatal outcomes.
Materials and Methods: Large-scale hospital data focused on HBV infection and severe alanine transaminase (ALT) elevation were analyzed at the regional hospital near Tokyo, Japan. More than 99,000 individuals whose blood samples were taken at more than 7,170,000 opportunities were analyzed.
Results: HBV surface antigen (HBsAg)-positive group had a more frequent prevalence of patients with higher ALT elevation than the HBsAg-negative group. However, among the HBsAg-negative group, patients who were positive for anti-HBV surface antibody and/or anti-HBV core antibody, had more severe liver diseases and fatal outcomes.
Conclusion: More careful attention should be paid to severe ALT elevation in patients who had current and history of HBV infection.

[PP-0674]

The surrogate marker for chronic hepatitis B flare between HBsAg and HBcrAg

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Objectives: Serum levels of hepatitis B core-related antigen (HBcrAg) have been reported with HBV active replication and HCC development. Here, we investigate its role in patients who had been received antiviral treatment.
Materials and Methods: 103 adults with HBV infection received antiviral treatment were enrolled, who had long-term follow-up at Lin-kou branch, Chang Gung Memorial Hospital from 2001 through 2019. HBV DNA, HBsAg, AST, ALT and HBcrAg were checked retrospectively.
Results: In this study we found that HBcrAg has low titer in post success treatment and anti-HBe positive group ($p < 0.0001$). HBcrAg has no significant in hepatocellular carcinoma group. HBcrAg also has strong association with elevated serum AST/ALT and HBV-DNA level ($p < 0.05$). We find that the predictability of HBsAg and HBcrAg are very similar (AUC = 85.49%). The correlation of HBsAg and HBcrAg concentrations are linearly correlated with R-squared equals 0.7056. Furthermore, the HBsAg for Roche and Fujiebio exhibit a linear relationship with R-squared equals 0.9734.
Conclusion: Level of HBcrAg is a good surrogate predict marker for post HBV anti-viral therapy and might strengthen help serum HBV-DNA level monitor in patients during or cessation of anti-viral therapy.

[PP-0691]

A pulse check on general publics knowledge, awareness, and attitudes towards liver health in South Korea

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Objectives: The 2013 Korean Liver Association Survey revealed a suboptimal level of awareness and knowledge among the general public towards liver health and diseases, sparking progressive reform of policies and education efforts in South Korea. This study aims to assess any improvement of the public's knowledge towards liver-related diseases.
Materials and Methods: A self-reported, cross-sectional study among 1,000 adult individuals (age and gender reflective of the national population) was conducted between February–March 2020. Items assessing knowledge, awareness, and attitudes towards liver-related health and diseases were administered via a 30-min web-based questionnaire.
Results: About half knew untreated/chronic viral hepatitis could lead to liver failure and/or cancer, and liver cirrhosis/fibrosis being key determinants of liver disease progression. Majority agreed regular screening (96%) and getting vaccinated (90%) were ways to protect liver health. This contrasted with 76% self-reported attended health screening within recent 2 years, 67% knowing hepatitis B (HBV) is preventable by vaccination (43.3% self-reported being vaccinated in 2013), and 16% aware hepatitis C (HCV) cannot be prevented by vaccination. Misperceptions pertaining to transmission risks hint at the presence of stigma and discrimination within the community. About one-quarter (26%) rightly identified dining with an infected individual could not transmit HBV (37% in 2013). Apart from cost-related concerns, reasons for low urgency towards seeking medical consultation upon risk-factor exposure or diagnosis included perceptions of being healthy or the condition is not life-threatening. Furthermore, only 22% (82% in 2013) were aware of available treatments for curing HCV infection.
Conclusion: The findings highlighted a possible deterioration of public's knowledge towards liver-related health and diseases in South Korea. The limited public's knowledge towards liver diseases potentially account for the low urgency towards seeking medical consultation, therefore implying an unmet need for more efforts to address misperceptions and dispel stigma, encouraging screening among high-risk populations, within the community.

[PP-0701]

Hepatitis B surface antigen kinetics after nucleos(t)ide analogues cessation and in subsequent retreatment in noncirrhotic chronic hepatitis B patients

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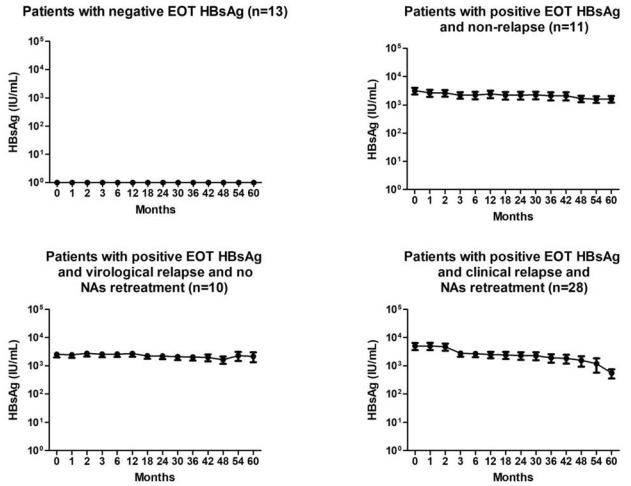
Objectives: Hepatitis B virus (HBV) infection remains a global public health problem. The study aimed to investigate hepatitis B surface antigen (HBsAg) kinetics after nucleos(t)ide analogues (NAs) cessation and in subsequent retreatment in noncirrhotic chronic hepatitis B (CHB) patients.
Materials and Methods: This was a prospective study. Noncirrhotic CHB outpatients receiving NAs treatment were enrolled and NAs treatment was stopped in this study. After enrollment, patients'

demographic, clinical and laboratory data were collected from baseline to each follow-up. All patients were monitored monthly for the first 3 months after NAs cessation, and every 3 months thereafter.
Results: A total of 104 noncirrhotic CHB patients receiving NAs treatment were enrolled and finally 62 patients who finished 5 years follow-up were included in this study. HBsAg kinetics after NAs cessation were shown in Fig. 1. HBsAg remained undetectable in 13 patients with negative end of treatment (EOT) HBsAg. For 49 patients with positive EOT HBsAg, 9 (18.4%) patients achieved HBsAg seroclearace, and proportion of patients with HBsAg level of $\leq$ 1000 IU/mL increased in the follow-up. The optimal cutoffs of EOT HBsAg level to virological relapse and HBsAg seroclearance were 186 IU/mL and 359 IU/mL, respectively. Comparing to EOT HBsAg level, end of follow-up (EOF) HBsAg level decreased more than 1 log10 IU/mL in 13 (26.5%) out of 49 patients with positive EOT HBsAg.
Conclusion: HBsAg seroclearance rate is high and proportion of patients with HBsAg level of $\leq$ 1000 IU/mL increased in the course of follow-up after NAs cessation. Lower EOT HBsAg level contributes to lower relapse rate and higher HBsAg seroclearance rate.



[PP-0708]

Role of HBs Ag quantification for predicting HCC risk in patients treated with TDF or ETV

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Objectives: This study evaluated the clinical implications of hepatitis B surface antigen quantification (qHBs Ag) in chronic hepatitis B (CHB) patients treated with entecavir or tenofovir and identified the association between qHBs Ag and the risk of hepatocellular carcinoma (HCC) in these patients.
Materials and Methods: Between January 2007 and December 2020, the qHBs Ag and clinical data of 212 CHB patients who initially received ETV or TDF were analyzed.
Results: The mean follow-up period of the 212 CHB patients was 47 months, of which 64 patients showed a reduction in qHBs Ag by more than 50% after one year of antiviral treatment. The HCC development or qHBs Ag reduction were similar in the ETV and TDF groups. Patients with a 50% or more decrease in qHBs Ag had a significantly lower incidence of HCC or decompensated cirrhosis complications than those with a less than 50% decrease or rather an increase in qHBs Ag. Multivariate analysis showed that a more than 50% reduction of qHBs Ag and the presence of cirrhosis were independent factors predicting the development of HCC.
Conclusion: HBs Ag level decreased gradually during ETV and TDF therapy in both HBe Ag-positive and -negative CHB patients, and a significant decrease (50% or more) in the HBs Ag level during ETV and TDF treatment may indicate a lower risk of critical events, particularly HCC development. Therefore, monitoring the changes in HBs Ag level during ETV and TDF treatment may provide useful information for predicting the risk of complications in both HBe Ag-positive and -negative treatment-naive CHB patients.

[OP-0732]

Adherence to hepatocellular carcinoma surveillance in patients with chronic hepatitis B infection in the Super Tertiary Hospital

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Objectives: According to international guidelines, imaging should be performed every six months in patients with chronic hepatitis B (CHB) for hepatocellular carcinoma (HCC) surveillance. Prior reports, however, showed that overall adherence was still low. The adherence rate of HCC surveillance in Thai CHB patients is unknown.
Materials and Methods: We conducted a retrospective cohort study including CHB patients who were followed up $>$ 1 year at our center, a tertiary care hospital in Thailand, between 2011–2019. The patients who had the diagnosis of HCC within 6 months of the first visit were excluded. The HCC surveillance adherence rate was calculated using percentage of time up-to-date with HCC surveillance (PTUDS).
Results: Of 532 eligible patients, the mean age at HCC surveillance commencement was 55.5 ($\pm$ 9.25) years. The most common indication for surveillance was male aged over 40 (41.2%), followed by female aged over 50 (28.9%), and cirrhosis (22.6%). The median PTUDS in our cohort was 70.3% (IQR: 53.6–81.3%). Cirrhosis was the indication with the highest rate of PTUDS (70.9%). The highest PTUDS among physicians' subspecialty was gastroenterology specialists (67.3%), whereas the mean PTUDS among internists were 48%. In the multivariable linear regression analysis, cirrhosis indication and gastroenterology subspecialty were independently associated with higher adherence rates with rates of + 6.60% ($p = 0.002$) and + 20.5% ($p < 0.001$), respectively. There was no significant difference in PTUDS regarding reimbursement status, family history of HCC, and comorbidities. All of the eligible patients had a good compliance with the imaging ordered.
Conclusion: HCC surveillance is well adhered to in Thailand's university-based hospital. There is still a gap in non-gastroenterology physicians' adherence to HCC surveillance. This study emphasizes the importance of education regarding HCC surveillance indications, particularly in non-cirrhotic patients.

Factors Associated With HCC Surveillance

Variables	Univariable analysis		Multivariable analysis	
	Beta coefficient (95% CI)	P values	Beta coefficient (95% CI)	P values
Male Sex	-0.63 (-4.23 to 2.96)	0.73		
Age at diagnosis	0.11 (-0.03 to 0.26)	0.15		
Age at surveillance	0.20 (0.01 to 0.39)	0.04*	0.12 (-0.07 to 0.30)	0.21
Reimbursement		0.14		
Universal Coverage	Reference			
Civil Servant	3.91 (-0.18 to 8.00)			
Social Security	5.80 (-4.52 to 16.1)			
Family History of HCC[1]	-1.64 (-7.33 to 4.05)	0.57		
Indication		0.001*		0.002
Non-cirrhosis	Reference		Reference	
Cirrhosis	7.01 (2.75 to 11.3)		6.60 (2.48 to 10.72)	
Underlying Diseases				
HTN	-2.05 (-6.50 to 2.40)	0.37		
DM	-1.77 (-7.04 to 3.50)	0.51		
CVD	8.71 (-5.17 to 22.6)	0.22		
CKD	-2.35 (-17.1 to 12.4)	0.75		
Stroke	8.42 (-33.0 to 49.8)	0.69		
Cancer[2]	2.37 (-6.10 to 10.8)	0.58		
HBV/HCV co-infection	-3.00 (-14.5 to 8.50)	0.61		
HIV	-23.1 (-35.6 to -10.7)	<0.001*	-11.1 (-23.5 to 1.19)	0.08
Specialties		<0.001*		<0.001
IM	Reference		Reference	
GI	19.6 (14.2 to 25.1)		20.5 (15.1 to 25.9)	

1: 1st Degree Relatives, 2: All cancers except HCC
IM: Internal Medicine, GI: Gastroenterology and Hepatology

[OP-0741]

Health-related quality of life in Thai chronic hepatitis B patients

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Objectives: Chronic Hepatitis B (CHB) results in various complications and impaired health-related quality of life (HRQoL). Health state utilities (HSU) and HRQoL are the fundamental input to decision models and economic evaluation analysis. The effect of CHB infection on HRQoL has not been well established in the Thai population. We collected data in the aspect of HRQoL across any stage of CHB infection.
Materials and Methods: CHB patients in various stages who were followed up at a super-tertiary care center between March 2021 and September 2021 were invited to participate in this cross-sectional study. Participants completed the EQ-5D-5L questionnaire and gave their demographic data, e.g., age, sex, and marital status. Medical records were reviewed to determine the disease stage and other helpful information. HSU were calculated from EQ-5D-5L using the conversion coefficients explicitly developed for the Thai population.
Results: A total of 352 patients were recruited: 201 had no cirrhosis; 76 had compensated cirrhosis; 11 had decompensated cirrhosis; 42 had early or intermediate stage hepatocellular carcinoma (HCC); and 22 had advanced or terminal stage HCC. The HSU for various CHB stages were 0.96, 0.90, 0.77, 0.91, and 0.54 for non-cirrhotic, compensated cirrhosis, decompensated cirrhosis, early/intermediate stage HCC, and advanced/terminal stage HCC patients, respectively. The HRQoL scores using a visual analog scale were shown in the Table.
Conclusion: The HRQoL of patients with CHB infection is more impaired in the later stages of the disease. Decompensated cirrhosis and advanced/terminal stage HCC affect physical health and quality of life, while compensated cirrhosis and early/intermediate stage HCC patients still have pretty high HRQoL.

[OP-0758]

Concordance and impact factor of two different sensitivity serum HBV DNA detection assays in HBV infection patients: A cross-sectional study

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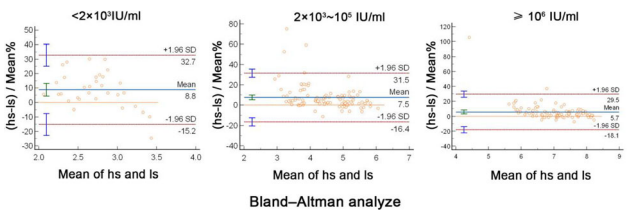
Objectives: Although various treatment guidelines have recommended the high-sensitivity (hs) HBV DNA assays (detection limit: 5 ~ 10 IU/ml) during the diagnosis and treatment of chronic hepatitis B (CHB) patients, still a large percentage of patients in China use the low-sensitivity (ls) assays (detection limit: 50 ~ 500 IU/ml) for economic reasons. We aimed to evaluate the consistency and influential factors between hs and ls HBV-DNA assays.
Materials and Methods: 511 patients whose plasma HBV-DNA tested with both hs and ls assays (detection limit: 20 IU/ml and 100 IU/ml, respectively) simultaneously were included in this study. The consistency among the two assays was evaluated by the Kappa coefficient, the intra-class correlation coefficient (ICC), and the Bland–Altman approach. We also performed stratified analyses separately for their HBV-DNA levels. For the sample that HBV-DNA negative (ls), we analyzed the differences in detection rates (hs as a standard assay) in different alanine aminotransferase (ALT), Hepatitis B e antigen (HBeAg), and quantitative Hepatitis B surface antigen (HBsAg) groups using the Chi-square test.
Results: The Kappa coefficients of the two assays is 0.499 ($p < 0.0001$) in all samples, but in HBV DNA < 2000 IU/ml sample (hs) it is 0.192 ($p < 0.0001$). The ICC was 0.5432, 0.7996, and 0.6563 in $< 2 \times 10^3$, $2 \times 10^3 \sim 10^5$, and $\geq 10^6$ IU/ml (hs) group, respectively (p-value all < 0.0001). Bland–Altman approach suggested similar results. For the HBV-DNA negative (ls) samples, the detectable rates (hs) were significantly higher in HBsAg ≥ 1000 IU/ml group and ALT > upper limit of normal (ULN) group compared with HBsAg < 1000 IU/ml and ALT ≤ ULN group ($\chi^2 = 6.67$, $p < 0.0001$ and $\chi^2 = 5.00$, $p = 0.0254$, respectively).
Conclusion: The two assays agreed well only in medium HBV-DNA ranges. Low HBV-DNA level associated with worse consistency for both assays. We should consider the high sensitivity HBV-DNA assay in the low HBV-DNA, abnormal ALT, HBeAg positive, or high HBsAg level CHB patients.



[OP-0768]

Direct-acting antivirals and the risk of hepatitis B reactivation in hepatitis B and C coinfected patients: A systematic review and meta-analysis

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Objectives: Hepatitis B virus (HBV) reactivation may occur in chronic hepatitis C (CHC) coinfected patients using direct-acting antivirals (DAAs). However, previous studies have reported inconsistent findings on this issue. We investigated the association between DAA and HBV reactivation by conducting a meta-analysis.
Materials and Methods: Relevant studies were identified by searching Medline, EMBASE, Cochrane Central Register of Controlled Trials, KoreaMed, KMbase, and RISS to September 4th, 2020. The primary outcome was HBV reactivation. Random effect method was used for pooling the data.
Results: We identified 39 articles, comprising 119,484 patients with chronic (n = 1,673) or resolved (n = 13,497) HBV infection who treated with DAA. When all studies were pooled, the rate of HBV reactivation was 12% (95% confidence interval (CI) 0.06–0.19). When stratified by baseline HBV DNA, undetectable HBV DNA (HBV DNA < 20 IU/mL) group showed significantly lower risk of reactivation compared to detectable HBV DNA group (odds ratio (OR) 0.30, 95% CI 0.11–0.86). Although patients on prophylactic anti-HBV therapy showed a lower reactivation rate, there was no significant difference (OR 0.27, 95% CI 0.07–1.01). The rate of HBV reactivation was only 0.4% in patients with resolved HBV infection.
Conclusion: The risk of HBV reactivation was not negligible in HCV coinfected patients using DAAs, indicating watchful attention for HBV reactivation is still needed.

[OP-0789]

Reactivation of HBV in patients with resolved HBV infection after receiving direct acting antiviral treatment for HCV

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Objectives: To determine the risk of HBV infection reactivation while treating with direct anti-viral therapy.
Materials and Methods: This was a clinical prospective observational study carried at the Gastroenterology section of medical unit IV, Jinnah Postgraduate Medical Centre, Karachi, Pakistan,?80 patients positive for chronic HCV who were candidates for treatment by DAA therapy. The patients identified to carry HBsAg at baseline or with positive HBc Antibodies were further assessed for other HBV markers: hepatitis Be antigen at baseline, and serum HBV DNA quantitative measurement at baseline, week 4 of treatment, and end of treatment. On the other hand, recent infection by HBV among those patients was also observed.
Results: From our study participants majority were males (63%) than females (37%) with a mean and SD of age was 48.17 ± 9.44 years. At beginning of the study, there were 32 (40.0%) patients who were co-infected with HCV and HBV with a quantitative PCR test for HBV DNA ≥ 20?IU/ml. After 1 month of DAA therapy, reactivation was detected in 15 (46.87%) cases (3 occult cases show reverse seroconversion (became HBs Ag positive), and 2 co- infected cases show increased HBV DNA ≥ 1000?IU/L above the baseline level). Surprisingly, 3 new cases acquired recent infection with the positivity of HBc IgM and detectable levels of HBV DNA. The rate of reactivation after three months was quite surprising and one patient with co-infection (where increased HBV DNA ≥ 1000?IU/L above the baseline level), and 2 new cases acquired recent infection late in the study.
Conclusion: HBV screening is strongly recommended for co-infected HCV/HBV patients before initiation and during DAA therapy. HBV reactivation can be prevented with pretreatment screening and prophylactic treatment when necessary. Additional data are required to evaluate the underlying mechanisms of HBV reactivation in this setting.

[OP-0807]

HBV seroprevalence and liver fibrosis status among population born before national immunization in thailand: findings from a health check-up program

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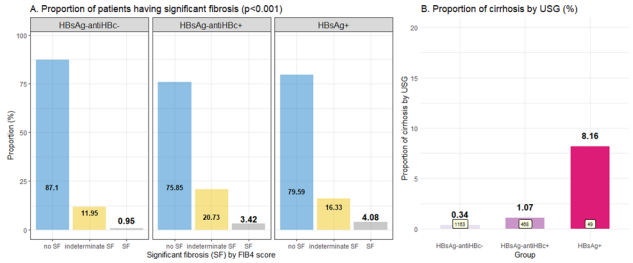
Objectives: Hepatitis B virus (HBV) infection is the leading cause of liver-related death worldwide. Both patients with current and past HBV infection are at risk for cirrhosis and hepatocellular carcinoma (HCC), and many of them might be unaware of their infection. We aim to study the seroprevalence of HBsAg, antiHBc, and liver fibrosis status in people in Thailand who were born before nationwide HBV immunization.
Materials and Methods: A cross-sectional study of patients born before 1992 who sought for health check-up program at Our Center, a tertiary-care hospital in Thailand, between January 2019 and December 2020 was conducted. Non-Thai nationals were excluded. The hepatitis B serology findings, liver fibrosis status determined by ultrasonographic finding and the FIB-4 score, and the clinical note regarding the management in patients after the detection of positive HBsAg were obtained.
Results: The seroprevalence of HBsAg positive, positive anti-HBc but not HBsAg (HBsAg-antiHBc +), and negative for both HBsAg and anti-HBc (HBsAg-antiHBc-) were found in 2.9%, 27.8%, and 69.3%, respectively. Cirrhosis by ultrasonography was found in 4 (8.2%) of 49 HBsAg positive patients, much higher than 1.1% and 0.3% in HBsAg-antiHBc + , and HBsAg-antiHBc- patients, respectively ($p < 0.001$), and significant fibrosis determined by FIB-4 score are shown in the Figure. Only 6 (12.2%) of 49 HBsAg positive patients were aware of their infection and regularly followed up with gastroenterology/hepatology specialists before participating in the health check-up program.

Conclusion: The current prevalence of HBsAg positive in the population of Thailand born before EPI is 2.9% but the prevalence of past infection is 27.8%. Those with active and past HBV infection increase risk of cirrhosis and significant liver fibrosis. And most patients with active HBV infection were not aware of their HBV status. HBV screening should be implemented broadly and all patients with HBV should be taken up in the cascade of care.



[OP-0808]

The long-term efficacy and glycolipid metabolism safety of tenofovir disoproxil fumarate in chronic hepatitis B patients: A real-world retrospective study

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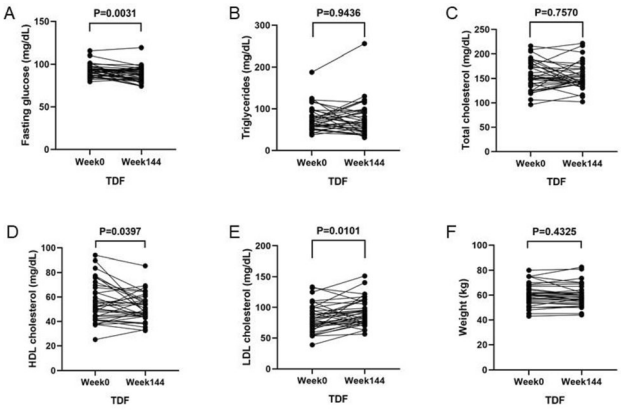
Objectives: This study aimed to investigate the antiviral efficacy and the impact on lipid profile and fasting glucose in chronic hepatitis B (CHB) patients who had received tenofovir disoproxil fumarate (TDF) treatment for three years.
Materials and Methods: These 37 treatment-naïve CHB patients without liver cirrhosis were derived from the CHB-follow-up cohort of our center. During the 144-week TDF treatment, the virologic response, biochemical response, non-invasive measurements index of liver fibrosis, lipid profile changes, and fasting glucose change were monitored and summarized every six months.
Results: After 144 weeks of TDF antiviral treatment, the complete virological response (HBV DNA < 20 IU/mL) and ALT normalization rates were 81.1% (30/37) and 86.5% (32/37), respectively. Non-invasive measurements of liver fibrosis (FIB-4 and APRI) were also gradually decreased during TDF treatment. The HDL cholesterol was decreased significantly at week144 compared to baseline ($-$ 4.086 mg/dL, $p = 0.0397$), while the LDL cholesterol was increased significantly (8.413 mg/dL, $p = 0.0101$). The changes of total cholesterol ($p = 0.7570$), triglycerides ($p = 0.9436$) and weight ($p = 0.4325$) were not statistically significant. The decrease of fasting glucose, from 92.306 mg/dL (95%CI: 89.97–94.74) to 88.049 mg/dL (95%CI: 85.08–91.02), was also statistically significant ($p = 0.0031$). Moreover, there were 4 (10.8%) patients who occurred hypoglycemia and 1 (2.7%) patient who occurred hypertriglyceridemia, and the rate of Grade 3/4 metabolic-related adverse events was 10.1% (3/37).
Conclusion: TDF was effective in treatment-naïve patients with CHB. However, it might impact lipid and glucose metabolism. Therefore, long-term usage of TDF should be more cautious in CHB patients with a potential risk of abnormal glycolipid metabolism.



[PP-0815]

Occult hepatitis B virus infection in HBsAg-negative liver cirrhosis or hepatocellular carcinoma patients

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Objectives: Occult hepatitis B virus (HBV) infection is defined as the presence of HBV DNA or genome in the liver tissue or the serum in subjects negative for hepatitis B surface antigen (HBsAg). The prevalence of occult HBV infection may be considered to depend on the virus endemicity, the assay sensitivity, and the population variability. This study was conducted to estimate the seroprevalence of occult HBV infection in HBsAg-negative patients with liver cirrhosis (LC) or hepatocellular carcinoma (HCC).
Materials and Methods: Serum samples from 114 patients with HBsAg-negative LC or HCC were obtained. HBsAg, anti-HBs, and IgG anti-HBc were measured by radioimmunoassay and serum HBV DNA was determined by real-time polymerase chain reaction. The lowest detection limit of HBV DNA is 116 copies/mL. The seroprevalence of occult HBV infection in these patients was compared to that of 94 age- and sex-matched healthy subjects negative for HBsAg.
Results: The seroprevalence of occult HBV infection was 2.6% in HBsAg-negative patients with LC or HCC, while that of healthy subjects was 2.1%. In all cases with occult HBV infection, hepatitis B viral loads were less than 116 copies/mL except one with 144 copies/mL and IgG anti-HBc indicating past exposure to HBV was positive regardless of the presence of anti-HBs. Occult HBV-infected patients with LC or HCC revealed Child–Pugh classification A. Table 1. showed clinical characteristics of the patients with occult HBV infection.
Conclusion: The overall seroprevalence of occult HBV infection was 2.4% in which viral load was extremely low. No difference of the seroprevalence of occult HBV infection was observed between LC or HCC patients and healthy subjects in endemic area for HBV.

[OP-0843]

Comparable risk of hepatocellular carcinoma between immune-tolerant and active phase in hepatitis B e antigen-positive patients

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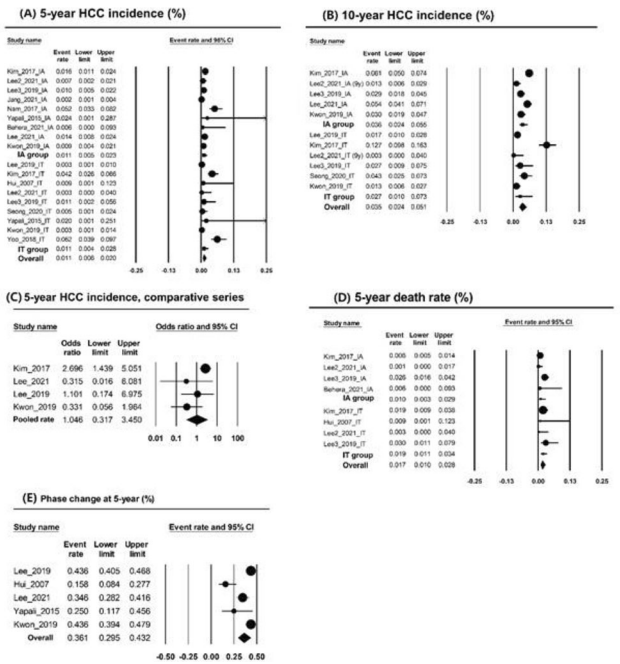
Objectives: Antiviral therapy is not indicated for patients with chronic hepatitis B (CHB) in the immune-tolerant (IT) phase. We compared the treatment outcomes between untreated IT-phase and treated immune-active (IA) phase in CHB patients.
Materials and Methods: We systematically searched four databases including Pubmed, Medline, Embase, and Cochrane database until August, 2021. The cumulative incidence of hepatocellular carcinoma (HCC) and mortality in IT and IA cohorts and that of CHB phase change in IT cohort was investigated. Studies regarding patients who have clinically or pathologically diagnosed liver cirrhosis were excluded. Random effects model was used for pooled analyses.
Results: A total of 13 studies involving 19 cohorts, including 11,903 patients were included. None of 13 studies were dropped from formal analysis for quality issue. The overall median of median follow-up period was 62.4 months. The pooled HCC incidence rate at 5-years was 1.1% (95% confidence interval [CI]: 0.6–2.0%) in all cohorts. No statistical difference in HCC incidence rate at 5-years was observed between IT [1.1% (95% CI, 0.4–2.8%)] and IA cohorts [1.1% (95% CI, 0.5–2.3%) (p = 0.976). The pooled odds ratio of comparative series between IT and IA cohorts was 1.05 (95% CI, 0.32–3.45; p = 0.941). Pooled HCC incidence rate at 10-years was 3.5% (95% CI, 2.4–5.1%) in all cohorts. No statistical difference in HCC incidence rate at 10-years was observed between IT [2.7% (95% CI, 1.0–7.3%)] and IA cohorts [3.6% (95% CI, 2.4–5.5%)] (p = 0.587). No statistical difference in pooled mortality rates at 5-years was observed between IT [1.9% (95% CI, 1.1–3.4%)] and IA cohorts [1.0% (95% CI, 0.3–2.9%)] (p = 0.285). Finally, pooled incidence rate of phase change in IT cohort was 36.1% at 5 years (95% CI, 29.5–43.2%).
Conclusion: The long-term risks of HCC and mortality were similar between the IT and IA phase. However, various definitions of CHB phase in different studies have to be considered.



[OP-0848]

Effectiveness and safety of tenofovir alafenamide in patients with hepatitis B virus associated hepatocellular carcinoma: Real-world study

Heechul Nam[1,2], Ji Won Han[1,2], Soon Kyu Lee[1,2], Hyun Yang[1,2], Hae Lim Lee[1,2], Pil Soo Sung[1,2], Hee Yeon Kim[1,2], Sung Won Lee[1,2], Do Seon Song[1,2], Jeong Won Jang[1,2], U Im Chang[1,2], Si Hyun Bae[1,2], Jong Young Choi[1,2], Seung Kew Yoon[1,2], Jin Mo Yang[1,2], Chang Wook Kim[1,2]

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Objectives: Real-world clinical data of tenofovir alafenamide (TAF) treatment in patients with hepatocellular carcinoma (HCC) are limited. We aimed to investigate efficacy and safety of TAF in patients with HCC.
Materials and Methods: This is a multi-center retrospective study on hepatitis B virus (HBV) associated HCC patients who were given TAF. Currently, TAF administration as the first-line antiviral agent for HBV-HCC patients is not available in Korea. Therefore, this study was conducted on patients who were diagnosed with HCC while taking TAF for more than 6 months.
Results: A total of 24 patients were included in the analysis, with the median age of 64 years. Of these, 15 were male (62.5%), 8 were diabetic (33.3%), 9 had hypertension (37.5%) and 22 had cirrhosis (91.7%) at the time of TAF initiation. The median duration of TAF treatment and follow-up period after HCC diagnosis were 18.7 months and 7.9 months, respectively. In this study, all patients maintained undetectable levels of HBV DNA (< 20 IU/mL) after diagnosis of HCC. Most of the patients (91.7%) were diagnosed with single nodular HCC, and the median size (largest diameter) of the tumor was 1.7 cm. The treatment modalities for HCC were as follows; 13 cases of trans-arterial chemoemolization (54.2%), 6 of surgical resection (25.0%), 3 of radiofrequency ablation (12.5%), and 2 of other options (8.3%). No TAF-specific adverse events occurred during the treatment of HCC.
Conclusion: In this real-world study, TAF provided acceptable efficacy and safety for patients with HCC. Future studies with large-scale, long-term follow-up are needed to substantiate these results.

[OP-0851]

Treatment efficacy and safety of tenofovir alafenamide switched from tenofovir disoproxil fumarate to in chronic hepatitis B patients: Real-world study

Heechul Nam[1,2], Ji Won Han[1,2], Soon Kyu Lee[1,2], Hyun Yang[1,2], Hae Lim Lee[1,2], Pil Soo Sung[1,2], Sung Won Lee[1,2], Do Seon Song[1,2], Jeong Won Jang[1,2], U Im Chang[1,2], Chang Wook Kim[1,2], Si Hyun Bae[1,2], Jong Young Choi[1,2], Seung Kew Yoon[1,2], Jin Mo Yang[1,2], Hee Yeon Kim[1,2]

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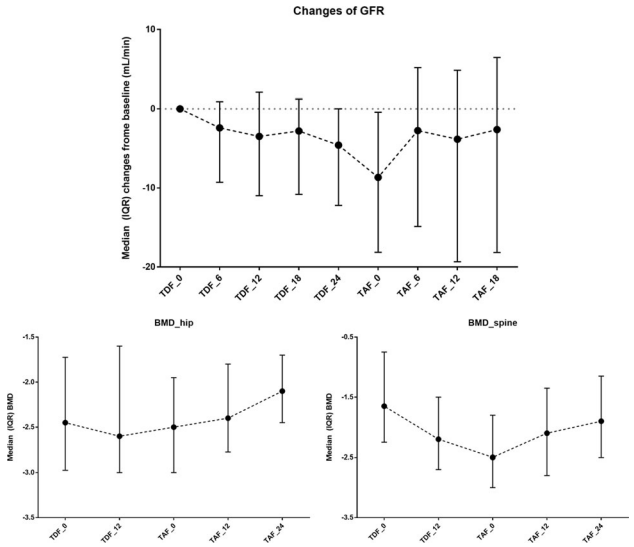
Objectives: Tenofovir alafenamide (TAF) is safer prodrug that reduces systemic toxicities of tenofovir disoproxil fumarate (TDF). We aimed to evaluate effectiveness and safety of TAF in chronic hepatitis B (CHB) patients who were switched from TDF in a real-world setting.
Materials and Methods: This is a multi-center retrospective study on CHB patients who were kept virologically suppressed (HBV DNA < 20 IU/mL) with TDF treatment for at least 1 year and then switched to TAF. Safety of TAF was determined by estimated glomerular filtration rate (eGFR) and bone mineral density (BMD).
Results: A total of 256 patients were included in the analysis (median age 59 years, 43.0% male, and 37.5% cirrhosis). The median duration of TDF treatment and follow-up period after TAF switching were 52.1 months and 22.5 months, respectively. The reasons for switching to TAF were as follows; renal insufficiency 33.9%, osteoporosis 59.1%, hypophosphatemia 1.9%, and others 5.8%. Majority of patients (98.4%) maintained alanine aminotransferase within normal range, and only seven patients experienced transient detection of HBV DNA during TAF. A significant decrease in eGFR was observed during TDF; 1-year of TDF (-4.92 ± 14.89 ml/min/1.73m^2; $P < 0.001$), at the time of TAF switching (-10.01 ± 18.38 ml/min/1.73m^2; $P < 0.001$). After switching to TAF, eGFR was significantly improved by 6 months ($+5.10 \pm 13.09$ ml/min/1.73m^2; $P < 0.001$), 12 months ($+6.44 \pm 12.95$ ml/min/1.73 m^2; $P < 0.001$). After switching to TAF, hip and spine BMD improved significantly; at 1-year ($10.8 \pm 11.5\%$ and $11.3 \pm 15.5\%$; $P < 0.001$, respectively), at 2-year ($17.1 \pm 11.1\%$ and $16.0 \pm 21.7\%$; $P < 0.001$, respectively). There was no specific TAF-related adverse events.
Conclusion: In this study, we observed sustained improvement in renal function and BMD following switch to TAF. These findings suggest that switching from TDF to TAF is effective and safe, especially in CHB patients with renal impairment or osteoporosis.



[OP-0865]

Antiviral therapy for HBeAg negative chronic HBV infection with normal or minimally elevated alaninetransaminase: A systematic review and meta-analysis

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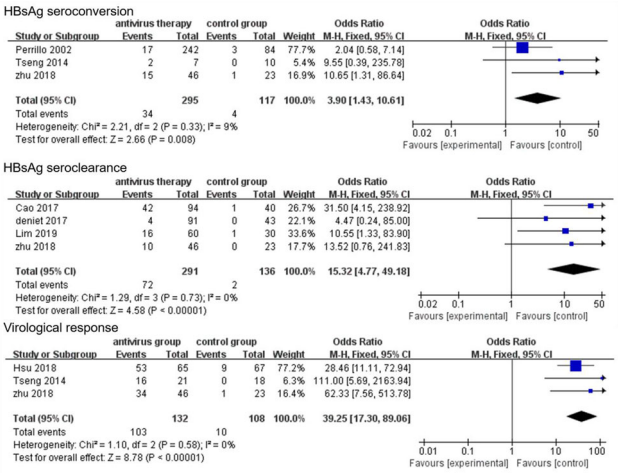
Objectives: We performed a systematic review and meta-analysis to provide a more accurate estimate of whether HBeAg negative chronic HBV infection with ALT lower than two times of the upper limit of normal value (ULN, 40U/L) would benefit from antiviral therapy.
Materials and Methods: A systematic literature review was conducted using 3 English database from January 1st, 1990 to October 3rd, 2020. We included observational studies and experimental trails in chronic hepatitis B (CHB) patients with ALT $\leq$ 2ULN reporting comparative rates of virological response, HBsAg seroconversion, HBsAg seroclearance, histologic activity and fibrosis, the incidence of cirrhosis and liver cancer and drug safety. Either the Joanna Briggs Institute Critical Appraisal Tools or the Newcastle–Ottawa scale was applied to evaluated methodological quality of the involving studies. Risk ratios (RRs) and odds ratios (ORs) were calculated using the Mantel–Haenszel formula with fixed effect models, and applied to each outcome.
Results: Of 6215 abstracts screened, seven studies both met criteria for inclusion in the systematic review and had a low risk-of-bias. Among studies included in the meta-analyses, we found that the rates of virological response (OR = 39.25, 95% CI: 17.30 – 89.06, $P < 0.00001$), HBsAg seroclearance (OR = 15.32, 95% CI: 4.77–49.18, $P < 0.00001$) and seroconversion (OR = 3.90, 95% CI: 1.43–10.61, $P = 0.008$) were both higher in the antivirus treatment group compared with the control one.
Conclusion: With normal or slightly elevated ALT, HBeAg negative CHB patients may benifit from being treated appropriately early and actively. The approach to such patients should be individualised, as further evaluation and treatment may be appropriate.



[OP-0866]

Reduction of liver stiffness in chronic hepatitis B patients treated with tenofovir disoproxil fumarate: A prospective observational study

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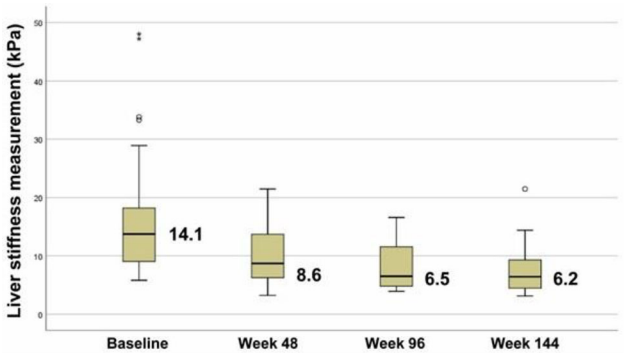
Objectives: Regression of hepatic fibrosis during antiviral therapy in patients with chronic hepatitis B has been demonstrated, but data about influence of long-term treatment with tenofovir disoproxil fumarate (TDF) on liver stiffness (LS) measured by transient elastography are scarce. We aimed to investigate changes in LS values during 144-week antiviral therapy with TDF in patients with chronic hepatitis B.
Materials and Methods: A total of 48 treatment-naïve patients with chronic hepatitis B who initiated TDF therapy were enrolled and followed up for 144 weeks. Laboratory tests and LS measurements were performed at baseline and repeated at weeks 12, 24, 48, 96 and 144. A significant decline of LS was defined as $\geq$ 30% drop of LS value from the baseline to week 96.
Results: Among the 48 enrolled patients, 11 patients were lost to follow-up before 96 weeks and 37 patients were included in the analysis (median age, 45 years [interquartile range, 35–55.5 years]; 20 men [54.1%]). During antiviral therapy with TDF, the median LS value decreased from 14.1 kPa to 8.6 kPa, 6.5 kPa, and 6.2 kPa at weeks 48, 96 and 144, respectively (all $P < 0.001$; Fig. 1). At week 96, virologic and biochemical response were achieved in 34 patients (91.9%) and 33 patients (89.2%), respectively. Moreover, 21 of 36 patients (58.3%) in whom the 96-week LS values were measured showed a significant decline of LS and higher baseline LS value was a single independent predictor of a significant decline of LS (odds ratio, 1.212; 95% confidence interval, 1.027–1.431; $P = 0.023$).
Conclusion: During the long-term antiviral therapy with TDF, LS values declined significantly in treatment-naïve patients with chronic hepatitis B.



[PP-0867]

Impact of long-term oral antiviral treatment on HCC risk in immune-tolerant and immune-active chronic hepatitis b patients utilizing aMAP, a recently validated risk prediction tool

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Objectives: The aMAP (Age, Male, Albumin-bilirubin, Platelets) score assesses 5-year HCC risk (J Hepatol 2020;73:1368–78). We utilized aMAP to assess HCC risk in CHB patients enrolled in tenofovir-based trials.
Materials and Methods: Data from GS-US-203-0101, a Phase 2 study of TDF vs TDF plus emtricitabine (FTC) in immune-tolerant (IT) patients, and 2 Phase 3 studies, GS-US-320-0108/GS-US-320-0110, comparing TAF vs TDF in immune-active (IA) patients, were used to generate aMAP scores at baseline and over 192 (IT), or 240 (IA) weeks. Risk scores were categorized as low-, medium-, or high-risk. Shifts in categories were evaluated during treatment.
Results: Of 126 (64 TDF; 62 TDF/FTC) IT patients (49% male, 89% Asian, 99% HBeAg-positive), mean (range) aMAP score was 41.4 (28.4–62.5) at baseline, with 113 (89.7%), 12 (9.5%) and 1 (0.8%) categorized as low-, medium-, or high-risk. At Week 192, mean (SD) change in aMAP was − 2.0 (3.62); 100%, 58%, and 100% remained categorically unchanged, while 5/12 (42%) medium-risk patients shifted to low-risk (Table). Changes in aMAP scores were similar with TDF vs TDF/FTC; none developed HCC. Of 1631 (1092 TAF; 539 TDF) IA patients (65% male, 83% Asian, 64% HBeAg-positive), mean (range) aMAP score was 47.6 (20.4–72.6) at baseline; 1033 (63.3%), 508 (31.1%), and 90 (5.6%) were low-, medium-, or high-risk (Table). At Week 240, mean (SD) change in aMAP was − 2.12 (3.04); 97%, 61%, and 37%, low-, medium-, and high-risk patients remained unchanged; 39% and 63% medium- and high-risk patients improved, respectively; $\leq$ 3% shifted to higher risk category. Changes were similar with TAF vs TDF. Overall, 22 HCC cases developed (0.2%, 1.8%, and 12.2% in low-, medium-, and high-risk patients at baseline).
Conclusion: aMAP scores supports few IT or IA patients at low HCC risk at initiation progressing to higher risk. Many at medium- or high-risk improved to lower risk after up to 5 years of treatment.

Table. Shifts in HCC Risk from Baseline to End of Treatment (EOT) by aMAP Categories

n (%)	Immune-Tolerant CHB (N=126)			Immune-Active CHB (N=1631)		
	Baseline			Baseline		
	Low-risk (n=113)	Medium-risk (n=12)	High-risk (n=1)	Low-risk (n=1033)	Medium-risk (n=508)	High-risk (n=90)
Week 192 (EOT)						
Low-risk	89 (100)	5 (42)	0			
Medium-risk	0	7 (58)	0			
High-risk	0	0	1 (100)			
Missing	24	0	0			
Week 240 (EOT)						
Low-risk				750 (97.0)	165 (39.2)	3 (4.5)
Medium-risk				23 (3.0)	255 (60.6)	39 (58.2)
High-risk				0	1 (0.2)	25 (37.3)
Missing				260	87	23

[PP-0872]

Atherosclerotic cardiovascular disease (ASCVD) risk profile of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in chronic hepatitis B (CHB) patients treated for 2 years

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Objectives: To explore how differing lipid profiles and other metabolic factors could impact cardiovascular (CV) risk associated with TAF or TDF use in CHB patients, we performed a post-hoc analysis from head-to-head studies.
Materials and Methods: Pooled data from 2 Phase 3 studies (GS-US-320-0108/0110) were included. Patients were randomized (2:1) to TAF 25 mg/day (N = 1093) or TDF 300 mg/day (N = 539), treated in a double-blind fashion for ≥ 96 weeks, after which patients were eligible for open-label TAF through an extension phase. Statin eligibility and estimated 10-year atherosclerotic CV risk (ASCVD) among patients aged 40–79 years were analyzed using ACC/AHA Equations, and shifts from baseline (BL) to Week 96 in ASCVD risk were assessed using intermediate and high risk cutoffs.
Results: 620/1632 (38%) met ACC criteria for 10-year ASCVD risk assessment at BL and ≥ 1 post-BL visit. At BL, the TAF (N = 400) and TDF (N = 220) groups were similar, except a higher % on TDF were aged ≥ 50 years; 60% male, 85% Asian, mean BMI 24.8 kg/m^2, 52% HBeAg-positive, 15% cirrhotic; 20%, 13%, 10%, and 4% had a history of hypertension, hyperlipidemia, diabetes, or other (non-ASCVD) CV disease, respectively; 14% smokers. At BL, median 10-year ASCVD risk was low and similar between groups (Table). At Week 96, no significant differences existed in median change in 10-year ASCVD risk score, or in shifts in risk categories by both cutoffs (Table). Based on 2019 AHA Guidelines, the % who became eligible for statins during the study was higher for TAF vs TDF (61/946 [6%] vs 5/458 [1%]; $p < 0.001$); however, within the statin-eligible population, few patients had lipid-lowering therapy initiated (3/61 TAF [5%] vs 0/5 TDF; p = 1.000).
Conclusion: Over 2 years of treatment, the potential for future CV risk assessed by 10-year ASCVD risk scores was similar with TAF vs TDF. Few TAF patients who were statin-eligible had lipid-lowering therapy started.

Table. Estimated 10-Year ASCVD Risk (%) at Baseline and Change Over 96 Weeks, and Shifts in 10-Year ASCVD Risk Categories Based on Intermediate and High Risks Cut-offs

Estimated 10-Year ASCVD Risk (%) at Baseline and Change Over 96 Weeks						
Median (Q1, Q3)		TAF (n=400)		TDF (n=220)		p-value
Baseline		2.1 (1.0, 4.4)		2.6 (1.1, 5.4)		0.0738
Change from baseline at:						
Week 24		0.2 (-0.1, 0.8)		0.1 (-0.1, 0.8)		0.294
Week 48		0.3 (0.0, 0.9)		0.1 (-0.2, 0.8)		0.0028
Week 96		0.5 (0.2, 1.5)		0.5 (0.1, 1.4)		0.129
Shifts in 10-Year ASCVD Risk Categories Based on Intermediate (7.5%) or High (20%) Risk Cut-offs						
		TAF		TDF		
		Baseline		Baseline		
		<7.5% (n=342)	≥7.5% (n=58)	<7.5% (n=184)	≥7.5% (n=36)	p-value
At Week 96 n (%)	<7.5%	293 (94)	2 (4)	146 (94)	1 (3)	0.753
	≥7.5%	18 (6)	47 (96)	10 (6)	30 (97)	
	Missing	31	9	28	5	
		Baseline		Baseline		
		<20% (n=396)	≥20% (n=4)	<20% (n=217)	≥20% (n=3)	p-value
At Week 96 n (%)	<20%	351 (98)	1 (33)	182 (99)	0	0.875
	≥20%	6 (2)	2 (67)	2 (1)	3 (100)	
	Missing	39	1	33	0	

[PP-0873]

Safety and efficacy at 4 years in post-liver transplant patients with chronic kidney disease receiving tenofovir alafenamide (TAF) For HBV prophylaxis

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Objectives: We previously reported that 48-week TAF monotherapy demonstrated similar efficacy to TDF-containing regimens with improved bone and renal safety in post-liver transplantation patients with chronic kidney disease (CKD). We present long-term results from this study.
Materials and Methods: In a Phase 2 open-label study (NCT02862548) in New Zealand, 51 liver transplant recipients on HBV antiviral prophylaxis with TDF ± lamivudine with ≥ Stage 2 CKD were randomized 1:1 to TAF 25 mg/day or continued previous treatment for 48 weeks. Subsequently all received TAF during an extension phase through Week 192. At Week 192, the efficacy endpoint was HBV DNA < 20 IU/mL; safety endpoints included serious adverse events (SAEs), changes in eGFR by the CKD-EPI and BMD at spine and hip by DXA.

Results: Baseline characteristics included: mean age 60 years, 75% males, 53% Pacific Islander; median eGFR 50 mL/min/1.73m^2. Overall, 46/51 (90%) patients completed the 192-week treatment (TAF: 2 deaths, 1 D/C for AE; TDF → TAF: 1 death, 1 D/C for investigator discretion). All had sustained viral suppression through Week 192. During the extension phase, SAEs occurred at a similar frequency (none treatment-related); 1 TAF patient D/C due to acute kidney injury not related to treatment. Median (Q1, Q3) eGFR increased in both groups at Week 192: TAF: 3.5 (− 1.2, 7.7); TDF → TAF 1.1 (− 6.3, 9.0) mL/min/1.73m^2. Increases from baseline in spine and hip BMD were observed with TAF (mean [SD]% change at Week 192: 4.26% [7.034] and 1.60% [2.384], respectively); while in the TDF → TAF group decreases occurred during the randomized phase, with increases after switching to TAF at Week 48 (mean [SD]% change at Week 192: 4.26% [6.289] and 1.81% [3.703] for spine and hip, respectively).
Conclusion: Long-term results in liver transplant recipients switched from TDF-containing regimens to TAF monotherapy demonstrated that prevention of viral relapse was maintained, with sustained improvements in key bone and renal parameters.

[PP-0874]

VALIANT: A targeted long-read approach to study translocations and mRNA isoforms associated with HBV integration

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Objectives: HBV DNA integration into the host genome may be a key driver of HCC oncogenesis. Standard sequencing approaches cannot capture the complete architecture of HBV DNA insertions and underestimate the contribution of integrated HBV to viral mRNA production. We present a method for detecting VirAL Integrations ANd Translocations (VALIANT): a quantitative workflow using targeted long-read sequencing to determine the structure of HBV DNA integrations and full-length HBV RNA transcripts.
Materials and Methods: DNA and RNA were isolated from 42 liver biopsies collected within the GS-US-174-0149 trial. A pan-genotypic panel of biotinylated oligos was developed to enrich for HBV sequences from sheared genomic DNA and full-length cDNA from poly-adenylated RNA. Samples were sequenced on the PacBio long-read platform and analyzed with VALIANT.
Results: HBV-targeted long-read DNA sequencing generated high coverage data spanning entire integrations, detecting thousands of chimeric HBV-host sequences in each patient. 13 of 42 samples contained HBV sequences flanked by two different chromosomes, indicating a chromosomal translocation associated with HBV integration. Chromosomal translocations were unique to each biopsy sample, each might originate randomly, and in some cases had evidence of clonal expansion. From HBV-targeted cDNA sequencing, we identified transcriptional activity from HBV integrations, including fusion transcripts associated with inter-chromosomal translocations. Inspection of the 3' ends of HBV RNAs showed that nearly 95% of HBV transcripts from HBeAg-positive patients originate from cccDNA, whereas HBeAg-negative patients expressed mostly HBsAg from integrations. In both, we detected non-chimeric HBV transcripts from HBV integrations within host genes, which utilize a non-canonical polyA site in the X ORF. These transcripts would not be properly classified by standard RNA-Seq.
Conclusion: VALIANT workflow is a powerful tool for studying HBV integration architecture and expression. The existence of multiple unique HBV-associated inter-chromosomal translocations in non-HCC CHB patient liver biopsies suggests a novel mechanism with mutagenic potential that may contribute to progression to HCC.

[PP-0875]

Predictive immune biomarkers of persistent HBV DNA suppression and low replicative state after treatment discontinuation in CHB

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Objectives: Numerous reports suggest that NA treatment discontinuation results in HBV viremia recurrence in the majority of patients with low HBsAg loss rates or maintenance of inactive carrier state. The ability to predict outcomes before discontinuation would be valuable for safe and effective treatment discontinuation. We aimed to identify biomarkers that can predict off treatment HBV response.
Materials and Methods: Patients (n = 359) from GS-US-174-0102/0103/0149 were used to identify predictive biomarkers for HBV DNA suppression (HBV DNA < 29 IU/mL) and low- replicative states (LRS) (HBV DNA < 2000 IU/mL and ALT $\leq$ ULN) 24 weeks after TDF $\pm$ Peg treatment discontinuation in HBeAg-positive/-negative patients. We profiled 182 relative expression levels in serum or plasma proteins at end of treatment (or last visit prior to treatment withdrawal), using Olink Proteomics. Wilcoxon-Mann–Whitney test was used to compare differences in protein expression, and multiple comparisons were adjusted using Benjamini–Hochberg method, at significant levels of 0.05 for adjusted p-values. Gene ontology and Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses were conducted.
Results: In virologically suppressed patients (n = 25) at treatment free follow up Week 24 (TFFU-24), levels of 29 proteins were significantly higher vs those without suppression (n = 334). These proteins included myeloid cell markers (e.g., CD164, CLEC5A, IL-33, CD1c), leukocyte trafficking chemokines (e.g., CCL4, CXCL5, CCL17), NK markers (i.e., KLRD1), and extracellular matrix (ECM) and/or ECM- associated proteins (e.g., ANGPT1, MMP12, PDGF8, SERPINB8). Pathway analyses show enrichment for ECM remodeling, innate immune response to virus and immune regulation in the DNA suppressed group. CD8a expression levels trended higher in subjects with LRS (n = 111) compared to those without LRS

(n = 247) at TFFU-24. Feature selection and assessment of predictive performance of the identified biomarkers is ongoing.
Conclusion: HBV DNA suppression and maintenance of inactive carrier state following treatment discontinuation is associated with higher levels of certain innate and T cell immune responses during treatment.

[PP-0876]

Long-term efficacy and safety of tenofovir disoproxil fumarate (TDF) in children with chronic hepatitis B (CHB): final results from a placebo-controlled trial

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Objectives: TDF was approved for treatment of CHB in children $\geq$ 2 years (y) weighing $\geq$ 10 kg based on 48-week results from GS-US-174-0144. We report efficacy and safety for TDF treatment through 4 years.
Materials and Methods: Pediatric CHB patients 2 to $<$ 12 y, $\geq$ 10 kg BW with HBV DNA $\geq$ 4 $\log_{10}$ IU/mL, ALT $\geq$ 1.5 $\times$ ULN ($\leq$ 30 U/L), and eGFR $\geq$ 80 mL/min/1.73m^2 were randomized (1:1) to TDF 8 mg/kg or placebo (PBO) once daily in a double-blind (DB) fashion for 48 weeks or 72 weeks, and then eligible for open-label (OL) TDF through Week 192. Viral suppression, serologic and biochemical responses were determined, viral resistance was performed yearly (HBV DNA $\geq$ 69 IU/mL), and safety, including renal and bone parameters was assessed.
Results: 89 patients (TDF 60; PBO 29, baseline characteristics in Table) were randomized and treated, 81/89 (91%; TDF 56; PBO 25) and 77/89 (87%; TDF 55; PBO-TDF 22) completed both DB and OL phases. Week 192 efficacy (TDF vs PBO-TDF, missing = failure): HBV DNA $<$ 29 IU/mL 82% vs 62%; ALT normalization 72% vs 50%; HBeAg loss 54% vs 34%; HBsAg loss 10% vs 0%. Most adverse events (AEs) during the OL phase were mild-moderate; none had a Grade 3/4 AE or SAE related to study treatment and none discontinued OL treatment due to AEs. 3 patients (2 TDF; 1 PBO-TDF) had confirmed eGFR $<$ 70 but $\geq$ 50 mL/min/1.73m^2. Mean % BMD increase from baseline was slightly less in TDF vs PBO-TDF patients: spine: + 19.2% ($\pm$ 12.28) vs + 26.1% ($\pm$ 14.26); whole body: + 23.7% ($\pm$ 9.82) vs + 27.7% ($\pm$ 11.14). No tenofovir resistance were detected through Week 192.
Conclusion: Long-term TDF treatment of CHB in children was associated with a high viral suppression rate without resistance, while also being safe and tolerated. Biochemical and serologic responses were comparable to those in adults. No patient experienced clinically significant bone or renal toxicity.

Table. Baseline patient characteristics

Age, mean (range) years	6 (2-12)
Weight, mean (range) kg	24 (10.5-55)
Male, %	56
Asian, %	65
HBeAg-positive, %	96
HBV-DNA, mean (SD) $\log_{10}$ IU/mL	8.1 (0.9)
ALT, mean (SD) U/L	123 (92)

[PP-0877]

Alanine aminotransferase flares and seroclearance in chronic hepatitis B patients

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Objectives: Higher levels of Alanine Aminotransferase ('ALT flares') in Chronic Hepatitis B (CHB) patients have been found to be associated with declines in HBsAg levels and seroclearance. ALT flares can be a marker of immune response to therapy and a prognostic marker for CHB.
Materials and Methods: Adult CHB patients were identified using ICD or SNOMED code from the IQVIA Ambulatory EMR database. 'ALT flares' (5XULN) were defined as ALT levels of $\geq$ 125 IU/L in females and $\geq$ 175 IU/L in males. Patients with subsequent negative HBsAg or positive anti-HBs were considered to have seroclearance/seroconversion (SC). Multivariate Stepwise Cox proportional hazard model was used to determine association between ALT flares and SC.
Results: CHB patients (N = 12,653) diagnosed between 2001–2020 were included; mean age 49.7 years, 48% men, 39% Caucasian, 27% Asian, 10% African American. 531 (4.2%) patients had documented SC [median time to SC = 820 (121–4516) days] and 189 (1.5%) had an ALT flare with 17 (9.0%) of flares occurring prior to SC. Median time to SC in patients with ALT flares was shorter than among those without (1.7 vs. 2.3 years). Patients with ALT flares had SC 2X more often than those without (OR, [95% CI] = 2.3[1.4–3.8]). This association was significant in a multivariate model among CHB patients with antiviral use (HR, [95% CI] = 3.5[1.4–8.9]) but not among those without (HR [95%CI] = 1.5[0.6–4.0]). Race (Caucasian vs. others), BMI ($\geq$ 30 vs. $<$ 30), diabetes, and absence of cardiovascular disease were associated with increased SC in the two multivariate models.
Conclusion: In this large cohort of CHB patients, ALT flares prior to SC were relatively uncommon. Whether antiviral use can invoke therapeutic flares in a subgroup of patients requires additional research. Further elucidation of underlying pathophysiology and role of other associated factors could provide insight to CHB disease progression and functional cure.

Table. Association between variables and seroclearance by antiviral use

Variable	Antiviral use (N=2,207)			No antiviral use (N=10,446)		
	Hazard Ratio	95% CI	p-Value	Hazard Ratio	95% CI	p-Value
ALT flare	3.5	(1.4–8.9)	0.009	1.5	(0.6–4.0)	0.431
Age ≥ 45 vs. <45 years				1.6	(1.2–2.1)	0.002
BMI ≥ 30 vs. <30				1.5	(1.1–2.0)	0.003
African American vs. others				1.5	(1.1–2.0)	0.013
Caucasian vs. others	2.4	(1.3–4.5)	0.006			
Diabetes mellitus				1.6	(1.2–2.3)	0.004
Cardiovascular disease				0.7	(0.5–0.8)	0.001

*CI, confidence interval

[PP-0879]

Switching from TDF and/or other OAVs to TAF in virally suppressed CHB patients with moderate or severe renal impairment, or with ESRD on hemodialysis: Final week 96 results from a phase 2 study

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Objectives: We previously showed in renally impaired (RI) CHB patients, including ESRD patients on HD, that switching to TAF from TDF and/or other OAVs maintains high viral suppression rates with stable bone and renal safety parameters at Week 48. Here we present the Week 96 results.

Materials and Methods: In this Phase 2 study (NCT03180619), virally suppressed CHB patients (HBV DNA < LLOQ × 6 months, < 20 IU/mL at screening) with mod-severe RI or with ESRD on HD at screening while receiving TDF and/or other OAVs for ≥ 48 weeks were switched to TAF 25 mg QD for 96 weeks. Safety assessment included adverse events (AEs) and changes in bone and renal parameters. Viral suppression, and serological and biochemical responses were serially assessed.

Results: 93 patients (mod-severe RI 78; ESRD on HD 15) enrolled; 74% male, 77% Asian, 51% ≥ 65 y, 83% HBeAg-negative, 34% cirrhosis, median ALT 17 U/L, up to 24% osteoporosis at hip and/or spine, 60% HTN, 22% CV disease, 25% DM. Twelve (13%; 11 mod-severe RI and 1 ESRD) patients discontinued early (5-withdrew consent, 3-deaths [none treatment-related], 2-AE, and 2-investigator decision). Key efficacy/safety results at Week 96 are in the Table. Viral suppression was maintained in all remaining on treatment (missing = excluded); a high proportion had target not detected. TAF was well tolerated; no Grade 3/4 AEs or SAEs related to study treatment. Switching to TAF resulted in small % increases in hip/spine BMD in those with mod-severe RI, and small decreases in ESRD patients. 2 with mod-severe RI had a fracture. Median $eGFR_{CG}$ increased while urinary markers of proximal tubular function progressively decreased in mod-severe RI patients.

Conclusion: Renally-impaired CHB patients, including ESRD patients on HD, who were switched to TAF from TDF and/or other OAVs maintained high viral suppression rates. Bone and renal parameters remained stable or slightly improved after 2 years of treatment.

Table. Final Results at Week 96: Efficacy and Bone and Renal Parameters

n/N (%), or median (Q1, Q3)	Moderate – Severe RI[a] (n=78)		ESRD on HD[b] (n=15)	
	M = F[c]	M = E[d]	M = F	M = E
HBV DNA <20 IU/mL	65/78 (83)	65/65 (100)	13/15 (87)	13/13 (100)
HBV DNA <20 IU/mL and target not detected (<LLOD)	54/78 (69)	54/65 (83)	10/15 (67)	10/13 (77)
Normal ALT (2018 AASLD criteria) [e,f]	58/78 (74)	58/65 (89)	13/15 (87)	13/13 (100)
Normal ALT (Central lab criteria) [e,g]	64/78 (82)	64/65 (98)	13/15 (87)	13/13 (100)
HBeAg loss[h]	0/13	0/9	1/3 (33)	1/3 (33)
HBsAg loss	0/78	0/66	0/15	0/13
qHBsAg, log10 IU/mL change		-0.10 (-0.16, -0.01)		-0.11 (-0.17, -0.02)
Hip BMD, % change		+0.94 (-1.285, 2.282)		-1.54 (-3.620, 1.721)
Spine BMD, % change		+1.21 (-1.230, 3.452)		-1.32 (-3.459, 1.910)
CTX, % change (ng/mL)[i]		-18.9 (-35.0, 0.0)		-9.9 (-38.6, 23.9)
P1NP, % change (ng/mL)[j]		-13.8 (-29.3, 8.0)		-20.8 (-28.7, 16.5)
sCr, change (mg/dL)		-0.04 (-0.120, 0.080)		NA
sPO4,change (mg/dL)		0.1 (-0.2, 0.4)		NA
$eGFR_{CG}$, change (mL/min)		+1.0 (-2.8, 4.5)		NA
RBP/Cr, % change[k]		-38.5 (-62.5, 29.5)		NA
β2MG/Cr, % change[l]		-57.0 (-77.0, 62.0)		NA

[a]Moderate to severe renal impairment: $eGFR_{CG}$ 15 - <60 mL/min at screening;
[b]ESRD on HD: $eGFR_{CG}$ < 15 mL/min maintained on chronic hemodialysis
[c]M=F, missing equal failure analysis; [d]M=E, missing equal excluded analysis (i.e. observed data)
[e]ALT value within normal range at Week 96 regardless of baseline ALT level; [f]ULN ≤35 U/L males and ≤25 U/L females
[g]ULN ≤43 U/L men and ≤35 U/L for men ≥65y; ≤34 U/L women and ≤32 for women ≥65y
[h]Only includes patients HBeAg-positive at baseline. [i]Serum C-type collagen sequence (bone resorption marker); [j]Serum procollagen type 1 N-terminal propeptide (bone formation marker)
[k]Urine retinol binding protein/creatinine (renal tubular marker); [l]Urine beta-2 microglobulin/creatinine (renal tubular marker).
Abbreviations: $eGFR_{CG}$, estimated creatinine clearance (Cockcroft-Gault method); ESRD, end-stage renal disease; BMD, bone mineral density by DXAscan); LLOD, lower limit of detection; NA, not applicable (hemodialysis patients)

[PP-0881]

Switching from TDF and/or Other OAV to TAF in virally suppressed chronic hepatitis B patients with hepatic impairment: Final 2 year efficacy and safety results from a phase 2 open-label study

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Objectives: We have previously shown that in hepatically impaired CHB patients, switching to TAF from TDF and/or other OAVs maintains high rates of viral suppression with stable bone and renal safety parameters through 48 weeks. Here we present our final 2-year (Week 96) results.
Materials and Methods: In this Phase 2 study (NCT03180619), virally suppressed CHB patients (HBV DNA $<$ LLOQ $\times$ 6 months and $<$ 20 IU/mL at screening) with Child-Turcotte-Pugh (CTP) scores $\geq$ 7 and $\leq$ 12 at screening (or previously documented to be $\geq$ 7) while receiving TDF and/or other OAVs for $\geq$ 48 weeks were enrolled and switched to TAF 25 mg QD for 96 weeks. Safety assessments including changes in bone (hip and spine BMD) and renal (CrCL by Cockcroft-Gault [$eGFR_{CG}$], serum creatinine) parameters, viral suppression, and serological and biochemical responses were serially assessed.
Results: Of 31 patients enrolled, mean age was 55 y (29% $\geq$ 60 y), 68% male, 81% Asian, and 90% HBeAg-negative; median (Q1, Q3) CTP and MELD scores were 6 (5, 8) and 10 (7.5, 14.2), respectively, median eGFRCG 98.5 mL/min; 19% had osteoporosis on spine DXA. Twenty-five (81%) patients completed 96 weeks of TAF treatment (6 discontinued early: 2-withdrew consent, 1-adverse event [AE; Grade 2 creatinine increase], 1-investigator decision, and 2-death [respiratory failure and aspiration pneumonia—both not treatment-related]). Week 96 efficacy/safety results are summarized in the Table. 96% of patients on TAF treatment had HBV DNA $<$ 20 IU/mL with a high proportion having normal ALT levels. Bone and renal parameters remained stable. TAF was well tolerated with no patients having a Grade 3 or 4 AE or a serious AE related to treatment.
Conclusion: At 2 years, CHB patients with hepatic impairment who were switched to TAF maintained high rates of viral suppression and normal ALT values while bone and renal parameters remained stable.

Table. Efficacy and Safety Results at Week 96

n/N (%), or median (Q1, Q3)	TAF 25 mg QD	
	Missing = Failure	Missing = Excluded
Efficacy		
HBV DNA <20 IU/mL	24/31 (77)	24/25 (96)[a]
ALT normal (2018 AASLD criteria)[b,c]	18/31 (58)	18/25 (72)
ALT normal (Central lab criteria)[b,d]	22/31 (71)	22/25 (88)
HBsAg loss[e]	2/30 (7)	2/24 (8)
qHBsAg, log_{10} change (IU/mL)		-0.15 (-0.32, -0.08)
CTP score change		0 (-1, 0)
MELD score change		-0.6 (-1.3, 0.0)
Bone safety		
Hip BMD, % change		+0.15 (-1.167, 2.677)
Spine BMD, % change		-0.13 (-2.192, 2.736)
CTX, % change (ng/mL)[f]		-6.3 (-25.0, 7.1)
P1NP, % change (ng/mL)[g]		-3.8 (-19.3, 25.4)
Renal safety		
sCr, change (mg/dL)		0.02 (-0.05, 0.90)
sPO_4, change (mg/dL)		-0.1 (-0.4, 0.3)
$eGFR_{CG}$, change (mL/min)		-2.4 (-11.4, 10.7)
RBP/Cr, % change[h]		-22.5 (-42.7, 14.7)
β2MG/Cr, % change[i]		-20.5 (-52.5, 27.3)

[a]1 patient had HBV DNA ≥20 IU/ml but <69 IU/mL; [b]ALT normal is proportion with ALT ≤ULN at Week 96 regardless of baseline ALT level; [c]ULN ≤35 U/L males, ≤25 U/L females; [d]ULN ≤43 U/L men and ≤35 U/L for men ≥65y; ≤34 U/L women and ≤32 for women ≥65y; [e]No patient had HBsAg seroconversion. [f]Serum C-type collagen sequence (bone resorption marker); [g]Serum procollagen type 1 N-terminal propeptide (bone formation marker); [h]Urine retinol binding protein/creatinine ratio (proximal tubular marker); [i]Urine beta-2 microglobulin/creatinine ratio (proximal tubular marker).
BMD, bone mineral density by DXA scan; sCr, serum creatinine; $eGFR_{CG}$, estimated creatinine clearance (Cockcroft-Gault method); sPO_4, serum phosphorus.

[PP-0883]

Occurrence rates of hepatocellular carcinoma in patients with lamivudine-resistant chronic hepatitis B

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Objectives: Suboptimal virological response to adefovir (ADV) rescue therapy has been commonly experienced in patient with lamivudine-resistant chronic hepatitis B. The aim of this study is to compare the occurrence of hepatocellular carcinoma (HCC) between patients with adefovir rescue therapy for lamivudine-resistance and treatment-naïve patients receiving entecavir (ETV).
Materials and Methods: Electronic medical records of 126 patients with lamivudine-resistant chronic hepatitis B who received ADV rescue therapy and of 169 treatment-naïve patients with ETV 0.5 mg were reviewed retrospectively. Virological response was defined as undetectable serum HBV DNA levels ($<$ 20 IU/mL). Cumulative occurrence of HCC was evaluated during antiviral therapy and the association between clinical variables and development of HCC were analyzed using Kaplan-Meyer curve and risk factor for HCC was evaluated with Cox-proportional hazard model.

Results: The median duration of ADV rescue therapy was 139 (12–173) months and ETV therapy was 129 (12–160) months (P = 0.102). Baseline DNA level was 6.04 log IU/mL in ADV rescue group and 6.46 log IU/mL in ETV group (P = 0.135). During rescue therapy, switching to tenofovir was needed in 49% of patients for ADV resistance or suboptimal response at median 76 (6–160) months. Cumulative occurrence rates of HCC were in 13.5% (17 of 126) with ADV rescue group and 11.2% (19 of 169) in ETV group during follow-period (P = 0.608). In multivariate analysis, age (P < 0.001) and underlying cirrhosis (P = 0.001) were independent risk factors for occurrence of HCC. In subgroup analysis, virological response at 12 months (P = 0.098), biochemical response at 6 months (P = 0.143), and switching to tenofovir (P = 0.518) was not associated with occurrence of HCC in ADV rescue group.
Conclusion: Constant and proper rescue therapy in patients with lamivudine-resistant chronic hepatitis B might not increase the occurrence rates of HCC.

[PP-0889]

Safety and efficacy of oral TLR8 agonist, selgantolimod, in viremic adult patients with chronic hepatitis B

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Objectives: Selgantolimod (SLGN) is an oral, Toll-like receptor 8 agonist in development for CHB treatment. We present the results through week 48 on the safety and efficacy of 24 weeks of SLGN treatment in viremic patients.
Materials and Methods: In this double-blind, phase 2 study, viremic CHB patients were randomized (2:2:1) to SLGN 3 mg, 1.5 mg, and placebo (PBO) once weekly for 24 weeks combined with TAF. Safety assessments included treatment emergent adverse events (TEAE) and laboratory abnormalities. The primary efficacy endpoint was the proportion of patients with $\geq$ 1 $\log_{10}$IU/mL decline in HBsAg levels from baseline at week 24. Exploratory endpoints included changes in pharmacodynamic markers (IL-12p40 and IL-1RA), peripheral T-cell, myeloid and NK-cell subsets.
Results: 67 patients were randomized. Baseline characteristics were similar across groups (Table). No patients achieved the primary endpoint at week 24; however, 3 (6%) SLGN-treated patients achieved HBsAg decline $\geq$ 0.5 $\log_{10}$IU/mL vs none in the placebo group. At week 48, 4 (7.4%) patients in the SLGN-treated group while none in the placebo group achieved HBsAg decline $\geq$ 0.5 $\log_{10}$IU/mL. Most frequent TEAE (SLGN vs PBO) were: nausea (26% v 0%), headache (15% v 15%), vomiting (17% v 0%), fatigue (15% v 0), and dizziness (11% v 0%). Grade $\geq$ 3 TEAE occurred in 0 (SLGN) v 7.7% (PBO) subjects; 1 (SLGN 3 mg) discontinued due to vomiting and abdominal pain. Most SLGN-treated patients showed decline of immune-cell subsets in the circulation 4 h postdosing, concurrent with increases of IL-12p40 and IL-1RA. Cell populations that decreased in the circulation included effector and memory T cell subsets. These parameters reverted to baseline values 24 h postdosing.
Conclusion: Oral SLGN up to 3 mg once weekly for 24 weeks is safe and well-tolerated. SLGN can induce sustained HBsAg declines of $\geq$ 0.5 $\log_{10}$IU/mL in some patients out to Week 48. Further evaluation of SLGN combined with immunomodulatory and antiviral agents is planned.

Table. Baseline Demographics

	TAF 25mg+		
	Placebo n=13	SLGN 1.5mg n=28	SLGN 3mg n=26
Mean age, y (range)	46 (27-65)	44 (19-65)	46 (24-62)
Men, n (%)	9 (69)	15 (54)	15 (58)
Asian, n (%)	13 (100)	28 (100)	25 (96)
HBeAg-negative, n (%)	6 (46)	10 (36)	12 (46)
Mean DNA, $\log_{10}$ IU/mL (SD)	6.8 (1.8)	7.0 (1.8)	6.5 (1.8)
Mean HBsAg, $\log_{10}$ IU/mL (SD)	4.0 (0.7)	4.2 (0.8)	3.8 (0.9)

[PP-0896]

Effect of tenofovir on liver stiffness in patients with chronic hepatitis B infection

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Objectives: Chronic hepatitis B treatment is a major global healthcare challenge. Antiviral treatment can alter natural history and reduce risks of cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Antiviral therapy in patients with chronic hepatitis B with decompensated cirrhosis improves hepatic reserve and reduces mortality. Liver fibrosis is closely related to the prognosis of patients with chronic liver disease. Elastography noninvasively quantifies tissue elasticity and stiffness. This research wants to study effect of tenofovir on liver stiffness in patients with chronic hepatitis B infection at Prof. Dr. R. D. Kandou Hospital.
Materials and Methods: This research was cohort retrospective study. The respondents are 35 patients with chronic hepatitis B infection who have been treated with tenofovir more than six months at Prof. Dr. R. D. Kandou Hospital, on January 2020—June 2021. Patient with hepatitis C and non alcoholic fatty liver disease were excluded. Data analysis were done using Wilcoxon test, with significance level $p < 0.05$.
Results: A total of 35 patients with chronic hepatitis B infection who have been treated with tenofovir, there are 25 male patients. Research subjects have a range of ages between 23 – 73 years. The mean value

of liver stiffness measured by transient elastography pre and post treatment were 11.11 ± 3.11 kPa and 8.03 ± 4.85 kPa. Wilcoxon test shows a significant difference of liver stiffness between pre and post treatment subjects. (p = 0.0001).
Conclusion: There is a significant difference of liver stiffness between pre and post treatment with tenofovir subjects.

[PP-0911]

Immunization capacity of HBV vaccination and immunization after HBV infection in Mongolia

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Objectives: We aimed to determine the generation of persistent immunity from HBV vaccination or after infecting with HBV infection in Mongolia.
Materials and Methods: 492 patients have enrolled who were investigated with quantitative HBsAb (qHBsAb) using Sysmex HISCL-800 (full automated analyzer) at Mongolian National University of Medical Sciences and Happy Veritas Diagnostic and Treatment Center. The vaccination scheme consists of three doses. Vaccination is successful if the antibody-titer (qHBsAb) is higher than 10 mIU/L. Also we have conducted questionnaires about HBV vaccination and risk factor for taking Hepatitis infections from patients.
Results: In this study 492 patients have participated, 313 female (63%) and 179 male (37%), out of which 471 (96%) people born before 1991 and remaining 21 (4%) people born after 1991. Twelve people (57%) who born after 1991 or vaccinated within 24 h after birth were qHBsAb low titer (< 10 mIU/L), remaining (43%) were qHBsAb titer (> 10 mIU/L), while 297 people (64%) who born before 1991 were qHBsAb titer (< 10 mIU/L), and remaining 36% of patients had persistent HBV vaccine. The 99 people who born before 1991 have enrolled in HBV vaccination voluntarily while 372 people did not take HBV vaccine at all.
Conclusion: Persistent immunity against HBV is generated not only in person who have taken HBV vaccination but also in person who have had slight HBV infection. It was considered that people aged between 50 and 60 years could not get persistent immunity against HBV. We assumed that persistent immunity against HBV depends on age, not other factor and sex.

[PP-0914]

Hepatitis B virus reactivation after successful treatment of hepatitis C virus with DAA in Ulaanbaatar, Mongolia

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Objectives: We aimed to assess the virological reactivation of HBV after HCV treatment in patients with HBV/HCV co-infection.
Materials and Methods: In our study we used two centers patient data. These patients are in treatment control of chronic hepatitis HBV/HCV co-infection in Mongolian National University of Medical Sciences and Happy Veritas Clinic and Diagnostic Center. From 369 HBV/HCV co-infected patients 84 patients are successfully finished their DAA therapy. In this study, we included 12 patients who had a HBV-DNA quantification results before and after DAA therapy.
Results: The overall SVR_{6-12} rate was 100% of HCV patients. Before DAA therapy, virological reactivation of HBV was observed in three patients. However after DAA therapy HBV-DNA was not detectable in all three patients. For the patients previously HBV-DNA undetectable (HBsAg +), HBV virological reactivation was found in 5 (55.5%) out of the 9 patients. For the all patients after DAA therapy the clinical laboratory results were decreased due to normal range.
Conclusion: International studies show that HBV virological reactivation occurs after DAA therapy. From our study HBV virological reactivation observed 5 out of the 9 patients and reactivation was not so high (from 500 to 4000 IU/ml). For chronic hepatitis patients with current HBV infection, the risk of HBV virological reactivation is present and monitoring the HBV-DNA quantity level during therapy might be useful. For patients with active HBV-DNA during DAA therapy further study should be done.

[PP-0980]

Improved bone and renal parameters across multiple chronic HBV (CHB) patient types treated with tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF)

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Objectives: TAF, a novel tenofovir (TFV) prodrug, is non-inferior to TDF in viremic and suppressed CHB patients with an improved safety profile. For a more comprehensive assessment of TAF bone and renal safety, we reviewed data across the TAF HBV Clinical Development Program.
Materials and Methods: Data from 1,911 patients treated with TAF or TDF from several studies were analyzed, including HBeAg + / HBeAg- patients (Studies 108/110), stable TDF patients switched to TAF (Study 4018), those with renal or hepatic impairment (Study 4035), and liver transplant recipients (OLT) with chronic kidney disease (CKD) (Study 3912). Standardized hip/spine bone mineral density (BMD) and estimated glomerular filtration rate ($eGFR_{CG}$) measurements were extracted and summarized. Exploratory biomarkers of bone formation (procollagen type 1 N-terminal propeptide-P1NP) and resorption (C-type collagen sequence-CTX) along with sensitive markers of proximal tubular function (retinol binding protein:creatinine [RBP:Cr] and β_2-microglobulin:Cr [β_2M:Cr]) ratios were examined across studies in different patient populations.
Results: Stable, or in most instances, improved bone and renal parameters were seen across multiple HBV patient types (Table 1). In Studies 108/110, hip/spine BMD were stable or improved following switch; minimal declines in $eGFR_{CG}$ occurred and improved following switch from TDF. Switch patients, including those with hepatic or renal impairment, bone and renal parameters were maintained or improved. Among OLT recipients with CKD, improvements in bone and renal parameters were also observed.
Conclusion: Across multiple HBV patient types, including those at higher risk of TDF-associated bone and/or renal toxicity, stable or improved bone and renal parameters were observed compared to TDF treatment.

Table 1. Changes from baseline in select bone (hip and spine bone mineral density as measured by DXA) and renal ($eGFR_{CG}$) parameters[‡]

	Hip DXA Mean % change (SD)	Spine DXA Mean % change (SD)	$eGFR_{CG}$ Median change (Q1, Q3), (mL/min)
Studies 108/110 (N=1248*) (Phase 3, viremic) – Week 240[#]			
TAF	-0.87 (3.69)	-0.26 (5.25)	-2.4 (-12.3, 8.5)
TDF→TAF OL 3-yrs	-1.39 (3.88)	-1.11 (4.97)	-2.9 (-10.7, 6.6)
TDF →TAF OL 2 yrs	-1.76 (3.73)	-0.70 (5.00)	-4.9 (-13.8, 7.1)
Study 4018 (N=488) (Phase 3, TDF→TAF switch) – Week 96**			
TAF - TAF	+1.16 (2.85)	+2.33 (3.93)	1.63 (-4.58, 6.95)
TDF - TAF	+0.18 (2.68)	+1.73 (3.82)	0.54 (-5.23, 7.68)
Study 4035 (N=124) (Renal/hepatic impairment Switch) – Week 96**			
Part A: Renal Impairment			
TAF: all moderate-severe	0.2 (3.25)	1.02 (4.44)	1.0 (-2.8, 4.5)[§]
TAF: prior TDF	0.95 (3.01)	1.88 (4.68)	2.53 (-1.54, 5.95)[§]
TAF: prior other OAV	-1.14 (3.29)	-0.49 (3.60)	-2.59 (-4.19, 0.25)[§]
Part B (Hepatic Impairment)			
TAF: all patients	0.28 (3.25)	-0.25 (3.91)	-2.4 (-11.4, 10.7)
TAF: prior TDF	1.09 (3.53)	-0.17 (4.52)	0.72 (-10.42, 14.86)
TAF: prior other OAV	-1.08 (2.31)	-0.39 (2.68)	-5.92 (-16.11, 5.79)
Study 3912 (N=51) (TDF→TAF Switch Post-OLT with CKD) – Week 192[‖]			
TAF	1.07 (2.42)	3.37 (6.55)	2.8 (-1.5, 12.3)
TDF-containing regimens	2.12 (3.55)	3.80 (5.89)	0.2 (-9.0, 7.7)

[‡]Data are M=E (missing equals excluded) using the safety analysis set. Due to differences in study designs, change from baseline measurements varied by study. [§]Note: In Study 4035, for $eGFR_{CG}$, only Part A Cohort 1 has been reported, which included subjects with moderate (30mL/min ≤$eGFR_{CG}$≤59 mL/min) to severe renal impairment (15mL/min ≤$eGFR_{CG}$< 30mL/min).
*Number of patients in the Week 240 analysis subset. [#]For Studies 108/110: changes from baseline represent the differences from Week 240 to baseline; **For studies 4018 and 4035: changes from baseline represent the differences from Week 96 to baseline. [‖]For Study 3912, changes from baseline represent the differences from week 192 to baseline. Note that subjects in the TDF arm switch to TAF at week 48.
Abbreviations: DXA=Dual Energy X-ray Absorptiometry; $eGFR_{CG}$=estimated glomerular filtration rate by Cockroft-Gault; OL=open label; OAV=oral antiviral

[PP-0988]

A national patient survey to identify the awareness gap and insights of patients on chronic hepatitis B management in Taiwan

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Objectives: Hepatitis B virus (HBV) infection and HBV-related hepatocellular carcinoma (HCC) are prevalent in Taiwan. Patients' awareness and insights on the management of chronic hepatitis B (CHB) help to provide a better clinical care. This study aims to understand disease awareness and healthcare needs of CHB in Taiwan.
Materials and Methods: The online survey was conducted in 2021. Patients > 20 years with CHB ≥ 1 year were eligible. Those who received liver transplantation, cancer chemotherapy or immunotherapy, and had human immunodeficiency virus were excluded. Participants were stratified according to their sex, living regions, and hospital types (medical center, regional or area hospital, and clinic) with prespecified percentages. Patients were categorized evenly into four groups: patients on first-time nucleoside analogues (NA) therapy, CHB relapse patients on NA retreatment, patients who stopped NA, and treatment-naïve patients, respectively.
Results: Overall, 240 patients were recruited with an average age of 51.2, and 68% of them had CHB diagnosed in hospital. Around 59% of patients are aware that CHB is associated with cirrhosis and HCC; however, 77% of them think HCC occurrence is due to irregular lifestyle. Patients over 70 years and > 20-year of CHB have the lowest degree of awareness. The perceived misconceptions for CHB cure ranges from normal liver function, negative HBV DNA, and even NA discontinuation. Healthcare professionals and Google are their main sources of information of CHB. If there is no economic concern, 53% treatment-naive patients are willing to receive self-paid NA therapy if indicated. Overall, only 28% of patients are satisfied with the current reimbursement criteria by the National Health Insurance.
Conclusion: We identify misconceptions and knowledge discrepancy of patients, which could lead to NA self-discontinuation or loss of follow-up. Enhance disease awareness and patient support, and extended National Health Insurance coverage will be fundamental to improve the management of CHB in Taiwan.

[OP-0990]

Efficacy and safety of tenofovir alafenamide fumarate prophylaxis in HBsAg positive recipients who received liver transplantation: An interim analysis

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Objectives: To evaluate the efficacy and safety of Tenofovir Alafenamide Fumarate in HBsAg positive recipients who underwent liver transplantation.

Materials and Methods: We retrospectively screened consecutive HBsAg positive patients who underwent liver transplantation. Inclusion criteria: 1) > 18; 2) HBsAg positive recipients who were treatment naive (TN group) or has received antiviral treatment (ETV or other NAs except TAF, TE group) for at least 48 weeks before transplantation; 3) patients started or switched to TAF treatment when entering the list for liver transplantation. Primary endpoint was the proportion of patients with viral suppression (HBV DNA < 20 IU/mL) 24 weeks after surgery.
Results: 10 eligible patients were enrolled, among whom 2 were in TN group and 8 in TE group. The median age was 48.8, 9 were male. The median time of prior NAs treatment was 8.07 years. 8 out of 10 patients had undetectable HBV DNA at baseline. The remaining 2 patients had HBV DNA of 800 IU/mL and 90,000 IU/mL respectively. 5 patients with undetected HBV DNA receiving HBsAg negative livers have sustained undetectable HBV DNA after surgery. 1 patient in TN group has HBV DNA decreased from 90000 IU/mL to 2180 IU/mL after 4 weeks of TAF treatment before surgery, and achieved viral suppression 8 weeks after transplantation. Another patient with HBV DNA 800 IU/mL at baseline also achieved viral suppression 24 weeks after transplantation. HBV DNA elevated immediately in 2 patients who received HBsAg positive livers, and then decreased significantly (496,000 IU/mL to 468 IU/mL at 3 month; 70,000 IU/mL to 55 IU/mL at 6 month). No drug related adverse events were reported. 90% patients had normalized ALT at 4 weeks after surgery. renal function remained stable through whole study.
Conclusion: TAF prophylaxis treatment was effective and safe in HBsAg positive recipients who underwent liver transplantation surgery.

[PP-1012]

Efficacy of tenofovir alafenamide on prophylactic administration for HBV reactivation and HBV reactivation related hepatitis during immunosuppressive or anti-tumor therapy

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Objectives: Tenofovir Alafenamide (TAF) is a prodrug of tenofovir and shows high efficacy and safety for patients with chronic hepatitis B.While, there is not enough data regarding prophylactic administration of TAF to prevent HBV reactivation, ahead of or during immunosuppressive therapy and anti-tumor therapy. In this multicenter prospective study, we aim to evaluate the efficacy and safety of TAF prophylactic administration for HBV reactivation and HBV reactivation related hepatitis.
Materials and Methods: In NORTE study participated hospital between August 2018 and September 2021, patients who were HBs Ag positive and/or HBV-DNA positive and received TAF administration for preventing HBV reactivation, ahead of anti-tumor therapy or immunosuppressive therapy, or patients with previous HBV infection, who experienced HBV reactivation during anti-tumor therapy or immunosuppressive therapy and received TAF administration for preventing HBV reactivation hepatitis were included. The efficacy and safety of TAF prophylactic administration at 24 weeks and 48 weeks after TAF initiation were evaluated.
Results: A total of 132 patients were included. Of those, a total of 108 patients were administrated with TAF for preventing HBV reactivation, ahead of anti-tumor therapy or immunosuppressive therapy, and 24 patients with previous HBV infection and who experienced HBV reactivation during anti-tumor therapy were administrated with TAF for preventive HBV reactivation related hepatitis. A total of 72 were treated with anti-tumor therapy, and a total of 60 were administrated with Immunosuppressive therapy. Of those, 119 patients were followed more than 6 months and, no patients experienced HBV reactivation and HBV reactivation related hepatitis. A total of 84 patients were followed more than 48 weeks and no patients experienced HBV reactivation and HBV reactivation related hepatitis. No patients cease TAF administration due to adverse event.
Conclusion: Prophylactic administration of TAF for HBV reactivation and HBV reactivation related hepatitis is highly effective and safe.

[OP-1049]

Risk factors related to low-level viraemia in chronic hepatitis B patients receiving entecavir treatment

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Objectives: About 20% of chronic hepatitis B (CHB) patients receiving nucleos(t)ide analogues (NAs) treatment experienced low-level viraemia (LLV), which is associated with persistent low-grade inflammation, liver fibrosis progression and increased risk of hepatocellular carcinoma. We aimed to investigate the risk factors related to LLV in entecavir (ETV) treated CHB patients.
Materials and Methods: In this retrospective study, patients receiving ETV treatment, presented to Fifth Medical Center of Chinese PLA General Hospital from January 2016 to January 2021, were enrolled. According to virologic response at the end of 48 weeks of NAs antiviral therapy, the enrolled patients were divided into a LLV (defined as HBV DNA level still detectable, but < 2000 IU/ml) cohort and a complete virological response (CVR) (defined as HBV DNA level undetectable) cohort. Characteristics of the patients were collected and multivariate logistic regression analysis was performed to identify the independent factors associated with LLV.
Results: Totally, 2,567 patients were enrolled, 948 and 1619 into the LLV and CVR cohorts respectively. Based on the multivariate analysis, HBeAg positivity (OR = 1.152, 95% CI:1.120–1.194, P = 0.012), high baseline HBV DNA level (≥ 6 Log_{10} IU/mL, OR = 1.270, 95% CI:1.025–1.484, P < 0.001) and high baseline qHBsAg level (≥ 15,000 IU/mL, OR = 1.209, 95% CI:1.067–1.520, P = 0.022) were associated with LLV (see below table).
Conclusion: This study suggested that high HBV DNA level, high HBsAg quantification, and HBeAg positivity are associated with LLV after entecavir and anti-HBV treatment may need to be adjusted in such patients to avoid poor long-term clinical outcomes.

[PP-1056]

Incidences and predictive risk factors for long-term liver-related events during ETV treatment

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Objectives: A few large long-term follow-up studies have investigated the effect of entecavir (ETV) treatment on specific liver-related events (LREs), namely, hepatocellular carcinoma (HCC), cirrhotic complications and mortality.
Materials and Methods: This was a 14-year longitudinal observational study of treatment-naïve patients with CHB who received ETV treatment. The primary outcome was the cumulative probability of LREs.
Results: Data from 893 treatment-naïve CHB patients who received ETV were analyzed. The mean age was 52.0 ± 11.4 years, and patients were predominantly male (n = 596 [66.7%]). A total of 439 patients (49.2%) had cirrhosis. Overall, 536 patients (60.0%) were HBeAg-positive. During the median 9.6-year follow-up period (range, 1.0–14.4 years), 120 patients (13.4%) developed HCC. The cumulative incidence rates of HCC at 2, 3, 5, 7 and 10 years were 2.6%, 4.3%, 8.8%, 11.0% and 16.4%, respectively, in the entire cohort (average 1.6% per year). The majority of patients with HCC had cirrhosis (105/120, 87.5%). During follow-up, 148 patients (13.4%) developed cirrhotic complications, of which the most commonly encountered were HCC (n = 120), followed by ascites (n = 45), variceal bleeding (n = 28), HE (n = 22), SBP (n = 15) and HRS (n = 3). Overall, 23 patients (2.6%) died during the study period, the majority of whom (25/27, 93%) had cirrhosis at baseline. On the multivariate analysis, cirrhosis at baseline ($P < 0.001$), the male gender ($P < 0.001$), lower albumin ($P < 0.001$), an older age ($P < 0.001$), higher $\log_{10}$ HBV DNA level ($P = 0.034$), DM ($P = 0.044$) and lower PLT ($P = 0.041$) were predictive of cirrhotic complications.
Conclusion: ETV therapy may reduce the risk of HCC and liver-related events. Nevertheless, the residual risk of HCC necessitates intensive on-going follow-up of patients with successfully suppressed viral replication.

[PP-1058]

Efficacy of tenofovir alafenamide for nucleos(t)ide-nave patients with chronic hepatitis B in real-life practice

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Objectives: Tenofovir alafenamide (TAF) has demonstrated potent antiviral activity in clinical trials, but data in Korean patients from community studies are lacking.
Materials and Methods: We retrospectively investigated the clinical outcomes of TAF treatment for more than 6 months in 131 nucleos(t)ide-naïve patients with CHB. The primary endpoint was a virological response (VR), defined as an HBV DNA level of < 12 IU/mL. Secondary endpoints were rates of ALT normalization (ALT < upper limit of normal), HBeAg seroconversion, virologic breakthrough, and safety.
Results: The median duration of TAF therapy was 28 months (range, 6–40 months). Sixty seven (50.8%) patients were HBeAg positive. The mean pre-treatment HBV DNA and ALT levels were 5.85 ± 2.03 $\log_{10}$ IU/mL. and 151.5 ± 342 IU, respectively. Forty six (35.1%) patients had normal ALT levels at baseline. Among the 85 patients with elevated ALT levels at baseline, 75 patients (88.2%) showed ALT normalization during TAF treatment. In addition, normalization of ALT levels at 3, 6, and 12 months was achieved, respectively, in 56.6%, 75.8%, and 89.1% of patients. During TAF therapy, VR was achieved in 99 patients (75.6%). The cumulative rates of VR at 3, 6, 12, and 24 months were, respectively, 28.1%, 47.3%, 73.2%, and 88.6%. In multivariate analysis, absolute HBV DNA levels at baseline ($P < 0.001$; OR, 0.817; 95% CI, 0.738–0.904) and HBeAg positivity ($P = 0.001$; OR, 0.497; 95% CI, 0.326–0.758) as factors significantly associated with VR. Treatment was well tolerated. Most adverse events were mild in severity.
Conclusion: TAF is effective and well tolerated in Korean CHB patients in real life practice, consistent with larger registration trials.

[OP-1067]

Validation of modified PAGE-B score in predicting HBV-related hepatocellular carcinoma

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Objectives: Modified PAGE-B (mPAGE-B) score had been shown to have good predictive value for hepatocellular carcinoma (HCC) risk in chronic hepatitis B (CHB) patients on antiviral therapy. We performed a retrospective analysis of the mPAGE-B score predictive value among Chinese CHB patients.
Materials and Methods: Chinese CHB patients who had received entecavir/tenofovir treatment for 5 or more years, from Jan 2015 to Jan 2020, were included in analysis. Diagnosis of HCC was based on APSAL HCC 2017 updated guidelines. Staging was according to Barcelona Clinic Liver Cancer (BCLC). The mPAGE-B score was calculated and the 5-year cumulative incidence of HCC among the low (≤ 8), immediate (9–12) and high (≥ 13) score groups were compared.
Results: Totally, 2232 eligible patients were included, 435 and 1040 in the low and high score groups respectively. 441 patients developed HCC within 5 years. Univariate logistic regression analysis showed that the risk of HCC increased by 0.725 fold for each unit increase in mPAGE-B ($B = 0.545$, $P < 0.001$).Multivariate logistic regression analysis showed that mPAGE-B score was an independent risk factor

for HCC ($P < 0.001$). The 5-year risk of HCC was 3.09 times higher in the medium-risk group than in the low-risk group with 95%CI of 1.776—5.375 ($P < 0.001$), and was 10.13 times higher in the high-risk group than in the low-risk group with 95%CI of 6.017—17.064 ($P < 0.001$).The correlation between BCLC and mPAGE-B in the HCC group was not statistically significant ($P = 0.377$).
Conclusion: Chinese CHB patients undergoing antivirals in the low mPAGE-B score group had a lower risk of developing HCC than those in the intermediate and high score groups. Barcelona staging and mPAGE-B score had no significant correlation. The high HCC incidence in our cohorts may be related to a high proportion (46%) of subjects with high risk scores.

[OP-1068]

Clinical effectiveness of tenofovir alafenamide-switching therapy in chronic hepatitis B patients with clinical relapse after discontinuation of oral antiviral therapy—an interim report

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Objectives: Retreatment is frequent in patients of chronic hepatitis B (CHB) who developed clinical relapse after cessation of oral antiviral therapy. Whether retreatment with the original regimen or switching to tenofovir alafenamide (TAF) would be beneficial remains unclear. We aimed to investigate the clinical effectiveness of switch to TAF after clinical relapse.
Materials and Methods: This multicenter study is enrolling patients who experienced off-therapy clinical relapse and switch to TAF for retreatment (prospective arm), or continue the original entecavir or tenofovir disoproxil fumarate (TDF) regimens (historical arm) for 48 weeks in Taiwan. The primary endpoint was the rate of virological remission (HBV DNA < 20 IU/mL), and the secondary endpoints were the rate of ALT normalization, the change of HBsAg level, renal function, body weight and lipid profiles.
Results: As of November 3, 2021, the CHANGE (Chronic Hepatitis b patients switch to tAf after discontinuation of Nucleoside analoGuE) study included 25 patients in the prospective arm. At retreatment, the median age was 52 years, HBV DNA was 6.7 log10 IU/mL and ALT was 228 IU/mL. The virological remission rate was 43% (n = 6/14), 89% (n = 8/9), and 50% (n = 4/8) at 24, 36, and 48 weeks of therapy with a median HBV DNA level of 17 IU/mL at week 48. The ALT normalization rate was 71% (n = 10/14), 100% (n = 9/9), and 100% (n = 8/8), respectively. Eight patients completed 48-week TAF therapy, and their HBsAg declined significantly (3.34 to 2.88 log10 IU/mL, $P = 0.034$). There was a significant change of TG (88 to 110 mg/dL, $p = 0.006$), and HDL (54 to 46 mg/dL, $P = 0.021$), while their body weight and eGFR remained stationary. The compliance was good and no significant adverse events were reported.
Conclusion: In this interim report, switching to TAF therapy is safe and effective, while long-term viral suppression, and change of lipid profile should be monitored.

[PP-1102]

The prevalence of hepatitis B among pregnant women in Cirebon Regency during COVID-19 pandemic

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Objectives: The COVID-19 pandemic has brought tremendous impact on healthcare, including screening for hepatitis B in pregnant women. Of 19,234 pregnant women, there were 2.38% identified as hepatitis B in 2017–2019. This study was aimed to investigate its current prevalence during pandemic.
Materials and Methods: A cross-sectional study was conducted among pregnant women between April 2020 and September 2021 in 3 public health centers in Cirebon Regency, Indonesia. History of chronic liver disease was excluded in this study. Data were collected from annual report of Department of Health, Cirebon Regency, Indonesia, including demographic characteristics, obstetric history, the presence of jaundice. The status of hepatitis B was detected by immunochromatographic, rapid assay HBsAg test kit.
Results: Of 2210 subjects, there were 21 found positive (0.95%). Median age of subjects were 28 years old (15–48). Among subjects, as many as 37.42% were primigravida and 47.19% were in first trimester. None of subjects had symptoms. The highest hepatitis B prevalence was identified in mother aged < 35 year and multiple parities.
Conclusion: Prevalence of hepatitis B among pregnant women in Cirebon Regency during pandemic was 0.95% and markedly reduced compared with previous prevalence.

[PP-1154]

Reduced risk of hepatocellular carcinoma during a long-term besifovir treatment in chronic hepatitis B patients

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Objectives: To date, there is no information regarding the influence of besifovir (BSV) on the occurrence of HCCs in chronic hepatitis B (CHB) patients. The present study aims to assess the degree of HCC incidence reduction in those under the BSV treatment.
Materials and Methods: The present study is a part of an extensional phase 3 trial for BSV. A total of 190 CHB patients were treated with BSV up to 288 weeks. We assessed the incidence of HCC during the follow-up and compared it with predictive numbers of HCC cases using the models developed in untreated CHB patients (REACH-B and GAG). In addition, we compared the performance of HCC prediction models developed in CHB patients receiving antiviral therapy.
Results: During the follow-up of 288 weeks, 7 patients developed HCC; 1 of 139 non-cirrhotic patients and 6 of 51 liver cirrhosis patients. We compared the HCC incidence with the prediction number of the REACH-B model in non-cirrhotic patients at 288 weeks. The standard incidence ratio (SIR) was calculated to be 0.128 (P = 0.039), which suggests a significant decrease of HCC incidence in non-cirrhotic patients. The incidence of HCC in the cirrhosis patient was compared using the GAG model, and the SIR was 0.392 (P = 0.026), suggesting decreased HCC incidence in liver cirrhosis patients. By multivariable analysis, liver cirrhosis (P = 0.006) and age (P = 0.002) were the significant factors for the development of HCC. When we compared the HCC prediction models developed in CHB patients under antiviral therapy, the HCC-RESCUE model showed higher AUROC (0.913) than PAGE (0.749), mPAGE (0.779), THRI (0.826), CAMD (0.911), or AASL (0.920) without statistical significance.
Conclusion: BSV decreases the risk of HCC in CHB patients with or without liver cirrhosis. The performance of the HCC-RESCUE model was the best among various prediction models.

[OP-1195]

Long-term bone safety of tenofovir disoproxil fumarate in chronic hepatitis B patients

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Objectives: To observe the long-term bone safety of tenofovir disoproxil fumarate in chronic hepatitis B patients.
Materials and Methods: This prospective observational study was started in January 2019 and the data is still being conducted in the Department of Gastroenterology & Hepatology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan. A total of 179 patients with CHB started on TDF therapy of both gender and having age more than 18 years and less than 60 years were recruited till date. Bone mineral density was assessed on the basis of pre and post Dual-Energy X-ray Absorptiometry (DEXA) scan. Dexa score (T-Score) of less than $-$ 1.0 of left hip & spine was considered abnormal. Patients were assessed at the time of recruitment then after three and six months for comparison.
Results: Out of 179 patients, 111 (62.01%) were males and 68 (37.98)% were females, with a mean age of 35.34 $\pm$ 11.07 years. A T score of $-$ 1.0 to $-$ 2.5 was recorded insignificantly while comparing with baseline at the end of three months (29% at lumbar and hip sites, p value > 0.05) but after six months the BMD was significantly reduced in patients receiving TDF (46% at hip and 49% at lumber site, $p < 0.05$). While T score of $\leq -$ 2.5 was found in 21% at the lumbar site and 17% at the hip (p value > 0.05) site after three months and 16% at the lumbar & 7% at hip sites after six months (p value < 0.05).
Conclusion: The results of this study conclude that the use of TDF is associated with reductions in bone density in patients with CHB patients having no prior bone disease.

[OP-1196]

Long-term renal safety of tenofovir disoproxil fumarate in chronic hepatitis B patients

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Objectives: The aim of this study is to evaluate the long term renal safety of TDF in chronic hepatitis B patients.
Materials and Methods: This prospective observational study was conducted from January 2019 till todate in the Department of Gastroenterology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan. A total of 179 patients with CHB started on TDF therapy of both gender, age $\geq$ 18 years. Renal safety was assessed on the basis of pre and post assessment of renal functions via eGFR measurement. Patients were assessed at the time of recruitment then after 3 and 6 months. The primary endpoint was renal outcome, based on eGFR.
Results: We enrolled 179 patients, 114 (63.68%) were males and 65 (36.31%) were females, with a mean age of 35.41 $\pm$ 11.06 years. During follow-up at 3 months there was no difference in eGFR $\geq$ 60 mL/minute/1.73m^2 from baseline. And, after 6 months of TDF therapy patients had slight lower eGFR (55.5 mL/minute). However, after one year of follow up significant decrease in eGFR was observed (48.9 mL/minute). Also, in a sub analysis, patients older than age 50 years had worse renal outcomes with TDF.
Conclusion: Comparing with baseline a significant reduction of eGFR has been observed at the end of one year (p value < 0.05).

[OP-1202]

Risk factors of hepatitis B in children: an experience of tertiary care hospital of Karachi, Pakistan

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Objectives: We evaluated the frequency of risk factors of Hepatitis B virus in children presenting to a tertiary care hospital of Pakistan.
Materials and Methods: This descriptive cross-sectional study was conducted at the Gastroenterology section of Medical Unit IV, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. After obtaining ethical approval and informed consent from the guardians, children between the ages of $\leq$ 15 years, diagnosed with Hepatitis B virus were included in the study. Patients with positive Hepatitis B Surface Antigen were included in the study. Patient's current HBV status, history of blood transfusion and history of surgery or dental procedures were recorded in pre-designed Pro-forma. Data were analyzed using SPSS version 25. We desire a larger sample size so this study is continued further.
Results: A total of 153 children were enrolled in this data out of which 96 (63%) were male while 57 (37%) were female. Mean age of patients was 12.0 $\pm$ 2.3 years. Out of these, 12 (8%) had HBeAg + ve chronic HBV infection while 20 (13%) were HBV Carrier, and 8 (5.22%) were in immunotolerant phase of CHB. Seventeen (11%) patients had a perinatal route of transmission and only 3 (2%) patient had a positive past surgical history. Nighty three (60%) patients had a positive family history.
Conclusion: Mass awareness campaigns are needed in order to educate the general population regarding Hepatitis B Virus Infection. Maternal infection is a serious threat to the unborn child. Hepatitis B vaccine should be administered to all newborns regardless of maternal HBsAg status. Data collection is still ongoing.

[L-OP-1273]

Hepatitis B vaccination coverage among Indian healthcare workers

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Objectives: The current survey was conducted to assess the coverage as well as associated barriers for Hepatitis B Vaccination among Indian Healthcare workers.
Materials and Methods: A descriptive cross sectional survey was conducted among 706 healthcare workers across 25 states of India using online platform (survey monkey) over a period of 5 months. A prevalidated questionnaire with 25 items was used for data collection. The obtained data was analysed with SPSS version 22.
Results: Mean age of participants was 30.8 $\pm$ 7.6 and majority of them were females (73.5%). Of all, 62% of HCWs were working in govt institutes while 38% were from private institutes. 35.4% healthcare workers reported that they were never tested or screened for Hepatitis B infection. Out of all, 66.71% of the HCWs were completely vaccinated, 14.9% had not taken complete dose while 16% had not taken any dose of hepatitis b vaccination. HCWs could not complete vaccination due to forgetfulness (7.2%), lack of time (4%),and long duration (2%) while 1.6% participants felt they are protected against HBV and do not require the further doses. Reasons reported for not getting vaccinated were non availability of vaccines through govt channels (4.4%), not at risk for getting infected (4%), non awareness towards availability of HBV vaccination (3.7%), can't get infected (2.4%), didn't give much emphasis (2.3%), long duration of vaccination (2.1%), high cost of vaccine (0.8%), doubtful vaccine efficacy (0.6%) and a fear that vaccine may have worse side effects (0.1%).
Conclusion: Based on the results of the study it was concluded that only two third of health care workers are vaccinated against hepatitis B in India. Hence there is a need for the government to establish and implement hepatitis B vaccination policies for Health care workers.

[L-OP-1310]

Pharmacokinetics, safety, and tolerability of the siRNA JNJ-73763989 in healthy Chinese adult participants

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Objectives: JNJ-73763989 is composed of 2 RNA interference triggers JNJ-73763976 and JNJ-73763924 designed to target all hepatitis B virus mRNAs and reduce viral proteins. This study investigated the pharmacokinetics, safety, and tolerability of JNJ-73763989 in healthy Chinese adults following single-dose administration.
Materials and Methods: In this single-center, open-label, parallel, randomized Phase 1 study, participants were administered single subcutaneous doses of 100 or 200 mg of JNJ-73763989. Plasma and urine pharmacokinetic parameters were determined for each trigger up to 48 h post-dosing using non-compartmental analysis (Phoenix). Safety and tolerability were evaluated by dose group until 28 days post-dose.
Results: In total, 18 participants were enrolled (9 per dose). The median age and weight were 33 years and 73.7 kg; 83.3% were male. JNJ-73763976 and JNJ-73763924 C_{max} and AUC all increased in a dose-proportional manner (Table). Median time to maximum plasma concentration (t_{max}) ranged from 6.02 to 10.00 h, and mean apparent half-life ($t_{1/2}$) ranged from 4.5 to 4.8 h for both triggers. Mean excretion in urine up to 48 h was 17.7% and 19.4%, and 13.2% and 13.1% in the 100 and 200 mg groups for JNJ-73763976 and JNJ-73763924, respectively. There were no deaths, serious adverse events (SAEs) or treatment-emergent AEs (TEAEs) leading to termination of study participation; all TEAEs were mild and resolved by end of study. Injection site erythema was the most common AE in 27.8% of participants.
Conclusion: In healthy adult Chinese participants, JNJ-73763989 had pharmacokinetics consistent with previous studies in other populations and was generally safe and well tolerated.

Table. Summary of Plasma and Urine Pharmacokinetic Parameters

	JNJ-73763976		JNJ-73763924	
PK Parameter*	JNJ-3989 100 mg (n = 9)	JNJ-3989 200 mg (n = 9)	JNJ-3989 100 mg (n = 9)	JNJ-3989 200 mg (n = 9)
Plasma				
C_{max} (ng/mL)	410 (183)	1,060 (607)	83.5 (37.5)	195 (103)
t_{max} (h)	10.00 (3.00 – 10.00)	10.00 (3.00 – 10.02)	8.00 (3.00 – 10.00)	6.02 (2.00 – 10.02)
AUC_{last} (h*ng/mL)	7,019 (2,167)	16,706 (3,978)	1,221 (435)	2,622 (543)
AUC_{∞} (h*ng/mL)	7,053 (2,172)	17,186 (4,029)†	1,310 (482)‡	2,641 (564)†
$t_{1/2}$ (h)	4.6 (0.9)	4.7 (0.4)†	4.5 (1.6)‡	4.8 (0.9)†
CL/F (L/h)	10.2 (3.09)	8.21 (2.29)†	28.6 (10.4)‡	26.3 (5.96)†
V_d/F (L)	69.5 (27.8)	56.5 (17.9)†	200 (149)‡	186 (70.4)†
C_{max}/dose (ng/mL/mg)	6.15 (2.74)	7.98 (4.55)	2.50 (1.12)	2.92 (1.54)
AUC_{last}/dose (h*ng/mL/mg)	105 (32.5)	125 (29.8)	36.6 (13.0)	39.3 (8.14)
AUC_{∞}/dose (h*ng/mL/mg)	106 (32.6)	129 (30.2)†	39.2 (14.4)‡	39.6 (8.45)†
Urine				
Ae (mg)	11.8 (7.21)	25.9 (9.13)	4.42 (2.52)	8.76 (2.74)
Ae (% dose)	17.7 (10.8)	19.4 (6.85)	13.2 (7.56)	13.1 (4.10)
CL_R (L/h)	1.60 (0.479)	1.56 (0.416)	3.39 (0.804)	3.29 (0.834)

SD, standard deviation; C_{max}, maximum plasma concentration; t_{max}, time to reach the maximum plasma concentration; AUC_{last}, area under the plasma concentration-time curve from time 0 to the time of the last quantifiable concentration; AUC_{∞}, area under the plasma concentration-time curve from time 0 to infinite time; $t_{1/2}$, the apparent terminal elimination half-life; CL/F, total clearance of drug following single-dose administration; V_d/F, apparent volume of distribution; C_{max}/dose, dose normalized C_{max}; AUC_{last}/dose, dose normalized AUC_{last}; AUC_{∞}/dose, dose normalized AUC_{∞}; Ae, cumulative urinary recovery; Ae (% dose), cumulative urinary recovery represented as a percentage of dose; CL_R, renal clearance.
*All parameters are shown as mean (SD) except for t_{max}, which is shown as median (range).
†n = 8 for AUC_{∞}, $t_{1/2}$, CL/F, V_d/F, AUC_{∞}/dose.
‡n = 7 for AUC_{∞}, $t_{1/2}$, CL/F, V_d/F, AUC_{∞}/dose.

[L-PP-1318]

Antiviral activity of GST-HG141, a hepatitis B virus capsid assembly modulator, in subjects with chronic hepatitis B: Interim data

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Objectives: Safety, tolerability, and pharmacokinetics of GST-HG141, a hepatitis B (HBV) capsid assembly modulator (CAM), in healthy subjects (NCT04386915) has been reported previously [Li et al., Antimicrob Agents Chemother.2021:65 (10)]. The aim of this study was to evaluate the antiviral activity of multiple doses of GST-HG141 in subjects with chronic hepatitis B (CHB).
Materials and Methods: A multi-center, randomized, double-blind, placebo-controlled, multiple ascending-dose phase Ib study (NCT04868981). Patients with CHB, who were not treated with interferon or nucleosides (> 12 or 6 months, respectively), HBeAg-positive or negative (serum HBV DNA $\geq 2 \times 10^5$ or $\geq 2 \times 10^4$ IU/mL, respectively) received oral BID doses of GST-HG141 (25, 50 and 100 mg) for 28 days. Ten patients in each cohort were randomized to receive a drug or placebo (4:1). A validated LC–MS/MS method was used to quantify GST-HG141 in plasma. The PK parameters were calculated with WinNonlin 8.0 software. Serum HBV DNA was determined using Quantitative Real-Time PCR, serum HBV antigens – by ELISA methods. Here we present preliminary data on the PK and antiviral activity for 25 and 50 mg cohorts. The dosing with 100 mg is ongoing.
Results: Administration of 25 and 50 mg of GST-HG141 BID for 28 days was well tolerated. A rapid and robust decline in serum HBV DNA was observed with the 25 and 50 mg dose cohorts (average 2.9 $\log_{10}$ IU/ml and 3.3 $\log_{10}$ IU/ml, respectively). No virus breakthrough was noted. No significant decline in serum HBsAg or HBeAg was observed. Plasma GST-HG141 exposure increased nearly proportionally with the dose. Modest accumulation (mean values 1.67–2.38) was seen with dosing for 28 days.
Conclusion: Oral BID dosing with 25 and 50 mg of GST-HG141 for 28 days resulted in rapid, robust and dose-dependent decline in serum HBV DNA. Plasma GST-HG141 exposure was nearly dose-proportional. Dosing of additional cohorts is ongoing. Further clinical development of GST-HG141 for CHB is warranted.

[L-OP-1326]

Hepcidin expression levels involve efficacy of pegylated interferon-treatment in hepatitis B-infected liver

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Objectives: Hepcidin is an iron regulator hormone produced by the liver. The association of serum hepcidin with interferon therapy in patients with chronic hepatitis C infection has been studied. However, the role of hepcidin in predicting the effect of interferon in patients with hepatitis B infection is yet to be elucidated. Our study aims to investigate the correlation between hepcidin expression levels and the curative effect of interferon-alpha therapy in CHB patients.
Materials and Methods: A total of 47 patients with CHB who accepted pegylated interferon-α (PEG-IFN- α) treatment were recruited. The serum level of hepcidin was estimated by ELISA. The alternation in the gene expression level of hepcidin was detected by RT-PCR, and immunofluorescence cell staining was performed to detect hepcidin peptide. The induction of antiviral proteins was analyzed by Western blotting. The predictive value of early on-treatment variation in serum hepcidin during treatment progress was assessed by receiver operating characteristic analysis.
Results: High levels of early on-treatment serum hepcidin were observed in patients who achieved a decline in HBsAg > 1 log10 IU/mL or HBV DNA > 1 log10 IU/mL. In vitro, an elevation of the hepcidin expression in HepG2.2.15 cells induced by PEG-IFN-α was noted. Furthermore, combined treatment with hepcidin and PEG-IFN-α increased the levels of antiviral proteins. The predictive cut-off value of hepcidin for HBsAg decline > 1 log10 IU/mL was 239 pg/mL, the sensitivity and specificity were 72.73% and 70.97%. As for HBV DNA decline > 1 log10 IU/mL, the value was 190.4 pg/mL, the sensitivity and specificity were 72.73% and 61.11%. The changes in the hepcidin level signified the predictive value of the PEG-IFN-α treatment.
Conclusion: A higher early-on treatment hepcidin level indicates a higher possibility of HBsAg and HBV DNA decline in CHB patients during PEG-IFN-α treatment. The hepcidin level is significant in predicting the PEG-IFN-α therapeutic effect in patients with CHB.

[L-PP-1328]

Comparison of the impact of tenofovir alafenamide and entecavir on viral response and HBsAg declines in the same group of HBV-infected patients

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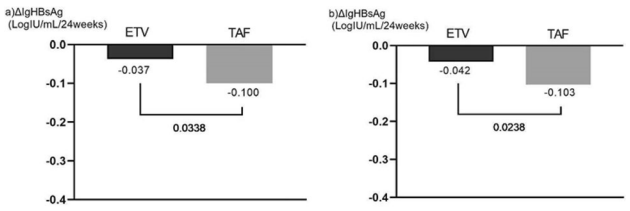
Objectives: To evaluate antiviral effectiveness, hepatitis B surface antigen (HBsAg) dynamics and safety of TAF in CHB patients previously treated with entecavir, including patients with low level viremia (LLV) in real-world setting.
Materials and Methods: This cohort included 69 consecutive CHB patients from Jan 2019 to Dec 2020 who switched to TAF after previous treatment with ETV for over 96 weeks. HBV DNA, HBsAg, ALT, liver stiffness measurement (LSM), eGFR and controlled attenuation parameter (CAP) were observed before and after switchover.
Results: HBV DNA undetectable (HBV DNA < 20 IU/ml) rate were 57.9%, 60.3% and 91.4% at 24 weeks before, at time point and 24 weeks after drug switching, respectively, showing significant increase [60.3% vs 91.4%, P < 0.05] during the 24-week period of treatment with TAF. HBsAg levels were reduced significantly more during the 24-week TAF phase than during the ETV phase (− 0.100 vs − 0.037, P = 0.0338, Figure a). ALT normal (ALT < 50 U/L) rate, LSM, CAP and eGFR did not change significantly during treatment. At week 24 before switchover there were 23.2% (16/69) patients with LLV, among which 25% (4/16) had virological response after maintained ETV treatment for 24 weeks. After 24 weeks switching to TAF, the rate increased to 83.3% (10/12). HBsAg levels in LLV population were also reduced significantly more during TAF phase than during ETV phase (− 0.103 vs − 0.042, P = 0.0238, Figure b).
Conclusion: CHB patients switched to TAF from long term ETV achieved significant improvement in virological response and more decline in HBsAg level. Similar result demonstrated in LLV population as well.



[ABST-0555]

Analysis of the determinants of hepatitis B risk factors in pregnant women during the Covid-19 pandemic in Indonesia

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Background: Hepatitis B is a disease that attacks the liver and is a world health problem, especially in developing countries, including Indonesia. Hepatitis B (HBV) infection in pregnant women has become a worldwide concern because transmission is the most common throughout the world, especially in endemic areas. In addition to horizontal transmission, one of the biggest causes is vertical transmission from mother to child or also called the mother to child transmission (MTCT) where a mother who is HBsAg positive will transmit it to the fetus she is carrying.
Methods: This study used the Case–Control method with a retrospective approach involving 133 cases and 534 controls with multiple logistic regression analysis.
Results: Statistical tests showed that education level (p-value = 0.027; OR = 2.705; 95% CI: 1.197–6.113), parity (p-value = 0.023; OR = 2.846; 95% CI: 1.228–6.697), and sexual partners (p-value = 0.031; OR = 9.333; 95% CI: 1.121–77.704) is a risk factor for the incidence of hepatitis B in pregnant women. Meanwhile, the age group (p-value = 0.177) and type of work (p-value = 0.059) were not risk factors for the incidence of hepatitis B in pregnant women. Another study states that the way to avoid the transmission of this infection, one of which is the Antenatal Care (ANC) examination.
Conclusions: Education level, parity, and sexual partners are risk factors for hepatitis B incidence in pregnant women. Among all the risk factors found, a sexual partner is the most risk factor for the incidence of hepatitis B in pregnant women. Therefore, it is very important for pregnant women to carry out Antenatal Care (ANC) examinations.

Hepatitis C—Basic

[PP-0196]

Helicobacter pylori versus platelet-to-spleen ratio as a risk factor for variceal bleeding in patients with liver-cirrhosis-related portal hypertension

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Objectives: Acute upper gastrointestinal (GIT) bleeding is a common medical emergency clinically manifested by hematemesis and/or melena. This study aims to elucidate the roles of Helicobacter pylori and the platelet–spleen ratio as risk factors for variceal bleeding in patients with portal hypertension secondary to liver cirrhosis.
Materials and Methods: The study was conducted on 200 patients with liver cirrhosis of various etiologies who were divided into two groups: group 1 included 100 patients with liver cirrhosis and portal hypertension with or without a history of upper GIT bleeding, and group 2 included 100 patients with liver cirrhosis without portal hypertension. Upper GIT endoscopy was performed, and biopsy samples were taken from the gastric antral mucosa for rapid urease testing. The platelet–spleen diameter ratio was calculated for all patients.
Results:: In group 1, most patients who had a history of variceal bleeding were H. pylori-negative whereas most patients without a history of variceal bleeding were H. pylori-positive, implying that H. pylori may play a significant role as a protective factor against variceal bleeding. The calculated odds ratio for the rapid urease test was low (0.851), whereas the calculated odds ratio for the platelet–spleen diameter ratio was higher (9.766) than that for the rapid urease test. Thus, the rapid urease test plays a significantly higher role than the platelet–spleen ratio as a risk factor for bleeding (p-value = 0.001).
Conclusion: H. pylori has a more significant relationship with upper GIT bleeding than the platelet–spleen diameter ratio.

[OP-0197]

Assessment of fibrosis after treatment with direct acting antiviral drugs with or without silymarin in patients with chronic hepatitis C related liver disease

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Objectives: Direct-Acting Antivirals (DAAs) are now the standard of care for management of chronic hepatitis C (CHC) infection. Patients who are treated from HCV infection with sustained virological response experience multiple health benefits, like a decrease in liver inflammation, regression of fibrosis. Aim: to evaluate change in hepatic fibrosis through liver and spleen stiffness measurements using fibroscan in relation to combination of DAAs and silymarin in chronic HCV patients.
Materials and Methods: this prospective study included 300 chronic HCV patients. They were classified into group 1 (n = 150) who received DAAs and group 2 (n = 150) who received DAAs then fixed oral dose of silymarin (420 mg daily in three divided doses) for 9 months after end of treatment with DAAs. Assessment of liver and spleen stiffness were done twice by transient elastography, at time of inclusion before starting treatment and one year later.
Results: Patients in group 1 and 2 achieved a significant improvement in all biochemical parameters in form of significant reduction in serum AST, ALT levels, ($p = 0.001$), significant improvement in INR ($p = 0.001$) and albumin ($p < 0.05$). However, there was no statistically significant difference between group 1 and 2 regarding biochemical parameters ($p > 0.05$). A statistically significant reduction in stiffness values of liver and spleen had been established in both groups. Group 2 showed a significant greater reduction in liver stiffness values compared to group1 ($p = 0.007$).
Conclusion: Among chronic HCV patients, DAAs yielded a significant improvement in overall disease parameters. This improvement has shown to be significantly greater when silymarin was added to DAAs.

[OP-0198]

Hyaluronic acid as a potential marker for assessment of fibrosis regression after direct acting antiviral drugs in chronic hepatitis C patients

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Objectives: Fibrosis is inevitable complication of chronic hepatitis C virus (HCV) infection. Direct acting drugs (DAAs) radically treated HCV and were suggested to ameliorate fibrosis. Silymarin (natural herbal remedy) was proposed to further decrease hepatic inflammation and fibrosis. Consequently, serial monitoring of liver fibrosis status by different biomarkers is needed. Aim: to assess hyaluronic acid as potential marker of fibrosis regression after DAAs in chronic HCV patients. In addition, evaluate Silymarin as an agent that, beside DAAs, could further improve fibrosis.
Materials and Methods: two groups were included (150 patients each). Group I received DAAs only, while group II received DAAs followed by Silymarin. Hyaluronic acid (HA) and FIB4 score were assessed at baseline before treatment and 1 year after inclusion in the study.
Results: we found that DAAs therapy alone or in combination with Silymarin resulted in significant reduction in serum hyaluronic acid level. However, the latter case showed statistically significant greater reduction ($p = 0.034$). Mean ± SD of serum HA level was 211.8 ± 179.9 and 143.3 ± 123.9 ug/L before and one year after inclusion respectively in group I ($p = 0.001$) and also, its level reduced significantly in group II from 188.3 ± 211.8 ug/L before receiving DAAs to 126.4 ± 136.9 ug/L at one year after inclusion ($p = 0.001$). There was no significant difference between the 2 studied groups as regards FIB-4 at 1 year after inclusion ($p = 0.103$).
Conclusion: hyaluronic acid might be a sensitive marker for monitoring fibrosis regression in treated chronic HCV patients. Adding Silymarin to treatment protocols could ameliorate fibrosis status.

[OP-0788]

Treatment outcome of patients undergoing hemodialysis with chronic hepatitis C on the sofosbuvir and velpatasvir regimen

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Objectives: This study aims to determine the outcome associated with combination therapy (sofosbuvir/velpatasvir) in HCV patients with end-stage renal disease and undergoing hemodialysis.
Materials and Methods: All HCV patients with ESRD and undergoing maintenance hemodialysis having age more than 18 years were included in our study. Study population was enrolled from Nephrology and Gastroenterology & Hepatology wards of a tertiary care hospital of Karachi. A structured questionnaire was used to obtain the data regarding baseline demographics & clinical profile and outcome associated with combination therapy (SOF (400 mg once daily) and VEL (100 mg once daily). Outcome was assessed at the end of treatment (week 12) and at week 24.
Results: Final analysis was performed on 34 patients out of 122, among all, more than 91% (n = 31) of the patients have achieved sustained virological response at week 24. Treatment relapse was very low and only five patients showed treatment relapse which was statistically insignificant. The most common cause of ESRD was hypertension (44.1%, n = 15/34) and the most common side effect observed by the end of treatment was fatigue (47.1%, n = 16/34).
Conclusion: Treatment with sofosbuvir and velpatasvir is a safe choice in achieving SVR after 24 weeks in patients with ESRD undergoing hemodialysis.

[OP-0838]

Low disease awareness as a contributing factor to the high prevalence of hepatitis C infection in Tzukuan, a hyper-endemic area of Southern Taiwan

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Objectives: Clarifying the barriers and tackling the hurdles of HCV care cascades are the key toward hepatitis C virus (HCV) elimination. The current study aimed to investigate the rates of disease awareness, link-to-care and treatment uptake of HCV in an hyper-endemic area, Tzukuan, in Taiwan.
Materials and Methods: A total of 1,789 Tzukuan residents seropositive for anti-HCV were enrolled in this study. Due to the

disease awareness with a lack in 2000–2004. among these anti-HCV seropositive subjects, 594 had received a questionnaire for the disease awareness, accessibility and antiviral treatment of HCV from 2005 to 2018.
Results: Overall, from 2000 to 2018, HCV prevalence was 17.3%, while 24.9% of disease awareness and 7.5% of community-effectiveness were noted. Over periods, it decreased from 21.2% in the early cohort to 9.3% in the recent cohort of HCV prevalence, increased from 15.6% to 41.7% of disease awareness and 0.9% to 20.2% of community effectiveness. Awareness increased as prevalence decreased over time. Young people, lower education levels and normal liver function were associated with lower rate of disease awareness or lower treatment uptake of HCV to lead to lower community effectiveness of treatment. About 70% of subjects with abnormal liver function and advanced fibrosis (FIB-4 > 3.25) still had no disease awareness of HCV infection.
Conclusion: We demonstrated there are huge gaps with significant barriers in disease awareness, link-to-care and treatment uptake in care cascade toward HCV elimination in an HCV hyperendemic area even in the era of DAA. Therefore, a comprehensive strategy to increase the rates of screening, diagnosis and accessibility to enhance treatment update is urgent for the achievement of WHO's goal for HCV elimination.

[PP-1172]

Detection of basal core promoter mutation in patient with chronic hepatitis B virus infection using droplet digital PCR (ddPCR)

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Objectives: Mutation in the hepatitis B virus basal core promoter (BCP) is associated with disease progression and severity. However, previous conventional method does not provide quantification of HBV mutants. The aim of this study was to evaluate the efficiency of droplet digital PCR (ddPCR) for the detection of the BCP mutation in patients with chronic hepatitis B.
Materials and Methods: Serum samples from a total of 69 patients with chronic hepatitis B virus infection (18 HBeAg-positive chronic infection and 51 HBeAg-negitive chronic hepatitis) were extracted for DNA and detected for mutation by Sanger sequencing. The percentage of BCP mutation were determined by ddPCR.
Results: The BCP mutation was detected in 60 of 69 samples (86.95%) by ddPCR, while only 25 of 69 samples (36.23%) was detected by Sanger sequencing. The 60 samples with the BCP mutation were detected by ddPCR at a fractional abundance from 0.15% to 100% as follows: ≥ 10% (51 samples, 83%), 5–10% (2 samples, 3.33%), and ≤ 5% (7 samples, 11.67%). The mutation rate of BCP was ranging from 0.15% to 100% for patients with HBeAg-positive and 1.26% to 100% for patients with HBeAg-negative. The BCP mutation was significantly higher in HBeAg-negative than HBeAg-positive groups (55.27% vs 33.23%, P < 0.022).
Conclusion: ddPCR might be used as an alternative method for the detection of the BCP mutation rate in patients with chronic hepatitis B virus infection.

Hepatitis C—Clinical

[PP-0065]

Seroprevalence of hepatitis B and C, and HIV in the Korean young men on Military Health Examination from 2017 to 2020

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Objectives: Little is known about the seroprevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV among young adults in Korea. This study aims to investigate the seroprevalence of HBsAg, anti-HCV, and anti-HIV along with the frequency of abnormal aspartate and alanine transferase [(AST and ALT) > 40 IU/L] among the Korean young men on military health examination from 2017 to 2020.
Materials and Methods: This retrospective study analyzed the data of 1,218,516 men with mean age of 19 years, who received the military service determination examination conducted by the Military Manpower Administration in South Korea from 2017 to 2020. At the first visit, HBsAg, anti-HIV, AST, and ALT were tested (n = 1,218,516), and anti-HCV tests were performed only in the men showing abnormal AST or ALT levels (n = 156,879).
Results: From 2017 to 2020, the overall positive rate for HBsAg (0.22%, n = 2,685), anti-HCV (0.003%, n = 38), and anti-HIV (0.006%) was found, respectively. The prevalence of abnormal AST and ALT was 5.1% and 12.7%, respectively. The annual HBsAg positivity was 0.27% in 2017, 0.19% in 2018 and 2019, and 0.23% in 2020. The annual anti-HIV positivity was 0.0066% in 2017, 0.0039% in 2018, 0.0057% in 2019, and 0.0065% in 2020. Among 156,897 men who underwent the anti-HCV tests, The annual anti-HCV positivity was 0.014% in 2017, 0.021% in 2018, 0.020% in 2019 and 0.029% in 2020, showing an increasing trend. The mean AST and ALT levels in anti-HCV positive patients were 55.8 IU/L and 97.1 IU/L, respectively. The annual proportion of men with abnormal ALT level was 11%, 12%, 13% and 15% in 2017, 2018, 2019, and 2020, respectively.
Conclusion: From 2017 to 2020, HBsAg prevalence is decreasing, but the anti-HCV positivity rate is increasing, and the proportion of abnormal ALT is increasing. The anti-HIV prevalence is increasing from 2018 to 2020.

[OP-0069]

Changes and factors associated with liver function improvement in patients with hepatitis C virus-associated decompensated cirrhosis after sofosbuvir plus velpatasvir therapy

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Objectives: High rate of sustained virologic response (SVR) can be achieved even in patients with hepatitis C virus (HCV)-associated decompensated cirrhosis using sofosbuvir plus velpatasvir (SOF/VEL) therapy. Liver function is improved in some patients with decompensated cirrhosis after SOF/VEL therapy, but studies addressing long-term changes and factors associated with liver function improvement are limited in Asia.
Materials and Methods: A total of 102 patients who were clinically diagnosed with HCV-associated decompensated cirrhosis and initiated SOF/VEL therapy from February 2019 to October 2019 at 25 Japanese hospitals were included.
Results: The mean age was 68 years and 50% were male. Patients with Child–Pugh class A (CP-A), CP-B, and CP-C were 8%, 74%, and 19%, respectively. The SVR12 rate was 89% (91/102). Patients with CP-A at baseline, end of therapy (EOT), 12 weeks after EOT, 24 weeks after EOT, and 1 year after EOT were 8%, 34%, 40%, 42%, and 34%, respectively. The percentage of patients with CP-A were increased from baseline to EOT, but little further increase after EOT was observed. Among 94 patients with baseline CP-B or CP-C, 28 patients experienced improvement to CP-A at 1 year after EOT. In the multivariate analysis, presence of overt hepatic encephalopathy ($p = 0.016$), higher total bilirubin level ($p = 0.032$), and lower albumin level ($p = 0.003$) were negative predictor of improvement to CP-A.
Conclusion: Liver function improves until EOT, but may not improve thereafter in patients with decompensated cirrhosis after SOF/VEL therapy. Overt hepatic encephalopathy, total bilirubin level and albumin level are associated with liver function improvement.

[OP-0072]

Prevalence, diagnosis, treatment and associated factors of hepatitis C in the United States from 2013 to 2018: A population-based cross-sectional study

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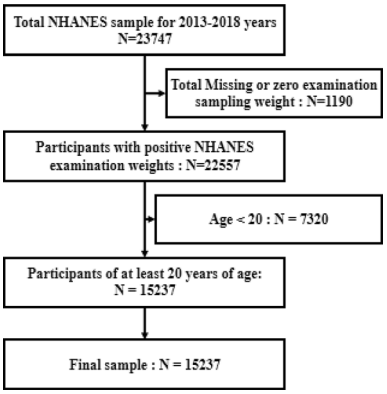
Objectives: To assess the prevalence, diagnosis, treatment and associated risk factors of HCV in the USA over the past six years.
Materials and Methods: Prevalence of HCV among adults living in American were estimated by the HCV RNA positive. Demographic characteristics, lifestyle, and laboratory results were collected in NHANES from 2013 to 2018.
Results: The weighted prevalence of total HCV (n = 168), HCV in 2013–2014 (n = 67), HCV in 2015–2016 (n = 50), HCV in 2017–2018 (n = 51) diagnosed by the HCV criteria were 0.94% (95%CI, 0.79% to 1.09%), 0.87% (95%CI, 0.62% to 1.12%), 0.95% (95%CI, 0.68% to 1.21%), 1.00% (95%CI, 0.72% to 1.28%) respectively, with estimated 2.20 million adults (95%CI, 1.84 million to 2.40 million), 2.00 million adults (95% CI, 1.42 million to 2.24 million), 2.22 million adults (95% CI, 1.59 million to 2.70 million), 2.39 million adults (95% CI, 1.72 million to 3.06 million), respectively. Among these patients, 43 to 63 years old, male, non-Hispanic blacks, lower educated, lower household income, divorced, single and living alone were more likely to be infected with HCV. Illicit drug use (including injecting drugs) and blood transfusion were significantly associated with HCV infection. Meanwhile, the weighted diagnostic rate of HCV infection was 0.58% and increased from 54.28% (95% CI, 42.35% to 66.20%, from 2013 to 2014) to 56.85% (95% CI, 43.12% to 70.57%, from 2015 to 2016) and to 63.48% (95% CI 50.26% to 76.69%, from 2017 to 2018).
Conclusion: The prevalence of HCV increased over the last six years in the USA. Also, the diagnostic rate and treated rate were low.



[PP-0073]

Comorbidities and prescription patterns among patients with chronic hepatitis C in Korea

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Objectives: Drug–drug interaction (DDI) is an important factor when choosing direct acting antivirals (DAAs) for patients infected with hepatitis C virus (HCV). This study aims to investigate the latest demographic trend of patients with HCV in Korea (including comorbidities and comedications) and compare the DDI among DAAs regimens.
Materials and Methods: In this retrospective, cross-sectional study, Health Insurance Review & Assessment Service (Korea) database from January 1st to December 31st, 2018, was analysed. Patients aged $\geq$ 18 years and diagnosed with "Chronic viral hepatitis C" (KCD-7 code B18.2) were selected. Comorbidities and comedication were assessed and potential DDI based on the comedications was analysed.
Results: Total of 50,476 patients were identified to have been diagnosed with HCV in 2018. The mean age of patients was 60.3 ± 12.7 years with 37.2% of patients $\geq$ 65 years. 53.3% were female. 97.5% of patients had $\geq$ 1 comorbidity and the mean number of comorbidities was 7.6. Diseases of digestive system (83.7%) was the most prevalent comorbid disease category. Hypertension, dyslipidemia and diabetes mellitus were present in 34.1%, 21.5%, and 19.9% of patients, respectively. Almost all patients (98.8%) were taking at least one prescribed medication. mean number of

medications was 9.5 and increased with age. Analgesics (91.6%), gastrointestinal agents (85.0%) and antibacterials (80.3%) were the most commonly prescribed comedications. Among the DAA regimens, SOF/VEL (2.2%) had the lowest contraindication DDIs followed by LDV/SOF (13.1%) and GLE/PIB (15.6). The three most commonly prescribed comedication with DDI of contraindication were atorvastatin (12.7%) with GLE/PIB, rosuvastatin (11.1%) with LDV/SOF and simvastatin (1.4%) with GLE/PIB.
Conclusion: Majority of HCV patients in Korea present with comorbidity and comedications. DDI should be thoroughly considered with caution.

[OP-0080]

Efficacy and safety of direct-acting antiviral therapy for hepatitis C virus in elderly patients (≥ 65 years old): a systematic review and meta-analysis

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Objectives: Direct-acting agents (DAAs) have launched a new era of hepatitis C virus (HCV) treatment. As aged individuals comprise a large percentage of HCV patients, the effectiveness and safety of DAAs in the elderly have come under scrutiny. This meta-analysis aims to evaluate the efficacy and safety of DAAs in elderly patients.
Materials and Methods: After a systematic search in PubMed (Medline), EMBASE, OVID Medline, the Cochrane Library, two investigators reviewed relevant abstracts and selected manuscripts. The sustained virologic response (SVR) and adverse events (AEs) rates were calculated with a random-effects model.
Results: Ninety studies evaluating SVR rates of elderly patients (≥ 65 years old) receiving DAAs were selected. DAAs in elderly patients exhibited a notable SVR rate of 96% (95% CI: 95% – 97%), accompanied with comparable rates in subgroup analyses. Comparison of SVR rates in elderly and non-elderly patients indicated no significant discrepancy (OR 1.01, 95% CI: 1.00 – 1.01). The overall event rate of AEs was 45% (95% CI: 31% – 60%), though AE rates varied by subgroups. Furthermore, AEs were comparatively more frequent (OR 1.15, 95% CI: 1.04 – 1.28) in the elderly than non-elderly, especially in subgroups such as SAE and dose reduction of ribavirin. However, in the ribavirin-free regimen, there was no significant difference in the incidence of AEs between the elderly and non-elderly groups.
Conclusion: DAAs exhibit high efficacy in elderly patients. Considering the possibility of AE, the RBV-free regimen should be given prior consideration for the treatment of elderly patients with HCV.

[OP-0096]

The Korean hepatitis C virus care cascade in a tertiary institution: Current status and changes in testing, link to care, and treatment

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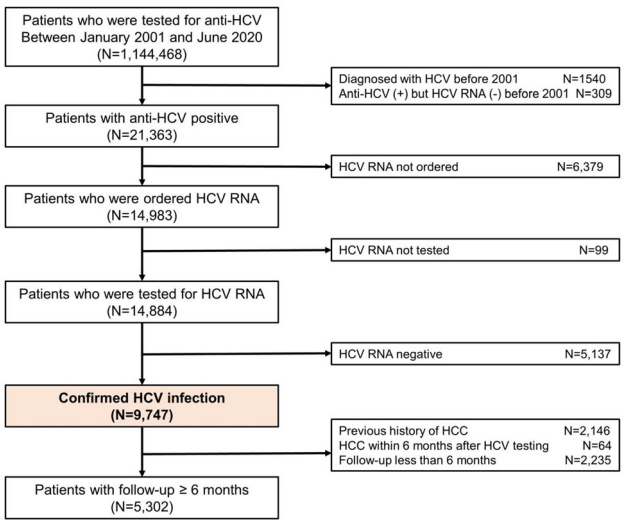
Objectives: The care cascade for hepatitis C virus (HCV) infection is impeded by multiple barriers, including suboptimal HCV Ab testing, link to care, and diagnosis. We explored the changes in the care cascade of HCV for the past 20 years and its current status in a large cohort from a tertiary referral center.
Materials and Methods: We analyzed 1,144,468 patients who had HCV Ab testing between January 2001 and June 2020. Metrics related to the care cascade of HCV infection and the long-term prognosis of patients were explored.
Results: The seroprevalence of HCV Ab was 1.8%, with a recent decreasing trend. In all, 69.9% of HCV Ab-positive patients performed HCV RNA testing, with a 65.7% positivity. Patients who did not have HCV RNA testing were older and more likely to have a non-hepatocellular carcinoma (HCC) malignancy, normal ALT level, and good liver function. Linkage times for HCV RNA testing from the HCV Ab positivity and for antiviral treatment from HCV diagnosis decreased, notably after 2015, when highly efficacious oral antiviral treatment was introduced to Korea. The average treatment uptake rate was 35.4%, which increased to 38.9% after 2015. Of the 5,302 patients analyzed regarding long-term prognosis, the annual incidences of HCC were 1.02 and 2.14 per 100 person-years in patients with and without a sustained virological response, respectively.
Conclusion: The care cascade of HCV infection has been suboptimal for the past 20 years, despite the recent changes. More effort should be made to increase HCV RNA testing and treatment uptake.



[OP-0133]

Real-life experience of ledipasvir and sofosbuvir for HCV infected Korean patients: a multicenter cohort study

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Objectives: We have evaluated the efficacy and safety of ledipasvir (LDV) and sofosbuvir (SOF) therapy in hepatitis C virus (HCV) infected Korean patients in real clinical settings.
Materials and Methods: A total of 273 patients who received LDV/SOF between May 2016 and February 2021 were consecutively enrolled and analyzed. Weight-based ribavirin was added for the treatment of decompensated cirrhosis and treatment-experienced compensated cirrhosis patients. Per protocol analysis was done for the evaluation of virologic response.
Results: Eighty-nine percent of the patients were treatment-naïve. Seventy-five percent were infected with genotype 1 and 25% with genotype 2 HCV, respectively. One hundred and eighty-one (66.3%) patients had chronic hepatitis, 74 (27.1%) compensated cirrhosis, and 8 (2.9%) decompensated cirrhosis, respectively. Ten patients (3.7%) had a history of hepatocellular carcinoma and 10 (3.7%) had received liver transplantation prior to HCV treatment.
Undetectable HCV RNA at week 4 was achieved in 90.2% (231/256) of the patients, 99.2% (250/252) achieved end of treatment response and 98.1% (202/206) achieved sustained virologic response at 12 weeks post-treatment (SVR12). According to underlying liver function, SVR12 rates were 99.3% (135/136) in chronic hepatitis, 96.4% (53/55) in compensated cirrhosis and 100% (6/6) in patients with decompensated cirrhosis. SVR12 rates according to genotypes were 98.2% (167/170) in genotype 1, and 97.2% (35/36) in genotype 2, respectively.

Eight weeks LDV/SOF treatment in treatment-naïve, chronic hepatitis patients who had less than 6,000,000 IU/mL HCV RNA at baseline resulted in 100% (24/24) SVR12 rates.

Overall, LDV/SOF was well-tolerated with 0.7% (2/273) treatment discontinuation rate due to adverse events. Both events were unrelated to LDV/SOF.
Conclusion: LDV/SOF for the treatment of HCV infected Korean patients was effective and safe with high SVR rates.

[PP-0135]

Prognosis after sustained virologic response of chronic hepatitis C patients treated with sofosbuvir based treatment; Interim analysis of multicenter prospective observational study

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Objectives: Direct-acting antiviral (DAA) therapy can cure chronic hepatitis C (CHC) and sofosbuvir (SOF) and ledipasvir (LDV)/SOF were introduced to Korea in 2016. Good prognosis is expected in patients achieved sustained virologic response (SVR) after DAA treatment. However, information about prognosis of Korean CHC patients achieved SVR after SOF based treatment is still limited. We aimed to investigate prognosis of these patients.
Materials and Methods: This is a multicenter prospective observational study. The CHC patients achieved SVR after SOF or LDV/SOF treatment were enrolled and final follow up date was August 2021. Primary end-point was hepatocellular carcinoma (HCC) occurrence. At last one time in year, we checked about this end-point.
Results: Total 486 patients were included in this analysis and mean follow up duration was 29.7 months. Male was 218 patients (44.9%) and mean age was 62.0 years. Genotypes were 1 (81, 16.7%), 2 (403, 82.9%) and 3 (2, 0.4%). SOF and ribavirin combination was the most common treatment (389, 80.0%). Cirrhosis was 152 patients (31.2%) and mean Child–Pugh score was 5.1. HCC occurrence cases were 11 patients (2.3%) up to 4 years. HCC patients had more cirrhosis prevalence (81.8% vs. 30.1%, p = 0.001), higher MELD score (8 vs. 7, p = 0.038) and higher FIB-4 (4.8 vs. 2.8, p = 0.019).
Conclusion: Prognosis of patients achieved SVR after SOF based treatment was generally good. However, HCC risk was not completely removed especially cirrhosis patients. Therefore, regular follow up surveillance is still warranted and early treatment is important.

[PP-0136]

Prognosis of daclatasvir/asunaprevir treated genotype 1b chronic hepatitis C patients after sustained virologic response; Up to 5 years data of multicenter prospective observational study

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Objectives: Direct-acting antiviral (DAA) therapy can cure chronic hepatitis C (CHC) and daclatasvir (DCV)/asunaprevir (ASV) is the first introduced interferon free DAA in Korea. Good prognosis is expected in patients achieved sustained virologic response (SVR) after DAA treatment. However, information about prognosis after SVR with DCV/ASV combination is still limited. We aimed to investigate prognosis of these patients.
Materials and Methods: This is a multicenter prospective observational study. The CHC patients achieved SVR after DCV/ASV treatment were enrolled and final follow up date was August 2021. Primary end-point was hepatocellular carcinoma (HCC) occurrence and secondary end-points was recurrence or reinfection. At last one time in year, we checked about this end-point.
Results: Total 304 patients were included in this analysis and mean follow up duration was 33.3 months. Mean age was 58.5 years and male was 149 patients (49.0%). Cirrhosis was 104 patients (34.2%) and mean Child–Pugh score was 5.1. HCC occurrence cases were 12 patients (3.9%) up to 5 years. HCC patients were older (75 years vs. 57 years, p = 0.001), had more cirrhosis prevalence (75.0% vs. 32.5%, p = 0.004), higher AFP (7.5 ng/ml vs. 3.6 ng/ml, p = 0.006) and higher FIB-4 score (3.9 vs. 2.4, p = 0.015). On cox-proportional analysis, age over 72 years (p = 0.001) and AFP over 5.9 (p = 0.031)

were significant variables. Recurrence or reinfection was occur in 3 patients (1.0%) and all occurred within 1 year after SVR.
Conclusion: Although prognosis of SVR achieved patients was generally good, HCC risk was not completely removed especially older patients with elevated AFP. Recurrence or reinfection is also possible. Therefore, regular follow up surveillance is still warranted and early treatment is important.

[OP-0146]

Hepatectomy outcomes in patients with hepatitis C virus-related hepatocellular carcinoma with or without cirrhosis

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Objectives: Although hepatocellular carcinoma (HCC) is rare in hepatitis C virus (HCV) patients without cirrhosis, little is known about the postoperative results of these patients. Present study to compare the outcomes of cirrhotic and non-cirrhotic HCV patients with solitary treatment-naïve HCC after liver resection (LR) and to assess ability of the non-invasive scoring markers to predict prognosis in these patients.
Materials and Methods: Two hundred seven adult hepatectomy patients with HCV-related HCC were prospectively identified at our institution between July 2005 and May 2019.
Results: The non-cirrhotic group had better liver function than the cirrhotic group based on platelet count, liver function tests, liver stiffness measurement, and indocyanine green retention rate at 15 min but were older than the cirrhotic group. Consistently, non-invasive markers in the cirrhotic group were significantly higher than in the non-cirrhotic group. The cumulative disease-free survival and patient survival in the non-cirrhotic group were significantly higher than in the cirrhotic group. HCC recurrence is related to major LR and alpha-fetoprotein (AFP) > 40 ng/mL and death is related to long hospitalization, and AFP > 40 in multivariate analysis. Non-invasive markers and the presence of cirrhosis were not related to HCC recurrence or patient survival in multivariate analyses. Interestingly, HCC recurrence and patient survival according to non-invasive markers were different after 5 years since hepatectomy.
Conclusion: The non-cirrhotic group had a better prognosis after curative LR, although the difference was not significant in multivariate analysis. The factors influencing HCC recurrence and patient survival were different in the cirrhotic and non-cirrhotic groups.

[PP-0150]

Difference of liver fibrosis burden in groups with and without confirmatory HCV RNA testing

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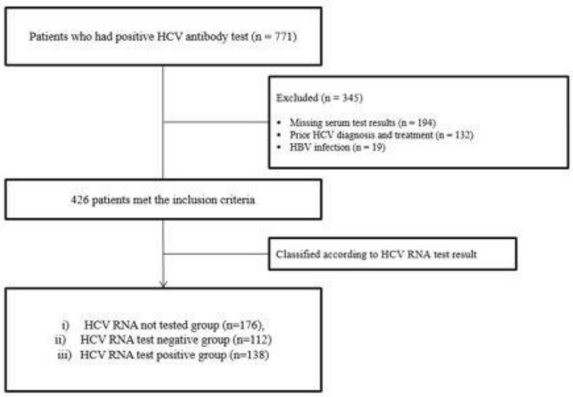
Objectives: Confirmatory hepatitis C virus (HCV) ribonucleic acid (RNA) testing is recommended for patients who have positive results for anti-HCV test in most guidelines. The aim of this study was to determine the need for HCV RNA test, assuming the same stage of liver fibrosis for patients with or without confirmatory HCV RNA testing.
Materials and Methods: Data were collected from a single tertiary hospital from 2015 to 2018. This study included 426 patients who were positive for HCV antibody. Patients who had already been treated for hepatitis C were excluded. Anti-HCV test positive patients were divided to two groups: i) those who did not undergo confirmatory HCV RNA test (HCV RNA not tested group) (n = 176); and ii) those who had confirmatory HCV RNA test (HCV RNA tested group) (n = 250).
Results: Mean age of patients was 63.5 years. Of 426 patients, 208 (48.8%) were males. Mean FIB-4 score was 2.70 for HCV RNA not tested group and 3.61 for HCV RNA tested group (HCV RNA test negative group: 3.68; HCV RNA test positive group: 3.55), showing no significant difference between the two groups (p-value = 0.231). Mean APRI score was 0.65 for HCV RNA not tested group and 1.31 for HCV RNA tested group (HCV RNA test negative group: 1.19; HCV RNA test positive group: 1.41), showing a significant difference between the two groups (p-value = 0.08).
Conclusion: The group of patients who did not undergo HCV RNA test had no significant difference in FIB-4 score compared to those in HCV RNA tested group. The degree of liver fibrosis in the HCV RNA not tested group was not mild compared to that of the HCV RNA tested group. Therefore, confirmatory HCV RNA testing is essential for every anti-HCV positive patient.

Figure 1



[PP-0153]

The effectiveness and safety of glecaprevir/pibrentasvir for the treatment of patients with chronic HCV infection: a real-world multicenter study

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Objectives: Glecaprevir/pibrentasvir is approved for the treatment of patients with chronic HCV genotypes (GT) 1–6. This study aimed to evaluate the efficacy and safety of glecaprevir/pibrentasvir in real-world settings.
Materials and Methods: Consecutive patients treated with glecaprevir/pibrentasvir for chronic HCV infection between July 2019 and November 2020 were enrolled at the liver unit of Catholic university in South Korea. Glecaprevir/pibrentasvir was given for 8 weeks in most patients, but for 12 weeks in some patients with liver cirrhosis (LC). The primary outcome was the sustained virological response at post-treatment week 12 (SVR12). Safety was also assessed.
Results: In total, 356 patients were treated and mean age was 58 ± 12. Of the patients, 144 (40.4%) were male, 57 (16.0%) were diagnosed as LC, and 11 (3.1%) had been treated for hepatocellular carcinoma. GT 2 (58.4%) was the most common type, followed by GT 1b (38.5%), GT 1a and 3 (1.4% for both), and GT 6 (0.3%). Twelve patients (3.4%) were on dialysis for end-stage renal disease. Twenty-eight patients (7.9%) were treatment-experienced for HCV, 13 (3.7%) patients with interferon-based therapy and 15 (4.2%) patients with direct-acting antivirals. The SVR12 rate was 98.6% for evaluable patients with post-treatment week 12 data. All 4 patients who failed to achieve SVR12 were GT 2, treatment naïve, and had no cirrhosis. In 3 of them, HCV RNA was not detected at the end of treatment. Adverse events (AEs) including nausea, dizziness, pruritis, ALT elevation and rash were reported in 12 patients (3.4%). Four patients had grade 2 ALT or AST elevations during the treatment period. AEs-related treatment discontinuation was reported in 7 patients (2.0%).
Conclusion: In real-world practice, treatment with glecaprevir/pibrentasvir for 8 or 12 weeks was well-tolerated and achieved extremely high SVR in patients with chronic HCV infection across all genotypes.

[OP-0235]

Acute hepatitis C risk factors and treatment challenges in Armenia

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Objectives: Acute hepatitis C (AHC) is rarely diagnosed due to its predominant asymptomatic course. However symptomatic AHC occurs on average in 20% of patients with Hepatitis C virus (HCV) and has high likelihood of spontaneous viral clearance (SVC). The disease burden in Armenia requires strategies to prevent new infections.
Materials and Methods: We conducted in-depth review of the epidemiology of AHC,risk factors and routes of transmission,current clinical diagnostics and treatment practices. We prospectively assessed the clinical,biochemical,serological,virological parameters.
Results: 254 HC patients, AHC was diagnosed in 38 (14,9%) in 2017–2019 years.The age of patients with AHC was 47,5 ± 16,39 (24–78) with predominance of men 22 (58,4%). The average time from exposure to manifestation of hepatitis was 88,5 ± 48,3 (14–180) days.25 patients had jaundice with elevated serum bilirubin 230 ± 75 (29–283) mcmol/L and ALT of 963,4 ± 480,8 (168–1883) U/l.The main risk factor was unsafe medical procedure 21 (55,2%) followed by i/v drug injection 5 (13,2%), Sexual and cosmetological exposure 1 (2,6%) respectively,unknown in 10 (26%). In 12 (32%) patients the diagnosis of AHC was confirmed by HCV RNA detection, without Anti-HCV antibodies. The mean period of clinical manifestations lasted 20–60 days, and in 23 (62%) patients with the rapid decline in ALT. The data of patients' observation within 6 months revealed SVC in 9 (24%) patients, with the rapid decline in ALT, 7 of them were 20–40 years old female. Virological clearance in the remaining 29 patients was associated to early (after 3 months of clinical manifestations) administration of anti-viral treatment (AVT).
Conclusion: HCV occurs so far in Armenia as well as in the world. Symptomatic AHC was mostly associated with unsafe medical procedures. Male sex and middle age are the other risk factors for AHC AHC characterized by high rates of spontaneous resolution (24%) Rapid decline in ALT was the main risk factor for SVC as well as female sex and young age (20–40 years old). Early Antiviral treatment after acute phase provides 100% elimination of HCV.

[OP-0295]

Best practice in treatment of chronic hepatitis C for resource-limited situations; Myanmar experience

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Objectives: In the treatment of HCV using DAAs, it is usually tested the following parameters; Genotype, Fibrosis assessment and Viral Load at the designated time points. In resource limited situations where the above mentioned parameters cannot be performed, special unique treatment regimen was needed. Myanmar GI & Liver Society recommended the fixed-dose combination of sofosbuvir and velpatasvir with ribavirin (SOF/VEL/RBV) for 12 weeks or those with limited accesses. This study was aimed to assess the efficacy of this treatment regimen in Myanmar population.
Materials and Methods: An observational study of 384 treatment-naïve patients infected with HCV was performed. The patients were treated with SOF/VEL/RBV for 12 weeks at Yangon GI and Liver Centre, between April 2018 and October 2019. Patients were evaluated clinically along with laboratory testings to assess safety of treatment. All adverse events were recorded and graded according to a standardized scale.
Results: The patients were well-tolerated to drugs and no one discontinued the treatment through the study with no incidents of serious adverse events. The mean age at the time of treatment initiation was 51.2 years and 49% of patients were male (n = 188) and 51% were female (n = 196). About 46% (n = 177) of patients had cirrhosis in ultrasound scan at the time of treatment initiation. Overall SVR rate was 98.7% of patients (379/384) with 5 relapsers. The dose of ribavirin had to be reduced in 36 patients (9.4%) and only one patient needed the erythropoietin-stimulating agent for the correction of anaemia but no blood transfusions were necessary.

Conclusion: According to Real World experiences in Myanmar, generic DAAs are cheap but efficacy is excellent, achieving high SVR rates. In resource-limited situations, the pangenotypic regimen, SOF/VEL combined with Ribavirin, is proposed; without genotype and assessment of fibrosis. Such regimen is highly recommended to increase accessibility to the DAA therapy in the general population.

[OP-0330]

Outreach onsite treatment with a simplified pangenotypic direct-acting antiviral regimen for hepatitis C virus micro-elimination in a Prison

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Objectives: Prisoners are at risk of hepatitis C virus (HCV) infection, especially among the people who inject drugs (PWID). We implemented an outreach strategy in combination with universal mass screening and immediate onsite treatment with a simplified pangenotypic direct-acting antivirals (DAA) regimen, 12 weeks of sofosbuvir/velpatasvir, in a PWID-dominant prison in Taiwan.
Materials and Methods: HCV-viremic patients were recruited for onsite treatment program for HCV micro-elimination with a pangenotypic DAA regimen, 12 weeks of sofosbuvir/velpatasvir, from two cohorts in Penghu Prison, either identified by mass screen or in outpatient clinics, in September 2019. Another group of HCV-viremic patients identified sporadically in outpatient clinics before mass screening were enrolled as a control group. The primary endpoint was sustained virological response (SVR12, defined as yundetectable HCV RNA 12 weeks after end-of-treatment).
Results: A total of 212 HCV-viremic subjects were recruited for HCV micro-elimination campaign; 91 patients treated with sofosbuvir/ledipasvir or glecaprevir/pibrentasvir before mass screening were enrolled as a control. The HCV micro-elimination group had significantly lower proportion of diabetes, hypertension, hyperlipidemia, advanced fibrosis and chronic kidney diseases, but higher levels of HCV RNA. The SVR12 rate was comparable between the HCV micro-elimination and control groups, 95.8% (203/212) versus 94.5% (86/91), respectively, in intent-to-treat analysis, and 100% (203/203). versus 98.9% (86/87), respectively, in per-protocol analysis. There was no virological failure, treatment discontinuation, and serious adverse event noted among sofosbuvir/velpatasvir-treated patients.
Conclusion: Outreach mass screening followed by immediate onsite treatment with a simplified pangenotypic DAA regimen, sofosbuvir/velpatasvir, provides successful strategies toward HCV micro-elimination among prisoners.

[PP-0346]

Extended virological response after sustained virological response in patients with direct acting antiviral

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Objectives: Late relapse or reinfection after sustained virological response (SVR) were remaining issues in antiviral therapy for chronic hepatitis C. The aim of this study was to investigate durability of virological response in patients with SVR after direct acting antiviral (DAA).
Materials and Methods: We consecutively enrolled patients with chronic hepatitis C received sofosbuvir with ribavirin (n = 43), ledipasvir-sofosbuvir (n = 23), elbasvir-grazoprevir (n = 23), and glecaprevir-pibrentasvir (n = 49) from September 2016 to September 2020, respectively. All of 138 patients who completed DAA treatment and achieved a SVR (HCV RNA level < 15 U/mL after at 12 weeks of completing DAA therapy). An extended virological response was defined as undetectable HCV RNA level after at least 24 weeks of SVR.
Results: Median age was 57 (17—83) years and 56% of subject were female. Median baseline HCV RNA level was 6.12 (3.3 – 7.4) log IU/mL and 50 patients had genotype 1b and 87 had genotype 2. Seven were interferon-experienced patients and 13 patients had cirrhosis. End of treatment response was achieved in all patients. Median follow-up period was 54 (27 – 79) weeks after SVR. In 138 patients with SVR, 98.5% patients showed extended virological response. Serum HCV RNA was detected in 2 male subjects received sofosbuvir with ribavirin at 31 and 54 weeks after achieving SVR. Rapid virological response at week 4 was not shown (6.64 at baseline to 3.88 log IU/mL at week 4) in one patient.
Conclusion: Extended virological response was achieved in most of the patients with SVR after DAA therapy, except ribavirin-containing regimen.

[PP-0396]

Real-life effectiveness and safety of sofosbuvir/velpatasvir in difficult to treat hepatitis C patients

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Objectives: In spite of recent advance in the treatment of hepatitis C virus (HCV), there are still difficult to treatment population such as prior direct antiviral agents (DAA) failure, decompensated cirrhosis or presence of hepatocellular carcinoma (HCC). Here we report our

experience about these patients treated Sofosbuvir/Velpatasvir (SOF/VEL) in real world setting.
Materials and Methods: All consecutive patients with HCV receiving SOF/VEL between August 2017-May 2021 in South Korea were enrolled. Sustained virological response (SVR) was defined as undetectable HCV-RNA 12 (SVR12) weeks after the end-of-treatment.
Results: A total of 37 patients were included: median age 65 (45–83) years, 59.5% males, median HCV-RNA 852,500 (11,100–10,800,000) IU/ml. HCV genotype was 1b in 67.6%, 2 in 29.7%, 1b &2b in 2.7%. 37.8% have concomitant HCC (BCLC stage A/B/C; 4/8/2). 56.8% have underlying cirrhosis and 7.5% was decompensated cirrhosis. 70.3% have failed prior DAA treatment (Daclatasvir + asunaprevir n = 16, sofosbuvir + ribavirin n = 3, sofosbuvir + ledipasvir n = 2, glencaprevir + pibrentasvir n = 3, boceprevir n = 1) Naïve patients received SOF/VEL for 12 weeks and the patients with prior DAA failure received SOF/VEL for 24 weeks, ribavirin was added in 78.4% of treatment schedules. Undetectable HCV-RNA was achieved by 97.2% of patients at week 4 and end of treatment response was 97.2%. Overall, 36/37 (97.2%) patients by intention to treat analysis and 36/36 (100%) by per protocol analysis achieved SVR12, respectively; One patient was expired due to HCC progression during SOF/VEL treatment. Most patient well tolerated treatment without adverse events.
Conclusion: SOF/VEL is an effective and safe retreatment for difficult to treat HCV population in a real-life setting.

[OP-0397]

Progress and prognosis according to care cascade in patients with anti-HCV positive

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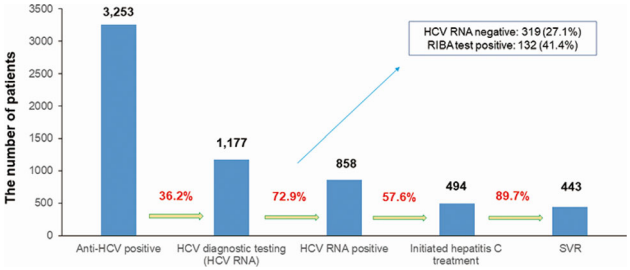
Objectives: There are few studies analyzing the frequency of HCV RNA test and actual treatment among anti-HCV positive patients in Korea, with a low prevalence of HCV infection. The purpose of this study is to analyze the diagnosis process, treatment results and prognosis according to care cascade in patients with anti-HCV positive.
Materials and Methods: 3,253 patients with anti-HCV positive were investigated in a tertiary hospital between January 2005 and December 2020. The number of patients who received HCV RNA test, treatment, and proportion of sustained virologic response (SVR) according to type of antivirals were investigated. We investigated the cumulative incidence of hepatocellular carcinoma (HCC) and liver cirrhosis.
Results: Of the total 3,253 people, 1,177 (36.2%) who received HCV RNA test and 858 (72.9%) were positive for HCV RNA. 494 (57.6%) received antiviral treatment and 443 (89.7%) experienced SVR without significant difference according to the type of antivirals. Of the 421 treated patients, 16 (14.2%) developed HCC. The cumulative incidence of HCC at 15 years showed significant difference according to the presence of liver cirrhosis (10/83, 29.5% vs. 6/338, 10.8%, $p < 0.001$). The cumulative incidences of HCC or liver cirrhosis did not show statistical differences according to the presence of SVR12 (14/388, 13.2% vs. 2/33, 52.5%, p = 0.084, 21/319, 15.0%, vs. 3/22, 28.7%, p = 0.051).
Conclusion: Due to introduction of DAA, high SVR12 were achieved, but the proportion of anti-HCV positive patients receiving HCV RNA test and treatment was not high. For chronic hepatitis C patients with cirrhosis, HCC surveillance after SVR12 is recommended.



[OP-0413]

HCV elimination from a highly endemic, well-defined demographic area of peri-urban Karachi

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Objectives: Pakistan has a nationwide HCV prevalence of 6% with recognized "hot spots" where prevalence and liver disease related mortality is reported to be much higher. This ongoing study aims to achieve highest possible HCV elimination in an endemic district by scaling up and implementing lessons learnt from a prior pilot project of a low-cost community-based test-and-treat model that concluded in 2019.
Materials and Methods: This study targets 40,000 individuals over 12 years of age, across three Union Councils (UCs) of Malir district, Karachi. HCV screening using finger-stick rapid-diagnostic test (RDT), began in October 2019 through door-to-door visits guided by community mapping. HCV RNA testing using GeneXpert, or HCV core antigen is done for those screened positive. Individuals with confirmed infection are given free of cost direct-acting antiviral (DAA) treatment after clinical evaluation during a house-visit. Monthly dose is delivered, and testing done 12 weeks after last dose to assess sustained viral response (SVR).
Results: 21,143 individuals have been screened with mean age 31.35 ± 15.33 years, 64% being females. Of those screened positive, mean age is 48.37 ± 14.46 years with 69% females. Average sero-prevalence in males and females is 10% and 12% respectively. 1993 individuals underwent HCV RNA testing of which 54% had active viremia. 1033 patients started treatment of which 872 have completed treatment with a drop out rate of 12%. Sustained virologic response (SVR) rate is 90%.
Conclusion: This study demonstrates feasibility of HCV-micro elimination program using a low-cost community-based model which can be scaled up and implemented in diverse resource-limited settings.

[OP-0416]

Oral saliva anti-HCV assay: Assessing reliability of community screening for hepatitis C in a peri-urban area of Pakistan

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Objectives: Screening of Hepatitis C infection (HCV) is commonly done via finger-prick serum anti-HCV Rapid Diagnostic Test (RDT). However, many subjects are hesitant and fearful of pin pricks, driving a shift towards non-invasive and easy to administer screening tests. In this study, we evaluated the sensitivity and specificity of the Fortune anti-HCV oral assay in a resource-limited, peri-urban community of Karachi, Pakistan.
Materials and Methods: This prospective cohort study was conducted in Malir district, highly endemic for HCV. Individuals 18 years or above were screened for HCV antibody using both Fortune anti-HCV oral assay (Fortune Bioscience Co., Zhengzhou, China) and RDT (SD Rapid Test 02FK10, Standard Diagnostics, Inc., Republic of Korea). Positive results from the two screening tests were subsequently tested for ARCHITECT HCV core antigen (HCV cAg) assay from Abbott Diagnostics to confirm active infection.
Results: 349 individuals were screened with mean age of 36.2 ± 15.0 and 68.2% females. Compared to the RDT, sensitivity, specificity, negative predictive value, and positive predictive value of the Fortune anti-HCV oral assay were 100%, 99.6%, 100% and 98.5% respectively. Kappa value was 0.99, showing high consistency between the two tests. Of the positively screened, 55.8% of Fortune anti-HCV oral assay positive and 56.7% of the RDT positive were reactive for HCV cAg assay respectively.
Conclusion: Fortune anti-HCV oral assay showed high sensitivity and specificity compared to RDT and comparable PPV to RDT with respect to HCV cAg assay. It can therefore be used as an alternative to RDT to screen masses in large HCV elimination programs.

[OP-0417]

Feasibility of HCV self-testing in an endemic peri-urban area

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Objectives: Pakistan has the second highest burden of Hepatitis C (HCV) globally. Since underdiagnosis remains a barrier in HCV elimination, use of low-cost rapid screening tests can improve access to testing and linkage to care. WHO approved self-testing kits are being successfully used for HIV screening. This study was conducted to determine the feasibility and acceptability of HCV self-testing using the OraQuick® HCV rapid antibody test which is currently licensed for professional use only.
Materials and Methods: This was a cross-sectional study conducted in a secondary hospital of HCV endemic, resource limited Malir district of Karachi. Individuals presenting to the hospital above 18 years of age with unknown HCV status were included. Participants were provided written and pictorial instructions to perform HCV self-test using oral fluid. Participants performed tests and interpreted their results while being observed. The kits were re-read by study staff blinded to self-reported results to determine inter-reader agreement. Participants were also tested by healthcare workers using professional version of the test to study inter-operator agreement. Acceptability and preferences of HCV self-testing were also explored through interviews.
Results: 105 participants were enrolled of which 54% were females. 52% participants had no formal education or up to primary school education. 90% participants completed the test correctly and 98% interpreted results correctly. The agreement with professional test was 97%. 100% of the participants showed willingness to re-use the test and recommend it.
Conclusion: The results exhibit high acceptability and feasibility of HCV self-testing. It can improve HCV screening coverage while ensuring confidentiality and convenience especially in hard to reach, vulnerable populations.

[PP-0423]

Microelimination among HCV low-prevalence area in East China: 1 year outcomes of weekly resembling sentinel surveillance

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Objectives: In 2017, a local epidemiological survey showed the positive rate of hepatitis C antibody in Zhenjiang, a city of Jiangsu province from China, was 51% and the positive rate of HCV-RNA was 68%. So, Zhenjiang city is a high-aggregation area in low-prevalence province. This study aimed to evaluate the 1-year results from screening and linkage to care in Zhenjiang area use weekly resembling sentinel surveillance measure.
Materials and Methods: 4 Community Health Centers in Zhenjiang perform resembling sentinel surveillance service from 2020.4–2021.4, including serological testing and education. The HCV-Ab and HCV RNA/GT results are available in 15 min and 1 week respectively, which could be used as reference for HCV diagnosis and management.
Results: A total of 1010 subjects were tested, and 66% (669/1010) had HCV antibody positivity which is numerically higher than the 2017 survey data (51%). The possible reason maybe these participants involved knew that they were antibody positive before and came for further consultation. The positive rate of HCV RNA was 18.8% (126/669) which is significantly decreased compared with the 2017 data (68%). The characteristics of these diagnosed HCV patients show, median age is 62.8 years and most are women (78.5%, 525/669), GT 1b patients was 73% (89/122) while GT non-1b was 27% (33/122), this is quite different from the 2017 survey data which show 92% (542/592) were GT-1b and only 8% (50/592) were GT non-1b respectively. Maybe it reminds us beyond illegal blood collection and donation, there are other transmission channels in newly diagnosed population. For those diagnosed HCV patients, all received SOF-based DAA treatment and the SVR rate is 100% (110/110).
Conclusion: Weekly resembling sentinel surveillance results in 97% linkage to care and is efficient in such high-aggregation area while located in low-prevalence province without HCV sentinel surveillance system. This model is a pragmatic complement to China hepatitis C sentinel surveillance.

[OP-0431]

Reduced clinical outcomes among direct anting antiviral treated geriatric patients with chronic hepatitis C: A prospective, multicenter cohort study

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Objectives: Studies on the clinical outcomes among old aged patients with hepatitis C virus (HCV) infection according to the treatment with direct-acting antivirals (DAA) are limited. This study aimed to elucidate the incidence of primary liver cancer including hepatocellular carcinoma (HCC) and the all-cause mortality among HCV patients with age $\geq$ 65 according to DAA treatment.
Materials and Methods: A total 590 senior patients with HCV RNA positivity and no liver cancer or decompensation at diagnosis (mean age 71.2 years, 44.6% male, 29.3% cirrhosis) were prospectively enrolled in 10 university hospitals from May 2007 to June 2020 and followed until Dec. 2020. They were classified into no-DAA treated group (n = 303, 50.8%) and DAA-treated group (n = 287, 49.2%). Kaplan–Meier curve analysis, time-varying Cox regression analysis, and propensity score matched analysis were performed.
Results: During 5.0 years (IQR 2.4–8.1) of median follow-up, 68 developed liver cancer and 119 patients died. The DAA group (n = 287) was significantly younger (71.4 vs 72.5 year) and having lower proportion of heavy alcohol consumption (10.8% vs. 15.4%, p = 0.018) than the no-DAA group (n = 303), and the SVR rate was 95.8%. Compared with the no-DAA group, the DAA group showed a significantly lower risk of liver cancer (HR 0.40, HR 0.19–0.87, P = 0.020) and death/transplantation (HR 0.04, HR 0.01–0.28, P = 0.001) by multivariate time-varying Cox regression analysis. It was confirmed by propensity-scored analysis of 196 matched pairs, in which the DAA group showed a significantly lower risk of liver cancer (HR 0.40, HR 0.19–0.87, P = 0.020) and death/transplantation (HR 0.04, HR 0.01–0.28, P = 0.001) than no-DAA group.
Conclusion: In the geriatric HCV patients, DAA treatment resulted in the overall SVR rate of 95.8%, and improved clinical outcomes. Therefore, active screening and treatment in old age HCV patients is warranted.

[PP-0459]

Efficacy and safety of sofosbuvir-based regimens in IDUs with genotype 3 and 6 HCV patients in East China

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Objectives: To evaluate the efficacy and safety of SOF/VEL or LDV/SOF regimens in IDUs with HCV G3 and G6 infection in East China.
Materials and Methods: We performed a retrospective analysis of patients with CHC between April 2020 and June 2021, who started the SOF/VEL or LDV/SOF regimen and liver cirrhosis added ribavirin (1000–1200 mg per day). Laboratory examinations were detected at baseline, 2 weeks of treatment, 4 weeks of treatment, end of treatment and 12 weeks of follow-up. Sustained virological response (SVR), safety was observed.
Results: In total, 36 CHC patients were enrolled in this analysis. Of the 36 patients, 6 patients (16.67%) had cirrhosis. 8 patients (22.22%) are GENOTYPE 3a, 20 (55.56%) genotype 3b, 8 (22.22%) genotype 6a. Among this study, 28 patients had available SVR12 data. Of these 28 patients, 2 patients with genotype 6a took LDV/SOF while the others were treated with SOF/VEL $\pm$ RBV. The undetectable rate of HCV-RNA was 92.86%(26/28), 100% (28/28) and 96.42% (27/28), respectively, at 2,4 and 12 weeks of therapy. The overall SVR12 rate was 85.7%. SVR12 of genotype 3a was 100% (6/6), SVR of genotype 3b was 73.3% (11/15), SVR12 of genotype 6a was 100% (7/7), The 4 patients who failed all occurred in genotype 3b and they were all relapsed. 1 patient was treated with glucocorticoid because of nephrotic syndrome. The other 3 patients received SOF/VEL 12 week without RBV. No Adverse Event (AE) caused treatment discontinuation and no serious AE occurred.
Conclusion: SOF/VEL or LDV/SOF for 12 weeks provide high rates of sustained virologic response among patients infected in IDUs with HCV genotype 3 and 6 with favorable safety profile.

[PP-0485]

Effectiveness and safety of sofosbuvir/velpatasvir with or low-dose ribavirin for HIV-positive patients with HCV genotype 3b infection a real-world study from China

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Objectives: Previous studies had shown that sofosbuvir-based regimens had achieved high sustained virological response rates in patients with hepatitis C. However outcomes among HIV-positive patients with HCV genotype 3b infection treated with Sofosbuvir/Velpatasvir regimen remains limited in real-world. We aimed to assess the effectiveness and safety of Sofosbuvir/Velpatasvir $\pm$ ribavirin for HIV-positive patients with HCV GT3b coinfection.
Materials and Methods: A total 299 of HCV/HIV co-infected patients with GT3b who were treated with Sofosbuvir/

Velpatasvir ± ribavirin were enrolled We evaluated the sustained virologic response at 12 weeks after the end of treatment (SVR12), adverse events (AEs).

Results: Among 299, the mean age was 43.9 years, 77.3% (231/299) of the patients were male. 36.5%(109/299) had liver cirrhosis, 14.7% (44/299) had decompensated cirrhosis. 27.8% (83/299) were treated with Sofosbuvir/Velpatasvir with ribavirin. 13.4% (40/299) had previously received treatment. 6.4% (19/299) had liver cancer. overall sustained virological response rate (SVR12) was 87.0% (260/299, 95% CI: 82.9–91.0%),and patients with or without ribavirin resulting in SVR12 were 87.5% (82.9–91.2) and 85.5% (78.3- 92.8),respectively. Of the 259 naïve patients, 242 (93.4%) (90.3–96.1) achieved SVR, as compared with18 of 40 (96%) (30.0–60.0) experienced patients. The rates of sustained virologic response among patients with and those without cirrhosis were 87.5% (82.9–91.2) and 85.5% (78.3- 92.8), respectively; 39/299 (13%) patients had virologic failure after the end of treatment. Univariate regression analysis showed that PLT (OR: 0.957, 95%CI: 0.931–0.984), LSM (OR: 1.446, 95% CI: 1.147–1.822), treatment-experienced (OR: 13.807, 95% CI: 2.970–64.174) was independent risk factors for relapse in patients with genotype 3b HCV/ HIV co-infection. There was a significant difference in the incidence of serious adverse events between patients with cirrhosis and non-cirrhosis (25.7% VS 6.8%).

Conclusion: Twelve weeks of Sofosbuvir/Velpatasvir + RBV was highly efficient and safe in patients with genotype 3b HCV/ HIV co-infection. PLT, LSM, and history of treatment might be risk factors for sustained virological response rate.

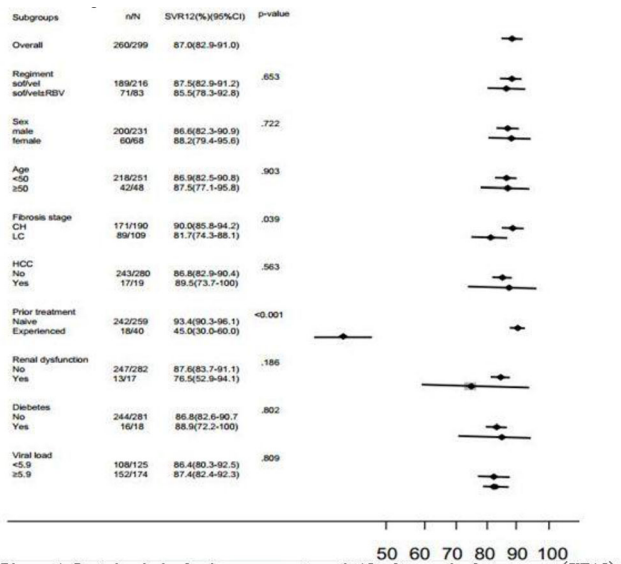

Figure 1 Sustained virologic respose at week 12 after end-of-treatment(SVR12) rates with HCV/HIV

[OP-0486]

Hepatitis C virus factsheet in Korea, 2021: Prevalence, incidence, linkage to care, and treatment rate

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Objectives: Accurate identification of the hepatitis C virus (HCV) situation in Korea is a way of assessing how far we are in achieving the 2030 HCV elimination plan of World Health Organization. We aimed to determine the current status of HCV infection in Korea in terms of prevalence, incidence, linkage to care, and treatment rate.

Materials and Methods: This study used data from the Korea Centers for Disease Control and Prevention. Linkage to care was defined as patients who had visited a medical institution at least twice or those had been treated for HCV within 1.5 years from the index date. Treatment rate was defined as patients who had been prescribed for antiviral medication within 1.5 years from the index date.

Results: Between 2015 and 2019, among a total of 32,335 people recruited, anti-HCV antibody was positive in 269 patients, constituting unadjusted anti-HCV antibody positivity rate of 0.7%. In 2019, new HCV infection was identified in 8,810 patients (4,278 men and 4,532 women). The crude incidence rate of HCV infection was 17.2 per 100,000 person-years. The number of new HCV infection was highest in patients aged 50–59 years (n = 2,480), and the crude incidence rate of HCV infection significantly increased with the increasing age ($P < 0.001$). Linkage to care in 2019 was 78.2% (78.2% in men and 78.2% in women). Treatment rate in 2019 was 58.1% (56.8% in men and 59.3% in women).

Conclusion: In 2019 Korea, among newly diagnosed patients with HCV, 78% were linked to care and 58% were treated. In order to achieve the goal of HCV elimination, it is necessary to investigate the serial statistics of HCV infection.

[PP-0496]

Low incidence of hepatocellular carcinoma after antiviral therapy in patients with chronic hepatitis C and hemophilia

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Objectives: Hepatocellular carcinoma (HCC) rarely develops in patients with chronic hepatitis C (CHC) who achieve sustained virological response (SVR). We assessed the incidence of HCC in CHC patients with hemophilia after treatment with pegylated interferon plus ribavirin (PegIFN/RBV) and direct-acting antivirals (DAAs).

Materials and Methods: Patients (n = 202) were enrolled between March 2007 and July 2019. A total of 139 patients were treated with PegIFN/RBV (genotype 1, n = 98; genotype 2, n = 41). Sixty-three patients were treated with DAAs (genotype 1, n = 44; genotype 2, n = 19).

Results: For genotype 1, SVR was achieved in 78.6% (77/98) and 90.9% (40/44) of patients in the PegIFN/RBV and DAAs groups, respectively. For genotype 2, SVR was achieved in 95.1% (39/41) and 94.7% (18/19) of patients in the PegIFN/RBV and DAAs groups, respectively. Six HCC cases were identified. The cumulative incidence of HCC was 4.1% at 14 years in PegIFN/RBV and 1.7% at 5 years in DAAs. The mean age was 77 years, 5 patients had genotype 1, 4 patients had liver cirrhosis, and 3 patients experienced SVR. One patient who was treated with DAAs and who achieved SVR experienced HCC at 2 years after the end-of-treatment. The 14-year cumulative incidence of HCC was 1.9% in the SVR group and 21.7% in the no-SVR group in the PegIFN/RBV group ($p < 0.001$).

Conclusion: Treatment with PegIFN/RBV led to stable SVR and a low incidence of HCC. Although the follow-up period was short, DAAs led to more stable SVR than PegIFN/RBV and a low incidence of HCC in CHC patients with hemophilia.

[PP-0504]

Prevalence and genotype distribution of hepatitis C virus within hemodialysis units in Thailand: Role of HCV core antigen in the assessment of viremia

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Objectives: Patients with end-stage renal disease undergoing long-term hemodialysis (HD) are at an increased risk of acquiring hepatitis C virus (HCV) infection. This study was aimed at investigating the prevalence and genotype distribution of HCV, as well as the clinical use of HCV core antigen (HCVcAg), within several HD centers in Thailand.
Materials and Methods: A cross?sectional study was conducted from January to June 2019. HCV infection was assessed by anti-HCV and HCV viremia using HCV RNA and HCVcAg. Nucleotide sequences of NS5B region was analyzed for HCV genotype by phylogenetic analysis.
Results: Overall, 140 of 3,305 (4.2%) patients in 15 dialysis centers had anti-HCV positive. Among them, HCV RNA was further performed in 93 patients and was detectable in 59 (63.4%) individuals. Compared to HCV RNA, HCVcAg testing displayed high sensitivity (94.9%), specificity (100%) and accuracy (96.8%) in determining HCV viremia. Patients with HCV infection had a significantly longer dialysis vintage as compared to anti-HCV negative controls. The predominant HCV genotypes were 1a, 1b, 3a, 3b, 6f and 6n. Based on phylogenetic analysis, 6 separate clusters of HCV isolates involving 13 patients with high sequence homology were identified, providing suggestive evidence of patient-to-patient transmission within HD facilities.
Conclusion: The prevalence and genotype distribution of HCV in Thai patients undergoing HD differed to those of the general population. HCVcAg testing could be an alternative assay to HCV RNA in resource-limited settings. Improved preventive control measures, dialyzer reuse policy and increased access to viral eradication are essential for micro-elimination of HCV from HD centers.

[PP-0518]

Hepatitis C infection remains a serious challenge in the Southern part of Xinjiang, China

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Objectives: To understand the infectious status and viral genotypes of Hepatitis C in Southern Xinjiang, China, and promote the Hepatitis C Elimination Program in China by 2030.
Materials and Methods: The venous blood sample was collected during the physical examination, the anti-HCV test was carried out in the primary hospital, the positive anti-HCV sample be transferred to the 1st hospital of Xinjiang medical university in Urumqi to get PCR test for HCV RNA. According to the multi-stage stratified random sampling method, the HCV RNA result is analyzed by each age group. HCV antibody was detected using the hepatitis C virus antibody test kit produced by InTec PRODUCTS, INC Co., Ltd., HCV infection and genotypic determination were confirmed with RNA test. Understand the possible route of infection by issuing a questionnaire to the patients. The survey results were statistically analyzed using SPSS26.0.
Results: 8900 residents in Southern Xinjiang were screened in by anti-HCV, and the positive rate of anti-HCV was 1.33%(118/8900). Stratified by age, It was found the anti-HCV positive rate in the 50–60 years aged group (40.68%; 48/118) was higher than other age groups. Stratified by occupation, compared with other occupations, the anti-HCV positive rate was the highest among farmers and shepherds (66.9%; 79/118). For HCV RNA results, 66.9% (79/118) of patients were HCV RNA positive with predominate Genotypes 1b (84.8%; 67/79), GT2a (6.32%; 5/79), GT3b (5.06%; 4/79), GT3a (2.53%; 2/79) and GT6a (1.27%; 1/79). Among the patients with epidemiological history, 38.14% had haircuts and cosmetic tattoos in public markets with shared razors or tools, and 22.88% had surgical history, which were all high-risk factors of HCV infection.
Conclusion: The HCV prevalence was as high as 1.13% in southern Xinjiang, with HCV genotype 1b dominated. Population aged 50–60 years old, farmers, and shepherds were at the highest risk of infection. Education of erasing unhealthy life methods, such as shared razors, knives, etc. would help to decrease HCV transmission in an epidemic area of Xinjiang.

[PP-0544]

Efficacy of elbasvir and grazoprevir treatment in hepatitis C patients with chronic kidney disease who underwent routine hemodialysis at Dr. Sardjito Hospital Yogyakarta

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Objectives: This study aimed to know the efficacy of elbasvir and grazoprevir in HCV patients who underwent routine hemodialysis at Dr. Sardjito Hospital Yogyakarta.
Materials and Methods: A retrospective descriptive study was conducted among the medical records of 44 routine hemodyalisis patients who were naïve and had elbasvir and grazoprevir therapy during 2019 using total sampling technique at Dr. Sardjito Hospital Yogyakarta. Variables assessed in this study included the prevalence of HCV infection, demographic characteristic and the SVR 12 of therapy.
Results: There were 173 routine hemodialysis patients, 52 (30%) with anti-HCV positive, but only 44 (84.6%) patients with HCV RNA detected. The highest proportion by age was in the 50–59 year age

group (43.2%). Males were dominant in this study (59.1%). Based on liver cirrhosis status, the proportion of patients with non-cirrhosis was dominant 32 (72.7%). Based on SVR 12 there were 41 (93.2%) patients with HCV RNA undetected. Based on adverse events, 1 (2.3%) experienced an incident and discontinued therapy.
Conclusion: Elbasvir and grazoprevir treatment was highly effective to eradicate HCV in CKD patients with HCV infection who underwent routine hemodialysis.

[PP-0549]

Direct-acting antiviral therapy for genotype-1 infected chronic hepatitis C patients: A real-world experience

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Objectives: Chronic hepatitis C (CHC) is a major cause of cirrhosis, hepatocellular carcinoma (HCC), and mortality. Eliminating hepatitis C virus (HCV) can greatly improve long-term outcomes. Several direct-acting antiviral agents (DAAs) have been approved for treating CHC genotype-1 (GT-1) patients in Taiwan. We aimed to evaluate the real-world efficacy in CHC GT-1 patients who underwent these DAA regimens in our hospital.
Materials and Methods: This retrospective study enrolling 1492 CHC GT-1 patients treated with either Elbasvir/Grazoprevir (EBR/GZR), Sofosbuvir/Ledipasvir (SOF/LDV), glecaprevir/pibrentasvir (GLE/PIB) or sofosbuvir/velpatasvir (SOF/VEL) with or without ribavirin from December 2013 to September 2020. Therapeutic efficacy was evaluated by whether sustained virological response (SVR) were achieved at 12 weeks after finishing DAAs treatment. Intention-to-treat (ITT) analyses enrolled all patients treated with the regimens. Per-protocol analyses (PPA) were performed after excluding patient with treatment discontinuation or loss of follow up.
Results: The overall SVR rate at week 12 (SVR12) by ITT and PPA were 95.2% and 99.2%, respectively. The SVR12 rates were similar in four DAAs regimen by ITT (97.3%, 95.6%, 93.2% and 94.1% respectively) and by PPA (99.7%, 98.6%, 99.6% and 99.4% respectively). All eleven patients without SVR12 were relapsers: one was IFN-experienced (by EBR/GZR), three were previous injection drug users (PIWD) (by SOF/LDV, GLE/PIB, and SOF/VEL), one were HIV co-infected (by GLE/PIB), two with HCC (by SOF/LDV and SOF/VEL). In the subgroup analysis, the SVR12 rate by PPA was significantly lower in patients treated with GLE/PIB and HIV co-infection (91.7%), which may be due to the relative small case number in this group.
Conclusion: Several kinds of DAAs have become available over the past few years for genotype 1 patients. In our study, DAA therapy can achieve a high SVR rate among CHC GT-1 patients, regardless of whether the patient were treatment experienced, had history of HCC, liver cirrhosis or advanced CKD.

[OP-0570]

Steatosis in baseline liver biopsy proven chronic hepatitis C could explain fibrosis progression detected in some patients who achieved SVR following INF based therapy: 10 years follow up

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Objectives: Backgrounds: The combination of pegylated IFN and ribavirin was the standard care for chronic HCV infection before the era of DAAs. There have been insufficient long-term follow-up studies (G4) regarding the effect of INF-induced SVR on disease progression. Objectives: To assess the clinical outcomes in a large cohort of CHC-G4 who achieved SVR and evaluating the factors that affect the clinical outcomes.
Materials and Methods: Methods: A retrospective single-center study was conducted at the Association of Liver Patients Care, El?Mansoura, Egypt, in patients with CHC infection treated with INF (from Jan 2007 to November 2011). Outcomes of all-cause mortality, Hepatocellular carcinoma, and decompensation of cirrhosis have been evaluated. The changes of fibrosis stages was also studied.
Results: Results: A total of 941 patients were included. SVR rate of 64.8% was found. The median time of patient follow-up was 120.00 months (IQR 115.0–126.0). 57 patients died during the study; 48 liver-related and 9 as non-liver-related. 40 cases of hepatocellular carcinoma and 41 cases of decompensated cirrhosis. Using multivariable analysis viral clearance was associated with a decrease in all-cause mortality (HR 0.194, 95% CI 0.058–0.646; p = 0.008), hepatocellular carcinoma (HR 0.081, 95% CI 0.011–0.614; p = 0.015), and decompensated cirrhosis (HR 0.094, 95% CI 0.013–0.706; p = 0.021). In 538 patients with baseline liver biopsy that attended follow-up visits, 49 patients (9.1%) showed reversal of hepatic fibrosis, 91 patients (16.9%) showed fibrosis regression, 308 patients (57.2%) remained stationary while 90 patients (16.7%) showed fibrosis progression. However, 26.4% of patients with baseline hepatic steatosis showed hepatic fibrosis progression despite achieving SVR.
Conclusion: Conclusion: IFN induced SVR to reduce overall mortality, risk of HCC, and rate of decompensation. Moreover viral clearance improved hepatic fibrosis, however, dual etiology (MAFLD, HCV) could explain fibrosis progression in some patients.

[PP-0580]

Cost-effectiveness and health-related outcomes of one-time screening and treatment for hepatitis C in Korean population: A pilot project for hepatitis C screening

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Objectives: This study investigated the cost-effectiveness of one-time screening and treatment strategy for hepatitis C patients as compared to no screening or risk-based screening strategies.
Materials and Methods: As a part of a pilot project for hepatitis C screening in Korea, 56-year-old general Korean population received hepatitis C virus (HCV) antibody (Ab) tests at the national general health checkup, followed by HCV RNA tests for HCV Ab-positive subjects as a confirmatory test. To model different screening and treatment strategies for hepatitis C patients for a cost-effectiveness analysis, a Markov disease progression model with screening and treatment decision tree was used. The screening strategies included "Scree-all", "Risk-based screening", and "No screening" strategies followed by treatment.
Results: A total of 133,705 subject, 104,918 subjects received hepatitis C screening test with acceptability of screening rate of 78.47%. Of the 104,918 examinees, 792 cases (0.75%) were positive for HCV Ab and 189 cases (0.18%) were positive for HCV RNA, resulting in HCV RNA positivity in persons with HCV Ab of 23.86%. In cost-effective analyses, the screen-all strategy led to the lowest rates of advanced liver disease events reducing the risk of decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, and death by 40–50%. The incremental cost-effectiveness ratio (ICER) of the screen-all strategy compared to the no screening strategy was ?8,164,704/quality-adjusted life-year (QALY), which was much lower than the cost-effectiveness threshold of gross domestic product per capita, ?35,831,274. When compared with the risk-based strategy, the screen-all strategy was consistently cost-effective with ICER of ?7,965,201/QALY. In sensitivity analyses, the cost-effectiveness of the screen-all strategy over the no screening or risk-based screening strategies was robust in all situations.
Conclusion: Screening all 56-aged Korean population once followed by effective treatment is expected to reduce the incidence of adverse liver disease and is cost-effective when compared with risk-based screening or no screening.

[PP-0624]

Efficacy of direct-acting antiviral agents for chronic hepatitis C genotype 3 in southern Taiwan

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Objectives: Chronic hepatitis C worldwide problems that cause hepatitis, liver cirrhosis, and even cancer. Direct antiviral agent (DAA) has been developed for a while and it shows the satisfactory treatment efficacy and tolerability in the prior studies. However, some papulations may have inferior treatment responses, including patients with severe liver decompensation, active hepatocellular carcinoma (HCC), and hepatitis C virus genotype 3 (HCV-3) infection and those who experience multiple DAA treatment failures. In this study, we aim to investigate the effectiveness and outcomes of DAA in patients with genotype 3 hepatitis C.
Materials and Methods: 55 patients were treated with Sofosbuvir/Daclatasvir (SOF/DCV), Glecaprevir + Pibrentasvir (GLE/PIB), Sofo-sbuvir/Velpatasvir ± Ribavirin (SOF/VEL ± RBV) for 8 ~ 16 weeks based on patient's characteristic according to the guideline. The laboratory test, virus RNA and fibrosis score were collected before treatment, in end of treatment and at the 12 weeks post treatment. Adverse effects are also recorded.
Results: Patients with higher FIB-4 score, serum bilirubin, liver cirrhosis, and hypertriglyceridemia are more in SOF/VEL ± RBV group. Totally 47 patients (94%) reached the SVR, 3 had relapsed disease (2 treated with Glecaprevir/Pibrentasvir and 1 with Sofosbuvir /Velpatasvir + Ribavirin). AST, ALT, rGT and FIB-4 score are improved after treatment. The patient with relapsed disease are all naïve to treatment, and have no CKD, HIV or HBV co-infection. One of them has liver cirrhosis. No significant difference is found in these 2 groups.
Conclusion: Pangenotypic DAAs have short treatment courses, good safety and high success rates when compared to the conventional pegylated interferon + ribavirin. Being a part of hard-to-cure populations, patients with genotype 3 hepatitis C has less treatment choice than patients with other genotypes and have lower SVR rate. However, we did not find the contributing factors between SVR and relapsed group. It needs more studies to find out the causes and to reach the goal for HCV elimination.

[PP-0636]

Efficacy of different direct-acting antiviral regimens for hepatitis C genotype-6 infected patients in Taiwan

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Objectives: Chronic hepatitis C (CHC) is one of main causes of liver cirrhosis, hepatocellular carcinoma (HCC), and mortality. Eradicating hepatitis C virus (HCV) would improve long-term outcomes prominently. Different direct-acting antiviral agents (DAAs), including Sofosbuvir (SOF) with NS5A inhibitors, or non-SOF-based DAAs, including glecaprevir/pibrentasvir (GLE/PIB), have been approved for treating CHC genotype-6 (GT-6) patients in Taiwan. We managed to evaluate the efficacy in patients with CHC GT-6 who received these DAAs treatment.
Materials and Methods: We retrospectively selected patients with CHC GT-6 who received SOF-based DAAs or GLE/PIB at a single medical center during 2018 to 2020. Total 98 patients were registered and baseline characteristics were collected including underlying diseases and biochemical data. Eight patients ever received peginterferon (Peg-IFN) ± RBV (ribavirin) treatment for HCV before. Fourteen patients lost follow-up. All of the patients were treated with either SOF/LDV (Ledipasvir) ± RBV for 12 weeks, SOF/VEL (Velpatasvir) for 12 weeks, or GLE/PIB for 8 or 12 weeks. The primary endpoint was clearance of the HCV RNA at 12 weeks after treatment (sustained virological response, SVR12).
Results: Eighty-four patients were enrolled for evaluation, including 21 patients with SOF/LDV ± RBV for 12 weeks, 33 patients with SOF/VEL for 12 weeks, 30 patients with GLE/PIB (25 patients for 8 weeks and 5 patients for 12 weeks). The overall SVR rate were 100%. All of these regimens achieved SVR whether the patients had underlying cirrhosis (28.6%), hepatitis B virus (HBV) co-infection (9.5%), chronic kidney disease (CKD) (22.6%), end-stage renal disease (ESRD) (3.6%), human immunodeficiency virus (HIV) co-infection (16.7%), or previous treatment for HCV (9.5%). There were

significant improvement of liver enzymes and liver fibrosis score (FIB-4) at 12 weeks after treatment compared with baseline data.
Conclusion: For patients with CHC GT-6, SOF/LDV, SOF/VEL, or GLE/PIB may reach high efficacies regardless of underlying cirrhosis, HBV co-infection, CKD status, HIV co-infection, or previous treatment for HCV.

	Overall (N = 84)	*SOF/LDV ± RBV (N = 21)*	*SOF/VEL (N = 33)*	*GLE/PIB (N = 30)*
*Week 4 of treatment n = 81***	56.8% (46/81)	65.0% (13/20)	48.4% (15/31)	60.0% (18/30)
*End of treatment n = 80***	91.3% (73/80)	100% (20/20)	90.3% (28/31)	86.2% (25/29)
Week 12 after treatment (SVR12) n = 84	**100% (84/84)**	**100% (21/21)**	**100% (33/33)**	**100% (30/30)**

[OP-0639]

Characteristics of HCV genotype 6 relapsers (treatment failures) treated with fixed-dose combination of sofosbuvir and ledipasvir (SOF/LDV) ± ribavirin

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Objectives: HCV infection is a globally prevalent disease and Genotype 6 is common in Southeast Asia. In Myanmar, Genotype 6 is estimated to account for 36% and is the most-difficult-to-treat genotype. Treatment with SOF/LDV ± ribavirin achieved SVR rates of 77% only. This retrospective study is aimed to determine the characteristics of HCV Genotype 6 patients who failed to achieve SVR (relapsers).
Materials and Methods: Total 161 patients were treated with SOF/LDV ± ribavirin for 12/24 weeks in Yangon GI and Liver Centre from January 2017 to September 2018 and 37 patients failed to achieve SVR. We studied 37 relapsers to review the factors of treatment failure.
Results: Among 37 relapsers, 40% of patients were male (n = 15) and 60% were female (n = 22). The mean age was 55.68 years (SD 10.3). All the patients were treatment-naïve and about 60% (n = 22) had cirrhosis before treatment initiation. The mean baseline viral load was 3.3 million IU/mL. Majority of relapsers, 84% (n = 31), were identified as subtype 'cL', 11% (n = 4) as 'n' and the rest 5% (n = 2) were 'm'. Among these relapsers, 81% (n = 30) were treated with SOF/LDV without ribavirin and only 19% (n = 7) received SOF/LDV + ribavirin. Only 10% (n = 4) were treated for 24 weeks and majority of relapsers (90%, n = 33) were treated for 12 weeks duration.
Conclusion: There was a significant association between SVR and each treatment regimen. But no conclusion regarding the superiority of the treatment regimen containing rebavirin over the regimen without ribavirin could be made due to the observational nature of our study. And we found that subtype 6-cL is the most common and difficult-to-treat subtype in Myanmar. In conclusion, the addition of ribavirin to SOF/LDV AND/OR extension of treatment duration may increase SVR rate. This should be applied in genotype 6 treatment AND more effective and pan-genotypic regimen should be used for these patients.

[PP-0711]

Incidence of HCC is quite different depending on the history of HCC; A prospective study by 611 SVRs

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Objectives: Oral preparation of anti HCV drug completely changed the paradigm of Hepatology. We prospectively observed HCC carcinogenesis after SVR in a single center.
Materials and Methods: We enrolled 611 patients who achieved SVR after DAA (Direct Acting Antiviral) between 2013 and 2020. Of the 611 patients, 34 (6%) had a history of HCC prior to DAA treatment. The remaining 578 patients had no history of HCC. These patients were prospectively observed for development of HCC.
Results: SVR was achieved in all 611 patients. The mean observation period for all 611 patients was 3.6 years, and HCC development was observed in 47 patients (8%) during follow-up, the rate was 2.1 per 100 person-years. By history of HCC, 21 of 34 patients with history positive had HCC development (62%), the rate was 43.9 per 100 person-years. On the other hand, 26 of 577 patients with no history of HCC showed HCC carcinogenesis (5%), the rate was only 1.2 per 100 person-years. A history of HCC was associated with a significantly higher rate of HCC carcinogenesis.
Conclusion: A prospective study showed an overall incidence of 2.1 cancers per 100 person-years. The rate was 43.9 per 100 person-years of carcinogenesis, especially in the patients with a history of HCC. Patients with a history of HCC need to be followed up with close attention to HCC carcinogenesis.

[PP-0713]

Incidence and prognosis of neoplastic lesions other than HCC; A prospective study of 611 patients with SVR

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Objectives: Oral preparation of anti HCV drug completely changed the paradigm of Hepatology. We prospectively followed 611 patients who attained sustained virological response (SVR).
Materials and Methods: We enrolled 611 patients who achieved SVR after DAA between 2013 and 2020. Of the 611 patients, 34 (6%) had a history of HCC prior to DAA treatment. The remaining 578

patients had no history of HCC. The patients were prospectively observed for development of ALL Malignant Tumor.
Results: The mean observation period for all 611 patients was 3.6 years. The incidence of all malignancies was 80 (13%), and the rate was 3.6 per 100 person-years. Of these, HCC development was observed in 47 patients (8%) during follow-up, the rate was 2.1 per 100 person-years. On the other hand, the incidence of malignancies other than HCC was 32 cases (5%), or 1.4 per 100 person-years. By age (< 75 years vs. 75 years and older), the overall cancer rate was 3.0 vs. 5.6 per 100 person-years. We further followed the patients and OS (overall survival) of the two groups was not different (< 75 years vs. 75 years and older).
Conclusion: A prospective study showed an overall incidence of 3.6 all malignant tumors per 100 person-years. It turns out that malignant tumors other than HCC also occur. In particular, the incidence of carcinogenesis was 2.5 times higher in patients over 75 years of age compared to those under 75 years of age. In the follow-up after SVR in the elderly, one should also be aware of carcinogenesis other than HCC.

[PP-0714]

Risk factors for occurrence of HCC after DAA therapy; A prospective study of 611 SVRs

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Objectives: Oral preparation of anti HCV drug completely changed the paradigm of Hepatology. We prospectively observed HCC carcinogenesis after SVR. The aim of this study was to identify the risk factors for liver carcinogenesis based on the clinical background of patients who achieved SVR after DAA treatment.
Materials and Methods: We enrolled 611 patients who achieved SVR after DAA between 2013 and 2020. Of the 611 patients, 34 (6%) had a history of HCC prior to DAA treatment. The remaining 578 patients had no history of HCC. These patients were prospectively observed for development of HCC. The various clinical backgrounds (Age, sex, BMI, HCV genotype, HCV-RNA, history of interferon treatment, history of liver cancer before DAA treatment, and Fibroscan value before DAA treatment) were compared between HCC and non-HCC cases.
Results: The mean observation period for all 611 patients was 3.6 years. The incidence of HCC development was observed in 47 patients (8%) during follow-up. When comparing HCC carcinoma cases with non-carcinoma cases, age (71 vs. 65 $p = 0.001$), HCV genotype 1 (39/48 vs. 351/562 $p = 0.009$), previous liver cancer (21/48 vs. 13/563 $p < 0.001$), Fibro-scan value at initial diagnosis (21.2 kPa vs. 10.6 kPa $p < 0.001$) were statistically significant. In multivariate analysis, we found that previous history of hepatocellular carcinoma (OR 23.5, 95%CI 9.2–60.3, $p < 0.001$), Fibro-scan > 11.8 kPa at first visit (OR 13.9 95%CI 5.4–35.5, $p < 0.001$), HCV genotype 1 (OR 2.6, 95%CI 1.0–6.9, (OR 2.6, 95%CI 1.0–6.9, $p = 0.045$) were significant risk factors for carcinogenesis.
Conclusion: In SVR patients treated with DAA, a history of hepatocellular carcinoma, high Fibro-scan at initial diagnosis, and HCV genotype 1 were found to be high risk factors for hepatocarcinogenesis.

[OP-0737]

Real-world impact of a subsidy decision for treatment of hepatitis C on clinical practice and patient outcomes

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Objectives: Sofosbuvir/velpatasvir was recommended for subsidy to treat chronic hepatitis C in Singapore in 2018. We studied the impact of the subsidy listing on clinical practice and patient outcomes by examining (1) changes in utilisation and prescribing pattern after subsidy and (2) real-world clinical effectiveness and safety outcomes.
Materials and Methods: Aggregated drug utilisation data from our public hospitals' dispensing systems and clinical data from the national electronic health record database were used to study utilisation trends and prescribing patterns. A single-cohort prospective study was conducted to evaluate sustained virological response rate 12 weeks post-treatment (SVR12) and adverse events (AEs).
Results: Usage of sofosbuvir/velpatasvir increased sharply after its subsidy listing and subsequently dropped. The absolute monthly growth in utilisation volume increased from 78 defined daily doses (DDDs) in the pre-subsidy period to 1,442 DDDs in the first nine months post-subsidy. Following which, there was a monthly drop in utilisation by 603 DDDs. On the other hand, utilisation of comparator drugs remained low. Prescribing rate of sofosbuvir/velpatasvir increased from 13.7% to 90.2%, and 39.1% of patients previously on peg-interferon and ribavirin switched to sofosbuvir/velpatasvir post-subsidy. There were 375 patients in the cohort study who met the inclusion criteria, of which 79.2% were males. Median age was 56 years (interquartile range: 49 to 61 years). The distribution for genotypes 1/2/3/4/5/6 was 41.3/1.9/52.3/1.9/0/0.5% respectively, with 8 (2.1%) missing records. 365 out of 375 patients (97.3%, CI 95.1–98.6%) achieved SVR12 and there were no significant differences in SVR12 for the different genotypes. AEs were reported in 3.7% of patients, and common reported AEs included fatigue, giddiness and itchiness. No serious AE was reported.
Conclusion: The subsidy decision has led to increased accessibility as well as the intended changes in clinical practice. Sofosbuvir/velpatasvir was clinically effective and safe in the real-world for all HCV genotypes.

[OP-0772]

Sofosbuvir-based therapy for pregnant women and infant with severe chronic hepatitis C: A prospective real-world study

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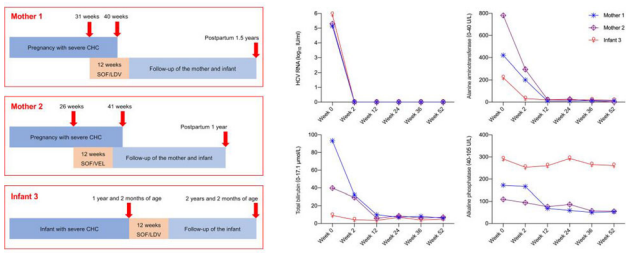
Objectives: To investigate the safety and effectiveness of direct acting antiviral agents for pregnant women and infant with severe chronic hepatitis C (CHC).
Materials and Methods: Two late pregnant women and one female infant were diagnosed with severe CHC at 30 (mother 1), 33 (mother 2) and 1.2 years of age (infant 3), respectively. Sofosbuvir-based therapy was administered according to patients' hepatitis C virus (HCV) genotypes, and the treatment duration was 12 weeks. The safety and effectiveness profiles of two mothers (including their male infants 1 and 2) and infant 3 were closely monitored until at least 12 months after treatment initiation.
Results: At treatment initiation, the gestational ages of mothers 1 and 2 were 31 and 26 weeks, and the infant 3 infected HCV perinatally had 8 months history of anorexia, detectable HCV RNA, and alanine aminotransferase (ALT) levels of more than 200 U/L; meanwhile, the mothers 1 and 2, and infant 3 had HCV RNA levels of 139,000, 198,000, and 8,450,000 IU/ml, genotypes of 1b, 2a, and 1b, ALT levels of 420, 781, and 220 U/L, and total bilirubin levels of 93.3, 39.7, and 9.2 μmol/L, respectively. Sofosbuvir/ledipasvir were administered for mother 1 and infant 3, and sofosbuvir/velpatasvir for mother 3. Sofosbuvir-based therapy was well tolerated, the most common adverse event was nausea (3/3), and no infants had birth defects. All 3 patients had undetectable HCV RNA and normal ALT levels (40 U/L) after 2 and 12 weeks of treatment, respectively. All 3 patients obtained sustained virological response at 12 weeks after treatment cessation. All infants 1, 2, and 3 had normal growth parameters until at 1.5, 1, and 2.2 years of age, and infants 1 and 2 had consistently negative anti-HCV antibody.
Conclusion: Sofosbuvir-based therapy is safe and effective for pregnant women and infant with severe CHC, future validation studies are warranted.



[PP-0773]

A study on linkage to care and awareness of patients with chronic hepatitis C in Korea

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Objectives: This study conducted a questionnaire on awareness of hepatitis C and clinical characteristics of patients with hepatitis C to improve linkage to care.
Materials and Methods: Hepatitis C patients over the age of 19 who visited ten referral centers in Korea from January to June 2021 were individually interviewed using a structured questionnaire. A total of 165 participants were asked to complete the questionnaire. Basic personal information, lifestyle habits such as drinking and smoking, information related to hepatitis C, and overall awareness of hepatitis C were assessed through statistical analysis.
Results: More than half (67%) of hepatitis C patients were diagnosed in their 50 s or older. The most common expected route of transmission was through needles for tattoos and piercings (123 participants, 76.4%). Approximately 53.9% of the participants were aware of the correct transmission route while 41.8% had wrong awareness. The most common route of diagnosis was incidental diagnosis through regular health examinations or at medical institutions (87.7%). Approximately 92.7% of the participants were treated for hepatitis C. However, only 55.3% received treatment within six months after diagnosis, and 20.7% received treatment five years after diagnosis. Additionally, 14% of the respondents answered that they experienced emotional and physical discrimination at work or school. The greatest proportion of participants (48.4%) responded that the direct expense for treatment was more than one million won ($850) per month.
Conclusion: The awareness and treatment rate of chronic hepatitis C patients were high. However, most of the patients were incidentally diagnosed during regular health examinations (87.7%), and a significant number of the participants (44.7%) underwent treatment more than six months after diagnosis.

Status on current diagnosis and treatment of chronic hepatitis C

Question and response	Number (%)
Expected transmission route (multiple responses were allowed)	
Wound and blood	123 (76.4%)
Shared use of nail clipper, toothbrush, and razor	22 (13.7%)
Sexual contact	17 (10.6%)
Vertical transmission	5 (3.1%)
Diagnosis route for hepatitis C	
Incidental diagnosis	144 (87.3%)
Onset of symptoms	17 (10.3%)
Voluntary examination	3 (1.8%)
Age at HCV diagnosis	
20s	6 (3.6)
30s	13 (7.9)
40s	35 (21.2)
50s	64 (38.8)
≥ 60s	48 (28.5)
Treatment status of respondents	
Treated	152 (92.7%)
Age at treatment	
30s	6 (4.2%)
40s	22 (15.4%)
50s	53 (37%)
60s	42 (29.4%)
70s	16 (11.2%)
80s	4 (2.8%)
Treatment agent	
Direct acting antiviral agents	114 (85.1%)
Interferon-based treatment	20 (14.9%)
Time gap from diagnosis to treatment initiation	
Within six months	83 (55.3%)
Six months - one year	19 (12.7%)
One to five years	17 (11.3%)
Five to ten years	13 (8.7%)
More than ten years	18 (12.0%)
Reasons for not undergoing treatment	
Lack of symptoms	6 (50.5%)
Economic burden	4 (33.3%)
Lack of recommendation from medical staffs	1 (8.3%)
Disease progression	1 (8.3%)

[PP-0781]

Virological efficacy and safety of ledipasvir and sofosbuvir in patients with chronic hepatitis C virus genotype 2 infection: Real-world experience from Korea

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Objectives: Genotype 2 (GT2) hepatitis C virus infection is the one of the two most common genotypes in Korea. While ledipasvir/sofosbuvir (LDV/SOF) is approved for the treatment of GT2 HCV infection in Taiwan, Japan, and Korea, the real-world experience of Korea is not well known. The aim of the study is to evaluate the efficacy and safety of LDV/SOF in patients with GT2 chronic hepatitis C infection in Korea.
Materials and Methods: From June 2019 to March 2021, 17 consecutive HCV GT2 patients who received LDV/SOF at 2 university-based hospitals were retrospectively included for analysis. HCV RNA was measured at baseline, 12 and 24 weeks after the first dose to determine the end of treatment response (ETR) and sustained virologic response at 12 weeks off-therapy (SVR12). The effectiveness of the treatment was determined by the SVR12 response.
Results: Among the 17 HCV GT 2 patients treated with LDV/SOF, 3 patients were lost to follow up before the assessment of SVR 12. In the remaining 14 patients, the overall SVR12 rate was 100%. Five - males and 9 females were included in the study. The mean age of the patients was 58-years old. Liver cirrhosis assessed with abdominal imaging which included ultrasonography, computed tomography or fibroscan was present in 64.2% (9/14) patients. All the patients had no prior treatment history with pegylated interferon or other direct-acting antiviral agents. No severe adverse events were reported and there was no drug interruption due to adverse events.
Conclusion: Treating GT2 chronic hepatitis C patients with LDV/SOF in Korea was safe and resulted in excellent efficacy regardless of the presence of liver cirrhosis.

[OP-0799]

Does routine ribavirin increase SVR12 among genotype 3 hepatitis C compensated cirrhosis receiving sofosbuvir/velpatasvir? A meta-analysis

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Objectives: Background: Sofosbuvir/Velpatasvir (SOF/VEL) is an effective pangenotypic direct-acting antiviral for chronic hepatitis C virus (HCV) infections. While the addition of ribavirin (RBV) to SOF/VEL improved sustained virological response (SVR12) in genotype 3 (GT3) decompensated cirrhosis patients, the benefits of routine RBV in GT3 compensated cirrhosis patients receiving SOF/VEL, remains unclear. Aims:To evaluate the efficacy and safety of SOF/VEL, with or without RBV in GT3 compensated cirrhosis patients.
Materials and Methods: Methods: We systematically searched four electronic databases, from inception to June 2021, using free text and MeSH terms. All studies reporting outcomes on GT3 compensated cirrhosis patients received 12 weeks of SOF/VEL, with or without RBV, were included. The primary outcome was SVR12. The secondary outcome was treatment-related adverse events, defined as symptomatic anaemia requiring transfusion or drop in haemoglobin beyond 2 g/dL.
Results: Results: From 1,752 citations, a total of 7 studies (2 RCTs, 5 cohort studies) with 1,088 subjects were identified. The SVR12 was similar in GT3 compensated cirrhosis patients, regardless of addition of RBV, for both the intention-to-treat (RR: 1.03, 95%CI: 0.99–1.07; I2 = 0%) and the per- protocol analysis (RR: 1.03, 95%CI: 0.99–1.07; I2 = 48%). The overall pooled rate of treatment-related adverse events was 7.2%. Addition of RBV resulted in four-fold higher risk of treatment- related adverse events (RR: 4.20, 95%CI: 1.29–13.68; I2 = 0%). Subgroup analysis showed that RBV was associated with a numerically higher SVR12 in GT3 compensated cirrhosis patients with baseline resistance-associated substitutions (96% vs 87%, p = 0.12). However, addition of RBV did not significantly increase the SVR12 among treatment-experienced GT3 compensated cirrhosis patients receiving SOF/VEL.
Conclusion: Conclusion: Ribavirin was not associated with higher SVR12 in GT3 compensated cirrhosis patients receiving SOF/VEL. Our findings suggest limited role for RBV as routine add-on therapy to SOF/VEL among GT3 compensated cirrhosis.

[OP-0813]

Effectiveness of ledipasvir/sofosbuvir and glecaprevir/pibrentasvir in real-world: A single center experience in Korea

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Objectives: Ledipasvir/sofosbuvir and glecaprevir/pibrentasvir are widely used to treat patients with hepatitis C virus (HCV) in South Korea. We aimed to evaluate sustained virologic response (SVR) rates following ledipasvir/sofosbuvir and glecaprevir/pibrentasvir in a real-world cohort of HCV patients.
Materials and Methods: Between January 2017 and December 2020, we reviewed the medical records of 232 HCV patients who were treated 12 weeks with ledipasvir/sofosbuvir or 8 weeks with glecaprevir/pibrentasvir at Kosin University Gospel Hospital. All enrolled patients were at least followed up 24 weeks after the end of treatment. We divided the study population into two groups (ledipasvir/sofosbuvir and glecaprevir/pibrentasvir), thereby compared two groups.

Results: A total of 232 HCV patients were treated either ledipasvir/sofosbuvir (n = 96, 41.4%) or glecaprevir/pibrentasvir (n = 136, 58.6%). Sixty-five (28.0%) patients had cirrhosis and 23 (9.9%) patients had hepatocellular carcinoma. The majority (95.7%) of patients were treatment-naïve. Two hundred and twenty-two (95.7%) patients had Child–Pugh class A, 10 (4.3%) patients had class B. Table 1 shows the genotypes of the study population. The median HCV RNA level was 6.0 $\log_{10}$ IU/ml, and 192 (82.8%) patients had HCV RNA levels less than 6,000,000 IU/mL. At the end of treatment, 231 (99.6%) of patients had undetectable HCV RNA levels. Furthermore, SVR12 was achieved in 231 of 232 patients (99.6%) and SVR24 was achieved in 230 of 232 patients (99.1%). One patient did not achieve both SVR12 and SVR24, while another achieved SVR12 but relapsed at post-treatment week 24.
Conclusion: Ledipasvir/sofosbuvir and glecaprevir/pibrentasvir showed high efficacy in patients with HCV.

Table 1. Baseline characteristics of study population

	Total (n=232)	LDV/SOF (n=96)	GLE/PIB (n=136)
Age, years[a]	63.0 (55.0-71.0)	61.5 (55.0-71.3)	63.0 (55.0-71.0)
Male, sex[b]	115 (49.6)	48 (50.0)	67 (49.3)
Liver cirrhosis[b]	65 (28.0)	29 (30.2)	36 (26.5)
Prior HCC[b]	23 (9.9)	12 (12.5)	11 (8.1)
Child-Pugh class[b]			
A	222 (95.7)	89 (92.7)	133 (97.8)
B	10 (4.3)	7 (7.3)	3 (2.2)
Habitual alcohol intake[b]	58 (25.0)	24 (25.0)	34 (25.0)
HBV coinfection[b]	9 (3.9)	7 (7.3)	2 (1.5)
Hypertension[b]	53 (22.8)	23 (24.0)	30 (22.1)
Diabetes[b]	52 (22.4)	24 (25.0)	28 (20.6)
Chronic kidney disease[b]	21 (9.1)	2 (2.1)	19 (14.0)
Treatment-naïve[b]	222 (95.7)	91 (94.8)	131 (96.3)
HCV Genotype[b]			
1	4 (1.7)	3 (3.1)	1 (0.7)
1a	2 (0.9)	1 (1.0)	1 (0.7)
1b	110 (47.4)	67 (69.8)	43 (31.6)
2	40 (17.2)	8 (8.3)	32 (23.5)
2a	5 (2.2)	0	5 (3.7)
2b	15 (6.4)	3 (3.1)	12 (8.8)
2a/2c	53 (22.8)	14 (14.6)	39 (28.7)
3a	1 (0.4)	0	1 (0.7)
1&2 co-infection	2 (0.9)	0	2 (1.5)
HCV RNA, $\log_{10}$ IU/ml[a]	6.0 (6.0-7.0)	6.0 (6.0-7.0)	6.0 (5.0-7.0)
HCV RNA <6,000,000 IU/mL[a]	192 (82.8)	78 (81.3)	114 (83.8)
WBC count, $\times 10^3$/L[a]	5.3 (4.3-6.6)	5.3 (3.9-6.5)	5.4 (4.6-6.8)
Hemoglobin, g/dL[a]	13.5 (12.4-14.6)	13.3 (12.4-14.7)	13.7 (12.3-14.5)
Platelet count, $\times 10^3$/L[a]	175.5 (133.5-220.0)	170.5 (131.8-209.0)	181.5 (134.5-226.0)
Albumin, g/L[a]	4.2 (3.9-4.4)	4.2 (3.9-4.4)	4.2 (3.9-4.4)
Total bilirubin, μmol/L[a]	0.7 (0.5-0.9)	0.7 (0.5-0.9)	0.7 (0.5-1.0)
AST, U/L[a]	32.0 (23.0-60.8)	33.0 (23.0-59.0)	31.5 (24.0-63.0)
ALT, U/L[a]	27.0 (17.0-52.5)	25.0 (16.0-49.3)	28.0 (17.3-55.5)
Sodium, mmol/L[a]	139.1 (137.8-140.5)	138.9 (137.0-140.5)	139.3 (138.0-140.5)
AFP[a]	3.7 (2.6-6.7)	3.8 (2.7-7.9)	3.5 (2.5-5.9)
EOT(+)[b]	231 (99.6)	95 (99.0)	136 (100)
SVR12[b]	231 (99.6)	95 (99.0)	136 (100)
SVR24[b]	230 (99.1)	94 (97.9)	136 (100)

Abbreviations: HCC, hepatocellular carcinoma; HBV, hepatitis B virus; HCV, hepatitis C virus; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; EOT, end of treatment; SVR, sustained virologic response
[a]Values are presented as median (range)
[b]Values are presented as number (%)

[PP-0878]

The effectiveness and safety in genotype 1b HCV infected treatment nave patients who are treated by ledipasvir/sofosbuvir

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Objectives: Combination of ledipasvir (LDV)/sofosbuvir (SOF) has been approved in Mongolia for the treatment of genotype 1b hepatitis C virus (HCV) infected patients.

Materials and Methods: This retrospective study analyzed 1254 patients with HCV infection who were treated with LDV/SOF from February 2016 to January 2020, were retrospectively enrolled from Dornod Medical center. Virology response was measured at 4 weeks (rapid virology response, RVR), at 12 weeks (end of treatment response, ETR), and at 12 weeks after the end of treatment (sustained virology response, SVR12). Safety was assessed by review of adverse events, physical examinations, and laboratory findings.
Results: Of the 1254 patients (male, n = 564 [45%] female n = 688 [55%]; mean age, 58.7 years; liver cirrhosis 338 [27%]), 916 patients (73.0%) were chronic hepatitis, mean AST (78.4 IU/L), mean ALT (69.8 IU/L), and mean HCV RNA level (3,578,370 IU/mL). In all patient, SVR12 was achieved in 1244 (99%). 6 patients early stopped the treatment because of headache problem, 6 patients were over 70 years old, stopped the medication due to gastrointestinal troubles. During or after DAA treatment, hepatocellular carcinoma developed in 3 patients whose age was over 65 years.
Conclusion: LDV/SOF treatment for HCV GT1b infected Mongolian subjects achieved very high SVR rates. However, in some older patients, HCC can develop during or after DAAs treatment.

[PP-0891]

Effect of DAAs treatment on liver stiffnes in hepatitis C patients

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Objectives: Hepatitis C virus infection can result in the inflammation and necrosis of liver cells, which can futher developing liver cirrhosis. Succesfull treatment of chronic hepatitis C with DAAs regiment lead to improvement in liver fibrosis in most of patients. Antiviral treatment can alter natural history and reduce risks of cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Liver fibrosis is closely related to the prognosis of patients with chronic liver disease. Elastography noninvasively quantifies tissue elasticity and stiffness. This research wants to study effect of DAAs on liver stiffness in patients with chronic hepatitis C infection at Prof. Dr. R. D. Kandou Hospital.
Materials and Methods: This research was cohort retrospective study. The respondents are 18 patients with chronic hepatitis C infection who have been treated DAAs for 3 months at Prof. Dr. R. D. Kandou Hospital, on January 2019—November 2021. Patients with CKD treated with Grazoprevir/elbasvir, whether non CKD group treated with Sofosbuvir/daclatasvir. Total sampling used in this study. Data analysis were done using Wilcoxon test, with significance level ($p < 0.05$).
Results: A total of 18 patients with chronic hepatitis C infection who have been treated with DAA regiment, there are 11 male patients. Research subjects have a range of ages between 42–75 years. The mean value of liver stiffness measured by transient elastography pre and post treatment were 28,1 + 24,7 kPA and 13,1 + 12,3 kPA. HCV-RNA pre and post treatment were 3,4 + 1,8 and 0. Wilcoxon test shows significant difference on liver stiffness (p = 0,01) and HCV-RNA (p = 0,0001) between pre and post treatment with DAAs regiment.

Conclusion: There are a significant difference on liver stiffness and HCV-RNA between pre and post treatment with DAAs regiment.

[PP-0929]

Polymorphism of genes involved in the reactions of congenital immunity, while viral hepatitis C in ethnic groups of Buryats and Mongolians

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Objectives: To study the proposed hypothesis by the study of the SNP genes IFNL4 (rs368234815), IFNL3 (rs12979860 and rs8099917), CD209 (rs4804803), TLR3 rs3775291 and rs13126816 in cohorts of Mongolian patients with HCV and in the ethnically similar Buryat group, and also in patients with Hepatitis C caused by different virus genotypes.
Materials and Methods: A total of 400 patients with chronic HCV were examined, including 200 from the Republic of Buryatia and 200 from Mongolia. The compared groups of patients completely matched in clinical-laboratory and sex-age indices. There were no associations of polymorphic variants of the genes CD209, IFNL3, and ethnicity of patients, as well as genotypes of the virus in the Buryat population. Obviously, the internalization of different genotypes of the virus into the cell is universal, and, at least, does not depend on the polymorphism of the CD209 gene.
Results: In contrast, as a result of the work performed, two SNPs in the candidate genes TLR3 (rs3775291) and IFNL4 (rs368234815) were detected, polymorphic variants of which occur with different frequency in patients with 1 and not 1 (2/3) genotypes of the virus. Carriers of G-allele rs3775291 TLR3 are 3.1 times more resistant to infection with 2/3 virus genotypes ($p < 0.0001$), and carriers of ΔG-allele rs368234815 IFNL4—2.0 times ($p < 0.02$). Consequently, the higher the proportion of human carriers of these alleles and their haplotypes in a population, the higher the tolerance for the spread of 2/3 genotypes of the virus in it.
Conclusion: Further studies at the level of practically healthy people in Mongolia and Buryatia, as well as the inclusion of other polymorphisms in the analysis will help establish the role of congenital immunity genes in the selective selection of individual genotypes of the virus.

[OP-0962]

Efficacy of sofosbuvir/velpatasvir treatment for chronic hepatitis C among intravenous drug users

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Objectives: This study aimed to evaluate the efficacy of sofosbuvir (SOF)/velpatasvir (VEL) treatment for chronic hepatitis C (CHC) among intravenous drug users.
Materials and Methods: This is a prospective study,which was performed at the West China Hospital of Sichuan University from April 2019 to August 2021. All included patients received SOF 400 mg plus VEL 100 mg daily for 12 weeks. And all patients were followed up for at least 12 weeks after completing the standard course of treatment.
Results: A total of 68 treatment-naïve patients with chronic hepatitis C were included, including 51 patients with genotype 3 and 17 patients with genotype 6. Among these patients, 16 had compensatory cirrhosis and 8 had renal damage. At the end of treatment, only 1 patient was still positive for serum HCV RNA. Serum HCV RNA in 2 patients turned positive at 12 weeks of follow-up, thus the sustained virological response 12 weeks after treatment (SVR12) was 95.6% (65/68). The three patients who failed antiviral treatment were HCV genotype 3 and all had liver cirrhosis. Compared to baseline values, measurements of liver stiffness were both significantly decreased in patients at the end of treatment and 12 weeks after treatment (both $P < 0.001$). The serum biomarker aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis-4 score were also significantly reduced at the end of treatment and 12 weeks after treatment (both $P < 0.001$). There was no significant difference in the changes of liver stiffness, APRI or fibrosis-4 between genotype 3 and genotype 6 patients. SOF/VEL therapy was well-tolerated, and no serious adverse events were reported.
Conclusion: In conclusion, SOF/VEL were safe and achieved a high SVR12 rate for treatment-naïve intravenous drug users with HCV GT3/6 infection. However, there seems to be some concern about the efficacy of SOF/VEL among genotype 3 intravenous drug users with liver cirrhosis.

[PP-0974]

Real-world experiences with direct-acting antiviral agents for chronic hepatitis C genotype 3 in Southern Taiwan

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Objectives: Chronic hepatitis C worldwide problems that cause hepatitis, liver cirrhosis, and even cancer. Direct antiviral agent (DAA) has been developed for a while and it shows the satisfactory treatment efficacy and tolerability in the prior studies. However, some papulations may have inferior treatment responses, including patients with severe liver decompensation, active hepatocellular carcinoma (HCC), and hepatitis C virus genotype 3 (HCV-3) infection and those who experience multiple DAA treatment failures. In this study, we aim to investigate the effectiveness and outcomes of DAA in patients with genotype 3 hepatitis C..
Materials and Methods: 55 patients were treated with Sofosbuvir/Daclatasvir (SOF/DCV), Glecaprevir + Pibrentasvir (GLE/PIB), Sofosbuvir/Velpatasvi ± Ribavirin (SOF/VEL ± RBV) for 8 ∼ 16 weeks based on patient's characteristic according to the guideline. The laboratory test, virus RNA and fibrosis score were collected before treatment, in end of treatment and at the 12 weeks post treatment. Adverse effects are also recorded.

Results: Patients with higher FIB-4 score, serum bilirubin, liver cirrhosis, and hypertriglyceridemia are more in SOF/VEL ± RBV group. Totally 47 patients (94%) reached the SVR, 3 had relapsed disease (2 treated with Glecaprevir/Pibrentasvir and 1 with Sofosbuvir /Velpatasvir + Ribavirin). AST, ALT, rGT and FIB-4 score are improved after treatment. The patient with relapsed disease are all naïve to treatment, and have no CKD, HIV or HBV co-infection. One of them has liver cirrhosis. No significant difference is found in these 2 groups.
Conclusion: Pangenotypic DAAs have short treatment courses, good safety and high success rates when compared to the conventional pegylated interferon + ribavirin. Being a part of hard-to-cure populations, patients with genotype 3 hepatitis C has less treatment choice than patients with other genotypes and have lower SVR rate. However, we did not find the contributing factors between SVR and relapsed group. It needs more studies to find out the causes and to reach the goal for HCV elimination.

[PP-1016]

Post-treatment assessment of hepatic fibrosis in patients with chronic hepatitis C who respond to direct-acting antivirals

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Objectives: Clearance of hepatitis C (HCV) can potentially slow or reverse liver fibrosis and cirrhosis, which may lead reduction reduce the risk liver related morbidities and hepatocellular carcinoma. Studies of fibrosis changes post-treatment with direct-acting antivirals (DAAs) are limited. We aimed to assess the impact of DAAs on fibrosis in HCV treatment responders.
Materials and Methods: This study included adult patients who received DAA treatment for HCV (naïve and experienced) from June 2015 to January 2019 and were labeled as responders at King Saud University Medical City and King Faisal Specialist Hospital. MAIN OUTCOMES MEASURES: The biochemical and noninvasive methods at baseline and follow-up: aspartate aminotransferase/platelet ratio index (APRI), and fibrosis-4 score (FIB-4) and, liver stiffness measurements (LSM).
Results: We included in the analysis 172 HCV responders to DAAs male (n = 76, 44.2%) and female (n = 99, 55.8%). At baseline, the mean age was 54.08 (14.1) years, body mass index was 28.81 (6.5) kg/m^2, (n = 58, 33.7%) were HCV treatment-experienced, and the majority of patients were genotype 4 with a mean follow-up of 141 (57.9) weeks. Comparing the baseline with the follow-up data, a significant change was observed in several biochemical tests such as; alanine aminotransferase, aspartate aminotransferase, and albumin. Similar results were found for the noninvasive tests; LSM (15.09 kPa [11.4] vs. 10.19 kPa [7.4], $P < 0.001$), APRI (0.81 [0.7] vs. 0.34 [0.2], $P < 0.001$), and FIB-4 (1.99 [1.4] vs.1.35 [0.9], $P < 0.001$), AST/ALT ratio (0.86 [0.32] vs. 0.95 [0.41], P = 0.05). Furthermore, similar findings have been shown when patients were categorized into the low fibrosis group (F0-F1) (n = 59, 34.3%) and the significant fibrosis group (≥ F2) (n = 113, 65.7%).
Conclusion: Our findings have confirmed that clearance of HCV with DAAs is associated with significant improvement in biochemical tests and noninvasive liver fibrosis tools, which support the concept of post-treatment fibrosis regression.

[PP-1032]

Hepatitis C virus-associated hypobetalipoproteinemia is correlated with plasma viral load, steatosis, and liver fibrosis

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Objectives: A relationship between chronic hepatitis C virus (HCV) infection and lipid metabolism has recently been suggested. The aim of this study was to determine the correlation between lipid profile and virology, histologic lesions, and response to alpha interferon therapy in noncirrhotic, nondiabetic patients with hepatitis C.
Materials and Methods: A total of 109 consecutive untreated chronic hepatitis C patients were studied to assess the following: 1) the effects of HCV genotype, viral load, steatosis, hepatic fibrosis, and body mass index (BMI) on lipid profile; and 2) whether lipid parameters could predict response to antiviral therapy.
Results: The control group showed a significantly higher apolipoprotein B (apoB) concentration compared with patients with chronic hepatitis C. Hypobetalipoproteinemia (apo B < 0.7 g/L) was found in 27 (24.7%) chronic HCV patients and in five (5.3%) control subjects (p = 0.0002). Levels of apo B were negatively correlated with steatosis and HCV viral load ($r = -0.22$; p = 0.03). This last correlation was strong for non-1 genotype and genotype 3 ($r = -0.48$; p = 0.0005, and $r = -0.47$; p = 0.007, respectively) but was not found in genotype 1. In multivariate analysis, low apo B concentration was significantly associated with fibrosis grade 2 or 3 versus grade 0 or 1 ($p < 0.001$), steatosis > 5% ($p < 0.001$), low body mass index ($p < 0.001$), and high HCV viral load ($p < 0.014$). No correlation was found in the 76 treated patients between apo B and response to interferon therapy.
Conclusion: In chronic HCV patients, hypobetalipoproteinemia occurs already in the early stages of HCV infection before the development of liver cirrhosis. The correlation between apo B levels and HCV viral load seems to confirm the interaction between hepatitis C infection and beta-lipoprotein metabolism.

[PP-1033]

Efficacy and safety of elbasvir/grazoprevir in patients with chronic hepatitis C and metabolic syndrome

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Objectives: To estimate efficacy and safety of Elbasvir/Grazoprevir 50/100 mg fixed dose combination (EBR/GZR) in patients with chronic hepatitis C (CHC) associated with metabolic syndrome (MS).
Materials and Methods: Open-label multicenter clinical trial in treatment-naïve patients with compensated liver disease caused by chronic HCV genotype 1b infection (in 29 patients—with MS defined according to NCEP ATP III criteria, and in 30—without MS). Standard clinical, laboratory and instrumental examination (including transient elastography) as well as virologic response at weeks 4, 12 (end) of treatment, 12 and 24 after treatment were evaluated.
Results: No statistically significant differences in terms of proportion of patients achieved virologic response at weeks 4, 12 (end) of treatment, 12 and 24 after treatment were revealed (based on significance level of 0.05) and all the patients achieved SVR 12 and 24 regardless fibrosis stage and presence of MS and its separate components. In patients with MS higher frequency of any adverse events was observed (more often ESR elevation, thrombocytopenia, and diarrhoea), however the most of them were mild, non?serious and did not related to antiviral therapy. The frequency of adverse drug reactions was similar in both groups and most of them were also mild.
Conclusion: EBR/GZR demonstrated similar efficacy and favorable safety profile in patients with CHC and MS compared to patients without MS.

[PP-1071]

Elbasvir and grazoprevir did not improve FIB-4 scores in hemodialysis patients with hepatitis C infection at Sardjito Hospital, Yogyakarta

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Objectives: This study aims to determine whether there is an improvement in the FIB-4 score in CKD patients undergoing hemodialysis with HCV infection after therapy using ELB/GRZ in Sardjito Hospital, Yogyakarta.
Materials and Methods: This is a retrospective cohort study of CKD patients undergoing routine hemodialysis at Sardjito Hospital, Yogyakarta, Indonesia infected with HCV. The reported variables include patient demographics and statistical tests of FIB-4 scores before and after ELB/GRZ therapy.
Results: There were 48 patients who met the inclusion criteria, of which 30 (62.5%) were male, the average age was 49.96 ± 10.96 years with the most age range being 35–65 years (41/85.4%). Most of the patients were 33 (68.8%) non-cirrhotic patients and 28 (58.3%) patients had FIB-4 score < 1.45. The mean FIB-4 score before and after treatment was 1.51 ± 1.13 and 1.52 ± 1.24, respectively. A Wilcoxon Signed-Ranks Test indicated that post therapy FIB-4 score was not significantly different statistically than pre therapy, $Z = -0.196$, $p = 0.845$. While patients with FIB-4 score < 1.45 is higher after therapy compare before therapy, 66.7% vs 58.3%, respectively.
Conclusion: Hepatitis C therapy using ELB/GRZ did not improve FIB-4 scores in CKD patients undergoing routine hemodialysis at Sardjito Hospital, Yogyakarta.

Table 1. Patients Baseline Characteristic

Parameters	Number
Sex	
Male (%)	30 (62.5)
Female (%)	18 (37.5)
Age (mean±SD)	49.96±10.96
<35 (%)	4 (8.3)
35-65 (%)	41 (85.4)
>65 (%)	3 (6.3)
Cirrhosis	
No (%)	35 (72.9)
Yes (%)	13 (27.1)
HBV	
No (%)	46 (95.8)
Yes (%)	2 (4.2)
FIB-4 (mean±SD)	1.51±1.13
<1.45 (%)	28 (58.3)
1.45-3.25 (%)	18 (37.5)
>3.25 (%)	2 (4.2)

HBV : Hepatitis B Virus; FIB-4 : Fibrosis-4;

[PP-1099]

Decreased of alpha-fetoprotein level among patients with liver cirrhosis that related to HCV treated with combination therapy with ledipasvir and sofosbuvir

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Objectives: Hepatocellular carcinoma (HCC) is considered one of the most lethal cancers, with most of cases diagnosed at advanced stage. The prevalence of HCC is high in Mongolia with men 116.6 cases and women 74.8 cases per 100,000 person-years. The hepatitis C virus (HCV) infection is one of the major causes of chronic hepatitis and hepatocellular carcinoma (HCC) in Mongolia. Viral infection with HCV can cause fluctuations in AFP that makes it difficult to differentiate between underlying liver disease and the development of HCC. The lack of specificity has limited the role of serum alpha-fetoprotein (AFP) for hepatocellular carcinoma (HCC) screening among patients with cirrhosis related to hepatitis C virus (HCV) infection.
Materials and Methods: Here we report 24 cases decreased of AFP level in patients with cirrhosis treated 24 weeks' combination therapy with ledipasvir and sofosbuvir between 2017 to 2019 were referred to the Liver Unit, Dornod Medical center Mongolia. All patients had been tested for blood chemistries, liver function markers, such as alanine aminotransferase (ALT), total bilirubin, prothrombin, international normalized ratio (INR), creatinine, AFP and HCV-RNA.
Results: Of all patients, thirteen were man and eleven were woman. The average age of the testimonies was 56 (between 44 and 69 years). Our twenty-four patients had HCV genotype 1b and had HCV-RNA

positive. The combination of the therapy with ledipasvir and sofosbuvir had significantly decreased level of HCV-RNA from 4,133,570 to not detected ($P < 0.05$), ALT from 126.4 to 26.36 ($P < 0.05$), AFP from 39.8 to 16.8 ($P < 0.05$).
Conclusion: In conclusion, the combination of the therapy with ledipasvir and sofosbuvir is decreased AFP level and improved liver function tests in HCV related liver Cirrhosis of those patients.

[PP-1108]

Long-term follow-up of patients with decompensated hepatitis C cirrhosis during and after DAAs treatment

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Objectives: To investigate the real-world safety of direct antiviral drugs (DAAs) in patients with decompensated hepatitis C cirrhosis.
Materials and Methods: Decompensated hepatitis C cirrhosis treated with DAAs consecutively (July 2017-April 2021) from a single center were enrolled. Recorded adverse events during treatment and in 7 months to 2 years after treatment.
Results: Twenty-one patients with decompensated hepatitis C cirrhosis were enrolled in this study. One of them accepted Dallatavir and Asurivir for treatment, two were treated with Sofosbuvir and Vipacavir, eighteen accepted combined treatment of Sofosbuvir Vipacavir and ribavirin. All patients achieved a sustained virological response (SVR). One patient developed coagulopathy during treatment. Eighteen patients developed cirrhosis related complications during the observation period after treatment (as shown in the table 1), six of which developed primary liver cancer. Besides, during the observation period after treatment, one patient appeared lymphoma metastasis, one patient died of sepsis, two died of hepatic carcinoma.
Conclusion: The safety of DAAs in the treatment of decompensated hepatitis C cirrhosis are fine. However, close follow-up is still needed after the treatment, and attention should be paid to the prevention and treatment of cirrhosis related complications, especially primary liver cancer.

Adverse Events		During treatment	After treatment
coagulopathy		1	
cirrhosis related complications	ascites		8
	gastrointestinal hemorrhage		1
	serious infection		1
	renal insufficiency		2
	primary liver cancer		6
lymphoma metastasis			1
Death	sepsis		1
	hepatic carcinoma		2

[PP-1121]

A clinical evaluation of a hepatitis C nosode in the treatment of hepatitis C

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Objectives: Upon identifying the need for an alternative treatment option in the management of hepatitis C to decrease viral load and improve health parameters, the investigator has developed the hepatitis C virus (HCV) nosode.
Materials and Methods: An open-label observational study in 24 HCV-positive individuals was conducted by using the HCV nosode at 30C and 50C potencies.
Results: In this clinical trial, the HCV nosode was administered to HCV-positive participants. From week 12 to week 24, the mean viral load decreased; the median viral load decreased by half, from 1,557,567.50 IU/mL to 789,265.50 IU/mL. However, at 24 weeks, the average viral load increased significantly ($p = 0.2206$) in the participants completing the trial. The study has shown a double population: a large set of responders with marked improvement (week 12 [$p = 0.0120$] and week 24 [$p = 0.0304$] and from week 12 to week 24 [$p = 0.0028$]) and a small set of nonresponders with increasing viral load (week 12 [$p = 0.0120$] and week 24 [$p = 0.0304$] and from week 12 to week 24 [$p = 0.0028$]). Most participants in this study showed improvement in appetite and weight gain. The treatment using the nosode was found to be safe in the tested population.
Conclusion: The HCV viral load was affected by using ultra-diluted preparation sourced from HCV, as per the Law of Similars, in responders. Further studies of longer duration in patients with uniform baseline characteristics and those that adjust the potency to the individual participant's requirement are recommended.

[PP-1125]

Autoantibodies and autoimmune disease during treatment of children with chronic hepatitis C

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Objectives: Autoantibodies were studied in a well-characterized cohort of children with chronic hepatitis C during treatment with pegylated interferon and ribavirin to assess the relation with treatment and development of autoimmune disease.
Materials and Methods: A total of 114 children (5–17 years), screened for the presence of high-titer autoantibodies, were randomized to pegylated interferon with or without ribavirin. Anti-nuclear, anti-liver-kidney-microsomal, anti-thyroglobulin, anti-thyroid peroxidase, insulin, anti-glutamic acid decarboxylase (GAD) antibodies were measured after trial completion using frozen sera.
Results: At baseline, 19% had autoantibodies: anti-nuclear antibodies (8%), anti-liver-kidney-microsomal antibodies (4%), and glutamic acid decarboxylase antibodies (4%). At 24 and 72 weeks (24 weeks after treatment completion), 23% and 26% had autoantibodies ($P = 0.50$, 0.48 compared with baseline). One child developed diabetes and 2 hypothyroidism during treatment; none developed autoimmune hepatitis. At 24 weeks, the incidence of flu-like

symptoms, gastrointestinal symptoms, and headaches was 42%, 8% and 19% in those with autoantibodies versus 52%, 17%, and 26% in those without (P = 0.18, 0.36, and 0.20, respectively). In children with negative hepatitis C virus polymerase chain reaction at 24 weeks, there was no difference in the rate of early virologic response/sustained virologic response, respectively, in those with autoantibodies 76%/69% vs 58%/65% in those without (P = 0.48).
Conclusion: Despite screening, we found autoantibodies commonly at baseline, during treatment for chronic hepatitis C and after. The presence of antibodies did not correlate with viral response, adverse effects, or autoimmune hepatitis. Neither screening nor archived samples assayed for thyroid and diabetes-related antibodies identified the 3 subjects who developed overt autoimmune disease, diabetes (1), and hypothyroidism (2).

[OP-1145]

Clinical characteristics and treatment experience of hepatitis C infection in people who inject drugs (PWID) in Beijing, China

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Objectives: In 2006, the seroepidemiological survey of viral hepatitis in China showed that the positive rate of anti-HCV in people aged 1 to 59 was 0.43%.However, the positive rate of anti-HCV in injection drug users was 48. 67%. There is a lack of relative data to show the clinical characteristics and treatment efficacy of these patients.
Materials and Methods: We selected 1509 patients with hepatitis C who were treated in our hospital from January 1, 2019 to December 31, 2020. After detailed inquiry, 25 patients were considered to be related to drug abuse. From HIS system, We carried out a detailed analysis of the patients. These patients have a history of intravenous drug use from one to eight years, All the patients had stopped taking drugs, of which six are still using methadone replacement therapy.
Results: Of the 25 patients, 20 were male. 19 cases (76%) were genotype 3 (3a/3b 6/13),2 cases (8%) genotype 1b, 2 cases (8%) genotype 6a,1 case (4%) was a mixed genotype of 1b/3a. 9 of 25 cases were liver cirrhosis and 8 cases were genotype 3.The naïve patients were 20 cases (20/25 80%).Of the naïve patients, two liver cirrhosis naïve patient (genotype3b) treated with Epclusa relapsed and one found liver cancer. The remaining 19 patients obtained SVR12. The 5 experienced patients obtained SVR12 by prolonged treatment period or combined with RBV. One Patient with liver cirrhosis (GT 3b) cured with Epclusa + RBV + Maviret and Another with Vosevi. The patient with mixed genotype of 1b/3a treated with Zepatier first and relapsed after treatment. we used Epclusa + RBV, obtained SVR12.
Conclusion: Most of the drug users in Beijing are male. Genotype 3 accounted for a relatively high proportion. patients with liver cirrhosis almost all were genotype 3. The treatment Regimens containing Epclusa should combined with RBV. Methadone replacement therapy had no effect on the antiviral efficacy.

Table 1 Clinical characteristics and treatment experience of 25 cases drug users with hepatitis C infection.

Case	Male1/ Female2	Age	HCV genotype	Liver cirrhosis Yes1/No2	Child-pugh score	Baseline RNA (IU/ml)	4week HCVRNA	HCV RNA	NAFLD Yes1/ No2	Treatment Regimens	Salvage therapy
1	1	49	1b	2		622000	TND	TND	2	NS5A+PI	Epclusa+RBV
2	1	52	3a	1	A	349000	TND	TND	1	Epclusa+RBV	
3	2	48	3a	2		1700000	TND	TND	1	Epclusa	
4	1	51	3a	2		23000000	<15	TND	2	Epclusa	
5	1	53	3a	1	A	437000	TND	TND	2	Sovadi+IFN+ RBV	
6	1	51	3a	2		150000	TND	TND	1	Epclusa	
7	2	52	3a	2		1250000	TND	TND	2	Epclusa	
8	1	46	3b	2		5920000	<15	TND	2	Epclusa	
9	1	52	3b	1	A	3520000	TND	TND	1	Epclusa+RBV	
10	2	38	3b	2		558000	<15	TND	2	Epclusa	
11	2	50	3b	1	A	3340000	TND	TND	3	Epclusa+RBV	
12	1	50	3b	1	B	3380000	150	345000	2	Epclusa+RBV	
13	1	50	3b	2		2780000	TND	TND	1	Epclusa+RBV	
14	1	53	3b	2		10200000	TND	TND	1	Epclusa	
15	1	53	3b	1	C	7010	TND	TND	2	Epclusa+RBV	
16	1	53	3b	2		20200	TND	TND	2	Epclusa+RBV	
17	1	47	3b	2		1830000	<15	TND	1	Sovadi+IFN+ RBV	Vosevi
18	1	59	3b	2		19000000	152	TND	1	Epclusa	Epclusa+RBV+Maviret
19	1	47	3b	1	A	2770000	180 0	2880000	1	Epclusa	Epclusa+RBV
20	1	49	3b	1	A	389000	3670	失访	1	Epclusa	withdraw
21	1	47	6a	2		70500	TND	TND	2	Epclusa	
22	1	50	6a	2		58500	TND	TND	2	Epclusa	
23	1	53	1b/3a	2		56300	TND	753000	1	Zepatier	Epclusa+RBV
24	1	49	1b	2		1210000		TND	2	Harvoni	
25	2	66	2a	1	A	5680000		TND	2	Epclusa+RBV	

[OP-1182]

Dyspepsia in cirrhotic hepatitis C patients

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Objectives: Background: To determine the frequency of patients with dyspepsia, its patterns of presentation and causes along with their associations with gender and age, amongst HCV cirrhotic patients presenting to a tertiary care health facility of Rawalpindi.
Materials and Methods: Methods: In this cross sectional study 207 HCV cirrhotic patients,above 25 years of age irrespective of gender, were included. Patients receiving prolonged treatment of acid suppression prior to hospitalization were excluded. After taking history and performing thorough physical examination, routine laboratory investigations, abdominal ultrasonography and endoscopies were performed to determine the cause of dyspepsia.
Results: Results: Results:Amongst 207 HCV cirrhotic patients 146 (70.5%) were presented with dyspepsia. Pain in epigastrium 92 (63.0%), heart burn 81 (55.5%) and water brash 65 (44.5%) were most common patterns of presentation of dyspepsia in HCV cirrhotic patients.Portal hypertensive gastropathy 77 (52.7%) came out as leading etiology of dyspepsia, followed by gastritis 9 (6.2%), ulcer 6 (4.1%) and cholelithiasis4 (2.7%). Amongst those diagnosed with Dyspepsia, 25 (17.1%) patients were found to have functional dyspepsia i.e. no organic cause was found.
Conclusion: Dyspepsia is very frequent phenomenon in HCV cirrhotic patients with most common patterns of presentation as pain in epigastrium and heart burn. The leading cause of dyspepsia was portal hypertensive gastropathy.

[OP-1185]

Seroconversion of hepatitis C during dialysis in major cities of Pakistan

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Objectives: Hepatitis C is highly prevalent in Pakistan. Several studies worldwide have shown that patients undergoing hemodialysis

are at a risk for developing Hepatitis C. So this study was carried out to determine the proportion of patients undergoing hemodialysis who seroconverted from HCV negative to HCV positive status in our hospitals.
Materials and Methods: This descriptive cross-sectional study was conducted at four tertiary care hospitals of Punjab from January 2016 to March 2016 on patients undergoing hemodialysis currently. With the help of WHO Sample Size Calculator, at confidence level 95%, absolute precision 5% and anticipated population proportion 14%, the minimally required sample size was calculated to be 186 patients but we included 190 patients in our study. Sampling technique was stratified random sampling based on hospital and gender. Our inclusion criterion was all those patients who were Hepatitis C negative (determined by HCV serology, based on the principle of immunochromatography) at the initiation of dialysis and remained negative for the subsequent six months after the initiation of hemodialysis. Our exclusion criteria was all those patients who seroconverted to HCV positive with six months of initiation of hemodialysis (the period corresponding to the incubation period of hepatitis C virus.) and those who were dialyzed on emergency basis.
Results: Out of 190 patients who were HCV negative at the initiation of dialysis, 93 (i.e. 48.9%) patients converted to HCV positive status whereas 97 (i.e. 51.05%) patients remained HCV negative throughout the study. The mean time taken for seroconversion was 18.04 months (SD $\pm$ 15.43) months). The median was 12 months, with an inter quartile range of 14 months.
Conclusion: The proportion of HCV seroconversion in our hemodialysis units is very high.

[L-PP-1233]

Hepatitis C virus treatment-related anemia is associated with higher sustained virologic response rate

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Objectives: Hepatitis C virus (HCV) treatment is frequently complicated by anemia from ribavirin (RBV)-related hemolysis and peginterferon-alfa (PEG-IFN)-related bone marrow suppression. We investigated the relationships among treatment outcomes, anemia, and their management with RBV dose reduction and/or erythropoiesis-stimulating agents (ESAs).
Materials and Methods: We analyzed data from a trial conducted at 118 Kazakhstan academic and community centers in treatment-naïve patients with HCV genotype 1. Patients were treated for as many as 48 weeks with 1 of 3 PEG-IFN/RBV regimens. ESAs were permitted for anemic patients (hemoglobin [Hb] $<$ 10 g/dL) after RBV dose reduction. Sustained virologic responses (SVR) were assessed based on decreases in Hb, anemia, and ESA use.
Results: While patients received treatment, 3023 had their Hb levels measured at least once. An SVR was associated with the magnitude of Hb decrease: $>$ 3 g/dL, 43.7%; $\leq$ 3 g/dL, 29.9% ($P < 0.001$). Anemia occurred in 865 patients (28.6%); 449 of these (51.9%) used ESAs. In patients with early-onset anemia ($\leq$ 8 weeks of treatment), ESAs were associated with higher SVR rate (45.0% vs 25.9%; $P < 0.001$) and reduced discontinuation of treatment because of adverse events (12.6% vs 30.1%, $P < 0.001$). ESAs did not affect SVR or discontinuation rates among patients with late-stage anemia.
Conclusion: Among HCV genotype 1-infected patients treated with PEG-IFN/RBV, anemia was associated with higher rates of SVR. The effect of ESAs varied by time to anemia; patients with early-onset anemia had higher rates of SVR with ESA use, whereas no effect was observed in those with late-onset anemia. Prospective trials are needed to assess the role of ESAs in HCV treatment.

[L-PP-1234]

Utility of hepatitis C viral load monitoring on direct-acting antiviral therapy

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Objectives: Hepatitis C virus (HCV) RNA loads serve as predictors of treatment response during interferon-based therapy. We evaluated the predictive ability of HCV RNA levels at end of treatment (EOT) for sustained virologic response (SVR12) during interferon-sparing direct-acting antiviral therapies.
Materials and Methods: HCV genotype 1-infected, treatment-naive patients were treated with sofosbuvir and ribavirin for 24 weeks (n = 55), sofosbuvir and ledipasvir for 12 weeks (n = 20), sofosbuvir, ledipasvir, and GS-9669 for 6 weeks (n = 20), or sofosbuvir, ledipasvir, and GS-9451 for 6 weeks (n = 19). Measurements of HCV RNA were performed using the Roche COBAS TaqMan HCV test and the Abbott RealTime HCV assay. Positive predictive value (PPV) and negative predictive value (NPV) of HCV RNA less than the lower limit of quantification ($<$ LLOQ) at EOT for SVR12 were calculated.
Results: All 55 patients treated with sofosbuvir and ribavirin had HCV RNA $<$ LLOQ at EOT by the Roche and Abbott assays, but only 38 achieved SVR12 (PPV, 69%). Among patients treated with sofosbuvir and ledipasvir with or without GS-9669 or GS-9451, 100% (59/59) had HCV RNA $<$ LLOQ by the Roche assay and 1 relapsed (PPV, 98%). By the Abbott assay, 90% (53/59) had HCV RNA $<$ LLOQ, of whom 1 patient relapsed (PPV, 98%). Notably, 6 patients with HCV RNA $\geq$ LLOQ at EOT (range, 14–64 IU/mL) achieved SVR12 (NPV, 0%). Quantifiable HCV RNA (range, 15–57 IU/mL) was measured 2 weeks posttreatment in 4 individuals, and 4 weeks posttreatment in 1 patient (14 IU/mL).
Conclusion: Contrary to past experience with interferon-containing treatments, low levels of quantifiable HCV RNA at EOT do not preclude treatment success.

[L-PP-1236]

Viral kinetics in hepatitis C or hepatitis C/human immunodeficiency virus-infected patients

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Objectives: Kinetic modeling of hepatitis C virus (HCV) response to interferon (IFN)-based therapy provides insights into factors associated with treatment outcomes. HCV/human immunodeficiency virus (HIV)-co-infected patients show lower response rates vs. HCV-monoinfected patients. Reasons for this remain unclear. This study evaluated kinetic parameters and treatment responses in co-infected vs monoinfected patients.
Materials and Methods: Co-infected patients were randomized within a US multicenter trial (ACTG 5071) to receive pegylated-interferon (PEG-IFN) alfa-2a + ribavirin vs. IFN alfa-2a + ribavirin. Monoinfected controls were matched prospectively for treatment,

genotype, age, sex, race, and histology. Quantitative HCV-RNA testing was performed at hours 0, 6, 12, 24, 48, and 72; days 7, 10, 14, 28, and 56; and weeks 12, 24, 48, and 72.
Results: Twelve HCV/HIV-co-infected and 15 HCV-monoinfected patients underwent viral kinetic sampling. Among HIV-positive patients the mean CD4(+) count was 325 cells/mm(3). Seventy-five percent of patients were genotype 1. The HCV-RNA level was undetectable at 72 weeks in 25 and 40% of co-infected and monoinfected patients, respectively. Phase 1/2 declines, free virus clearance rate, and infected hepatocyte death rate were not affected by co-infection status but differed by treatment. Efficiency (epsilon) > or = 90% at 60 h was associated with viral clearance (P = 0.02). Modeling with pooled parameters suggests baseline viral load is a key factor in time to response in this cohort. Predicted clearance time increased by 28% in co-infected patients.
Conclusion: Co-infection status did not affect key kinetic parameters. Among kinetic parameters, efficiency was associated significantly with viral clearance. Co-infected patients may require longer treatment duration than monoinfected patients given their generally higher baseline viral loads.

[L-PP-1237]

Disappearance of gastric mucosa-associated lymphoid tissue in hepatitis C virus-positive patients after anti-hepatitis C virus therapy

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Objectives: Mucosa-associated lymphoid tissue, which has a follicular structure closely resembling Peyer patches, is absent in the normal gastric mucosa, but it can develop in several chronic conditions. Since we recently detected hepatitis C virus-RNA in gastric mucosa-associated lymphoid tissue of patients with chronic hepatitis C, we tried to treat hepatitis C virus infection to evaluate the effect of antiviral therapy on gastric mucosa-associated lymphoid tissue.
Materials and Methods: Eighteen patients (12 men and 6 women; mean age: 52 years, range: 33–71 years) affected by chronic hepatitis C virus and with gastric mucosa-associated lymphoid tissue were enrolled. We enrolled only patients hepatitis C virus-positive, mucosa-associated lymphoid tissue-positive, and Helicobacter pylori-negative (8 patients) or hepatitis C virus-positive patients in whom anti-H. pylori therapy did not obtain disappearance of gastric mucosa-associated lymphoid tissue (10 patients).. The hepatitis C virus RNA was assayed at entry and at 3 months after stopping treatment. Virologic response was defined as undetectable levels of serum hepatitis C virus RNA 3 months after stopping treatment; esophagogastroduodenoscopy was repeated at this time to evaluate the effect of anti-hepatitis C virus therapy on acquired gastric mucosa-associated lymphoid tissue.
Results: Two (11.11%) patients were withdrawn from the study. Hepatitis C virus cure was obtained in 11/16 patients (68.75%), and in all of them we obtained disappearance of gastric mucosa-associated lymphoid tissue (P < 0.01). Hepatitis C virus infection persisted, but with very lower levels, in 5 of 16 patients (31.25%): in 3 patients gastric mucosa-associated lymphoid tissue persisted (but in 2 it decreased from grade 3 to grade 2), while in 2 it disappeared.
Conclusion: We showed clearly that there is a strict correlation between hepatitis C virus infection and acquired MALT, obtaining the disappearance of this acquired immunologic acquired gastric tissue curing hepatitis C virus infection.

[L-PP-1249]

Changes in the estimated renal function after hepatitis C virus eradication with direct-acting antiviral agents: Impact of changes in skeletal muscle mass

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Objectives: Hepatitis C virus (HCV) infection can cause renal dysfunction, expected to improve upon HCV eradication. However, adverse effects of HCV eradication using direct-acting antiviral agents (DAAs) on renal function have been recently reported. This retrospective study aimed to evaluate renal function with glomerular filtration rate (eGFR) estimated using creatinine (eGFRcre) and cystatin C (eGFRcys).
Materials and Methods: Complete clinical information and preserved serum samples were collected from 207 patients with HCV infection treated with interferon-free DAA at baseline and SVR48 (SVR48). Patients who underwent paired computed tomography (CT) at baseline and ≥ 12 months after DAA were evaluated for changes in skeletal muscle mass using the psoas muscle mass index (PMI).
Results: eGFRcre significantly worsened at SVR48, while eGFRcys was similar at baseline and SVR48. At baseline, eGFRcre was significantly higher than eGFRcys; eGFRcre and eGFRcys were similar at SVR48. Multivariate analysis revealed that the presence of liver cirrhosis and low-albumin level, as well as cirrhosis and age, was significantly associated with the overestimation of renal function by eGFRcre at baseline and SVR48, respectively. In the 57 patients who underwent paired CT at baseline and ≥ 12 months after DAA, relative values of PMI significantly increased after DAA. After DAA, in patients with increased PMI (65% 37/57), eGFRcre significantly worsened but did not change in patients without increased PMI.
Conclusion: eGFRcre significantly worsened after DAAs; however, this might not reflect accurate changes in renal function, partially because of changes in skeletal muscle mass. eGFRcys did not change after DAAs, and it is a potential alternative to eGFRcre.

[L-OP-1307]

Persistently high SVR of sofosbuvir/velpatasvir in GT3 or GT 6 HCV in PWID: Real-world data by followed up 48 weeks from China

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Objectives: SVR persistence in PWID for GT3 or GT6 HCV infection treated with SOF/VEL is scanty in China, especially in GT3b, because SOF/VEL was approved in China about 2 years.To evaluate persistence of sustained viral response in PWID with GT3 and GT6 infection treated with sofosbuvir/vipatavir ± ribavirin.
Materials and Methods: A total 49 PWID with GT3 or GT6 HCV infection who received sofosbuvir/vipatavir ± ribavirin treatment was enrolled and continue to follow up 48 weeks at our center between 01/19–10/21. All participants had access to our group of care addressing their medical, addiction -related needs. Long-term engagement in care after achieved SVR_{12}.The Sustained Viral Response (SVR) rate were analyzed at 12 weeks, 24 weeks,

48 weeks, respectively and HCC incidence were evaluated at 48 weeks.

Results: 49 eligible PWID were performed for analysis at our hospital. Median age was 57 years, 21 (42.9%) patients were genotype 3, 18 (36.8%) of those were genotype 3b, 28 (57.1%) were genotype 6a. Detail baseline demographics are provided in the Table1. Overall, SVR_{12} was 93.8%, 3 patients have relapse (2 GT3 patients and 1 GT 6a patients); 45 (92%) patients completed follow-up visits at 48 weeks; 97.7% (44/45) patients have sustained viral response at 48 weeks; none were treatment related or resulted in serious AE and death. No patients with or without cirrhosis developed HCC at 48 weeks.

Conclusion: SOF/VEL ± RBV has high persistence of SVR in PWID with GT3 or GT6 HCV infection, even in GT3b PWID. A special group of care could maximize HCV cure for PWID.

Baseline demographics and clinical characteristics

Patient Characteristics	N=49
Age (y), mean (range)	57 (32-79)
Sex – male, n (%)	40(81.6%)
Fibrosis stage, n (%)	
F0-F2	28 (57.1)
F3	5 (0.02%)
F4	16 (32.7%)
Presence of compensated cirrhosis, n (%)μ	
Yes	10 (20.4%)
No	39(79.6%)
Treatment-naïve, n (%)	49 (100%)
HCV GT, n (%)	
GT3	21(42.9%)
GT3a	3 (6.1%)
GT3b	18(36.8%)
GT6	28(57.1%)
GT6a	28(57.1%)
SOF/VEL+RBV	26(53.1%)

Other Infection in Liver Disease

[PP-0117]

Percutaneous catheter drainage and hospital stay in patients with pyogenic liver abscess

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Objectives: We aimed to investigate the factors associated with prolonged hospital stay and mortality among patients with pyogenic liver abscess (PLA) who underwent percutaneous drainage (PCD).

Materials and Methods: We retrospectively reviewed data from PLA patients admitted from 2005 to 2020 at Jeonbuk National University Hospital. We selected patients who underwent PCD during the admission period and early PCD was defined whether the procedure was done within 3 days of admission.

Results: A total of 460 patients was enrolled for the study. The patients had a mean age of 64.3 ± 15.0 years and 290 (63.0%) were men. Next, two groups were divided depending on the time period of PCD and 316 patients (68.7%) underwent PCD within 3 days of hospitalization. In baseline characteristics, hospitalization period was significantly lower in the early PCD group though in-hospital mortality was not different. We checked laboratory results at 1 week after the admission and CRP levels were significantly lower in the early PCD group. We further analyzed the factors related to the long-term hospitalization more than 14 days. In multivariate analysis, elevated total bilirubin and low albumin levels, and PCD inserted after 3 days of admission were independent factors associated with prolonged hospital stay.

Conclusion: Early PCD insertion shortened hospital stay which may be due to the facilitated improvement of inflammation. Early PCD may be beneficial in patients with PLA.

Table. Factors associated with prolonged hospital stay (> 14 days)

	Univariate analysis				Multivariate analysis			
	P value	HR	Lower CI	Upper CI	P value	HR	Lower CI	Upper CI
Age	0.727	1.00	0.99	1.02				
Male sex	0.842	1.04	0.68	1.59				
Malignancy	0.020	2.24	1.18	4.64	0.652	1.257	0.465	3.396
Biliary disease	0.943	1.02	0.64	1.65				
DM	0.159	1.38	0.89	2.18				
HTN	0.234	1.31	0.84	2.06				
Chronic liver disease	0.989	1.01	0.45	2.47				
Previous liver abscess history								
Significant alcohol consumption	0.297	0.76	0.45	1.29				
Decreased mentality at admission	0.399	0.58	0.16	2.29				
Shock at admission	0.675	1.28	0.44	4.60				
WBC, /mm^3	0.101	1.03	0.99	1.07				
Hb, mg/dL	0.051	0.90	0.80	1.00				
Na, mmol/L	0.186	0.97	0.93	1.01				
ALT, IU/L	0.095	1.00	1.00	1.01				
Total bilirubin	**0.004**	**1.47**	**1.16**	**1.94**	**0.028**	**1.545**	**1.048**	**2.278**
Albumin	**< 0.001**	**0.34**	**0.22**	**0.51**	**0.006**	**0.411**	**0.217**	**0.777**
Creatinine	0.089	1.35	1.02	2.04				
LD	0.105	1.001	1.000	1.002				
hsCRP, mg/L	0.013	1.004	1.001	1.008	0.146	1.004	0.999	1.010
PCT, ng/mL	0.021	1.018	1.003	1.033	0.156	1.011	0.996	1.026
Number of abscess, single vs multiple	0.064	1.57	0.98	2.55				
Maximal abscess diameter, cm	0.003	1.15	1.05	1.26	0.230	1.080	0.953	1.223
PCD insertion within 3 days of adm	**< 0.001**	**0.27**	**0.15**	**0.46**	**0.008**	**0.383**	**0.188**	**0.779**

DM, diabetes mellitus; HTN, hypertension; WBC, white blood cells; Hb, hemoglobin; CRP, C-reactive protein; PCT, procalcitonin; PCD, percutaneous catheter drainage

[PP-0140]

Factors associated with death and COVID-19 patients with acute liver injury

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Objectives: The objective of this study is to find the association between mortality and COVID-19 and risk factors among patients with acute liver injury.

Materials and Methods: The research method uses a cross-sectional study design. The participants were COVID-19 patients with acute liver injury admitted in the Field hospital and Somdejphrajaotaksin

Maharaj Hospital between 1 March 2020 and 30 September 2021. The data collected included patient's medical history and laboratory results. The analysis used was descriptive statistics and inferential statistics such as chi-square and multiple-logistic regression.
Results: The results showed that the number of total participants was 806. Patients with advanced age (more than 60 years) (OR_{adj} = 9.72; 95%CI = 4.16–22.12), hypoalbuminemia ($\leq$ 3.5 g/dl) (OR_{adj} = 26.92; 95%CI = 6.78–106.87), hepatitis (AST > 40 U/L) (OR_{adj} = 5.57; 95%CI = 1.91–16.28) and those with a length of hospital stay of at least 7 days (OR_{adj} = 0.13; 95%CI = 0.03–0.50) showed a statistically significant association with death. Note that mortality showed the greatest effect size with hypoalbuminemia compared with other variables. The severity of coronavirus infection 2019 (mild, moderate to severe), ALT > 40 U/L and ALP > 126 U/L. It was found that there was no correlation to mortality with statistically significant.
Conclusion: Therefore, the treatment for COVID-19 patients with acute liver injury should be prioritized for high risk patients, especially the elderly, patients with hypoalbuminemia ($\leq$ 3.5 g/dl), hepatitis (AST > 40 U/L) and patients with long admission days, relative to other patients, in order to prevent mortality.

Table 2. Risk factors associated with mortality in COVID-19

Risk factors	Odd ratio (95% Confidence interval)	P value
Age >60	9.72 (4.16-22.12)	0.002
Albumin < 3.5 g/dL	26.92 (6.78-106.87)	<0.001
ALT > 40 U/L	2.36 (0.82-6.76)	0.11
AST > 40 U/L	5.57 (1.91-16.28)	0.002
ALP > 126 U/L	0.77 (0.96-6.23)	0.81
Length of stay >7 days	0.13 (0.03-0.50)	0.003

ALT = alanine aminotransferase, AST = aspartate aminotransferase, ALP = alkaline phosphatase

[OP-0168]

Sero-prevalence of hepatitis B and hepatitis C Virus among the blood donors in Pokhara Valley, Nepal

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Objectives: This study was carried out to determine the sero-prevalence of HBV and HCV among blood donors in Pokhara valley, Nepal.
Materials and Methods: A cross-sectional study was conducted among voluntary blood donors in Pokhara valley. The samples were collected and analyzed in Nepal Red Cross Society, Regional Blood Transfusion Services, Pokhara, Nepal. A total of 13,431 individuals were included from July 2017 to June 2018.
Results: All the serum samples were processed by ELISA methods for hepatitis B surface antigen (HBsAg) and anti-Hepatitis C. Descriptive statistics and Chi-square test was used. Of the total, 84% were male and 16% were female; and 43.6% were in the age group of 21 to 30 years. Mean age of male and female was 30.34 ($\pm$ 9.00) and 28.71 ($\pm$ 8.60) years, respectively. The sero-prevalence of HBsAg was found to be 0.3% (44/13431) comprising of 0.4% in male and 0.1% in female. The sero-prevalence of anti-HCV was found to be 0.1% (17/13431) comprising of 0.1% in male and less than 0.01% in female. A significance difference was observed in the sero-prevlence of HBsAg in male and female ($p < 0.05$) but no significance difference was observed in the HCV ($p > 0.05$) in Nepal.
Conclusion: The sero-prevalence of HBVand HCV infection among male and female blood donors seems constant as compared to the previous studies in Nepal. However, the sero-prevalence among general and healthy looking population may still pose threat to public health in Nepal. It is identified the threats and preventive awareness programs are recommended.

[OP-0227]

Evaluation of ISH treatment protocols among hypertensive liver compromised patients at clinical setups of Hyderabad, Sindh, Pakistan

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Objectives: Due to different chronic hypertension in adults slowly and gradually liver functions are diturbed due to long term use of antihypertensive medications. The current stduy was designed to assess the international society of hypertension (ISH) treatment protocol among those adults who had confirmed diagnosis of Hypertension with liver compromised at different clinical setups of Hyderabad, Sindh, Pakistan.
Materials and Methods: A retrospective study was conducted for a period of one year during 2020. A total of 500 prescriptions of hypertensive patients having various liver problems with abnormal liver function test were collected in the study based on purposive sampling method. The study was conducted in six different clinical setup of Hyderabad, Pakistan. The data were transformed into pre-designed data sheet and assess based on ISH treatment protocols.
Results: Among 500 enrolled data maximum number were classified under grade 1 i.e. 348 followed by grade II i.e. 152. For grade 1 patients, data showed that only 26% prescribed medications according to ISH guidelines while remaining were not followed. For grade II patients, 37% of the prescriptions showed compliance with ISH guidelines while remaining did not followed the procedure. Mostly in Hepatitis B patients with hypertension, the treatment was not follow due to complications while in Hepatitis C, some compliance with ISH were observed.
Conclusion: The study was clearly revealed that the treatment protocol of ISH guidelines in liver compromised hypertensive adults was not accordingly so proper CMEs must be conducted to aware the health care professionals about the treatment protocols.

[OP-0375]

Dynamic changes of serum metabolites associated with infection and severity of patients with acute hepatitis E infection

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Objectives: Dynamic changes of metabolites may impact liver disease progression, and propose new methods for predicting liver damage.
Materials and Methods: We used ultra performance liquid chromatography mass spectroscopy (UPLC − MS) to assess serum metabolites in patients with healthy controls (HC), acute hepatitis E (AHE) or HEV- acute liver failure (HEV-ALF).
Results: The PCA, PLS-DA, and OPLS-DA models illustrated significant differences in the metabolite components between AHE patients and HC or between HEV-ALF and AHE patients. In pathway enrichment analysis, we further identified 2 altered pathways including linoleic acid metabolism and phenylalanine, tyrosine and tryptophan biosynthesis when comparing AHE patients with HC. Linoleic acid metabolism and porphyrin and chlorophyll metabolism pathways were found to be significantly distinct in HEV-ALF when compared with AHE. The discriminative performances of differential metabolites showed that taurocholic acid, glycocholic acid, glycochenodeoxycholate-3-sulfate, docosahexaenoic acid could be used to distinguish HEV-ALF patients from AHE patients. The serum levels of glycocholic acid, taurocholic acid, deoxycholic acid glycrine conjugate and docosahexaenoic acid were associated with the prognosis of HEV-ALF patients.
Conclusion: Dynamic changes of serum metabolites were associated with infection and severity of AHE patients. The identified metabolites can be used to diagnose and predict the prognosis of HEV-ALF.

[OP-0376]

Acute pancreatitis manifestations in HEV genotype 4 infection and its triggering mechanism

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Objectives: The prevalence of hepatitis E virus (HEV) genotype 4 in acute pancreatitis (AP) patients and its trigger mechanism is unclear.
Materials and Methods: In this study, we investigated the relationship between HEV gt4 infection and AP through a multi-center cohort and HEV mouse model.
Results: Prevalence of HEV in AP patients showed that the positive rates of anti-HEV IgG, anti-HEV IgM and HEV RNA in AP group were all significantly higher than that in HC group. The percentage of severe AP in the AP + anti-HEV IgG-positive and AP + anti-HEV IgM-positive groups were both significantly higher than that in AP + anti-HEV IgG-negative and anti-HEV IgM-negative groups, while mild AP patients in the AP + anti-HEV IgG-positive and AP + anti-HEV IgM-positive groups were both significantly lower than that in the AP + anti-HEV IgG-negative and anti-HEV IgM-negative groups. We successfully established acute gt4 HEV infections BALB/c mouse model, which showed the acinar structure of the pancreatic tissues in the HEV infected group was incomplete, the adenotropic cell degeneration and surrounding adipose tissue necrosis 28 days later. TUNEL staining showed that more apoptotic cells with yellow brown nuclei were detected in the pancreatic tissues of the HEV-infected group. The expression of BAX was increased and Bcl2 was decreased in HEV-infected mice, which indicating that HEV infection may mediate pancreatic cell apoptosis through classical and non-classical pathways.
Conclusion: HEV gt4 infection plays an important role in the occurrence and development of AP, which will provide new strategies for clinical diagnosis and treatment of AP patients.

[PP-0400]

Implementation on hepatitis prevention, control, and elimination program in Mongolia

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Objectives: Mongolia is implementing 'Whole Liver-Mongolia' nationwide, which aims to eliminate infections of Hepatitis B and C among population, one of major objectives of the Government's action plan 2017–2020. To define implementation of the program.
Materials and Methods: descriptive study, analyzed policy and strategic documents and statistics issued by governmental organizations.
Results: Within the framework of Whole Liver –Mongolia Program, Hepatitis B and C tests are free of charge and medicines for hepatitis are being discounted 60% by the Health Insurance Fund (HIF). The program covered 1,162,042 people, 1,142,512 people were screened (anti-HCV and HBsAg) by rapid test, 6,844 people were confirmed test by ELISA and 181,296 people were get HCV-RNA and HBV-DNA viral load test by PCR for hepatitis C and B virus as of Jan 2021. HBV screening testing positive rate is 7.8%, The HIF spent MNT18.8 billion on the program implementation in 2017, MNT 19.8 billion in 2018, MNT 17.2 billion in 2019, MNT 15.6 billion in 2020 for the program.
Conclusion: The HPCE Program in Mongolia is serving as a model for other countries in their fight against viral hepatitis. The HPCE Program through 2020, which is the largest amount of funding ever allocated for a national program.

[PP-0428]

Surgical treatment of pulmonary tuberculosis associated with chronic viral hepatitis C

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Objectives: Chronic viral hepatitis C (HCV) is widespread among patients with pulmonary tuberculosis and has an indirect effect on the characteristics of the tuberculosis process, expanding the contraindications for surgical treatment of pulmonary tuberculosis (PTB).
Materials and Methods: The study included 450 patients aged 18–70 years who underwent radical or palliative surgery for PTB at the Irkutsk Regional TB Hospital (Russia). The study was from January 2017 to June 2020.
Results: The association of PTB with HCV was reported in 88/19% of patients (PTB + HCV group). 362/81% of patients were not diagnosed with parenteral hepatitis with any type of virus (PTB group). In the PTB + HCV group, 20/23% of patients and in the PTB group, 15/5% of patients were HIV-infected ($\chi2 = 34.1$; $p < 0.0001$; OR = 6.8). The chronic course of tuberculosis was registered in 37/42% of patients in the PTB + HCV group and in 97/27% of patients in the PTB group ($\chi2 = 7.9$; $p = 0.005$; OR = 2.0). In the PTB + HCV group, radical surgery (60/68%) was performed significantly less frequently than in the PTB group (302/83%) ($\chi2 = 10.5$; $p = 0.001$; OR = 2.4). In the same group, large-scale radical surgeries were more often performed (28 out of 60/47%) versus those in the PTB group (51 out of 302/17%) ($\chi2 = 26.0$; $p < 0.0001$; OR = 4.3). In prospective observation of patients with HCV, it was found that, in comparison with patients with monoinfection of TB, they more often have a complicated course of the postoperative period (14/16% and 25/7%, respectively) ($\chi2 = 7.2$; $p = 0.007$; RR = 2.3); less often, the cessation of excretion of the pathogen into the external environment after surgery is observed (40 out of 57/70% and 173 out of 200/86%, respectively) ($\chi2 = 8.3$; $p = 0.004$; RR = 1.2).
Conclusion: The association of pulmonary tuberculosis with chronic viral hepatitis C reduces the possibility of radical cure of the tuberculous process, increases the likelihood of a burdened postoperative course and persistence of infectiousness in some patients with a surgical profile.

[OP-0450]

Causes of sepsis requiring admission in cirrhotic patients—a prospective study

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Objectives: Sepsis in cirrhotic patients is a frequent cause of hospitalization, often leading to multiple organ failures and even death. Our aim was to find out the causes of sepsis in cirrhotics requiring admission,
Materials and Methods: The study was conducted prospectively based on two teriary care liver units over 12 months. The age group was 18–80 years. The patients were admitted via emergency or referrals from other gastroenterology centers. Patients with pneumonia and acute gastroenteritis were also included. Blood, urine, and ascitic fluids were used in our study.
Results: Analyzed Sample size = 75 Among them, 33 patients were cultured positive for sepsis. The total duration time was 12 months. The age group was 18–80 years (Male = 45, Female = 30). Of the 75 patients, 33 patients had proven cultured positive sepsis. Of them: 6 patients were admitted with positive blood culture due to.
1. Escherichia coli = 4.
2. Proteus mirabilis = 2 10 were admitted due to spontaneous Bacterial peritonitis had a positive ascitic fluid culture.
1. Pseudomonas aeruginosa = 2.
2. Escherichia coli = 6.
3. Enterococcus = 2 7 were admitted due to Urosepsis.
1. Escherichia coli = 5.
2. Proteus mirabilis = 2 4 patients were admitted due to pneumonia and 6 patients due to gastroenteritis. Cultures were not positive in 42 patients.
Conclusion: Sepsis is the predominant reason for admission in cirrhotic patients, often cultures are not positive. We found 44% of our cirrhotic patients with suspected sepsis had positive culture reports. In our study, spontaneous bacterial peritonitis was found to be the leading cause of culture-positive sepsis is cirrhotic. Escherichia coli was the primary organism in blood, urine, ascitic fluid culture. Larger multicentric studies are required to validate our findings.

[OP-0464]

Effect of COVID-19 infection on liver enzymes: A prospective study in Western Part of Nepal

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Objectives: Background: Coronavirus disease 2019 (COVID-19), a global pandemic, has hit the whole world since December, 2019. COVID-19 has got multi-organ impact and liver is no exception. Studies have shown raised liver enzymes primarily alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phoshatase (ALP); the mechanism being multifactorial. Aims: To evaluate the effect of COVID-19 infection on liver enzymes.
Materials and Methods: It is a prospective study conducted at Mediplus Hospital and Trauma Center from 1st January, 2021 to 30th June, 2021. Ethical approval was obtained and a total of 210 PCR positive COVID-19 inpatients were included. Liver enzymes (ALT, AST and ALP) were measured. Data was entered in Microsoft excel and result studied.
Results: Out of 210 PCR positive COVID-19 patients, 57 (27.1%) had raised liver enzymes, while 153 (72.9%) had normal. Among the raised ones, 13 (22.9%) had ALT raised more than one time of upper normal limit (UNL, 45 IU/L), 29 (50.8%) had ALT raised more than two times of UNL and 15 (26.3%) had ALT raised more than three

times of UNL, while 42 (73.7%) had AST raised more than one time of UNL (35 IU/L) and 15 (26.3%) had AST raised more than two times of UNL, and ALP was found to be raised in only 5 (8.7%) patients (Table 1).

Conclusion: Raised liver enzymes have been commonly noticed in patients with PCR positive COVID-19 due to its direct or indirect impact on liver.

Table 1. Liver enzymes in PCR positive COVID -19 patients

Parameters		Number (n=210)
Liver enzymes	Raised	57 (27.1%)
	Normal	153 (72.9%)
ALT	Raised > one time of UNL	13 (22.9%)
	Raised > two times of UNL	29 (50.8%)
	Raised > three times of UNL	15 (26.3%)
AST	Raised > one time of UNL	42 (73.7%)
	Raised > two times of UNL	15 (26.3%)
ALP	Raised	5 (8.7%)

[PP-0500]

Progress in the research of diagnostic methods to clonorchiasis sinensis

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Objectives: Clonorchiasis is a kind of foodborne parasitic disease caused by Clonorchis sinensis, also known as hepatic schistosomiasis. According to reports, adults of Clonorchis sinensis can survive in the hepatobiliary duct of the final host for at least 26 years. Therefore, it can cause chronic inflammation of the bile duct and cause complications of the hepatobiliary system. Studies have shown that the incidence of cholangiocarcinoma is closely related to the infection of Clonorchis sinensis. Clonorchis sinensis is classified as a class I carcinogen of cholangiocarcinoma by the World Health Organization ((WHO). Most patients with clonorchiasis have no obvious early clinical symptoms (except for severe infections), so it is easy to misdiagnose and delay the condition. It listed as one of the most serious neglected tropical diseases by the World Health Organization (WHO). Therefore, early and accurate diagnosis of the disease has important clinical significance.

Materials and Methods: We conduct summary analysis by looking up information and reading literature.

Results: The traditional etiological diagnosis methods have some limitations and disadvantages. Immunological methods are widely used as an important supplement to etiological methods,but the sensitivity and specificity are still not ideal.With the further study of clonorchiasis, molecular biotechnology has opened up a new way for diagnosis.

Conclusion: With the development of molecular parasitology, molecular biology methods have also become a hot spot in diagnostic research. Molecular biology methods have greatly improved the sensitivity of detection, which can not only qualitatively but also quantitatively detect samples. It can be used as an important means for laboratory testing and epidemiological investigation. Based on molecular biology, further research on diagnostic specific molecules and drug targets is the focus of future research.

[PP-0695]

A case of hepatitis A associated with subchorionic hematoma during pregnancy

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Objectives: Hepatitis A virus (HAV) is an enterovirus of the family Picornaviridae that is transmitted primarily via the fecal–oral route. Most affected age is in 20–40 years and most viral hepatitis A patients have experienced benign course without complication. Moreover, HAV infection is not associated with severe outcomes or complications during pregnancy. But also maternal-infant HAV transmission is thought to be uncommon. Recently, we introduce a case that pregnant woman with HAV associated with subchorionic hematoma.

Materials and Methods: This review is based on medical records including lab data, sonographic view.

Results: A 36-year-old woman was at 8 weeks with Gestational age (1-0-3-1) and she was followed local obstetrics clinic. She represented to our emergency department with fever lasting 2 days and vaginal bleeding. Vaginal sonographic examination at our OBGY department revealed that she had subchorionic hematoma. She was also presented vaginal bleeding about 35 cc. We examined emergent vaginal ultrasonography and hematoma was occurred in Cervical Os. Considering her's abortion History, We doubted lupus and antiphospholipid antibody syndrome. In our laboratory data, Anti-nucleic acid antibody, Anti double strand DNA Ab, and Anti PL IgM/G were all negative. Especially, in our laboratory data, the mild elevation of total bilirubin and striking elevation of liver enzymes were observed. Moreover, HAV IgM was positive and acute hepatitis A was confirmed. As a result of abdominal ultrasonography, she had mild hepatomegaly and fatty liver and diffuse edematous wall thickening of Gallbladder. After consulting to department of obstetrics, they recommend that if patient does not represent vaginal bleeding & abdominal pain, observe the status and follow up in outpatient department. We planned that the patient will be discharged and followed up at outpatient department.

Conclusion: We report that it is the first case of presenting subchorionic hematoma in pregnant woman with HAV.

[PP-0736]

Clinical features and outcomes of epstein–barr viral hepatitis

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Objectives: The clinical characteristics and disease course of Epstein-Barr (EB) viral hepatitis have still not been evaluated. We aimed to better understand the clinical features and outcomes of EB viral hepatitis.
Materials and Methods: From January 2008 to December 2020, patients who had been diagnosed with EB viral hepatitis were enrolled. We retrospectively collected clinical manifestations, laboratory results and clinical course.
Results: A total of 65 patients were enrolled and 38 patients (58.5%) are male. Their mean age was 43.5 ± 17.4 years. Most (26.5%) patients were in their 20 s and 60 s. Fever was the most common chief complaint followed by sore throat, abdominal pain, and liver enzyme elevation. The patients had experienced symptoms for 7.3 ± 5.8 days before admission, and they had lasted for 5.3 ± 3.0 days after admission. Sixty one patients underwent radiologic examinations and 60 patients (98.3%) showed abnormal findings. The initial mean aspartate transaminase (AST), alanine transferase (ALT) levels were 468.7 ± 553.1 IU/L and 421.8 ± 618.7 IU/L, and they gradually decreased with conservative treatment. Total bilirubin increased from 1.9 ± 2.4 mg/dL to 3.7 ± 8.7 mg/dL after 14 days and decreased to 2.9 ± 6.7 mg/dL after 21 days. The AST and ALT normalization rates were 75.3% and 52.1% at 21 days, respectively. Only one patient expired, which reflected a 1.5% mortality rate.
Conclusion: EB viral hepatitis should be considered part of the differential diagnoses if elevated LFTs are associated with fever, sore throat and lymphadenopathy. EB viral hepatitis is usually mild and resolves without serious complications even with conservative treatment, and in rare cases it could cause death.

[OP-0823]

Hypoalbuminemia and risk for the development of surgical site infections following spinal surgeries: A meta-analysis

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Objectives: Surgical site infections (SSI) following spinal surgeries are linked with deeper SSI and prolonged length of stay, which may contribute extensive clinical and economic burden. Hypoalbuminemia has been associated with these devastating complications in surgical procedures. Serum albumin, prealbumin, and total lymphocytes are considered as malnutrition biomarker in patients undergoing surgery. Therefore, we aimed to determine the hypoalbuminemia is a risk factor for the development of SSI following spinal surgeries.
Materials and Methods: A systematic search on PubMed/Medline, and EMBASE databases were performed to identify English language articles. Eligible studies assessing malnutrition risk factor for the development of SSI in patients undergoing spinal procedures. The population of studies were restricted to Asia Pacific geographical area. This included studies defining malnutrition (serum albumin < 3.5 g/dl, prealbumin, and total lymphocyte count). Heterogeneity was assessed by using Cochrane Q test statistic and inconsistency index (I2). A random- effects model was used to calculate odds ratio (OR) with 95% confidence interval (CI).
Results: A total of three studies met the inclusion criteria, with 881 participants were undergoing spine surgeries. All three studies were conducted in Japan (n = 2) and china (n = 1). Two studies were defining malnutrition on the basis of hypoalbuminemia (< 3.5 g/dl), and one for prealbumin. Patients undergoing surgeries are at greater risk of developing SSI, when albumin level is < 3.5 g/dl. The overall results from pooled estimate shown no significant difference on development of SSI (OR = 2.57, 95% CI: 0.65–10.18). However, the results from meta-analysis observed hypoalbuminemia is significantly associated with risk of SSI in patients undergoing spine surgeries (OR = 4.69, 95% CI: 1.87–11.74), I^2 = 3%, p < 0.001.
Conclusion: The present findings suggest hypoalbuminemia is associated with increased risk of developing SSI in postoperative spinal surgery. Further, more studies are required to estimate the overall malnutrition status and risk of SSI.

[PP-0828]

Severity of acute viral hepatitis in patients with glucose-6-phosphate dehydrogenase deficiency: A case control study

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Objectives: To compare the parameters of morbidity and outcomes in patients of acute hepatitis with and without co-existing G6PD deficiency.
Materials and Methods: This was a retrospective case control study. A total of 9 patients with acute viral hepatitis and G6PD deficiency were compared with 18 matched controls.
Results: Mean age in G6PD and acute viral hepatitis only group is 28.89 (± 6.7) and 28.11 (± 8.6) respectively. Hepatitis E is the most common virus identified in both groups. One patient from the G6PD deficiency patients presented with acute liver failure due to hepatitis E and was managed conservatively. Acute kidney injury is also found to be common in patients with G6PD deficiency. Hemolysis is found in 44.4% of patients with G6PD deficiency and none in acute viral hepatitis only group. The hemoglobin levels are lower in patients with G6PD deficiency but not statically significant. However, total bilirubin (45.3 (± 14.9) vs 6.03 (± 3.64)p < 0.05), direct bilirubin (34.3 (± 9.79) vs 5.14 (± 3.14)p < 0.05), indirect bilirubin, serum creatinine (1.37 (± 0.87) vs 0.84 (± 0.24) p < 0.05), prothrombin time, INR (1.73 (± 0.80) vs 1.22 (± 0.25)p < 0.05) and length of hospital stay is significantly higher in patients of acute viral hepatitis with G6PD deficiency. Data was collected from age and gender matched 18 patients with G6PD deficiency alone from the same study period presenting in hospital with various reasons to identify the trend of all the parameters in them. The mean hemoglobin levels were 12.4 (± 8.6), platelets 256 (± 116.0), creatinine 0.86 (± 0.24), total bilirubin 2.0 (± 3.0), direct bilirubin 0.8 (± 0.8), indirect bilirubin 1.25 (± 2.43), ALT 68.6 (± 62.9), AST 69.3 (± 109.7), prothrombin time 11.4 (± 1.2) and INR 1.0 (± 0.12).
Conclusion: Based on our observations and the re-enforcing trend seen in our study to those it follows, we conclude that acute hepatitis in patients suffering from G6PD deficiency have a more severe initial presentation, hyperbilirubinemia and a protracted course complicated by hemolysis, Acute liver failure and AKI.

[PP-0845]

Changes of clinical characteristics of acute hepatitis A patients—single center experience

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Objectives: In Korea, the number of the patients with acute hepatitis A is increasing due to improved hygienic environment and low seroprevalence of anti-HAV IgG. This study aim to analyze the clinical features of acute hepatitis A patients in a single hospital for 22 years.
Materials and Methods: Patients with acute hepatitis A who had been hospitalized at Dankook University Hospital from 1998 to 2019 were included. We reviewed patients' medical records and analyzed the data such as the number of inpatients, age, symptoms, length of hospital stay, recovery rate, liver function test.
Results: For 22 years, total 798 patients had admitted with acute hepatitis A. The mean age of the patients was 25.8 ± 11.9 years in 1998 and gradually increased to 40.1 ± 9.4 years in 2019. The mean peak AST and ALT were 1,329.2 IU/L and 1,539.6 IU/L in 1998, and increased to 2,962.6 IU/L and 2,532.6 IU/L in 2019, respectively. The mean INR increased from 1.09 in 1998 to 1.30 in 2019. However, other parameters such as total bilirubin, WBC, platelet, serum Cr, and albumin did not show meaningful change by year. The mean duration of hospital stay was 8.2 ± 4.8 days and there was no significant changes for 22 years. The number of acute hepatitis A patients was highest in 2008, 2009 and 2019. There were 5 patients who were transferred to other center for consideration of liver transplantation. They are all male and their mean age was 38.4 ± 18.5 years old.
Conclusion: The average age of patients with acute hepatitis A has increased as many as 14.3 years. AST and ALT of the patients were higher than past, and INR was also increased, indicating severe liver dysfunction. Therefore, hepatitis A vaccination for middle-aged people should be actively considered.

[PP-0882]

Safety and efficacy of bulevirtide monotherapy and in combination with peginterferon alfa-2a in patients with chronic hepatitis delta: 24 weeks interim data of MYR204 phase 2b study

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Objectives: Bulevirtide (BLV) is an entry inhibitor used for the treatment of chronic HDV infection. Combination of BLV and Peginterferon alfa-2a (pIFN) showed synergistic effects on HDV RNA and HBsAg levels in MYR203 trial. We present the 24 weeks interim on data of the MYR204 phase 2b trial in HBV/HDV co-infected patients receiving BLV as monotherapy or in combination with pIFN.
Materials and Methods: 175 patients with chronic HDV infection were randomized in a 1:2:2:2 ratio to receive (see Figure). The primary endpoint is undetectable HDV RNA (< LoD) at week 24 after end of treatment; secondary endpoints include HDV RNA decline by $\geq 2\log_{10}$IU/ml, ALT normalization, combined response (undetectable HDV RNA or decrease by $\geq 2\log_{10}$IU/mL from baseline and ALT normalization) and HBsAg decrease.
Results: Safety: In the first 24 weeks of treatment, 998 AEs were reported by 151 patients (86.8%), being mostly mild (536) or moderate (296). 181 of 998 AEs were judged as possibly related to BLV and 724 AEs to pIFN. Overall, 7 SAEs (judged as not related to BLV) were reported, one of which led to death. Efficacy: At week 24, the proportion of patients with HDV RNA decline of $\geq 2\log_{10}$IU/mL from baseline was 37.5%, 86.0%, 90.0%, and in 72.0% of patients in arms A-D, respectively. Undetectable HDV RNA was demonstrated in 12.5%, 24%, 34% and 4% of patients at week 24 in arms A-D, respectively. Both, ALT and combined response had a higher proportion of responders in arm D, followed by arm B, arm C and arm A (Figure). HBsAg response (decline by $\geq 1\log_{10}$IU/ml) was observed in some patients (Figure).
Conclusion: BLV monotherapy and in combination with pIFN is safe and well tolerated through 24 weeks of therapy. Combination therapy and BLV monotherapy resulted in high rates of HDV viral decline, while BLV monotherapy resulted in the highest rate of ALT normalization.

Figure. Study design. 24 weeks interim data

Study design. Baseline and 24 weeks interim data		Baseline - levels			Results at week 24 - % of patients with response			
		HDV RNA (log_{10} IU/ml) Mean (SD)	ALT (U/ml). Mean (SD)	Compensated cirrhosis (% of patients)	HDV RNA decrease from baseline >2 log_{10} IU/mL	ALT normalization	Combined response	HBsAg decrease >1 log_{10} from baseline
arm A (n=25)	pIFN; Follow Up; week 0, week 48, week 96	5.197 (1.064)	121.5 (95.9)	33.3%	37.5%	12.5%	12.5%	4.2%
arm B (n=50)	2 mg BLV + pIFN; 2 mg BLV; Follow Up; week 0, week 48, week 96, week 144	5.268 (1.355)	107.5 (77.0)	34.0%	86.0%	30.0%	30.0%	12.0%
arm C (n=50)	10 mg BLV + pIFN; 10 mg BLV; Follow Up; week 0, week 48, week 96, week 144	5.090 (1.343)	112.6 (98.6)	36.0%	90.0%	24.0%	24.0%	8.0%
arm D (n=50)	10 mg BLV; Follow Up; week 0, week 48, week 96, week 144	5.448 (1.098)	118.4 (108.1)	34.0%	72.0%	64.0%	50.0%	0

[PP-0884]

Bulevirtide monotherapy at low and high dose in patients with chronic hepatitis delta: 24 weeks interim data of the phase 3 MYR301 study

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Objectives: Bulevirtide (BLV) has shown pronounced virological and biochemical responses in two phase 2 trials (MYR202/MYR203). We here present findings of a predefined 24 weeks interim analysis of the MYR301 phase 3 study in HBV/HDV co-infected patients receiving 2 mg/qd or 10 mg/qd dose BLV monotherapy in comparison to observation with no antiviral treatment.
Materials and Methods: 150 patients with chronic HDV infection were randomized in a 1:1:1 ratio to no antiviral treatment for 48 weeks followed by 10 mg/qd for 96 weeks (arm A, n = 51), treatment with BLV 2 mg/qd (arm B, n = 49), or with BLV 10 mg/qd (arm C, n = 50) for 144 weeks with a treatment-free follow-up of 96 weeks. The primary endpoint, combined response, is defined as undetectable HDV RNA or decrease by $\geq 2\log_{10}$IU/ml and ALT normalization at week 48; secondary endpoints include undetectable HDV RNA, decline by $\geq 2\log_{10}$IU/ml and ALT normalization.
Results: Baseline demographics; 57.3% male, 82.7% white, mean age 41.8 years, HDV RNA levels 5.05 $\log_{10}$IU/mL, mean ALT 110.9 U/L. BLV was well tolerated during 24 weeks: 421 treatment emergent adverse events (TEAE) were reported; 48 TEAE in arm B and 100 TEAE in arm C were assessed as possibly related to BLV. After 24 weeks, the proportion of patients achieving combined virological and biochemical response was 36.7% in arm B and 28.0% in arm C (vs. 0% in arm A, $p < 0.0001$). A HDV RNA decrease by ≥ 2 $\log_{10}$IU/mL from baseline was observed in 55.1% of patients in arm B and 68% in arm C (vs. 3.8% in arm A, $p < 0.0001$). ALT normalization was reached in 53.1% of arm B, 38% of arm C (vs. 5.9% in arm A, $p < 0.0001$).
Conclusion: This trial confirms that BLV is safe and well tolerated in patients with compensated hepatitis delta. 24 weeks of BLV treatment was associated with HDV RNA declines and improvements biochemical disease activity.

[OP-0910]

Hepatitis E infection: Sero-prevalence and viremia among healthy blood donors: A South Asian Country's perspective

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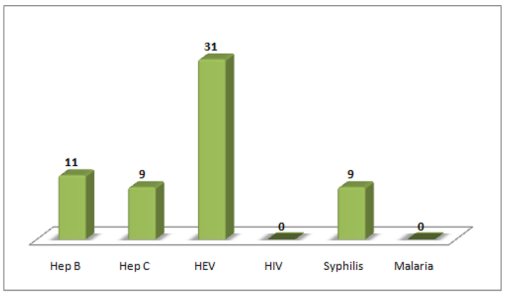
Objectives: To assess seroprevalence and viremia of HEV among healthy blood donors in a tertiary care set-up. Hepatitis E Virus (HEV) is a major health issue globally and it is endemic in Pakistan. Immunosuppressed individuals and pregnant women are at higher risk of developing acute liver failure and chronic hepatitis secondary to HEV. Routine screening of blood donors for HEV has not yet been implemented in Pakistan and other endemic South Asian countries. There is dearth of literature regarding the seroprevalence and viremia of HEV among healthy blood donors.
Materials and Methods: A cross-sectional study was conducted at Liaquat National Hospital, Karachi. Blood samples were obtained for HBsAg, Anti-HCV Antibody, Anti-HIV Antibody, Syphilis, Malaria, ALT and HEV antibodies (IgG and IgM by ELISA kits (NovaLisa by Novatec immundiagnostica GmbH)) after written informed consent. Positive samples for anti-HEV IgM were subjected to detect HEV-RNA by real-time reverse transcription polymerase chain reaction assay (RealStar® HEV RT-PCR Kit 2.0 by Altona Diagnostics).
Results: Total of 515 adult participants were enrolled with a mean age of 30.08 ± 7.56 years. Mean ALT levels of 43.05 ± 32.45 IU/L were observed. HEV IgG was positive in 365 participants (70.9%) with ALT levels of 43.61 ± 34.03. 31 participants (6%) were positive for Anti HEV IgM with ALT levels of 44.06 ± 69.21. All IgM positive were subjected to PCR testing which came out negative (PCR detection limit > 100copies/mL). Patients who tested positive for HBsAg, Anti-HCV Ab, Syphilis and HIV were 11 (2.1%), 9 (1.7%), 9 (1.7%) and 0 (0%) respectively.
Conclusion: High seroprevalence of Anti HEV IgM among healthy blood donors emphasizes the need for robust measures of routine screening for HEV of all blood products in endemic countries to prevent transfusion dependent transmission with special consideration when the recipients are either immunocompromised or pregnant.



Sero-prevalence of HBV, HCV, HEV, HIV, Syphilis and Malaria among healthy blood donors at a tertiary care set-up. (sample size n=515)

[PP-0921]

Prevalence of and risk factors for invasive liver abscess syndrome in patient with pyogenic liver abscesses: 10-year retrospective analysis

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Objectives: The etiology of pyogenic liver abscess has changed over the past few decades, and the clinical importance of invasive liver abscess syndrome (ILAS) is emerging with the increase of K.pneumoniae pyogenic liver abscess (KP-PLA). The aims of this study to investigate the prevalence of invasive liver abscess syndrome among patients with pyogenic liver abscess, and to identify differences in clinical characteristics between ILAS and non-ILAS, and risk factors for ILAS.
Materials and Methods: We retrospectively reviewed the medical records of 744 patients diagnosed with pyogenic liver abscess from January 2011 to December 2020. Cases that were not confirmed microbiologically in culture tests were excluded.
Results: A total of 342 patients were included into the study population. K.pneumoniae was identified in 71.6% (n = 245), followed by E.coli in 16.4% (n = 56). Among KP-PLA, 39 cases (15.9%) were diagnosed with ILAS. The most common septic metastatic infection were septic pneumonia (46.2%) and endophthalmitis (48.7%). ILAS showed longer duration of fever (9.2 days vs 4.8 days) and hospital stay (35.2 days vs 29.8 days) than Non-ILAS. There was no significant difference in diabetes mellitus between the ILAS and non-ILAS groups, but uncontrolled DM was more common in the ILAS group (28.2% vs 15.5%, p = 0.047). In multivariate logistic regression analysis, patients using antiplatelet agents were less likely to present ILAS (adjusted odds ratio, 0.131; 95% CI, 0.017–0.993; p = 0.049). Poor glycemic control was not found to be an independent predictor of ILAS.
Conclusion: K. pneumoniae was the leading cause of pyogenic liver abscess over the period of 10 years, and the prevalence of invasive liver abscess syndrome was found to be 15.9% among KP-PLA. Diabetes mellitus, which is considered a classical risk factor, did not show a significant association in ILAS. The administration of antiplatelet agents showed an inverse correlation with the incidence of ILAS, and consistency should be confirmed through additional studies in the future.

[OP-1051]

Rare underlying aetiology for liver nodules

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Objectives: to determine unusual underlying etiology of multiple liver nodular lesions.
Materials and Methods: A 40 years old male presented with recurrent nagging pain localized to the upper abdomen for 2 years. He also gave a history of recurrent low-grade fever associated with recurrent mild jaundice for the last 1 year. There was a history of loss of appetite and weight. No history of abdominal distension, constipation, diarrhea, hematemesis or melena. Physical examination did not reveal any significant findings in the abdomen. Investigations showed mild anemia, mildly deranged liver enzymes, and an increased level of alkaline phosphatase. Radiology showed multiple 15 to 30 mm size nodular lesions in the right lobe of the liver (mainly in segments 5 and 7). Resection of the liver showed multiple whitish nodular lesions, occasionally confluent with normal adjoining liver parenchyma. No unduly dilated biliary system.
Results: Histology showed multiple confluent epithelioid cell granulomas dominantly portal tract distributions with involvement of the bile ducts. The right main hepatic duct and surrounding hilar soft tissue are also involved by the granulomatous process. Zielh Nielsen staining was non-contributory however gene expert for Mycobacterium tuberculosis was positive confirming the granulomas to be of tubercular etiology.
Conclusion: We presented a rare condition of multiple granulomatous liver nodules of mycobacterium tuberculosis.

[OP-1135]

Hepato-gastric fistula and spontaneous rupture of liver abscess caused by extended-spectrum beta-lactamase producing E. coli

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Objectives: Hepatogastric fistula was rare complication of liver abscess and associated with high morbidity and mortality. This report describe diagnosis and treatment of spontaneous rupture of liver abscess with hepatogastric fistula. ESBL producing pathogens showed high resistant to common antibiotic families and 27.5% pathogens were multidrug resistant (MDR).
Materials and Methods: Male, 33 years old suffered from and right upper quadrant abdominal pain since 3 weeks prior and getting worse in the last 3 days. Nausea without vomiting and decreasing of body

weight within 1 month. History of alcoholic since he was 12 years old. Physical examination revealed tachycardia, abdominal distension, decreasing of bowel sound and dullness of Traube's space.
Results: Leucocyte was 11.800/uL, ALT 191 iu/mL, AST 89 iu/mL, total and direct bilirubin 1.85 mg/dl and 1.55 mg/dl respectively and albumin 1.72 g/dl. Ground glass opacity on was detected on abdominal plain radigraphy. MSCT abdominal scan showed thick fluid density; diameter 8cmx10.1cmx10.5 cm located on right lobe of the liver and spreading into pericapsular wall with rupture and fistulation to the gastric wall. Extra luminal free fluid and air detected within abdominal cavity. Surgical laparotomy was performed immediately. During exploration there was 2000 ml of pus and free air within peritoneal cavity with grade 3 inter intestinal adhesion. Liver rupture was located on segment II-III of right lobe with diameter 8 cm; site by site (adhesion) location with gastric rupture (BOEY 3, diameter 5 cm). Primary suture was performed on gastric rupture because of hemodynamic instability. Drain was inserted on sub hepatic and Retzii cavity. Biopsy obtained from gastric tissue showed acute inflammation. Pus culture was ESBL producing E.coli. The condition was getting better with antibiotic, correction of albumin and nutritional support.
Conclusion: We reported spontaneous rupture of liver abscess and hepato-gastric fistula in young patient. ESBL producing E.coli and chronic alcohol consumption contributed to prognostic and clinical outcome.

[PP-1164]

High seroprevalence of hepatitis E virus in rural residents in Dong Van, Vietnam

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Objectives: The aim of the present study was to investigate the seropositive rate of HEV infection in residents belonging to different ethnic groups of the rural province ?ông V?n, Vietnam.
Materials and Methods: A total of 607 blood serum samples were obtained in 2019 from practically healthy inhabitants (179 men and 428 women) in different communities of ?ông V?n district (age range: 18–83 years; mean age: 40,83 ± 1,18 years). Most of the participants belonged to H'mong ethnic group (90,04%), which is dominant in this region. National ethnic minorities were also represented by Tay (3,57%), Giay (2,44%), Kinh (1,13%), and others (2,82%). The majority of the participants were farmers (98,12%). The serological markers of HEV, HBV, HCV were detected using commercial ELISA assays (RPC Diagnostic Systems, Russia). The confidence limit (95% CI) was calculated using the Wilson method.
Results: Overall, 87,6% participants (95% CI, 84,8–90,0; 532/607) were positive for anti-HEV IgG, and only 1,32% participants (95% CI, 0,67–2,58; 8/607) were anti-HEV IgM positive. Hepatitis E cases seroprevalence increased with age: 75,7% (95% CI, 68,3–81,8) in aged group 18–29 years; 87,7% (95% CI, 81,9–91,8) – 30–39 years; 94,6% (95% CI, 89,3–97,4) – 40–49 years; 93,6% (95% CI, 88,5–96,5) –50 years and older. Among 532 anti-HEV positive individuals there were 63 (11,84%, 95%CI, 9,37–14,87) positive for the HBsAg, 248 (46,62%, 95%CI, 42,42–50,86) for the anti-HBc, and 7 (1,32%, 95%CI, 0,64–2,69) positive for the anti-HCV. The statistically significant difference between the presence of anti-HEV IgG and the participant's gender, age and professional were not determined.
Conclusion: Our study revealed a high HEV seroprevalence among the rural population of Ha Giang province, belonging to different ethnic minorities. It is necessary to increase the surveillance of rural provinces as a high risk of HEV territory and suggest measures to prevent HEV infection.

[OP-1187]

Trends and antifungal susceptibility of fungemia in cirrhosis patients: A call for action!

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Objectives: Fungal infections are emerging threat in cirrhosis patients and fungemia in particular is associated with high mortality. Mycological characteristics and antifungal susceptibility of these infections is poorly understood. Hence, we evaluated mycological attributes of cirrhosis patients with fungemia.
Materials and Methods: We enrolled cirrhosis patients with fungemia from intensive care unit of a tertiary care hospital between 2014 and 2020. Fungal characterisation was done through MALDI-TOF MS and antifungal susceptibility was evaluated by micro-broth dilution (CLSI-guidelines). Descriptive analysis was performed.
Results: Eighty-six cases of fungemia were identified, of which majority were due to Candida species. The commonest pathogen isolated was Candida tropicalis (n = 25, 40.7%) followed by Candida albicans (n = 18, 20.9%), Candida glabrata (n = 6, 7%), Candida parapsilosis (n = 6, 7%), Candida krusei (n = 6, 7%), Candida guilliermondii (n = 4, 4.7%), Candida kefyr (n = 3, 3.5%), Candida lusitaniae (n = 3, 3.5%), Trichosporon mucoides (n = 1, 1.2%), Cryptococcus neoformans (n = 1, 1.2%), Candida nivariensis (n = 1, 1.2%), and Candida orthopsilosis (n = 1, 1.2%). A significant increase in the isolation of non-albicans Candida was noted between 2019–2020 and 2014–2018 (90% vs. 10%, p = 0.032). Of all isolates maximum resistance was noted against fluconazole (8.1%), itraconazole (7.0%), caspofungin (5.8%), voriconazole (4.7%), amphotericin B (3.5%), anidulafungin (2.3%), micafungin (2.1%) and posaconazole (0%). Gradual increase in minimum inhibitory concentration (MIC) was observed for amphotericin B, fluconazole and caspofungin. The Geometric mean, MIC-50 (mg/L) and MIC-range of amphotericin B was 0.584, 1, 0.06- 2; fluconazole was 0.428, 0.5,

0.12–64; voriconazole was 0.024, 0.03, 0.03–16, itraconazole was 0.152, 0.12, 0.03–16; posaconazole was 0.0799, 0.12, 0.03–0.5; caspofungin was 0.02, 0.3, 0.12–16; anidulafungin was 0.12, 0.12, 0.12–2 and micafungin was 0.012, 0.12, 0.12–4; respectively.
Conclusion: Mycological characterisation and their susceptibility profile can guide antifungal treatment and stewardship decisions among cirrhosis patients with fungal infections. There is a concerning rise in non-albicans Candida blood stream infections with creeping MIC of antifungals.

[L-OP-1221]

Gastrointestinal manifestation of Covid-19 and LFTs association with Covid-19, its severity and outcome—a study from Tertiary Hospital, Pakistan

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Objectives: Aim of this study to assess gastrointestinal manifestations of Covid-19 and to evaluate frequency, pattern, association of LFTs with Covid-19, its severity and outcome.
Materials and Methods: It is a cross-sectional study was conducted at The Aga Khan University Hospital, Karachi. All the patients above 18 years of age, who were admitted in the hospital with the diagnosis of COVID-19, from 26 Feb 2020 till June 2020, were enrolled. Patient demography, clinical presentation, laboratory tests, duration stay and clinical outcomes (discharged stable and expired) were assessed. Statistical analysis of given variables performed with SSPS.
Results: Total 533 hospitalized patients median age of the cohort was 42 years (IQR 25 – 64 years)0.328 (61.5%) were predominantly male. Common comorbid were HTN 224 (42%) and DM 192 (36%). Gastrointestinal symptoms mainly noticed nausea in 130 (24%), vomiting and diarrhea in 80 (15%) and 84 (15.4%) respectively. LTFs found abnormal in (92%) of total patients, mainly GGT (59%), SGOT (54%) and SGPT (53%) whereas there was no significant changed in rest of liver enzymes. Significant association seen between abnormal LFTs and CRP, LDH, Na, Bicarb and Tlc. On comparing the clinical outcome significant association noticed between abnormal LFTs and mortality ($p = 0.05$).
Conclusion: Nausea, vomiting and diarrhea are the common gastrointestinal feature of C0vid-19. Abnormal LFTs found almost 90% 0f patient mainly with raised GGT, SGPT, SGOT whereas PT and Albumin are least affected. Abnormal LFTs have signification association with inflammation markers (raised TLC, LDH, CRP), hyponatremia and low bicarb. Abnormal LFTs signify the severity of disease leading to severe morbidity and mortality.

Table.1

Baseline Characteristic of COVID-19 Patients

Variables	Number	Percentage
Age (Mean 42 years)	(IQR 25 – 64)	
Total (533)		
Male	328	(61.4%)
Female	205	(38.6%)
Comorbids		
HTN	225	(42%)
DM	192	(36%)
IHD	86	(16%)
CKD	43	(8%)
CLD	21	(3.9%)
CVA	11	(2%)
GI Clinical Features		
Nausea	130	(24%)
Vomiting	84	(15.4%)
Diarrhea	80	(15%)
Jaundice	50	(9.4%)
Abdominal Pain	24	(4.5%)
Ageusia/dysgeusia/hypogeusia	10	(1.9%)
Other Clinical Features		
Fever	388	(72.7%)
Cough	297	(55.7%)
SOB	294	(55.1%)
Clinical Outcome		
Discharge Stable	452	(85%)
LAMA	25	(4.6%)
Expired	56	(10.5%)

Table no.2

Abnormal LFTS Frequency and Pattern in Covid-19 Patients

Variable	Total	Abnormal Value	Normal Value
LFTs (Overall)	533 (100%)	497 (93.2%)	36 (6.8%)
GGT	449 (100%)	265 (59.1%)	184 (40.9%)
SGPT	462 (100%)	248 (53.6%)	214 (46.3%)
SGOT	451 (100%)	248 (54.9%)	214 (47.4%)
AP	449 (100%)	94 (21%)	355 (79%)
TB	449 (100%)	32 (7.1%)	417 (93.2%)

Nonalcoholic Fatty Liver Disease—Basic

[OP-0042]

The effectiveness of pentoxifylline in NAFLD: A meta-analysis

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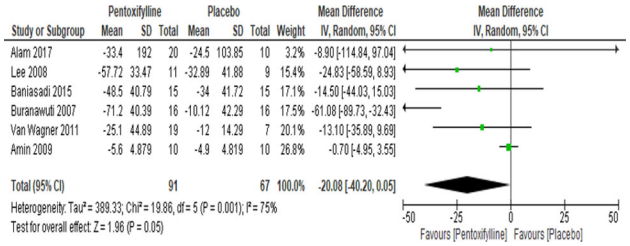
Objectives: Rising prevalence of non-alcoholic fatty liver disease (NAFLD) suggests correlation with liver failure worldwide. To date, there is no proven pharmacologic therapy for NAFLD. Pentoxifylline (PTX) with anti-tumor necrosis factor properties has shown improvement of histological parameters, reductions in transaminase levels and serum cytokines among patients with NAFLD. Main objective is to determine the effectiveness of PTX in the improvement of aminotransaminases, liver histology and cytokines like TNF-α.
Materials and Methods: Comprehensive literature search showed seven randomized controlled trials (N = 222) comparing PTX (1,200 mg/day) with placebo. Two reviewers independently selected studies, assessed quality, and pooled outcomes including AST/ALT levels, serum cytokines and liver histology. Selected studies were found to be of low risk of bias based on Cochrane risk of bias assessment tool for randomized trials. Statistical analysis and forrest plot were generated using the Review Manager Software 5.3.

Results: Pooled results showed that PTX significantly reduced the ALT (WMD = − 20.08; 95% CI: − 40.20, 0.05; p = 0.05) and AST (WMD = − 11.38; 95% CI: − 20.47, − 2.29; p = 0.01) in NAFLD patients. PTX significantly improved lobular inflammation (WMD = − 0.45; 95% CI: − 0.89, − 0.01; p = 0.04), fibrosis (WMD = − 0.39; 95% CI: 0.83, 0.05; p = 0.08) and NAS score (WMD = − 0.52; 95% CI: − 1.06, 0.0; p = 0.051) and greater reduction was demonstrated in TNF-α (WMD = − 20.20; 95% CI: − 50.46, 10.41; p = 0.20).
Conclusion: Pentoxifylline (PTX) improves aminotransferases, liver histology and TNF-α of NAFLD patients. Demonstrating effects on serum TNF-α which plays a key role in progression to hepatic steatosis, it may be used as an adjunct to diet and lifestyle modifications in the treatment of NAFLD.



[OP-0119]

Simple steatosis and non-alcoholic steatohepatitis differ by dietary patterns

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Objectives: To compare dietary patterns in patients with simple steatosis (SS) and non-alcoholic steatohepatitis (NASH).
Materials and Methods: The study (registered at https://rscf.ru/contests/search-projects/19-76-30014) enrolled patients gave written informed consent. The data of 178 patients with non-alcoholic fatty liver disease (per EASL) served as a source for the study. Subjects were divided into either NASH or SS group. Nutrilogic (Nutrilogic, Russia) was used for nutritional assessment. Dietary patterns were assessed in accordance to "healthy eating index" principles (ASN) for the following main groups of products: grains, fruits, vegetables, dairy products, meats, fats and confectioneries. Non-parametric statistics was used to perform the comparison of the main and the control group.
Results: There were 156 patients in the SS (mean age 56.5 ± 12.3 y.o., mean BMI 40.58 ± 14.9 kg/m^2) and 22 in NASH group (age 48.6 ± 13.4 y.o., BMI 40.0 ± 7.3 kg/m^2). No difference was found between NASH and SS groups in energy values of their diets (Mean ± SD: 2339 ± 1067 kcal/day in NASH vs 2499 ± 959.6 kcal/day in SS, p = 0.548), consumption of fats (109.3 ± 54.2 g/day vs 114.1 ± 46.67 g/day, p = 0.89), proteins (106.6 ± 51.0 g/day vs 109.7 ± 44.4 g/day, p = 0.91) and carbohydrates (214.9 ± 100.7 g/day vs 251.3 ± 121.5 g/day, p = 0.21). However, dietary fibre intake was higher in those with Simple steatosis (26.7 ± 13.2 g/day vs 20.9 ± 10.4 g/day in NASH, p = 0.03). Analysis of the consumption of subgroups of foods revealed greater amounts of potatoes (0.14 ± 0.08 vs 0.11 ± 0.15, p = 0.006), and lower – of onions (0.02 ± 0.03 vs 0.07 ± 0.1, p = 0.006) and dairy butter (0.14 ± 0.44 vs 0.15 ± 0.21, p = 0.009) intake in NASH compared to SS group. There was no other difference in the structure of vegetables (beans, root crops, leafy and other vegetables), and fats (animal fats, vegetable oils, margarines) consumption, as well as in the structure of other subgroups of foods.
Conclusion: Food patterns of patients with non-alcoholic steatohepatitis and simple steatosis differ significantly. The obtained data may be used for diet modification in patients with NAFLD.

Table 1. Comparative analysis of the data obtained in NASH and Simple steatosis groups

	Simple steatosis N=156 (Mean±SD)	Non-alcoholic steatohepatitis N=22 (Mean±SD)	P
Grains	0.96±0.50	1.23±1.45	0.714
Vegetables	1.12±0.77	1.01±0.81	0.223
Fruits	0.73±0.57	0.74±0.76	0.424
Dairy products	0.67±0.56	0.83±0.73	0.37
Fats	0.64±0.507	0.76±1.11	0.333
Confectioneries	0.29±0.35	0.32±0.72	0.237
Meats	1.7±1.0	2.2±3.1	0.655

*- According to the concept of the "Healthy eating index" [U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at: http://health.gov/dietaryguidelines/2015/guidelines]

[OP-0144]

The effect of herbal medicine on NAFLD in subjects with T2DM

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Objectives: Type 2 Diabetes Mellitus (T2DM) and Non-alcoholic fatty liver disease (NAFLD) are often seen together. It's a characteristic of metabolic syndrome.Steatosis, steatohepatitis, and cirrhosis are all signs of NAFLD. NAFLD affects 70% of T2DM patients. Folk medicine has often used herbal remedies to treat a variety of ailments. Triphala is the kind of folk medicine with the combination of Embelica officinalis Terminalia bellirica Terminalia chebula. This present study done for the therapeutic potency Triphala in T2DM.
Materials and Methods: Thirty-five subjects those who have T2DM were randomly selected from the week end diabetic clinic Health center, Jiwaji University. 3 g Triphala was given BD, for 6 month. Fasting and PP blood glucose and lipid profile (total cholesterol, triglycerides, HDL & LDL cholesterol) liver marker (Bilirubin, SGOT, SGPT) and oxidative stress markers (SOD, Catalase, GSH, TBARS) were also monitored in the study subjects. Paired t-test was made the compare the significance. This study was sponsored by study AYUSH, Gov. of INDIA.
Results: Administration of Triphala regularly for 6 months resulted in significant reductions of blood glucose ($P < 0.001$) glycosylated hemoglobin levels ($P < 0.001$) and in body weight ($P < 0.0001$). Lipid function markers level were reduced significantly ($P < 0.001$) Also, liver function markers (Bilirubin levels reduced 12.6% $P < 0.05$, SGOT levels reduced 18.0% $P < 0.05$ and SGPT levels reduced 17.8% $P < 0.05$) and the antioxidant markers were also improved significantly ($P < 0.05$).
Conclusion: Triphala for the treatment of T2DM show the significant improvement in glycemic control and lipid levels. The liver functions also improved in subjects. It may be the due to the anti-oxidant property of the herbal medicine.

[OP-0148]

The relationship between total cholesterol level and oxidative stress in the liver tissue of the hyperlipidemic rat model after the intervention with synbiotic beverage

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Objectives: Hyperlipidemia condition can makes liver cell damage and can be marked by an imbalance of oxidative stress levels in the liver tissue such as malondialdehyde (MDA) levels and of superoxide dismutase (SOD) activity. Previous research has shown that synbiotic intervention can improve the lipid profile level. This research aims to know the relationship between total cholesterol level and oxidative stress level in the liver tissue of the hyperlipidemic rat model after the intervention with a synbiotic beverage from kefir milk and jicama concentrate.
Materials and Methods: This research used 25 rats divided into 5 groups (K + , K-, P1, P2, and P3). Group of K + , P1, P2, P3 were given quail egg yolk for the first 4 weeks. For the next 4 weeks, K + and K- groups were only given fed ad libitum. Group of P1, P2, and P3 were given synbiotic with the formulation of P1: 85% kefir milk (K) and 15% jicama Concentrate (J), P2: 75% K, 25% J, and P3: 65% K, 35% J. The dose of quail egg yolks and synbiotic was 5 ml/200 grBW. Total cholesterol (TC) was taken at the 4^{th} and 8^{th} weeks. The animal model was terminated to get liver organs to measure the MDA level and SOD activity.
Results: Mean of TC level (mg/dl) were 203.2 ± 1.74 (K +), 80.2 ± 1.39 (K-), 171.8 ± 1.71 (P1) 142 ± 2.04 (P2), 109.4 ± 1.74 (P3). Mean of MDA level (nmol/gr) were 11.8 ± 0.17 (K +), 2.5 ± 0.12 (K-), 7.7 ± 0.18 (P1) 5.7 ± 0.10 (P2), 4.1 ± 0.09 (P3). Mean of SOD activity (%) were 21.43 ± 2.52 (K +), 71.43 ± 3.91 (K-), 30.71 ± 1.53 (P1) 50.35 ± 2.84 (P2), 63.93 ± 1.53 (P3). Pearson test showed There are correlation between TC with MDA level (0.971) and TC with SOD activity (-0.957) with the p-value < 0.001.
Conclusion: There is a relationship between TC level and oxidative stress in the liver tissue after the intervention with a synbiotic beverage from kefir milk and jicama concentrate.

[PP-0320]

Cynanchum atratum attenuates high-fat and high-fructose diet induced metabolic disorders in mice model associated with gut microbiota modulation

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Objectives: Cynanchum atratum, a traditional herbal medicine, has been frequently used in eastern Asia as an antifebrile, diuretic, antidote for curing rheumatalgia and scrofulid. The present study aimed to investigate the pharmaceutical effects and potential mechanism of 30% ethanol extract of cynanchum atratum (CAE) on high-fat and high-fructose diet (HFHFD) induced metabolic disorder in the mice model.
Materials and Methods: Ten weeks of high-fat (40% kcal fat) and High-fructose (20%) diet-treated mice were orally treated with (100, 200 mg/kg) CAE from the 5^{th} week until the 10^{th} week. Metformin was a positive control for comparison in the present study.
Results: CAE treatment dramatically relieved the increase of body, liver, and mesenteric fat weight, serum AST, ALT, LDL, TG, and hepatic TG levels, but no other portion of fat weight, food, and fructose intake as compared to the HFHFD group. The hepatic injury and lipid accumulation were ameliorated by CAE as evidenced by H&E and Oil red O staining in liver tissue. Besides, HFHFD triggered a high level of blood glucose and was also significantly improved by CAE administration. Additionally, CAE significantly lowered the elevation of hepatic TNF-α, TNF-α/IL-10 ratio, fecal endotoxins, and the abundance of Gram-negative bacteria. As we know, the gut microbiota is an essential factor for metabolic homeostasis. We found that the reduction of the dominant gut microbiota diversity was restored by CAE treatment. Meanwhile, hepatic lipogenesis and β-oxidation-related proteins and gene expression, including PPAR-α, SREBP-1, SIRT1, FAS, CTP1, etc., were normalized markedly by CAE. In particular, the AMPK, a central regulator of energy metabolism, was phosphorylated by CAE at an even higher rate than metformin.
Conclusion: Taken together, we supposed that cynanchum atratum exerts an effect of anti-hepatic steatosis, anti-hyperglycemia, improvement of dyslipidemia, and the corresponding mechanisms are associated with the regulation of gut microbiota and inhibition of inflammation.

[OP-0324]

Peripheral blood mononuclear cells mitochondrial copy number and adenosine triphosphate inhibition test in non-alcoholic fatty liver disease

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is known to be associated with mitochondrial dysfunction. The purpose of this study was to develop biomarkers for the assessment of mitochondrial dysfunction in patients with NAFLD.
Materials and Methods: Mitochondrion-associated transcriptome analysis was performed from the NAFLD and healthy control liver. Peripheral blood mononuclear cells obtained from 88 patients with NAFLD and healthy controls were used to measure mitochondrial

DNA (mtDNA) copy number. Mitochondrial inhibition substrate test (ATP assay) was performed in HepG2 cells using patients' serum. Cellular ATP concentration was measured in patient serum was applied at the same quantity as the media.
Results: Hepatic mRNA transcriptome analysis showed that patients with NAFLD exhibited upregulated expression of genes related to mitochondrial tricarboxylic acid (TCA) cycle (E2F1, E2F2, and ORC6) and those related to the mitochondrial envelope (E2F1, MAPK4, and CYP2K6) compared to healthy controls. Gene set enrichment analysis revealed upregulated expression of genes related to the pathways of TCA cycle and DNA replication in patients with NAFLD as compared to that in healthy controls. The mtDNA copy number in the peripheral blood mononuclear cells was 1.28-fold lower in patients with NAFLD than in healthy controls ($p < 0.0001$). Cellular adenosine triphosphate (ATP) concentration decreased 1.2-fold times in NAFLD patients than in healthy controls ($p < 0.0001$). The mtDNA copy number and ATP inhibition test showed negative correlation with degree of hepatic steatosis. And ATP concentration showed positive correlation with mtDNA copy number.
Conclusion: Peripheral blood mononuclear cells mitochondrial copy number and ATP inhibition test can be used biomarkers for the assessment of mitochondrial dysfunction in patients with NAFLD.

[OP-0326]

Lemon balm extract ALS-L1023, an angiogenesis inhibitor, inhibits liver fibrosis in a non-alcoholic fatty liver disease model

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Objectives: ALS-L1023 is an ingredient extracted from Melissa officinalis L. (Labiatae; lemon balm), which grows wild in Europe and the Mediterranean. ALS-L1023 is also known as a natural medicine that suppresses angiogenesis. Herein, we aimed to determine whether ALS-L1203 could alleviate non-alcoholic fatty liver disease (NAFLD).
Materials and Methods: C57BL/6 wild-type male mice (age, 6-weeks-old) were fed a choline-deficient high-fat diet for 10 weeks to induce NAFLD. Two doses (a low dose, 8 g/kg/day; and a high dose, 12 g/kg/day) of the lemon balm extract, ALS-L1023, were selected and mixed with feed for administration. RNA sequencing was performed for the choline-deficient high-fat diet group, ALS-L1023 responder group, and ALS-L1023 non-responder group.
Results: There was no significant difference between the groups in mean final body weight or food intake. Biochemical analysis revealed that the ALS-L1023 low-dose group had significantly decreased alanine transaminase and aspartate transaminase compared to the choline-deficient high-fat diet group. Based on Sirius red staining, the area of fibrosis significantly decreased due to the administration of ALS-L1023, and the anti-fibrotic effect of ALS-L1023 was greater than that of obeticholic acid. RNA sequencing was performed after mice were divided into responder and non-responder groups. The responder group had lower expression of genes related to the hedgehog-signaling pathway than the non-responder group.
Conclusion: ALS-L1023 may exert anti-fibrotic effects in the NAFLD model.

[OP-0327]

Ticagrelor, but not clopidogrel, attenuated hepatic steatosis in a model of non-alcoholic fatty liver disease

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Objectives: Several studies have suggested that platelets are associated with inflammation and may play a important role in hepatic inflammation. We tried to evaluate whether antiplatelet drugs could improve non-alcoholic fatty liver disease (NAFLD).
Materials and Methods: Mice were fed a high-fat diet (HFD) to establish an NAFLD model, which was verified through pre-study liver biopsy at 18 weeks. Animals with an NAFLD activity score (NAS) ≥ 4 were randomized into HFD-only, clopidogrel (CLO; 35 mg/kg/day), and ticagrelor (TIC; 40 mg/kg/day) groups, which were then treated with the respective drug for an additional 15 weeks. Liver and blood samples were collected from all animals at 33 weeks.
Results: The TIC group, but not the CLO group, showed significantly lower degree of steatosis and NAS than the HFD group (HFD: 5.3 ± 0.9, CLO: 4.6 ± 0.7, TIC: 3.4 ± 1.2; $p = 0.0047$). Hepatic de novo lipogenesis markers (SREBP1c, FAS, SCD1, and DGAT2 expression) and mRNA expression of inflammatory markers only decreased significantly in the TIC treatment group. Endoplasmic reticulum (ER) stress markers (CHOP, Xbp1, and GRP78) also decreased significantly in the TIC group, but not in the CLO group. Nile red staining intensity decreased in HepG2 cells following TIC treatment. Hepatic de novo lipogenesis markers were decreased significantly in HepG2 cells after TIC treatment.
Conclusion: TIC, but not CLO, attenuated steatosis and NAS via inhibiting fat de novo synthesis as well as ER stress in the biopsy proven NAFLD animal model.

[OP-0466]

Semaglutide and pioglitazone improve cardiometabolic parameters in diet-induced obese NASH hamsters

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Objectives: Cardiovascular disease is the leading cause of deaths in nonalcoholic steatohepatitis (NASH) patients. Mouse models, while widely used for drug development, do not fully replicate human NASH nor integrate the associated cardiac dysfunction, i.e. heart failure with preserved ejection fraction (HFpEF). To overcome these limitations, we established a nutritional hamster model developing obesity, NASH and HFpEF. Here we evaluated the effects of two clinical benchmarks for NASH treatment: semaglutide (SEMA), a glucagon-like peptide-1 receptor agonist, and pioglitazone (PIO), a peroxisome proliferator-activated receptor-gamma agonist.
Materials and Methods: Hamsters were fed with a free choice diet, which presents hamsters with a choice between control chow (CC) or high fat/cholesterol (HFC) diet, and normal water (NW) or 10% fructose water (FW). After 20 weeks of diet, obese hamsters were treated once daily for 5 weeks with vehicle, SEMA or PIO.
Results: While PIO had neutral effects, SEMA induced a lower HFC/FW and higher CC/NW intake, leading to a 17% body weight loss ($p < 0.01$ vs. vehicle) and a 48% lower visceral fat mass ($p < 0.001$). Compared with vehicle, both SEMA and PIO significantly reduced fasting glycemia, hyperinsulinemia and HOMA-IR index. PIO reduced hypertriglyceridemia (− 49%, $p < 0.01$ vs. vehicle). SEMA decreased both plasma total cholesterol levels (− 24%, $p < 0.001$) and hypertriglyceridemia (− 50%, $p < 0.001$). Although both treatments did not improve NAFLD activity scoring and fibrosis score significantly, improvement in liver steatosis was observed for PIO and SEMA, with significantly lower hepatic triglycerides levels (− 25% vs. vehicle for both treatments). Additionally, PIO and SEMA showed substantial benefits on HFpEF with significantly improved E/A and E'/A' ratios, as measured by echocardiography.
Conclusion: SEMA and PIO both improve cardiometabolic parameters in the diet-induced obese NASH hamster. This preclinical model will be useful for validating novel drugs or combination therapies for the treatment of NASH and associated HFpEF.

[PP-0495]

Insight into the therapeutic effects of artesunate in relieving nonalcoholic steatohepatitis and related fibrosis from transcriptomic and proteomic analyses

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Objectives: Artesunate, a water-soluble derivative of artemisinin, well-known for its efficacy in treating malaria, could also exert various pharmacological features such as anti-inflammatory, anti-tumor and immunomodulating activities. Here we aimed to probe its treating effects in a mouse model of nonalcoholic steatohepatitis (NASH).
Materials and Methods: Male C57BL/6 mice were randomly divided into two groups, the NASH group and the NASH + Artesunate group, for 4 weeks of vehicle or artesunate treatment (intragastrical administration, 30 mg/g body weight, once daily), respectively, before subjected to 12-week high fat high cholesterol diet (HFHCD) feeding. Morphological materials and tissue samples were acquired from euthanized mice for further analyses. Transcriptomics and proteomics were utilized to dig altered gene-protein pairs in mouse liver. Quantitative real-time PCR and Western blot were performed to confirm the identified gene and protein alterations.
Results: Artesunate significantly improved body weight, liver index, serum aminotransferase, alanine aminotransferase, and endotoxin, liver triglyceride and cholesterol, and blood glucose in NASH mice. The anti-steatosis, anti-inflammation and anti-fibrotic effects of Artesunate were supported by Oil red staining, Hematoxylin–eosin staining, Sirius red staining and Masson's trichrome staining. 1132 differentially expressed genes and 577 differentially expressed proteins were identified in the livers of Artesunate + NASH mice compared to the NASH mice. Representative hepatic gene markers regarding NASH phenotypes (Srebp-1c, Fasn, Scd-1, Cd36, Tnfa, IL1b, Ccl2, Col1a1, Tgfb1 and Mmp13), as well as hepatic autophagy function indicators (Becn1, Atg5, Sqstm1, and Sirt1) were found down-regulated in the Artesunate + NASH group compared with the NASH group. Moreover, several hepatokines, including Lect2, Lcn2 and Tsk, were found downregulated in the livers of NASH + Artesunate mice.
Conclusion: The current study showed that artesunate could alleviate steatosis, inflammation and fibrosis of mouse NASH via impacting lipid metabolism, inflammation, hepatokine secretion, and autophagy. Our results may pave the way for further mechanistic researches.

[OP-0516]

The signatures of bile microbiome associated with nonalcoholic fatty liver disease

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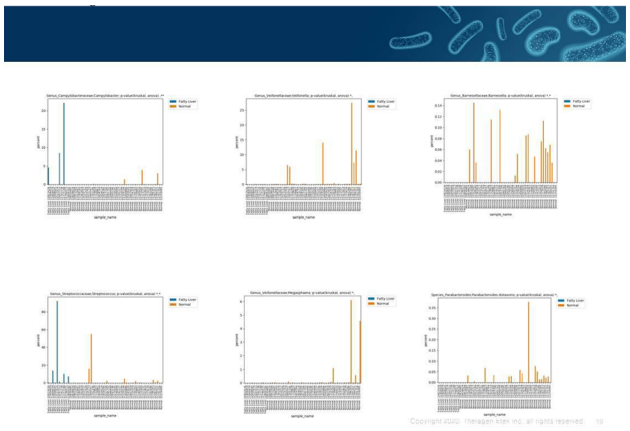
Objectives: Hepatic steatosis is a multifactorial condition that is often observed in obese patients and is a prelude to non-alcoholic fatty liver disease. The current changes in biliary flora are thought to be involved in the formation of many liver diseases. Therefore, we want to investigate whether the hepatic steatosis has a certain correlation with biliary microecology, and to detect specific strains.
Materials and Methods: All participants underwent three-phase CT examinations to identify the hepatic steatosis. Hepatic steatosis were determined using the unenhanced CT examination: a liver-spleen attenuation difference of greater than 10 HU and the absolute attenuation of the liver less than 40 HU. A total of 52 adults were enrolled in this study, including 10 hepatic steatosis subjects and 42 controls. Bile samples were collected and analyzed with metagenomics. We used Shannon index to reflect the alpha diversities of microbiota. Wilcoxon rank sum test and Kruskal–Wallis test were performed to evaluate alpha diversities between groups. At last, the differences of microbiota composition between hepatic steatosis subjects and healthy controls were assessed by Kruskal–Wallis test.
Results: Significant differences in microbiota composition between two groups have been observed. Deep sequencing of microbiota revealed high abundance of streptococcus in hepatic steatosis group, comparing with the control group. Compared to the control group, in hepatic steatosis group, the abundance of Veillonella, Barnesiella, Megasphaera, Parabacteroides were significantly reduced. There was no significant difference in terms of alpha diversity between two groups.
Conclusion: Significantly differences were observed in biliary microbiota composition of hepatic steatosis group in comparison to the control group.



[OP-0521]

Dysregulation of the ESRP2-NF2-YAP axis in the pathogenesis of non-alcoholic fatty liver disease-associated hepatocellular carcinoma

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is an increasing risk factor for hepatocellular carcinoma (HCC). The mechanism of progression of NAFLD is not yet fully understood, hampering the development of effective treatments for NAFLD and NAFLD-associated HCC. Recently, it has been reported that the activity of neurofibromatosis type 2 (NF2), a tumor suppressor and upstream regulator of Hippo kinases, is controlled by epithelial splicing regulatory protein-2 (ESRP2) in hepatocytes. In both NAFLD and AFLD, ESRP2 is suppressed by pro-inflammatory cytokines, thus inactivating NF2 by skipping a specific exon that is critical for NF2 activity and function. This, in turn, promotes dephosphorylation and nuclear localization of YAP, a transcription co-activator of genes involved in cell proliferation and anti-apoptosis. Here, we aim to evaluate the expression and activity of the ESRP2-NF2-YAP axis in a mouse model of NAFLD-associated HCC.
Materials and Methods: Male C57BL/6 mice received a single low-dose streptozotocin on days 2–3 of age and were fed a high-fat diet from 4 weeks of age (the STAM model). Mouse- or human-derived liver cell lines and frozen liver tissues from HCC patients were also analyzed.
Results: STAM mice exhibited insulin resistance and developed non-alcoholic steatohepatitis (NASH) and HCC by the age of 20 weeks. The expression of ESRP2 decreased, NF2 splicing occurred, YAP translocated in hepatocyte nuclei, and the expression of YAP target genes was upregulated in livers of STAM mice. We also found that inactive NF2 splice variants were significantly enriched in HCC cell lines and tumor tissues of HCC patients.
Conclusion: Our findings suggest a potential role for the ESRP2-NF2-YAP axis in NAFLD progression to HCC, whereby loss of NF2 function allows for YAP activation that promotes neoplastic growth of hepatocytes.

[OP-0528]

The effect of hyperammonemia on steatohepatitis in mice fed with high fat diet

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Objectives: Recent studies have suggested the therapeutic potential of ammonia lowering drug in the treatment of nonalcoholic steatohepatitis (NASH). However, few studies have directly investigated the effect of high blood ammonia on liver injuries in NASH. This study aims to construct a chronic hyperammonemia mouse model and inquiry the effect of hyperammonemia on the phenotypes of NASH induced by the high-fat diet.
Materials and Methods: The NASH model was established by feeding C57B/L6 mice with the high-fat diet. Hyperammonemia was induced via intragastric administration of the ammonium chloride solution or liver-specific carbamoyl phosphate synthetase 1 (CPS1) knockdown performed using adeno-associated virus.
Results: Chronic hyperammonemia was successfully induced in NASH mice using both methods. Except for elevated plasma cholesterol and liver ammonia level, ammonium chloride has no obvious effect on hepatic histological changes as well as the level of plasma liver enzymes, hepatic lipids and the expression of various hepatic metabolism genes of NASH mice when compared with the controls. CPS1 knockdown also exerted no significant effect on characteristic histological changes of NASH in mice with high-fat diet. Compared with the control group, hepatic triglyceride and cholesterol level in CPS1 knockdown mice were significantly decreased. CPS1 knockdown upregulated the expression level of PPARα that involved in hepatic fatty acid oxidation, while down-regulated the expression of inflammation-related genes IL-6 and CCR2.
Conclusion: Hyperammonemia does not exacerbate steatohepatitis and liver injury of NASH mice. The mechanism of ammonia lowering drug for the treatment of NASH requires further study.

[OP-0531]

Ammonia scavenger restores liver and muscle injury in a mouse model of nonalcoholic steatohepatitis with sarcopenic obesity

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Objectives: Recent studies have revealed that sarcopenia is closely associated with obesity and nonalcoholic steatohepatitis (NASH). However, few attempted to explore the role of sarcopenic obesity in NASH. In this study, we investigated muscular alterations in a rodent NASH model to elucidate their intrinsic relations and explore the potential therapeutic target.

Materials and Methods: Forty-six 8-week-old and sixteen 42-week-old male C57B/L6 mice (defined as young and middle-aged mice, respectively) were fed with a high-fat diet (HFD) for 12 or 20 weeks. A subset of young mice was subjected to ammonia lowering treatment by L-ornithine L-aspartate (LOLA). Before sacrifice, body composition and muscle strength were evaluated by nuclear magnetic resonance and grip strength meter, respectively.
Results: At the end of the 12th week, all HFD-fed mice developed typical steatohepatitis. Meanwhile, sarcopenia occurred in HFD-fed middle-aged mice, whereas young mice only demonstrated decreased grip strength. Until the end of week 20, young mice in the HFD group exhibited significant sarcopenia and obesity phenotypes, including decreased lean body mass and grip strength, and increased body fat mass and percentage body fat. Additionally, Plasma ammonia level was markedly increased in HFD-fed mice of both ages at week 20. Plasma ammonia level was negatively associated with muscle strength and myofiber diameter in young mice. LOLA can significantly reduce plasma levels of ammonia, alanine aminotransaminase, aspartate aminotransaminase, and cholesterol in mice fed an HFD. Hepatic infiltration of inflammatory cells and collagen deposition area were significantly decreased in HFD group by LOLA treatment. Meanwhile, LOLA significantly increased lean body mass, grip strength, and average muscle fiber diameter of HFD-fed mice.
Conclusion: These findings suggest that the occurrence of NASH precedes sarcopenia in HFD mice, and the steatohepatitis-related hyperammonemia might contribute to the pathogenesis of sarcopenia. LOLA might be an effective drug for both steatohepatitis and sarcopenic obesity.

[PP-0578]

Efficacy of sodium glucose co-transporter 2 inhibitor on a progression of nonalcoholic steatohepatitis in a murine steatohepatitis model

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Objectives: It is unclear whether SGLT2 inhibition could exert a beneficial effect on nonalcoholic steatohepatitis (NASH)-associated liver fibrosis and hepatocellular carcinoma.
Materials and Methods: We examined the protective effect of SGLT2 inhibitor, empagliflozin, in a murine NASH model. The choline-deficient, amino acid-defined diet containing 58% fat by calories was formulated, and the diets were administered to 8-week-old male C57Bl/6 J mice for up to 24 weeks. A total of 21 mice were divided into two groups, the control group and the SGLT2 inhibitor group, and 35 mg/kg/day of empagliflozin was administered to the SGLT2 inhibitor group. Five animals in each group were treated for 12 weeks, and the remaining five in the control group and six in the SGLT2 inhibitor group were treated for 24 weeks.
Results: There was no significant difference in mean body weight between the control and treatment group after 12 weeks ($P = 0.65$). Laboratory findings, including serum aspartate transaminase, alanine transaminase, creatinine, glucose, and triglyceride, also showed no statistical differences between groups (all $P > 0.1$). When hepatic fibrosis was assess by Sirius red staining, the area of collagen deposition was smaller in the SGLT2 inhibitor group. Moreover, 12 weeks of SGLT2 inhibitor treatment downregulated the expression of various fibrosis-related proteins in the liver compared to the control, indicating that SGLT2 inhibitor treatment attenuated hepatic fibrosis. After 24 weeks, the inhibitory effect of SGLT2 inhibitor on hepatic fibrosis was consistently observed as downregulated fibrosis-related proteins. However, multiple hepatic tumors developed in both groups without significant differences in tumor number and size.
Conclusion: High fat-CDAA feeding in C57Bl/6 J mice was identified as a suitable model of NASH developing robust fibrosis and hepatic tumor within 24 weeks. SGLT2 inhibitor showed the potential to attenuate hepatic fibrosis in the progression of NASH, whereas administration of SGLT2 inhibitor alone was insufficient to suppress the development of hepatic tumors.

[PP-0628]

The HIOMT metabolite on the pathogenesis in high-fat diet NASH mouse model

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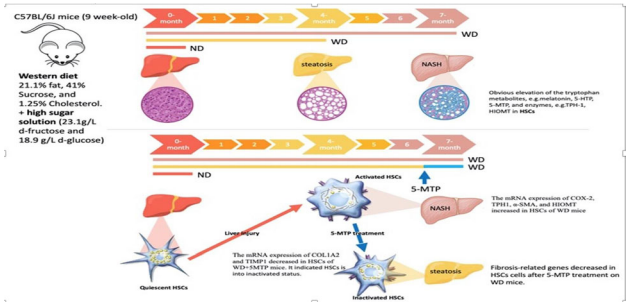
Objectives: 5-methoxytryptophan is a regulator of the inflammation and signaling in macrophages by cyclooxygenase-2 inhibition. 5-MTP expression in liver steatosis is unclear. This study used a high-fat diet mice to demonstrate 5-MTP attenuated the liver inflammatory and fibrosis by inactivating hepatic stellate cells.
Materials and Methods: C57BL/6 J mice were fed a normal chow diet and normal tap water or Western Diet. The mice developed human NAFLD's metabolic and histologic features for 4 months and human NASH's metabolic and histologic features for 7 months. 5-MTP given by IP 3 times/week at the 6 months for one month to identify 5-MTP effects on the severity of NAFLD and NASH.
Results: The serum concentration of the tryptophan metabolites decreased on the M7. The qPCR demonstrated high fold changes of HIOMT on the liver HSCs compared with hepatocyte and Kupffer cells. These results showed HIOMT played a critical role in tryptophan metabolism in hepatic inflammatory and fibrosis, and the reaction site was on HSC cells. Given 5-MTP for one month in WD mice, the inflammatory and fibrosis decreased in liver tissue. The fibrosis, lobar inflammation, and ballooning decreased after 5-MTP treatment. The immunofluorescence images showed the attenuation of COX-2 and α-SMA in liver tissue of WD + 5-MTP mice. These data confirmed 5-MTP attenuated the inflammatory and fibrosis in the NASH mice. The mRNA of COX-2, α-SMA, TPH1, and HIOMT increased in HSCs of WD mice and decreased in HSCs of

WD + 5-MTP mice. α-SMA decreased after 5-MTP given on the HSC cells of WD mice. The HSC activated genes, COL1A2 and TIMP1, increased on WD mice and reduced in HSCs of 5-MTP given WD mice. These data indicated 5-MTP inactivated HSC cells on WD-related NASH. The data confirmed 5-MTP attenuated inflammatory and fibrosis by inactivating HSCs.
Conclusion: 5-MTP attenuates the inflammatory and fibrosis in the NASH mouse model by inactivating HSC cells.



[OP-0664]

Peridroplet mitochondria are associated with the progression of NAFLD

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Objectives: Lipid droplets (LDs) can contact mitochondria to form peridroplet mitochondria (PDM) and regulate the function of mitochondria in brown adipose tissue. However, the role of PDM in non-alcoholic fatty liver disease (NAFLD) characterized by the abundance of LDs in hepatocytes is still unknown. In this study, we investigated whether there exist PDM in the steatotic liver of NAFLD mice, and the possible role of PDM in NAFLD.
Materials and Methods: C57BL/6 mice received methionine- and choline-deficient (MCD), choline-deficient, L-amino acid-defined (CDAA) and western diet (WD) to establish the model of NAFLD, respectively. The contact between LDs and mitochondria was observed by electron microscope and co-staining with LD and mitochondria. PDM and cytoplasmic mitochondria (CM) were isolated from the liver tissue based on the adherence to LDs, and the function of PDM and CM was detected. The expressions of Perilipin 5 which regulate the formation of PDM were also detected.
Results: Electron microscopic images of livers showed there are few LDs which do not contact with mitochondria in healthy liver. In NAFL liver, there are many LDs which always contact with mitochondria and form PDM. In NASH liver, there are few LDs and PDM, accompanying with significantly dilated endoplasmic reticulum. The mitochondria in the liver were divided into two groups by low-speed centrifugation. The upper fat layer were co-stained with LDs and mitochondria, confocal microscopy revealed that some LDs were surrounded by MitoViewTM Green-stained structure. PDM have enhanced mitochondrial function relative to CM. Perilipin 5 increased in the liver at the early stage of MCD diet induced NAFLD, and then decreased at the late stage of NAFLD.
Conclusion: PDM exist in the steatotic liver of NAFLD mice. PDM are negatively associated with the severity of NAFLD. The regulation of PDM may represent an attractive pharmacological target for NAFLD.

[PP-0665]

The evaluation of risk factors of metabolic syndrome and non-alcoholic fatty liver disease: the screening results of office workers in Almaty city

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Objectives: Assessment of metabolic syndrome and non-alcoholic fatty liver disease (NAFLD) risk factors in "conditionally" healthy young and middle aged individuals.
Materials and Methods: The cross-sectional study enrolled 447 office workers in Almaty, Kazakhstan. The study was carried out in 2 stages: (1) a questionnaire and physical examination to identify risk factors for NAFLD and metabolic syndrome (MS); (2) laboratory tests (cholesterol, LDL, HDL, glucose), and transient elastography with CAP (controlled attenuation parameter) modality for steatosis and fibrosis evaluation, in individuals with 2 or more risk factors obtained at the stage 1.
Results: Among 447 Almaty office workers studied, 2 or more factors of MS [overweight/obesity, arterial hypertension (AH), dyslipidemia, hyperglycemia/ type 2 diabetes mellitus] were identified in 113 individuals (25.3%). The most frequent risk factors were increased BMI (42.9%), waist circumference above normal (31.1%) and AH (16.4%). In those with 2 or more risk factors, the most frequent laboratory abnormalities were dyslipidemia (84%) followed by hyperglycemia (7.9%). Steatosis (by CAP modality) was diagnosed in 80.8% individuals: S0, S1, S2, S3 stages – in 19.1, 19.1, 31.9, 29.8%, respectively; liver fibrosis was diagnosed in 64% by transient elastography: F0, F1, F2, F3, F4 – in 17%, 63.8, 14.9, 21 and 2.1%, respectively. Regardless of the presence of risk factors, there were no differences in intensive physical activity in both groups; passive rest was predominant in the risk group (30%), and moderate physical activity—in the group without risk factors (walking—46%).
Conclusion: Risk factors of MS and NAFLD, including undiagnosed and severe cases, turned to be widespread, even among able-bodied relatively young individuals.

[PP-0679]

Gut microbiome signatures distinguish type 2 diabetes mellitus from non-alcoholic fatty liver disease

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Objectives: The identification of microbiome profiles that are specific to liver injury or impaired glucose metabolism may assist understanding of the role of the gut microbiota in the relationship between NAFLD and T2D.
Materials and Methods: We analyzed three independent Korean cohorts, with the aim of distinguishing the gut microbiomes of NAFLD and T2D. First, the 'Boramae NAFLD cohort' was recruited by the Seoul Metropolitan Government Seoul National University Boramae Medical Center in South Korea. Second, a validation T2D cohort was recruited from Chungnam National University Hospital. Finally, data from the healthy Korean twin cohort were obtained from ERP010289 and used for enterotyping.
Results: We identified Enterobacter, Romboutsia, and Clostridium sensu stricto as the principal taxa associated with the severity of NAFLD and T2D, whereas Ruminococcus and Megamonas were specific to NAFLD. In particular, the taxa that were associated with both severe liver pathology and T2D were also significantly associated with markers of diabetes, such as fasting blood glucose and Hb1Ac. Enterotype analysis demonstrated that participants with NAFLD had a significantly higher proportion of Bacteroides and a lower proportion of Ruminococcus than a Korean healthy twin cohort. However, T2D could not be clearly distinguished from NAFLD. Analysis of an independent T2D cohort permitted us to validate the T2D-specific bacterial signature identified in the NAFLD cohort. Functional inference analysis revealed that endotoxin biosynthesis pathways were significantly enriched in participants with NAFLD and T2D, compared with those with NAFLD alone.
Conclusion: These findings may assist with the development of effective therapeutic approaches for metabolic diseases that are associated with specific bacterial signatures.

[OP-0750]

Dipeptidyl peptidase-IV inhibitor and antioxidant properties from phenolic rich fraction of Allium sativum improve non-alcoholic fatty liver disease in type 2 diabetic mellitus

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease worldwide, affecting up to more than half of these patients have type 2 diabetes mellitus (T2DM) through Insulin resistance which is aggravated by oxidative stress and aberrant inflammatory signals. Novel approach for treatment of T2DM is based on incretin hormone, glucagon-like-peptide 1 (GLP-1). Dipeptidyl peptidase-IV (DPP-IV) inhibitors from phenolic rich fraction of Allium sativum might have the pleiotropic effect because incretin hormones receptor present on various tissues, including liver. We examined whether DPP-IV inhibitors with antioxidant capacity affects NAFLD in T2DM rat model.
Materials and Methods: T2DM model was induced in Wistar rats with high sucrose diet along with dexamethasone. Biochemical, toxicology and histological variable were evaluated between all groups. Apart from serum DPP-IV inhibition, glycosylated hemoglobin, HOMA-IR, hepatic lipid peroxidation, SGOT, SGPT and endogenous antioxidant in tissue were measured with serum lipid profiles to correlate with antiperoxidative effects of phenolic rich fraction of Allim sativum.
Results: Diabetes induction by corticosteroid and high sucrose diet confirmed by HOMA-IR = 2.5%, HOMA β % = 36.3% and HOMA sensitivity = 44.3%. Consequently, in-vitro assay of DPP-IV inhibition has showed 63.1 ± 2.8% % and activity in serum observed 41.9 ± 1.3%. DPP-IV inhibitor reduced the level of aminotransferases i.e. SGOT & SGPT and alkaline phosphatase with increasing the level of insulin and decrease HbA1c. Triglyceride and cholesterol level also significantly in the normal range as compared to control group. Allim sativum extract has shown a better antioxidant capacity to protect lipid peroxidation and histoarchitectural of liver also relevant good result after treatment of DPP-IV inhibitor.
Conclusion: DPP-IV inhibitors along with antioxidant properties improve insulin sensitivity, reduce oxidative stress and toxicity which lead to improve the liver dysfunction in T2DM.These findings also suggest that GLP-1 in the liver has beneficial effects on NAFLD.

[OP-0756]

Metabolic risk factor for progression of liver fibrosis and hepatic steatosis, a five year follow up

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Objectives: The objective of this study is to evaluate the risk of metabolic factors in progression of liver steatosis and liver fibrosis.
Materials and Methods: Evaluation of metabolic parameters and transient elastography of 292 patients diagnosed to have NAFLD by ultrasound were followed up for 5 years. The evaluation was performed at baseline, yearly thereafter and for 5 years. Metabolic factors (LDL level, triglyceride level, and HBa1C levels) was analyzed including BMI, concomitant Hypertension and Diabetes were correlated with transient elastography. Pearson's correlation coefficient was used to interpret the outcome.
Results: Of the two hundred ninety two patients the average age is 51 (± 11), mostly female (55.3%) with resulting average baseline BMI of 27.3. The correlation of BMI in CAP score is significant ($p = 0.0005$) but not with liver stiffness ($p = 0.4571$). The correlation between Low Density Level, Triglyceride level and Hypertension with liver stiffness ($p = 0.70$, $p = 0.57$, $p = 0.28$, respectively) and CAP score ($p = 0.73$, $p = 0.07$, $p = 0.27$ respectively) is not significant. However, occurrence of Diabetes Mellitus was significantly correlated with liver stiffness ($p = 0.05$) but not with CAP score ($p = 0.55$). Finally, HBa1C levels are not significantly correlated with CAP score ($p = 0.18$) and liver stiffness ($p = 0.27$).
Conclusion: Among patients with NAFLD, BMI was directly correlated with hepatic steatosis but not with liver fibrosis. Control of hypertension, LDL and triglyceride levels have no direct correlation with CAP score and liver stiffness. The occurrence of Diabetes Mellitus correlated with progression of liver stiffness but control of Diabetes Mellitus did not correlate with CAP score and liver stiffness. This suggests that the duration rather than the control of Diabetes Mellitus is a key metabolic factor for progression of liver fibrosis.

[OP-0767]

Gut microbiota-derived metabolomic signatures in non-alcoholic liver disease

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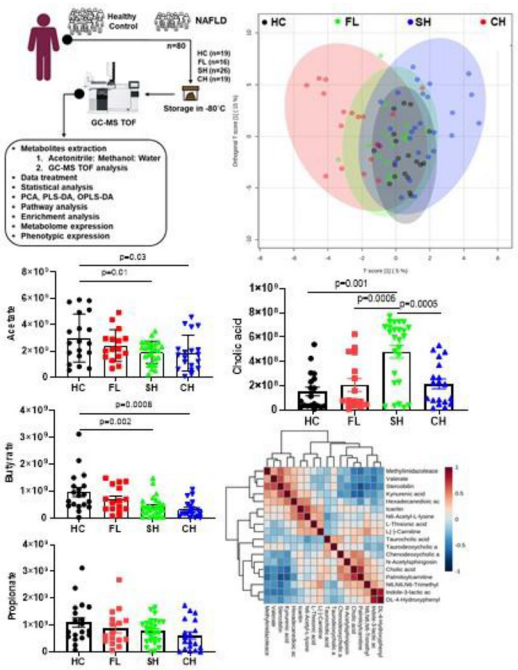
Objectives: Non-invasive microbiota-derived metabolites play crucial role in the pathophysiology of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), especially patients with decompensated cirrhosis. The gut microbiota and its metabolites represent a niche for the diagnosis of NAFLD. We aimed to identify gut microbiota-derived metabolomic signatures which are related to the progression of NAFLD.
Materials and Methods: We analyzed the stool metabolomes and untargeted metabolomics based on clinical parameters of 80 patients [Fatty liver (FL: n = 16); steatohepatitis (SH: n = 26); cirrhosis (CH: n = 19) and healthy control (HC: n = 19)]. Metabolomics analysis was performed by using GC-TOF–MS and LC–MS.
Results: 103 untargeted metabolites are quantified. Metabolic discrimination of FL, SH, and CH were assessed in principle component analysis. Short chain fatty acids (SCFA) such as acetate, p = 0.03; butyrate, p = 0.0008; and propionate levels were significantly reduced in among NAFLD patients. The stool cholic acid (p = 0.001) level was significantly increased in NAFLD. In among SH and CH, the palmitoylcarnitine and L-carnitine were significantly amplified. These metabolites phenotypic risk was related to higher β-oxidation levels. Correlation coefficient of significant metabolites has analyzed. Fold value of sitagliptin has increased in FL and CH than SH. The stercobilin and kynurenic acid were relatively down-regulated in stool NAFLD. 3-indole propionic acid (3-IPA, p = 0.001) was significantly down-regulated in SH and CH. Curiously, 3-IPA was increased in FL. Another indole-associated microbial metabolite was perplexed in NAFLD. Microbial metabolites in stool that are produced as results of host and microbe verity in NAFLD. In brief, microbiota-SCFA signaling to reverse the reduction of acetic acid (p = 0.01, SH and p = 0.03, CH) and propionic acid in NAFLD. Microbial metabolites were highly effective in treatments and prevention of NAFLD/NASH.
Conclusion: The association of microbiome and its metabolites phenotype that amino acids, fatty acids, and several metabolites suggest a novel microbial metabolome in FL, SH, and CH metabolic pathway influencing in NAFLD/NASH.



[OP-0840]

Comparison of diagnostic efficacy acoustic radiation force impulse and other non-invasive methods proven by liver biopsy in patients with nonalcoholic fatty liver disease

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Objectives: Acoustic Radiation Force Impulse (ARFI) is a noninvasive method to assess liver fibrosis by measuring stiffness. This study was conducted to assess the accuracy of ARFI in NAFLD patients, in comparison with NAFLD score, FIB-4, APRI, by using liver biopsy as the reference standard.
Materials and Methods: We enrolled 144 patients (mean age [± SD], 46.4 ± 14.0; 52.78% male; body mass index (kg/m^2) [± SD], 29.3 ± 3.89). The AUROC for the corresponding measures of stiffness were calculated and fibrosis (Metavir score) was used as the outcome measure. Fibrosis defined F2-F4 as significant and F3-F4 as advanced.
Results: The AUROC with ARFI score, NAFLD score, FIB-4 and APRI in significant fibrosis were 0.706, 0.680, 0.746, 0.776 and advanced fibrosis were 0.743, 0.701, 0.772, 0.815, respectively. Based on the NAFLD activity score, the group was divided into 2: The one is 4 or less and the other is 5 or more. The AUROC values (95% CI) with ARFI score, NAFLD score, FIB-4 and APRI in advanced fibrosis, the one was 0.923, 0.712, 0.769, 0.707 and the other were 0.705, 0.713, 0.759, 0.741, respectively. The difference in ARFI between the two groups classified based on NAS was statistically significant (p value = 0.010), but there was no statistical difference in the comparison of ARFI classified based on BMI 30.
Conclusion: The diagnostic predictive value of ARFI increased as fibrosis progressed, but it did not show a superior trend compared to other non-invasive methods. And the NAS system was classified into two groups based on 5 points, ARFI showed high diagnostic predictability in the low score group. ARFI has a moderate predictive value in all diagnostic classifications in this study, but has low accuracy when accompanied by inflammation or steatosis. In addition, it is not superior to other non-invasive methods and has limitations in replacing it with liver biopsy.

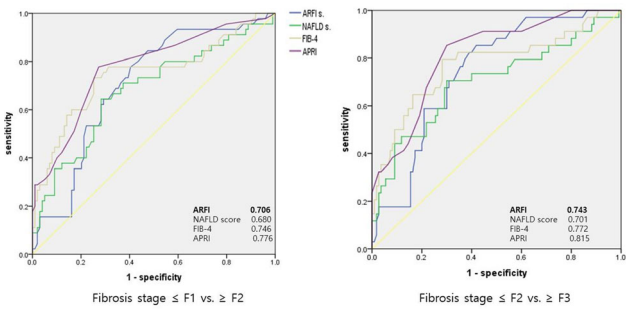

Fig 1. Diagnosis accuracy according to fibrosis stage in NAFLD patients using AUROC

[PP-0841]

Mechanism of imbalanced autophagy paradox mediated by ceramide in nonalcoholic steatohepatitis

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Objectives: Ceramides play important roles in multiple biological processes, which are known to be closely linked to the pathogenesis of nonalcoholic steatohepatitis (NASH). Here we aimed to identifying the mechanism of autophagic regulation by ceramide in NASH.
Materials and Methods: Sprague Dawley rats were randomly divided into three groups: standard chow, high-fat diet and HFD + myriocin. Lipidomics and transcriptomics were performed using liver samples to probe differentially expressed ceramides and autophagy associated genes. Western blots were performed to confirm the identified genes and corresponding proteins. Palmitic acid stimulated HepG2 cells were incubated with or without myriocin to test the impact of ceramide synthesis inhibition on autophagic flux.
Results: Myriocin not only reversed the elevated body weight and serum transaminases but also attenuated dyslipidemia and liver pathology in HFD group. Hepatic expression of multiple genes involved in fatty acid metabolism were found significantly altered in HFD-fed rat when compared with standard group, but corrected in HFD + myriocin group. Among 1590 differentially expression genes (DEGs) identified in HFD group (vs. standard chow, 363 up-regulated and 1227 down-regulated) and 634 DEGs identified in HFD + myriocin group (vs. HFD, 520 up-regulated and 114 down-regulated), the alterations of genes involved in protective autophagy or lethal autophagy were found correlated with NASH phenotypes in rats but were later recovered by ceramide inhibition. The ability of myriocin to restore the impaired hepatic autophagy function in rats with HFD-induced NASH was further confirmed by Western blots using rat liver homogenates. Inhibition of ceramide by myriocin reduced the level of the inflammatory factor, up-regulated cytoprotective autophagic flux increased and lethal autophagic flux reduced, which were verified in HepG2 cells in vitro experiments.
Conclusion: The disturbed autophagic balance serve as an important pathogenic mechanism of NASH and the inhibition of ceremide synthesis by myriocin could specifically predispose liver to protective autophagy against lethal autophagy.

[OP-0844]

Kimchi had a protective interaction with PNPLA3 risk allele against NAFLD development: the Korean Genome and Epidemiology Study (KoGES)

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Objectives: Genetic studies of NAFLD suggested the PNPLA3 as the major candidate gene. We tested the interaction between the PNPLA3 rs738409 genotype and dietary factors using a large Korean cohort.
Materials and Methods: NAFLD can be diagnosed when the individuals have a historical medical record of fatty liver disease without alcohol overdrinking. For each nutrient, daily intake above the recommended daily value was defined as high intake. We performed GWAS in our KoGES City cohort to identify influences of dietary factors in PNPLA3 rs738409 risk allele.
Results: From the subjects with 2,950 NAFLD and 12,907 control cases, PNPLA3 rs738409 G allele showed a significant association with NAFLD in all model analyses (OR of additive model = 1.22; $p = 1.96 \times 10^{-10}$). For the nutritional impact on NAFLD, high intake of protein decreased the risk of NALFD, while high intake of carbohydrate increased risk. In mineral, significantly more healthy control subjects had high intake of sodium ($p = 0.003$) and vitamin B than those in NAFLD group. Further the interaction between nutrients and PNPLA3 genotype was analyzed, and then only high intake of sodium had statistically significant protective interaction with PNPLA3 genotype against NAFLD development ($p = 0.002$). The association between food intake and PNPLA3 genotype was investigated. In the PNPLA3 risk allele group (GG + GC), baechu kimchi and green pepper were protective foods against NAFLD (all $p < 0.05$). Among these, baechu kimchi had statistically significant protective interaction with PNPLA3 genotype on NAFLD ($p = 0.012$). Based on these analyses, we concluded that effect of high sodium intake on NAFLD prevention is probably derived from the intake of baechu kimchi.
Conclusion: We can find significant association between PNPLA3 - gene and NAFLD among Korean population database. Further, we discovered that dietary factors can significantly influence development of NAFLD, and those factors even have interactions with PNPLA3.

2-2. NAFLD case frequencies by food habit in the PNPLA3 risk group

Food	Total			High			Low				
	NAFLD	NORMAL	Case %	NAFLD	NORMAL	Case%	NAFLD	NORMAL	Case%	Odd ratio	P
쌀밥	2097	8459	19.87%	333	1876	15.07%	1764	6583	21.13%	0.774	0.001
배추김치	1918	7832	19.67%	1713	7287	19.03%	205	545	27.33%	0.685	<0.0001
풋고추	1737	6869	20.18%	303	1234	19.71%	1434	5635	20.29%	0.783	0.003
커피	1970	8058	19.64%	1352	6322	17.62%	618	1736	26.25%	0.666	<0.0001
차에넣는설탕	1985	8098	19.69%	1057	4934	17.64%	928	3164	22.68%	0.72	<0.0001
차에넣는프림	2012	8141	19.82%	888	4236	17.33%	1124	3905	22.35%	0.746	<0.0001
오렌지	1890	7499	20.13%	185	863	17.65%	1705	6636	20.44%	0.835	0.063
과김치갓김치	1989	8060	19.79%	147	631	18.89%	1842	7429	19.87%	0.706	0.001
딸기	1768	6994	20.18%	285	1173	19.55%	1483	5821	20.30%	0.911	0.258
배	1849	7360	20.08%	258	1096	19.05%	1591	6264	20.25%	0.892	0.182
잡곡밥	2096	8450	19.87%	1173	4185	21.89%	923	4265	17.79%	1.191	0.002
요구르트요플레	1932	7671	20.12%	350	1136	23.55%	1582	6535	19.49%	1.194	0.023
땅콩아몬드잣	1993	8135	19.68%	125	346	26.54%	1868	7789	19.34%	1.352	0.014
무단무지	1965	7885	19.95%	134	485	21.65%	1831	7400	19.84%	1.188	0.142
야채샐러드	1944	7771	20.01%	101	326	23.65%	1843	7445	19.84%	1.297	0.061
녹차	1939	7843	19.82%	394	1620	19.56%	1545	6223	19.89%	1.056	0.456
튀김(집밖)	2019	8262	19.64%	611	2839	17.71%	1408	5423	20.61%	1.21	0.002
튀김(집안)	2024	8257	19.69%	572	2447	18.95%	1452	5810	19.99%	1.26	<0.0001

(COV.: AGE, SEX, SMOKE, DRINK, BMI)

[PP-0936]

Premorbid steatohepatitis facilitates the seriousness of dextran sulfate sodium-induced ulcerative colitis in mouse

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Objectives: The concurrence of nonalcoholic steatohepatitis (NASH) and ulcerative colitis (UC) has been increasingly recognized in clinical practice, but the underlying mechanisms remain unclear. The current study aimed to develop a mouse model mimicking the phenomenon by incorporating high-fat high-cholesterol diet (HFHCD) induced NASH and dextran sulfate sodium (DSS) induced UC, paving the way for further mechanistic studies.
Materials and Methods: Male C57BL/6 mice were randomly assigned to two groups receiving either chow diet or HFHCD for the 12-week NASH modeling. Then mice were further divided into 4 subgroups for UC modeling, (1) Control: chow diet with normal drinking water; (2) Colitis: chow with 2% DSS in drinking water; (3)

Steatohepatitis: HFHCD with normal drinking water; and (4) Steatohepatitis + Colitis: HFHCD with 2% DSS in drinking water.
Results: The combination of NASH and UC showed marked mortality (58.3%), while neither NASH nor UC modeling was found fatal. Although DSS-induced colitis did not exacerbate histological liver injury in HFHCD fed mice, premorbid NASH significantly increased UC related gut injury compared with UC group alone, supported by remarkably shorter colon, more colonic congestion and higher histopathological score ($p < 0.05$). Inflammatory (TNFα, IL-1β, CCl2, and NFκB) and apoptotic (Bcl2, Bad, Bim, and Bax) signaling pathways were found significantly altered in distal colon tissues collected from the Steatohepatitis + Colitis mice, when compared with other experimental groups.
Conclusion: Premorbid steatohepatitis could markedly aggravate DSS-induced colitis and bring about a lethal phenotype. Potential links between NASH and UC pathogeneses could be explored using the proposed model.

[PP-0951]

Multi-omics analysis revealed the role of gut-liver-muscle axis in non-alcoholic steatohepatitis and the therapeutic effects of probiotics

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Objectives: Molecular mechanisms of NSAH remain poorly understood and probiotic therapy may serve as a promising management approach. This study aimed to probe the underlying mechanisms of NASH development and therapeutic effects of probiotics in a murine model.
Materials and Methods: 30 male C57BL/6 mice were randomly divided into 3 groups and modeling for 12 weeks: (1) Standard chow, (2) High fat high cholesterol diet (HFHCD), and (3) HFHCD + probiotics (a mixture of Lactobacillus acidophilus, Bifidobacterium, Enterococcus faecalis, and Bacillus cereus, 10^9 CFU/day orally administration). 16 s rDNA sequencing, transcriptomics and metabolomics were performed using liver, colon and skeletal muscle samples.
Results: Morphological, serological and histological features of HFHCD-induced NASH could be restored by treatment of probiotics. NASH modeling significantly reduced the diversity and equitability of gut microbiota (5.546 vs. 3.79, $p < 0.001$), which was reversed by probiotics (3.79 vs. 4.592, $p < 0.05$). Multi-omics study identified dysregulated mRNAs and metabolites in colons (810 metabolites and 1332 mRNAs), livers (2202 metabolites and 1766 mRNAs), and skeletal muscles (1580 metabolites and 1611 mRNAs) of HFHCD group and in corresponding tissues (428 metabolites and 882 mRNAs in colon, 938 metabolites and 1095 mRNAs in liver, and 1284 metabolites and 1417 mRNAs in muscle) collected from HFHCD + probiotics group. There were 436 overlapped differentially expressed metabolites between HFHCD (vs. standard chow) and HFHCD + probiotics (vs. HFHCD) in mouse liver, 91 in colon and 641 in skeletal muscle, among which 486 metabolites (310 in liver, 79 in colon and 97 in muscle) showed opposite changing trend between two cohorts. These metabolites may be associated with the therapeutic effects of probiotics and serve as the key players in NASH development.
Conclusion: Our data delineate an integrated multi-omics profile of Gut-Liver-Muscle axis in HFHCD induced NASH, which may help uncover the molecular basis of NASH pathogenesis and offer novel therapeutic insights, such as probiotic therapy.

[OP-0956]

Utilization of community-based health centers (Puskesmas) to improve accessibility of health services for liver patients

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Objectives: Liver disease is the fifth most prominent cause of death for the elderly in Indonesia and is 3.3 times more likely to cause death with the Sars-Cov2 virus. Fatty liver progression is very gradual and new cases are known after an advanced stage. Utilizing Community-Based Health Centers (Puskesmas) that provide sub-district-based integrated services, is expected to be early detection for liver disease. However, little is known about the effectiveness of Puskesmas in the framework of controlling liver disease.
Materials and Methods: We utilize a longitudinal survey dataset from the 2014 Indonesia Family Life Survey to analyze and evaluate the effectiveness of the Puskesmas in improving the function of early liver disease detection.
Results: The analysis shows that the liver disease prevalence among observations is 1,9%. However, the percentage increases in senior citizens by two times or 3,8%, and 60% are men. The elderly with liver disease, whether they have government social insurance or not, tend to access treatment at the Puskesmas. Given that Indonesia uses the Gate-Keeper system, the first-level health facilities are at the sub-district or community level. Posyandu Lansia, as an extension of Puskesmas, is also utilized by older people for routine health checks, obtaining food/supplements, and various meetings and counseling. The Posyandu Lansia is also a space for the elderly to access savings and loan financial services, religious activities, and political activities. Community-based health care is highly effective in improving the senior QoL in various aspects of life. However, 56% of older people who do not have insurance prefer traditional practitioners.
Conclusion: The Posyandu Lansia can be a forum that carries out early detection of liver disease and is very accessible in preventive programs and improving the elderly QoL through various health activities, hobbies, counseling, economics, religion, and politics. It also needs to address the covered social insurance for treatment and caregiver.

[OP-0986]

miR-4449 regulates NASH-fibrosis via TAZ signaling

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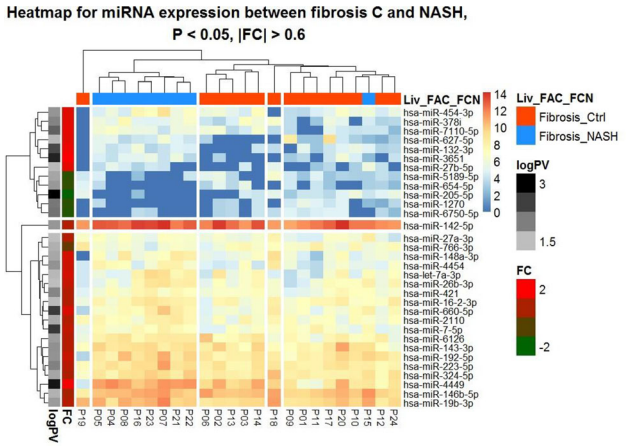
Objectives: Nonalcoholic fatty liver disease (NAFLD) is chronic and progressive liver disease with high prevalence of about 30% of the

general population. Nonalcoholic steatohepatitis (NASH) account for 20%–25% of NAFLD patients, and NASH with hepatic fibrosis has poor prognosis compared with nonalcoholic fatty liver (NAFL) or NASH without hepatic fibrosis. In this study, we aimed to analyze the regulation of TAZ by miR-4449 during NASH-fibrosis progression.
Materials and Methods: Small RNA sequencing was performed using seral from patients with 24 NAFLD patients. SH patients, and the miRNA expression was compared. To induce in vitro lipotoxicity in hepatocytes, HepG2 were treated with palmitic acids (PA). We transfected miR-4449 mimic or inhibitor into HepG2 cells to explore the effect of miR-4449.
Results: Among 24 NAFLD patients, 14 patients were NAFL or NASH without fibrosis, whereas 9 patients were NASH with fibrosis. NASH with fibrosis patients were older (59 years vs. 46 years, $P < 0.001$) and had lower BMI (28.23 kg/m^2 vs. 31.19 kg/m^2, $P = 0.032$) than NAFL or NASH without fibrosis. NASH group showed higher prevalence of diabetes/impaired fasting glucose, hypertension, and dyslipidemia. 31 miRNAs showed significant difference between two groups. Among them, we selected miR-4449 for further experiments due to their abundant expression in NASH-fibrosis group. PA treatment induced inverse expression pattern of miR-4449 between supernatant and hepatocytes. miR-4449 expression significantly increased in supernatant from PA-treated hepatocytes comparing with that from vehicle-treated hepatocytes. In contrast, expression of miR-4449 significantly decreased in PA-treated hepatocytes comparing with vehicle-treated hepatocytes. miR4449 overexpression blocks TAZ expression, and interfering miR4449 increased TAZ expression.
Conclusion: Expression of miR-4449 increased in NASH-fibrosis patients and miR-4449 regulate TAZ expression in hepatocytes during lipotoxicity. miR-4449 could be used for novel therapeutic target of NASH-fibrosis.



[OP-0991]

Are fatty liver patients who initially fail to meet metabolic associated fatty liver disease criteria part of its spectrum?

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Objectives: The recent change in diagnostic criteria for fatty liver disease has resulted in changes in epidemiology. We aimed to compare the clinical, biochemical, and metabolic differences among patients with fatty liver who met either nonalcoholic (non-MAFLD NAFLD) or metabolic associated fatty liver (non-NAFLD MAFLD) alone, or both (NAFLD/MAFLD), or none (non-NAFLD/MAFLD), and to report on the incidence of non-MAFLD patients eventually meeting MAFLD criteria on follow-up.
Materials and Methods: Consecutive patients with fatty liver on ultrasound from March 2007 to July 2017 were included. Only patients who had at least 2 follow-up visits were included in determining the incidence of non-MAFLD NAFLD and non-NAFLD/MAFLD patients progressing to MAFLD.
Results: The distribution of patients was 3.9% (N = 26) non-NAFLD/MAFLD, 7.8% (N = 52) non-MAFLD NAFLD, 74.5% (N = 494) NAFLD/MAFLD, and 13.7% (N = 91) non-NAFLD MAFLD. All patients in the non-NAFLD MAFLD and non-NAFLD/MAFLD groups had HBsAg positivity. As expected, NAFLD/MAFLD and non-NAFLD MAFLD patients were more likely to be hypertensive, with dyslipidemia and cardiovascular/cerebrovascular diseases, and to have higher alanine aminotransferase (ALT) levels compared to the other 2 groups ($p < 0.05$). NAFLD/MAFLD patients were more likely to be older and to have higher total cholesterol, triglyceride levels and NAFLD fibrosis score compared to the other groups. After a median follow-up of 39.6 weeks, 4.8% (1/21) and 21.9% (7/32) of eligible non-NAFLD/MAFLD and non-MAFLD NAFLD patients eventually satisfied MAFLD criteria. These patients were more likely to have baseline cirrhosis (50% vs. 4.4%; $p = 0.003$), older (63.3 vs. 50; $p = 0.007$) and have higher creatinine (1.1 vs. 0.8 mg/dL; $p = 0.002$) compared to patients who did not meet MAFLD criteria.
Conclusion: Majority of fatty liver patients met both NAFLD and MAFLD criteria. Our data shows that fatty liver patients who do not meet MAFLD criteria initially, especially HBsAg negative patients, need close monitoring of risk factors because a fifth will eventually meet MAFLD criteria.

[OP-1006]

Proteomic identification of adipocyte proteins involved in the pathogenesis of MAFLD

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Objectives: Metabolic dysfunction-associated fatty liver disease (MAFLD) is now the most common liver disease globally. Growing evidence suggests that adipose tissue dysfunction plays a role in hepatic injury in MAFLD. There is emerging evidence that altered secretion of adipokines secondary to iron accumulation in adipocytes contributes to MAFLD. This study determined the effect of iron and hepcidin, a master regulator of iron, on adipocytes and how this interaction might play a role in MAFLD pathogenesis.
Materials and Methods: 3T3 L1 MBX cells were differentiated into adipocytes prior to treatment with ferric ammonium citrate (FAC) and hepcidin. Adipokines and inflammatory genes were analysed by qRT-PCR. Filter -Aided sample preparation (FASP) was used to process protein samples for proteomics. Expression of differentially expressed (DE) proteins was analysed by qRT-PCR and Western blot.
Results: FAC and hepcidin treatment of adipocytes downregulated protective adipokines adiponectin, leptin, and Pparγ. There was upregulation of inflammatory genes Mcp-1, Il6 in both treatments. Proteomics analysis of FAC and hepcidin treated adipocytes showed

that 423 and163 proteins, respectively, were DE and of these 109 were common to both FAC and hepcidin. Tagln-2 was upregulated in both FAC and hepcidin treated adipocytes with a log2 foldchange of 1.16 and 1.85 respectively ($p < 0.00005$). Additionally, Capg was also upregulated in both FAC and hepcidin treated adipocytes with a log2 foldchange of 1.36 and 1.33 respectively ($p < 0.00005$). RT-PCR and western blot analyses also showed that Tagln-2 and Capg were upregulated in both treatments.
Conclusion: FAC and hepcidin treatment of adipocytes resulted in reduction of protective genes, adiponectin, leptin and Pparγ, and upregulation of inflammatory genes Mcp-1, Il6. Proteomics has identified adipocyte proteins that could be involved in MAFLD including Transgelin-2 and Macrophage-capping protein. Future mechanistic work on these proteins will further define the effect of iron on adipocytes, this may further clarify the role adipocytes play in MAFLD progression.

[PP-1078]

Distinct gut microbial community differentially characterizes patients with non-alcoholic fatty liver disease

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Objectives: Discordant reports of signature gut microbes in non-alcoholic fatty liver disease (NAFLD) due to bacterial responsiveness to spectrum of hepatic pathophysiology hampered developing diagnosis and understanding pathogenesis using gut microbiome. Thus, we aimed to investigate diagnostic factors and potential mechanisms for heterogenous NAFLD using gut environment including microbes and functional pathways.
Materials and Methods: Stools from 16 biopsy-proven NAFLD patients were analyzed for bacterial taxonomy and functional pathway based upon 16 s rRNA gene sequencing. Data from physical exam, serum biochemistry and gut environment were subjected to decision tree classifier to discover diagnostic markers, followed by being correlated with functional pathways.
Results: Diversity of gut microbial composition revealed two NAFLD subpopulations; NAFLD with similar or different gut microbial composition to healthy control (HC), defined as $P_{HC\text{-}like}$ and P, respectively. Stools of $P_{HC\text{-}like}$ were significantly populated with Enterobacteriaceae, and inferred to be enriched with metabolites degraded from dicarboxylic acid sugars, while colonization of Prevotella were significantly observed in stools of P in parallel with enrichment of metabolites from Heme b biosynthesis and sulfate reduction. As potential mechanism, we suggest that protoporphyrin IX and/or protoheme from the Prevotella participates in hepatic injury, and endogenous hydrogen sulfide induces serum IL-6 in P. On the other hand, endotoxin-producing Enterobacteriaceae is reasoned to produce glycerate, resulting in peroxisome proliferator activated receptor-alpha-mediated decrease of IL-6 and induction of fat accumulation in $P_{HC\text{-}like}$.
Conclusion: Heterogenous NAFLD populations defined by gut microbial composition revealed potential pathogenic mechanism that raises the possibility to use personalized treatment for NALFD patients.

[PP-1165]

Identification of intrahepatic microRNAs expression in non-B, non-C hepatocellular carcinoma

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Objectives: It has been shown that microRNAs (miRNAs), a class of non-coding molecules, play a crucial role in pathogenesis of many cancer types including hepatocellular carcinoma (HCC). The purpose of this study was to examine the expression profiles of miRNAs in non-B, non-C HCC (NBNC-HCC).
Materials and Methods: Liver tissue specimens obtained from patients with NBNC-HCC undergoing surgical resection were recruited. All these patients had early stages (BCLC stage 0 or A) and did not receive any therapy for HCC before collecting the samples. The expression profiles of miRNAs in paired tumorous and adjacent tissues were assessed by NanoString quantitative platform. Candidate miRNAs were selected if their differential expression in cancerous and non-cancerous tissues were more than 2-folds.
Results: Based on the Nanostring platform, the expression levels of 800 miRNAs were obtained. A volcano plot demonstrated that several miRNAs were significantly differentially expressed in cancerous and non-cancerous tissues. After filtering, the top 4 candidate miRNAs, were identified. Among these, hsa-miR-181a-5p, hsa-miR-6721-5p and hsa-miR-1183 were up-regulated expressed, while hsa-miR-519c-3p was shown to have down-regulated expression in cancerous tissues.
Conclusion: These results revealed that several miRNAs were differentially expressed in cancerous compared with paired adjacent non-cancerous liver tissues. Further validation of these candidate miRNAs in serum samples are needed to elucidate whether there is any clinical benefit for the diagnosis and prognostic prediction in patients with NBNC-HCC.

[L-OP-1256]

The saga of an outlier: Lean nonalcoholic fatty liver disease in urban, population of Karachi, Pakistan

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Objectives: Lean NAFLD is unique wherein the absence of obesity and unrecognized traditional risk factors, diagnosis is either get delayed or even overlooked; hence resulting in compromised effectiveness or complete absence of required treatment. We aim to investigate the prevalence of lean NAFLD and to compare the clinical, metabolic characteristics of lean and obese NAFLD in the urban, adult population of Karachi, Pakistan.
Materials and Methods: This was a population-based cross-sectional study piggybacked with a large community-based trial "Pakistan Diabetes Prevention Programme" conducted in collaboration with the University of Helsinki in "Karachi", Pakistan during 2013–2016.

Approximately 20,000 residents of Karachi were screened for diabetes using systematic sampling. Individuals aged 35–75 years, having Indian Diabetes Risk Score (IDRs) score ≥ 60 were enrolled. Ultrasound liver was performed by an experienced sonologist to identify NAFLD. Anthropometric measurements, laboratory investigations were carried out. Lean NAFLD was defined if BMI was < 25 kg/m^2. Obese NAFLD is defined if BMI was ≥ 25 kg/m^2. The study was funded by IDF) and URC, AKUH, Pakistan.

Results: Out of 1225 individuals 741 (60.5%) had NAFLD. Lean NAFLD was found in 128 (17.2%). Comparing lean NAFLD with obese NAFLD higher proportion of males, smaller waist circumferences, and lower ranges of metabolic factors were found in lean NAFLD (Table 1). The risk estimates for lean NAFLD were higher among smokers, subjects having larger waist circumference, HTN, elevated LDL, and ALT (Table 2).

Conclusion: Lean NAFLD is common in the South Asian urban community of Pakistan. In the absence of significant metabolic derangements, early detection of lean NAFLD is challenging.

Table 1: Clinical and Metabolic characteristics of Lean vs. obese NAFLD

	Lean NAFLD(n=128)	Obese NAFLD(n=593)	p value
Age (in years)	45.6 ± 10.3	44.6 ± 8.7	0.29
Gender Male Female	**60(46.9)** 68(53.1)	175(29.5) 418(70.5)	**<0.001**
Group Normal IGT and DM	53(41.4) 75(58.6)	159(26.8) **434(73.2)**	**0.001**
Waist circumference (cm) Normal ≥90 men and ≥80 women	29(22.7) 99(77.3)	15(2.5) **578(97.5)**	**<0.001**
Waist circumference (cm)	89.9 ± 10.8	**102.7 ± 10.7**	**<0.001**
Waist to hip ratio	0.95 ± 0.09	0.94 ± 0.08	0.35
Severity of NAFLD I II III	90(70.3) 36(28.1) 2(1.6)	327(55.2) **239(40.4)** **26(4.4)**	**0.005**
History of HTN	53(25.8)	**254(42.8)**	**<0.001**
History of antihypertensives	22(17.2)	**188(31.7)**	**0.001**
History of impaired blood sugar	**35(27.3)**	107(18)	**0.01**
History of dyslipidemia	23(18)	**167(28.2)**	**0.01**
Any metabolic illness in family	98(76.6)	490(82.6)	0.10
Family history of DM	65(50.8)	307(51.8)	0.83
Family history of BP	63(49.2)	323(54.5)	0.28
Family history of cholesterol	22(17.2)	121(20.4)	0.40
Family history of obesity	28(21.9)	**235(39.6)**	**<0.001**
Family history of IHD	32(25)	**207(34.9)**	**0.03**
Smoker	**18(14.1)**	43(7.3)	**0.01**
HTN Normal 120 139 systolic or 80 89 mmHg diastolic >140 Systolic or >90 mmHg diastolic	61(47.7) 48(37.5) 19(14.8)	201(33.9) **260(43.8)** **132(22.3)**	**0.01**
Systolic blood pressure	121.1 ± 17.9	**125.6 ± 19.9**	**0.01**
Diastolic BP	71.7 ± 9.8	**74.4 ± 11.3**	**0.007**
FBS	114.1 ± 49.7	107.2 ± 43.1	0.14
RBS	148.2 ± 84.0	136.0 ± 65.1	0.12
TG	187.1 ± 38.0	192.3 ± 38.4	0.55
HDL	181.4 ± 203.0	170.3 ± 118.7	0.87
LDL	109.3 ± 28.6	**119.1 ± 33.6**	**0.001**
ALT	27.4 ± 16.8	**32.6 ± 22.7**	**0.01**

Table 2: Univariatee and multivariate analysis for factors associated with Lean NAFLD

	Univariate analysis		Multivariate analysis	
	OR [95% CI]	*p* value	OR [95% CI]	*p* value
Smoking No Yes	1.0 2.09[1.16 3.76]	*0.01*	1.0 2.19[1.26 4.91]	*0.008*
Glycemic status Normal IGT/DM	1.0 1.9[1.29-2.86]	<0.001		
Waist circumference (cm)	11.2[5.8 21.8]	<0.001	10.17[5.15 20.11]	<0.001
Hip circumference (cm)	1.13[1.11-1.16]	<0.001		
HTN Normal BP 120-139 systolic or 80-89 mmHg diastolic >140 Systolic or >90 mmHg diastolic	1.0 1.64[1.07-2.50] 2.10[1.20-3.69]	0.02 0.009	1.0 1.42[1.06 1.89]	0.01
RBS	0.99[0.99-1.00]	0.07		
LDL	1.01[1.003-1.015]	0.002	1.01[1.003-1.106]	0.006
ALT	1.01[1.003-1.026]	0.01	1.01[1.003-1.032]	0.007

[L-PP-1257]

Novel exploration of pterostilbene (PTS), purpurin (PUR) and arbutin (ARB) in the management of diabetic and non-diabetic induced liver injury in rodents

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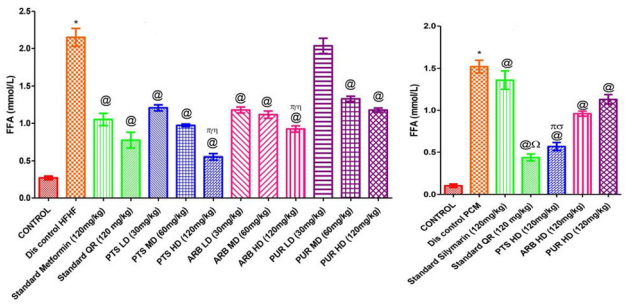
Objectives: The onset and development of liver damage is considered to be influenced by drugs and bad dietary habits.

Materials and Methods: The current study also aims to investigate the relation between paracetamol and high fructose + high fat produced diabetic and non-diabetic liver damage in context of innovative pharmacological therapies (Pterostilbene, Arbutin and Purpurin) with respect to their anti-adipogenic and hepatoprotective effect. The various biochemical, oxidative stress and qRT-PCR parameters were considered for the evaluation of selected interventions.

Results: High fat and fructose diet intake for 28 weeks markedly ($P < 0.05$) upsurge the level of glucose as compared to control diet treated experimental rodents. The scenario was reversed in the case of paracetamol treated rodents there was no significant ($P < 0.05$) increased in the level of glucose which depicted the difference of diabetic and non-diabetic liver injury models. The lipid, liver, inflammatory (IL-6) level, oxidative stress and serum free fatty acid (Fig. 1) parameters was shown to possess significant ($P < 0.05$) improvement in PTS, ARB and PUR treated groups as compared to the disease treated rodent groups.

Conclusion: It is hypothesized that reducing free fatty acid levels by Fatty Acid Synthase inhibition will improve insulin resistance and attenuate diabetic and non-diabetic Liver Injury.



[L-OP-1300]

HCBP6 maintaining of cholesterol homeostasis by down-regulating SREBP2/HMGCR

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Objectives: Dysregulation of cholesterol homeostasis is associated with different metabolic diseases, including fatty liver, atherosclerosis and type 2 diabetes. HCBP6, also known as FUNDC2, DC44, and HCC-3, is a protein that can conjoin with the HCV core protein, which our group screened from the liver cDNA Lib. Recent studies have suggested that the nucleocapsid of HCV (core) acts as a pathogenic factor involved in lipid droplet accumulation, changes in lipogenic gene expression and/or the activity of lipogenic proteins. But the function of HCBP6 remains unclear.

Materials and Methods: Fatty liver first model of high fat diet using HE staining and immunohistochemical method in mice and normal mice liver tissue paraffin sections were detected, the expression level of HCBP6 in two groups of mice in liver tissue different. We establish a cell model of transient overexpression and silencing of HCBP6 in L02 and cholesterol in cells and genes inside cells and lipid metabolism related to the detailed detection. We constructed lipid metabolism related gene SREBP2 promoter expression vector promoter reporter gene, was cotransfected with HCBP6 L02 and HepG2

cell lines, the effects of HCBP6 on the activity of the SREBP2 promoter. We constructed a 3'-UTR HCBP6 reporter, miR-185 and mimics were transfected into HepG2 cells, observe whether miRNAs regulates HCBP6.In order to investigate whether HCBP6 is involved in regulation of cholesterol homeostasis, we construct the in vitro cell model to remove cell overload and total cholesterol, and observed the changes in the expression level of HCBP6 in different time, the change of cholesterol concentration under.
Results: Mir-185 mediated HCBP6 expression maintaining of cholesterol homeostasis by down-regulatingSREBP2/HMGCR.
Conclusion: HCBP6 is the sensor and oscillator in the cholesterol homeostasis.Focus on the role of HCBP6 to keep the cholesterol homeostasis, and provide a new candidate therapeutic target for the NAFLD.

[L-OP-1340]

Association of triglyceride-glucose index and glycosylated hemoglobin with the degree of fibrosis in patients with non-alcoholic fatty liver disease

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Objectives: This study aims to determine the association of TyG index and Hba1c with the degree of hepatic fibrosis in patients with NAFLD evaluated using ARFI imaging. To determine the cutoff value of TyG index score and Hba1c level in identifying the risk for advanced fibrosis.
Materials and Methods: A retrospective analytical study was used to determine the correlation of TyG index and HbA1c to the degree of hepatic fibrosis in NAFLD evaluated using acoustic radiation force impulse (ARFI) imaging. Correlation was confirmedusing t-test for two independent variables and analysis of variance. Moreover, to accurately identify predictive values, a combination of univariate binary logistic regression and receiver operating characteristic were applied.
Results: A total of 186 subjects with mean age of 56.5 years were included in the study. Using ARFI imaging, 96 of 186 (51.6%) subjects had METAVIR score of F2. The comparison of clinical and biochemical characteristics of patients in different stages of fibrosis showed that HbA1c level, TyG index, and fasting blood sugar level were higher in advanced fibrosis. Furthermore, when univariate binary logistic regression analysis was applied, the odds ratio of TyG index indicates that, for every unit increase in TyG index that is 1.74 the likelihood that the patient will have an advanced fibrosis increases by approximately six times. The odds ratio of HbA1c score also indicates that, for every unit of increase in HbA1c level that is 1.40%, the likelihood that the patient will have advanced fibrosis increases by approximately four times. Lastly, computed cut-off value of TyG index was 4.73 while that for HbA1c level was 6.54% suggesting advanced fibrosis.
Conclusion: TyG index and Hba1c have a significant association with the degree of hepatic fibrosis in patients with NAFLD. These variables are effective in identifying individuals at risk for liver fibrosis.

	Cut-off value *(percentile) cut-off score*	Area under the ROC curve (AUC)	Comparison of two ROCcCurves *P-value*
TgY index	(33%) 4.73	0.639	0.000**
HbA1c score	(20%) 6.54	0.850	

Note: ** Significance level at 0.05

[L-OP-1341]

The correlation of serum total cholesterol and liver enzyme on high-fat diet induced rat

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Objectives: Hypercholesterolemia resulting from a high-fat diet could induce oxidative damage, i.e. generating reactive oxygen and lipid peroxidation. This condition may interfere with the liver enzyme. This study assessed the correlation between total serum cholesterol and liver enzyme levels in high-fat diet-induced rats.
Materials and Methods: The study utilized a post-test randomized control group design. Ten rats were divided into two groups. After one week of acclimatization, the normal group was fed a standard diet of 20 g/day, while the interfered group was fed 20 g of a high-fat diet for four weeks. The high-fat diet consists of 20% of standard food, 40% of quail egg yolk, and 40% of duck egg yolk. At the end of the study, total serum cholesterol and liver enzyme (aspartate aminotransferase (AST) and alanine aminotransferase (ALT)) were measured.
Results: The mean of total cholesterol (TC) were 95.71 ± 2.77 for the normal group and 203.86 ± 7.43 for the interfered group. The mean of AST and ALT respectively were 23.11 ± 0.55 and 17.96 ± 0.34 for the normal group, 75.16 ± 2.60 and 36.80 ± 0.63 for the interfered group. One-way ANOVA and posthoc Bonferroni test showed significant differences between all groups regarding serum TC, AST, and ALT (p-value = 0.000). Bivariate Pearson correlation coefficient showed positive correlation between serum total cholesterol and liver enzyme level (r = 0.990, p-value = 0.000 and r = 0.988, p-value = 0.000 for AST and ALT respectively).
Conclusion: This study suggests a positive correlation between total serum cholesterol and liver enzyme with a significant linear relationship.

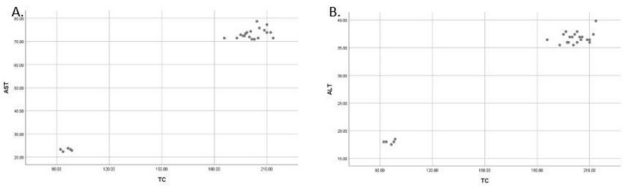

Figure 1. A. Scatter plot of Pearson Correlation Between Total Cholesterol and AST Level, B. Scatter plot of Pearson Correlation Between Total Cholesterol and ALT Level

[L-OP-1345]

The relationship between trygliceride levels and lipid fraction area of liver tissue in the dyslipidemic rats model after intervention of probiotic beverage from date palm and kefir milk

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Objectives: Dyslipidemia is often associated with the occurrence of fatty liver disease. One of the signs of dyslipidemia is an increase in trygliceride levels, while fatty liver disease is characterized by the accumulation of lipids in hepatocytes. The purpose of this research is to know the correlation between trygliceride levels and lipid fraction

area (LFA) of liver tissue in the dyslipidemic rats model after the intervention of probiotic beverage from date palm and kefir milk.
Materials and Methods: This study used a quasi-experimental method with post-test only control group design. This research was conducted in the laboratory of physiology, Universitas Islam Indonesia (UII) for 2 months. This research used male Wistar strain rats aged 1–2 months with BW of 100–150 g. Rats were divided into three groups. All groups were given fed ad libitum for 2 months. In the first month, the first group and third group were given 5 ml/200 g BW/day quail egg yolks (G1 and G3), while the second group was not given the quail egg yolks (G2). In the second month, the third group was given 5 ml/200 g BW/day probiotic beverage from date palm and kefir milk. At the end of the research, rats were terminated.
Results: The mean of trygliceride (mg/dL) in G1, G2, and G3 consecutively were 89.65 ± 6.02, 135.75 ± 1.14, and 112.93 ± 1.10. The mean of LFA (%) in G1, G2, and G3 consecutively were 1.00 ± 0.07, 3.03 ± 1.44, and 1.69 ± 0.37. The result showed there is a strong correlation between trygliceride levels and LFA of liver tissue with $r = 0.624$ (strong positive correlation) and $p < 0.05$ ($p = 0.040$) (Fig. 1).
Conclusion: Trygliceride levels and LFA of liver tissue in dyslipidemic rats after the intervention of probiotic beverage from date palm and kefir milk have a strong correlation.

Correlations

		Lipid_Fraction_Area	Triglyceride
Lipid_Fraction_Area	Pearson Correlation	1	.624*
	Sig. (2-tailed)		.040
	N	11	11
Triglyceride	Pearson Correlation	.624*	1
	Sig. (2-tailed)	.040	
	N	11	11

*. Correlation is significant at the 0.05 level (2-tailed).

Figure 1. *Pearson*-Correlations Test between Lipid Fraction Area of Liver Tissue and Triglyceride Levels

Nonalcoholic Fatty Liver Disease—Clinical

[OP-0055]

Prevalence trends of non-alcoholic fatty liver disease among young male adults in Korea; Korean Military population-based cross-sectional study

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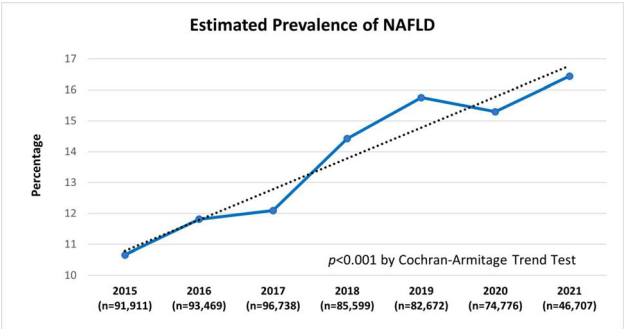
Objectives: Non-alcoholic fatty liver disease (NAFLD) has become major concern in Korea since its emergence as a major cause for chronic liver disease. Here, we performed cross-sectional study aiming to investigate the prevalence of NAFLD in young male Korean population.
Materials and Methods: We selected data from 596,359 Korean soldiers who participated in health examination from January 2015 to July 2021. Total of 571,872 individuals were analyzed after excluding those with missing data and HBsAg(+). Hepatic steatosis was determined using Hepatic Steatosis Index (HSI) (Lee et al. 2010). Participants with HSI > 36 were considered having NAFLD.
Results: All participants were male and mean age was 20.9 ± 1.3 years-old. Total 77,020 individuals are classified as having NAFLD out of 571,872 participants (13.47%). Comparing by year, prevalence of NAFLD has increased from 2015 to 2021 consistently (10.66% vs 16.44%, P for trend < 0.001, respectively). The prevalence of hypercholesterolemia has risen during study periods (1.78% vs 2.56%, P < 0.001) as well as dysglycemia (10.17% vs 11.68%, P < 0.001) and hypertension (2.87% vs 3.51%, P < 0.001, 2015 and 2021 respectively,). BMI also rose from 23.3 ± 3.0 kg/m2 to 23.9 ± 3.1 kg/m2 between 2015 and 2021 (P < 0.001). Estimated advanced fibrosis was assessed by BARD score and 24,092 out of 77,020 MAFLD patients (31.2%) had score of 2 or greater which indicates advanced fibrosis.
Conclusion: During the study period, male population in their early twenties showed increase in prevalence of NAFLD as well as other metabolic dysfunctions such as hypercholesterolemia, dysglycemia and hypertension.



[PP-0061]

The use of vegetative gathering in complex treatment of patients with non-alcoholic fatty liver disease

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Objectives: to study efficiency of vegetative gathering in complex treatment of nonalcoholic fatty liver disease.
Materials and Methods: On the basis of Medical Center of Turkmenistan named after S. A. Niyazov 49 patients with non-alcoholic fatty liver disease (35 women and 14 men) were examined. 1 group accepts hepatic protectors (essensiale forte) and 2 group—in a combination to herbal medicine (gathering № 2: 3 tablespoons (tbsp) of hips, 2 tbsp of hawthorn fruit, 2 tbsp. of nettle leaves, 1 tbsp of St. John's wort).
Results: Group accepting hepatic protectors, has yielded positive results for 7 days of therapy; at 49% patients the nausea has decreased, at 43% patients feeling of discomfort whereas other complaints remained has decreased. The group accepting hepatic protectors in a combination to herbal medicine, has yielded positive results for 3 days of treatment. The feeling of weight in epigastric areas has decreased at 54% patients, nausea has decreased at 28%, and feeling of discomfort—at 31% patients. Activity decrease of transaminases (at 14% of patients) was marked also.
Conclusion: Efficiency of vegetative gathering in a combination with hepatic protectors is shown already at an early stage of treatment of non-alcoholic fatty liver disease. Clinical semiology decreases, laboratory indicators of blood are normalized, disease current improves.

[PP-0097]

Metabolic dysfunction-associated fatty liver disease increases colon cancer risk: A nationwide cohort study

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Objectives: The association between nonalcoholic fatty liver disease (NAFLD) and colorectal cancer (CRC) has been controversial. Using the new consensus-driven definition, we evaluated the association of metabolic dysfunction-associated fatty liver disease (MAFLD) with the risk of developing CRC.
Materials and Methods: From a nationwide health screening database, we included 8,933,017 participants (48.6% male) aged 40–64 years between 2009 and 2010. Participants were categorized by presence of fatty liver disease (FLD)—NAFLD and MAFLD, separately—and by the combination of the two definitions: Neither-FLD, NAFLD-only, MAFLD-only, or Both-FLD. The primary outcome was the development of CRC.
Results: Among the participants, 2,517,330 (28.2%) had NAFLD and 3,337,122 (37.4%) had MAFLD, while 2,465,151 (27.6%) met both NAFLD and MAFLD definitions. Over a median follow-up period of 10.1 years, 60,888 new CRC cases developed. NAFLD and MAFLD were each associated with a significantly higher risk of developing CRC. When the Neither-FLD group was the reference, multivariable-adjusted hazard ratios (95% confidence interval) for CRC were 1.16 (1.06–1.28) in the NAFLD-only group, 1.18 (1.16–1.20) in the Both-FLD group, and 1.32 (1.28–1.35) in the MAFLD-only group. The presence of advanced liver fibrosis further increased CRC risk in each FLD group.
Conclusion: FLD was associated with a higher risk of CRC development. CRC risk was higher in the presence of MAFLD, especially when accompanied by liver fibrosis.

[PP-0099]

Anti-HBc-positivity and liver fibrosis severity in patients with nonalcoholic fatty liver disease

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Objectives: It is not known, whether previous hepatitis B virus (HBV) infection (PBI) affects natural course of nonalcoholic fatty liver disease (NAFLD). We aimed to assess the prevalence of PBI and liver fibrosis severity in patients with NAFLD.
Materials and Methods: In a single-center, cross-sectional study enrolled 110 HBsAg and anti-HCV-negative patients with confirmed NAFLD. To confirm the previous and occult HBV infection, the serum samples were tested for anti-HBc (IgG) and HBV DNA. To assess the liver fibrosis severity biopsy was performed in 35 patients (31.8%), other patients had transient elastography with steatometry and/or a serum FibroMax™ assay (FibroTest + SteatoTest + NashTest).
Results: One hundred and ten subjects (women—87 (79.1%)), of median [IQR] age 60[53–66] y.o. were enrolled. Among them, 78 (70.9%) had obesity, 64 (58.2%)—type 2 diabetes, and 77 (70%)—dyslipidemia. Mild (F0–F2 METAVIR) liver fibrosis was found in 85 subjects, and 25 had severe fibrosis (F4 in 23, F3 in 2). Patients with severe fibrosis were older than those with F0–F2 (64[60–69] vs 59[49–65] y.o., $p = 0.003$) and more frequent (76% vs 53%, $p = 0.041$) had type 2 diabetes. Anti-HBc was detected in 10 (40%) patients with F3–F4 and in 7 (8.2%) subjects with F0–F2 ($p < 0.001$). Blood HBV DNA was negative in all anti-HBc positive patients. Anti-HBc positivity was the major factor directly associated with severe liver fibrosis (OR 7.339; [95% CI 2.189–24.604]; $p = 0.001$).
Conclusion: Anti-HBc-positive patients with NAFLD have a much higher risk of severe liver fibrosis compared to patients without markers of previous HBV infection.

[PP-0107]

Young adults with nonalcoholic fatty liver disease can be at increased risk for myocardial infarction or stroke

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is associated with increased risk of cardiovascular diseases (CVDs). Because studies of young adults are limited, we investigated the relationship between NAFLD and cardiovascular events among a nationally representative sample of young adults in Korea.
Materials and Methods: This population-based cohort study from the Korean National Health Insurance Service included adults who were 20–39 years old when they underwent a health examination from 2009–2012. NAFLD was defined as fatty liver index (FLI) ≥ 60, and participants were divided into three groups according to FLI (< 30, $30 - 59$, and ≥ 60) to investigate the effect of steatosis by grade.
Results: Among 5,324,410 participants, 9.8% had an FLI ≥ 60. There were 13,051 myocardial infarctions (MI, 0.39%) and 8,573 strokes (0.26%) during a median follow-up of 8.4 years. In multivariable analysis, NAFLD was associated with a higher risk of MI and stroke (hazard ratio [HR] = 1.69; 95% confidence interval [CI]: $1.61 - 1.77$ and HR = 1.73; 95% CI: $1.63 - 1.84$, respectively). MI and stroke had dose-depended relationships with FLI (HR = 1.28 in FLI $30 - 59$ and 1.73 in FLI ≥ 60 for MI and HR = 1.18 in FLI $30 - 59$ and 1.41 in FLI ≥ 60 for stroke, respectively).
Conclusion: NAFLD was an independent predictor of MI and stroke in young adults. These results suggest that primary prevention of CVD should be emphasized in young adults with NAFLD.

[OP-0120]

Efficacy of newly developed specialized food product SPP2 in treatment of patients with NASH

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Objectives: To assess safety and efficacy of developed specialized food product SPP2 in patients with non-alcoholic steatohepatitis.
Materials and Methods: New specialized food product (SPP2) consisted of (% of the RDAs): protein 11%; fat 2% (including ω-3 PUFA 17%); soluble dietary fiber 100%; phospholipids 25%; alpha-lipoic acid 33%; taurine 30%; L-carnitine 33%; vitamins (A, E, D3, K1, C, B1, B2, B6, B12, PP, Folic acid, Pantothenic acid, Biotin) 35%–130%. The study (NCT04308980) was approved by LEC and enrolled patients with diagnosis of NASH. Subjects were randomized to the following groups: those received iso-calorie diet (according to REE, by indirect calorimetry) alone (ICD) and iso-calorie diet + SPP2 (2 portions of SPP2 a day, 14 days, ICD + SPP2 group). Safety was assessed based on clinical and laboratory data. Repeated measurements (baseline vs those on the 15th day of the study) of body composition, and blood chemistry were compared with non-parametric statistics.
Results: The results of complex examination of 20 subjects (12 in ICD + SPP2 and 8 in ICD group) served as a source for the study. Initially, groups did not differ by age, sex, and BMI. The product was well tolerated. In contrast to ICD group, those in ICD + SPP2 group demonstrated greater decrease of weight: BMI initially (BMI_0), Mean ± SD: 39.8 ± 12.3 kg/m^2 vs BMI at the end-point (BMI_{EOT}) 38.9 ± 11.8 kg/m^2, P = 0.02 in ICD + SPP2 group, whereas in the ICD group BMI_0 38.9 ± 7.2 kg/m^2 vs BMI_{EOT} 38.9 ± 7.3 kg/m^2, P = 0.08. This was caused mainly by reduction of body fat weight $(BFW)_0$ 50.7 ± 29.7 kg vs BFW_{EOT} 29.5 ± 28.8 kg, P = 0.017 in ICD + SPP2 group, whereas BFW_0 48.9 ± 11.4 kg vs BFW_{EOT} 47.8 ± 11.6 kg, P = 0.07 in ICD group.
Conclusion: The new specialized food product "SPP2" is safe, and well tolerated by patients with NASH. In combination with iso-calorie diet, it may increase efficacy of weight loss, predominantly by fat.

[PP-0123]

The evaluation of genetic and epigenetic factors in disease development and progression in nonalcoholic fatty liver disease

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is chronic and progressive liver disease with high prevalence of about 30% of the general population. This study evaluated the role of genetic and epigenetic factors in the development and progression of NAFLD using the Korean Genome Epidemiology Study (KoGES).
Materials and Methods: The KoGES is consisted with more than 10,000 participants from Ansan and Anseoung city from 2001. After excluding chronic viral hepatitis and alcohol abuser. 8840 patients were analysed genome wide association study (GWAS). 444 patients were analysed DNA methylation and 50 patients were reanalysed DNA methylation 5 years later. Participants with FLI > 60 were classified into NAFLD group, whereas participants with FLI < 30 were classified into control group.
Results: In GWAS data, 3234 and 3064 participants were classified into NAFLD group and control group, respectively. In chromosome 12, CCDC63, HECTD4, OAS3, MYL2 genes were significantly different patterns between controls and NAFLD participants based on FLI. In chromosome X, six SNPs of intergenic regions showed significance as a P-value of 5E−08 or less. In DNA methylation data, 180 and 156 participants were classified into NAFLD group and control group, respectively. The value of FLI has correlation patterns to 13 probes with r2 greater than 0.12.
Conclusion: Here, we demonstrate that GWAS and DNA methylation profiles showed significant difference between NAFLD group and control group. Our results suggest that GWAS and DNA methylation level and clinical variables can be used for the clues for molecular pathways in NAFLD.

[PP-0124]

MR-based nonalcoholic steatohepatitis score for diagnosis of NASH in patients with NAFLD

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Objectives: It is important to develop a non-invasive biomarker for the diagnosis of nonalcoholic steatohepatitis (NASH) among patients with nonalcoholic fatty liver disease (NAFLD). This prospective cross-sectional study aimed to develop a scoring system for NASH diagnosis through multiparametric magnetic resonance (MR) and clinical indicators.
Materials and Methods: Medical history, laboratory tests, and MR parameters of patients with NAFLD were assessed. A scoring system was developed using a logistic regression model. In total, 127 patients (58 with nonalcoholic fatty liver [NAFL] and 69 with NASH) were enrolled. After evaluating 23 clinical characteristics of the patients (4 categorical and 19 numeric variables) for the NASH diagnostic model, an equation for MR-based NASH score was obtained using 4 demographic factors, 2 laboratory variables, and 2 MR parameters.
Results: The MR-based NASH score showed a satisfactory accuracy for NASH diagnosis (c-statistics, 0.841; 95% CI, 0.772–0.910). At a cut-off MR-based NASH score of 0.68 for NASH diagnosis, its sensitivity was 0.68 and specificity was 0.91. When an MR-based NASH score of 0.37 was used as a cut-off for NASH exclusion, the sensitivity was 0.91 and specificity was 0.55. Only 35% (44/127) of patients were in the gray zone (between 0.37 and 0.68). Internal validation via bootstrapping also showed satisfactory accuracy for NASH diagnosis (optimism- corrected statistics, 0.811).
Conclusion: MR-based NASH score is a novel non-invasive biomarker for diagnosis of NASH in patients with NAFLD.

[OP-0147]

Diagnostic performance of AFP, PIVKA-II, AFP-L3, and their combinations in detecting hepatocellular carcinoma in nonalcoholic fatty liver disease: A multi-institutional observational study

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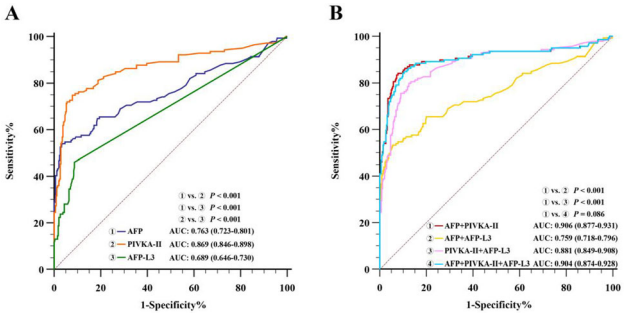
Objectives: Current surveillance strategies for hepatocellular carcinoma (HCC) among patients with nonalcoholic fatty liver disease (NAFLD) are insufficient. This study aims to investigate diagnostic performance of alpha-fetoprotein (AFP), protein induced by vitamin K absence or antagonist-II (PIVKA-II), lens culinaris agglutinin-reactive fraction of AFP (AFP-L3), and their combinations in diagnosing HCC in patients with NAFLD.
Materials and Methods: Serologic AFP, AFP-L3, and PIVKA-II levels in NAFLD patients with and without HCC were measured. By receiver operating characteristic (ROC) analyses, the area under the curve (AUC), sensitivity, and specificity were obtained to evaluate the diagnostic accuracy of each biomarker and their combinations.
Results: This study was conducted on 139 patients with NAFLD-HCC and 345 NAFLD controls. The elevation of these three biomarkers were observed in patients with NAFLD-HCC compared to NAFLD controls (all $P < 0.001$). When they were analyzed individually, PIVKA-II showed the best performance in diagnosing any-stage HCC with an AUC of 0.869, followed by AFP (0.763; vs. PIVKA-II, $P < 0.001$) and AFP-L3 (0.689; vs. PIVKA-II, $P < 0.001$). When they were analyzed by combinations, AFP + PIVKA-II yielded the highest AUC (0.906), followed by AFP + PIVKA-II + AFP-L3 (0.904; vs. AFP + PIVKA-II, $P = 0.086$), PIVKA-II + AFP-L3 (0.881; vs. AFP + PIVKA-II, $P < 0.001$), and AFP + AFP-L3 (0.759; vs. AFP + PIVKA-II, $P < 0.001$). Similar findings were obtained in the subgroup with early-stage NAFLD-HCC, as well as the non-cirrhotic subgroup.
Conclusion: These data validated the better diagnostic ability of PIVKA-II than AFP or AFP-L3 alone for diagnosing any-stage or early-stage HCC among patients with NAFLD, and the combination of AFP + PIVKA-II allowed a remarkable improvement for diagnosing NAFLD-HCC.



[OP-0174]

Lower serum copper concentrations are associated with higher prevalence of NASH: A matched case–control study

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Objectives: Copper is an essential trace element involved in oxidative stress reactions and energy metabolism of the human body. While nonalcoholic fatty liver disease (NAFLD) is closely related to metabolic dysfunctions, the role of copper in the development and progression of simple steatosis to nonalcoholic steatohepatitis (NASH) is unclear. We aim to investigate the effect of serum copper for the risk of NASH.
Materials and Methods: Biopsy-proven NAFLD were included for this study by a 1:1 matched case–control analysis by age, sex and residential city-matched NAFL controls. Multivariable conditional logistic analysis was performed to explore associations between serum copper levels and presence of NASH.
Results: Serum copper levels in patients with NASH were significantly lower than that in control group of patients (15.75 ± 2.52 umol/L vs. 16.58 ± 3.45 umol/L; $P = 0.012$). The per unit, per standard deviation, and per doubling of serum copper concentrations was associated with an approximately 20%, 50% and 90% respectively, decrease in risk of NASH, after adjustment for potential confounders. Additional subgroup analysis showed significantly difference between participants in male and corresponding controls.
Conclusion: Decreased serum copper concentrations are significantly associated with an increased risk of NASH among biopsied-proven NAFLD patients, particularly in males.

[OP-0189]

Reliability of the non-alcoholic steatohepatitis clinical research network and steatosis activity fibrosis histological scoring systems for non-alcoholic fatty liver disease

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Objectives: We aimed to determine whether lobular inflammation and ballooning grades in the Non-alcoholic Steatohepatitis Clinical Research Network scoring system (NASH CRN) can be directly translated into the same for the Steatosis Activity Fibrosis scoring system (SAF), and to look at intra- and inter-observer agreement for each individual histological component and for diagnosis of non-alcoholic steatohepatitis (NASH) using the two scoring systems.
Materials and Methods: Four pathologists from two Asian centres scored 20 digitalized slides, twice using the NASH CRN, twice using the SAF. Intra- and inter-observer agreement was analyzed using Fleiss' kappa, weighted kappa or Cohen kappa, where appropriate.
Results: The intra-observer discrepancy rate when using the NASH CRN compared with the SAF was higher than when using the individual scoring system for lobular inflammation (15% comparing both scoring systems vs. 10% and 1.8% for the NASH CRN and the SAF, respectively) and hepatocyte ballooning (33.8% vs. 12.5% and 5%, respectively), but not for diagnosis of NASH (6.3% vs. 6.3% and 0%, respectively). Intra- and inter-observer agreement was substantial to almost perfect, except for inter-observer agreement for lobular inflammation and diagnosis of NASH, which was only fair to moderate in most instances.
Conclusion: These findings do not support the direct inter-translation between the NASH CRN and the SAF. However, the diagnosis of NASH during examinations using the NASH CRN may be comparable with diagnosis of NASH using the SAF, vice versa. The inter-observer agreement for lobular inflammation and NASH diagnosis needs to be improved.

[OP-0214]

MAFLD is associated with greater impairment of lung function than NAFLD

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Objectives: We compared lung function parameters in nonalcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated fatty liver disease (MAFLD), and also examined the association between lung function parameters and fibrosis severity in MAFLD.
Materials and Methods: In this cross-sectional study, we randomly recruited 2,543 middle-aged individuals from 25 communities across four cities in China during 2016 and 2020. All participants received a health check-up including measurement of anthropometric parameters, biochemical variables, as well as liver ultrasonography and spirometry. The severity of liver disease was assessed with the fibrosis (FIB)-4 score.
Results: The prevalence of MAFLD and NAFLD was 20.4% (n = 519) and 18.4% (n = 469), respectively. After adjustment for age, sex, adiposity measures, smoking status and significant alcohol intake, subjects with MAFLD had a significantly lower percent predicted forced vital capacity (FVC: 88.27 ± 17.60% vs. 90.82 ± 16.85%, $P < 0.05$) and lower forced expiratory volume in one second (FEV_1: 79.89 ± 17.34 vs. 83.02 ± 16.66%, $P < 0.05$) than those with NAFLD. Furthermore, MAFLD with increased FIB-4 score was significantly associated with decreased lung function parameters (Fig. 1), i.e. for each 1-point increase in FIB-4, FVC was diminished by − 0.507 (95% CI [− 0.840, − 0.173], P = 0.003) and FEV_1 was diminished by − 0.439 (95% CI [− 0.739, − 0.140], P = 0.004), after adjustment for sex, age, adiposity measures, smoking status, significant alcohol intake, pre-existing diabetes and other potential confounding factors. The results remained unchanged even when we performed separate statistical analyses for men and women.
Conclusion: MAFLD is significantly associated with a greater impairment in lung function parameters than NAFLD.

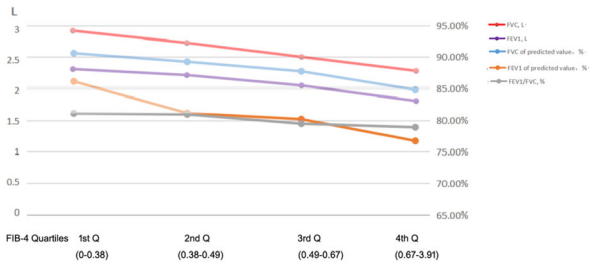

Figure 1 . Lung function tests according to increasing FIB-4 quartiles in MAFLD

FIB-4 = fibrosis 4 score, FVC= forced vital capacity, FEV1 = forced expiratory volume measured in the first second of exhalation, MAFLD = metabolic dysfunction-associated fatty liver disease,

[OP-0229]

Modest alcohol intake and mortality in individuals with elevated alanine aminotransferase levels

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Objectives: Alanine aminotransferase (ALT) levels are widely used to screen liver disease, and many asymptomatic individuals show elevated ALT level. As elevated ALT level indicates liver injury, even a small amount of alcohol intake may be harmful in subjects with elevated ALT levels, but there is limited evidence of the effect of light to moderate amount of alcohol intake in this subgroup.
Materials and Methods: A cohort of 367,612 men and women without established liver diseases (including chronic viral hepatitis, alcohol-associated liver disease, cirrhosis, liver transplantation or rare forms of liver disease) who underwent at least 1 health screening exam between 2009 and 2015 were assessed for liver-related and all-cause mortality. Elevated ALT levels were defined as $\geq$ 34 U/L for men and 25 U/L for women.
Results: In participants with normal ALT levels, the fully-adjusted hazard ratios (95% CI) for liver-related mortality comparing light and moderate drinkers to non-drinkers were 0.73 (0.51–1.05), and 1.06 (0.73–1.52), respectively. In participants with elevated ALT levels, the corresponding hazard ratios were 1.57 (1.08–2.28), and 2.09 (CI 1.46–2.99), respectively (P-value for alcohol intake by ALT interaction < 0.01). For all-cause mortality, the fully-adjusted hazard ratios comparing light and moderate drinkers to non-drinkers in participants with normal ALT levels were 0.72 (0.66–0.77), and 0.89 (0.82–0.97), respectively. In participants with elevated ALT levels, the corresponding hazard ratios were 0.93 (0.81–1.08), and 1.31 (1.14–1.50), respectively (P-value for alcohol intake by ALT interaction < 0.01).
Conclusion: Small amounts of alcohol intake were associated with increased liver-related and all-cause mortality among individuals with elevated ALT levels. Subjects with elevated ALT levels should be advised complete abstinence from alcohol.

[PP-0232]

Sex-specific cutoff values of visceral fat area for lean versus overweight/obese nonalcoholic fatty liver disease in Asians

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Objectives: Visceral obesity is a risk factor for nonalcoholic fatty liver disease (NAFLD). We investigated sex-specific optimal cutoff values for visceral fat area (VFA) associated with lean and overweight/obese NAFLD in an Asian population.
Materials and Methods: This retrospective study included 678 potential living liver donors (mean age, 30.8 $\pm$ 9.4 years; 434 male and 244 female) who had undergone abdominal computed tomography (CT) imaging and liver biopsy between November 2016 and October 2017. VFA was measured using single-slice abdominal CT. NAFLD was evaluated by liver biopsy ($\geq$ 5% hepatic steatosis). Receiver operating characteristic curve analysis was used to determine cutoff values for VFA associated with lean (body mass index [BMI] < 23 kg/m^2) and overweight/obese (BMI ≥ 23 kg/m^2) NAFLD.
Results: Area under the curve (AUC) values with 95% confidence intervals (CI) for VFA in male subjects were 0.82 (95% CI, 0.75–0.88) for lean NAFLD and 0.74 (95% CI, 0.69–0.79) for overweight/obese NAFLD. In female subject, AUC values were 0.67 (95% CI, 0.58–0.75) for lean NAFLD and 0.71 (95% CI, 0.62–0.80) for overweight/obese NAFLD. The cutoff values for VFA associated with lean NAFLD were 50.2 cm^2 in male and 40.5 cm^2 in female subjects. The optimal cutoff values for VFA associated with overweight/obese NAFLD were 100.6 cm^2 in male and 68.0 cm^2 in female subjects.
Conclusion: Sex-specific cutoff values for VFA may be useful for identifying subjects at risk of lean and overweight/obese NAFLD.

[OP-0269]

Non-alcoholic fatty liver disease in the South Asian Region: A systematic review and meta-analysis

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is the commonest chronic liver disease worldwide. We estimated overall prevalence and effect sizes of associations for NAFLD among adults in South Asia.
Materials and Methods: We searched for search terms "Prevalence of NAFLD (Non-Alcoholic Fatty Liver Disease)" AND "South Asia" AND individual South Asian countries from January 2004-May 2021 in PubMed database. Strict eligibility criteria were applied. Gender, urban or rural setting, general population and individuals with metabolic diseases stratified analysis. A random-effects meta-analysis was performed.
Results: Out of 158 studies, selected 25 studies from five countries (Bangladesh, India, Nepal, Pakistan and Sri Lanka) were included with 15,758 participants, of whom 4703 had NAFLD. The pooled NAFLD prevalence was 40.5% [95% CI 33.7–47.5] in overall, 26.2% [95% CI 18.7–34.4] in general population, 21.9% [95% CI 14.4–30.5] in rural communities, 32.9% [95% CI 22.8–43.8] in urban

communities and 54% [95% CI 46.4–61.5] in individuals with one or more metabolic abnormality. 11.1% [95% CI 7.1–16.0] among non-obese had NAFLD while 41.4% [95% CI 28.1–55.2] of NAFLD patients were non-obese. Gender specific prevalence was similar. Prevalence of NAFLD among individuals with metabolic disease was significantly higher than the general population ($p < 0.0001$). A significant association with NAFLD was found for metabolic syndrome, general obesity, central obesity, diabetes mellitus, dysglycemia, dyslipidemia and hypertension (Table).
Conclusion: The overall prevalence of NAFLD among adults in South Asia is high, especially in urban populations and those with metabolic abnormalities. Targeted health-strategies should be implemented in the region to address this.

Table : Pooled estimates for risk values for NAFLD in South Asia

Variable	RR*	95% CI	P value
Diabetes mellitus	2.0440	1.6437 – 2.5419	<0.0001
Dysglycemia	1.7834	1.4390 – 2.2102	<0.0001
Hypertension	1.3844	1.0987 – 1.7443	0.0058
Dyslipidemia	1.6827	1.5007 – 1.8868	<0.0001
General Obesity	2.5621	1.9519 – 3.3630	<0.0001
Central Obesity	2.2800	1.4979 – 3.4704	0.0001
Metabolic Syndrome	2.8585	1.7839 – 4.5805	<0.0001
Male gender	1.0374	0.9041 – 1.1903	0.6011

[PP-0284]

The change of skeletal muscle mass is associated with hepatic steatosis in nonalcoholic fatty liver disease

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Objectives: Nonalcoholic fatty liver disease (NAFLD) and sarcopenia have been known to be closely related. The aim of this study was to find out the association between skeletal muscle mass changes and NAFLD status.
Materials and Methods: A single-center, retrospective study was performed. Those who had received health screening twice with temporal gap of 5.5 to 6.5 years were enrolled for the study. The degree of sarcopenia was assessed by appendicular skeletal muscle mass (ASM) adjusted for weight and body mass index (BMI). Alternations in hepatic steatosis and fibrosis status were evaluated using non-invasive serum markers.
Results: In a sample of 606 patients, the mean age was 47.0 years, and 67 (11.1%) patients had diabetes. Over the course of 6 years, ASM of the study population had decreased, and those showing a decrease in ASM/BMI had higher proportion of diabetes, higher HIS and FLI score at baseline state ($p < 0.05$). The group with baseline sarcopenia had greater elevation in NFS over 6 years than those without baseline sarcopenia (0.7 versus 0.4 in ASM/Weight, 0.8 versus 0.4 in ASM/BMI). In regression analysis, we identified that as ASM/Weight or ASM/BMI had increased for 6 years, HIS and FLI score had decreased further. Same results were shown in subgroup analyses according to gender and age group.
Conclusion: Changes in skeletal muscle mass are associated with NAFLD, and sarcopenia may affect the worsening of NAFLD, and vice versa. We expect that skeletal muscle status can be used to predict the course of NAFLD and to establish individualized treatment strategies.

[PP-0286]

Effect of exercise-based interventions on liver function and intrahepatic lipids in nonalcoholic fatty liver disease: A meta-analysis

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. Exercise training has been shown to have beneficial effect in patients with NAFLD. The aim of this study was to systematically investigate the effect of exercise on hepatic steatosis, according to exercise type and duration.
Materials and Methods: We searched MEDLINE, EMBASE, Cochrane databases, KMBASE, and KISS (Korean studies Information Service System) from earliest records to September 2020 for randomized controlled trials assessing the effects of exercise on hepatic steatosis which measured using magnetic resonance imaging in NAFLD patients. Effect sizes were reported as standard mean difference and 95% confidence intervals. Subgroup analyses were conducted according to types and duration of exercise.
Results: We included 9 studies totaling 516 participants. Exercise improved intrahepatic fat contents (− 2.27, − 3.58 to − 0.96) and alanine aminotransferase (− 4.18, − 6.61 to − 1.75). However, there were no significant differences between exercise group and control group in insulin resistance (− 0.05, − 0.45 to 0.35) and body mass index (− 0.65, − 1.89 to 0.58). There was significant reduction of intrahepatic fat content in aerobic exercise group (− 2.63, − 4.26 to − 1.00), but not in resistance exercise group (− 2.18, − 4.63 to 0.27). Exercise more than 3 months significantly reduced intrahepatic fat content (− 3.66, − 5.82 to − 1.51), but exercise less than 3 months was not significant (− 1.45, − 3.10 to 0.20).
Conclusion: Exercise training reduces intrahepatic fat content and alanine aminotransferase. In subgroup analysis, aerobic exercise and duration more than 3 months can significantly reduce intrahepatic fat content.

[PP-0287]

MAFLD predicts the risk of cardiovascular disease better than NAFLD in asymptomatic subjects undergoing medical health check-ups

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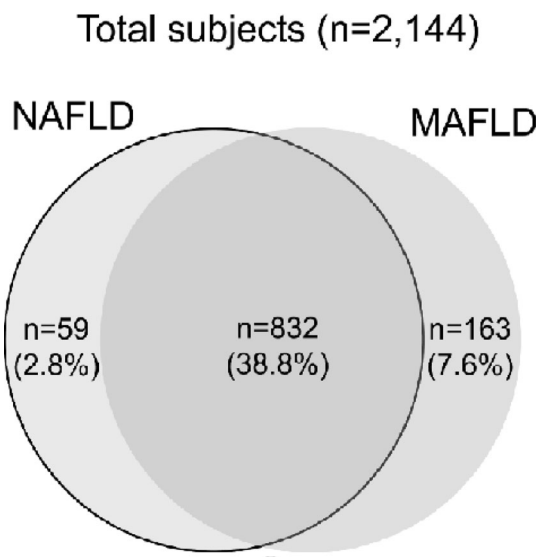
Objectives: Metabolic dysfunction-associated fatty liver disease (MAFLD) was proposed to compensate for the conventional concept of nonalcoholic fatty liver disease (NAFLD). We investigated the

superiority of MAFLD vs. NAFLD in predicting the risk of cardiovascular disease (CVD).
Materials and Methods: A total of 2,144 subjects without a history of CVD, who underwent a comprehensive medical health check-up, were selected for the study. The associations between fatty liver status and coronary risk surrogates, such as coronary artery calcium score (CACS), coronary artery disease, quantitative stenosis grade, and 10-year atherosclerotic cardiovascular disease (ASCVD) risk, were analyzed.
Results: MAFLD and NAFLD were identified in 995 (46.4%) and 891 (41.6%) subjects, respectively. Subjects with MAFLD or NAFLD were more likely to be male and had a significantly higher prevalence of central obesity, obesity, hypertension, diabetes, and dyslipidemia (all, $p < 0.05$) than their counterparts. In terms of coronary risk surrogates, the MAFLD or NAFLD population had a significantly higher proportion of subjects with CACS > 100, coronary artery disease, higher grade of coronary artery stenosis, and higher 10-year ASCVD risk (all, $p < 0.05$) than their counterparts. Multivariable logistic regression models showed an independent association between MAFLD/NAFLD and coronary risk surrogates (all, $p < 0.05$). However, NAFLD only, defined as 'NAFLD, but not MAFLD', was not associated with an increased coronary risk, compared to MAFLD.
Conclusion: Although both MAFLD and NAFLD discriminated different CVD risks, MAFLD predicted the risk of CVD better than NAFLD in asymptomatic subjects who underwent medical health check-ups.



[OP-0296]

Higher consumption of animal organ meat is associated with a lower prevalence of nonalcoholic steatohepatitis

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Objectives: Lifestyle modification is the foundation of treatment for nonalcoholic steatohepatitis (NASH) (a progressive form of nonalcoholic fatty liver disease (NAFLD)), but there are remaining uncertainties regarding the benefits, or harms, of specific foods. Animal organ meat (offal) is a food with high nutrient density that is popular in different parts of the world, but its relationship with NASH is unclear.
Materials and Methods: Chinese adults with biopsy-confirmed NAFLD were included. NASH was defined as NAFLD activity score ≥ 4 and at least one point for steatosis, ballooning, and lobular inflammation, respectively. Animal organ meat consumption (liver, kidney, heart, tripe, intestine or gizzard) was estimated using a self-administered validated food frequency questionnaire. Logistic regression analysis was performed to assess the association between animal organ meat intake and liver disease severity.
Results: 136 participants (80.9% men) had a mean (SD) age of 39.0 ± 12.5 years and body mass index of 27.4 ± 3.6 kg/m^2. Prevalence of NASH was 65.4%. Daily median organ meat intake was 1.3 g/1000 kcal. Animal organ meat intake was inversely associated with NASH after adjustment of demographics, lifestyle variables, metabolic and dietary factors, as well as liver fibrosis stage; adjusted-odds ratios (95% confidence intervals) for NASH were 0.15 (0.03, 0.69) for the highest tertile and 0.18 (0.05, 0.70) for the medium tertile, compared to the lowest (reference) tertile of animal organ meat intake (p-value for trend = 0.024).
Conclusion: Our results show for the first time that higher animal organ meat consumption is associated with a lower prevalence of NASH in Chinese individuals with biopsy-proven NAFLD.

[OP-0308]

Clinical prognosis in non-obese non-alcoholic fatty liver disease

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Objectives: Non-alcoholic fatty liver disease (NAFLD) can progress even in non-obese subjects. Previous reports have shown that the pathological profile of lean non-obese NAFLD patients is relatively good, but reports on long-term prognosis are controversial.
Materials and Methods: In this study, we retrospectively investigated the risk of clinical events and mortality. clinical events include cardiovascular events, liver-related events, and cancers without hepatocellular carcinoma. The criteria for non-obese and obese NAFLD

were body mass index (BMI) less than 25 kg/m2 and greater than 25, respectively.
Results: Of the 255 NAFLD patients, 66 (25.9%) were non-obese. Compared to obese patients, non-obese patients had a lower fibrosis stage (0.8 ± 0.80 vs 1.2 ± 0.91; P = 0.004). There was no difference in each pathological finding: steatosis, hepatocyte ballooning, inflammation and NAFLD activity score. In addition, non-obese NAFLD patients tended to have significantly lower ALT, Cre, bilirubin and higher HDL levels. After a median follow-up of 9.7 years, 3 patients (4.5%) in the non-obese group and 5 patients (7.6%) in the obese group died. 12 patients (18.2%) in the non-obese group and 29 patients (15.3%) in the obese group had clinical events, which tended to be more frequent in the non-obese group (P = 0.67). After the first 10 years of follow-up, the clinical event rate tended to be higher in the obese group, but after that, the clinical event rate was higher in the non-obese group. The non-obese group was characterized by a higher incidence of carcinogenesis, with 9 of the 12 patients experiencing carcinogenesis.
Conclusion: Long-term follow-up of more than 10 years suggests that non-obese NAFLD patients have a higher risk of developing clinical events, mainly carcinogenesis. This is a single-center analysis and needs to be validated in multiple centers.

[OP-0317]

Prevalence and clinical characteristics of nonalcoholic fatty liver disease in morbidly obese patients before and after bariatric surgery

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Objectives: The aim of this study is to investigate the prevalence and clinical characteristics of nonalcoholic fatty liver disease (NAFLD) of morbidly obese patients who underwent bariatric surgery, and to compare body compositions before and after bariatric surgery using computed tomography (CT) images.
Materials and Methods: We analyzed clinical data of 189 patients who underwent bariatric surgery at a tertiary hospital from January 2019 to September 2021. Among them, 137 patients had preoperative and postoperative non-contrast CT at 6 months of follow-up. Body compositions including fatty liver, visceral and subcutaneous adiposity, skeletal muscle mass and myosteatosis will be measured using non-contrast CT images. In nine cases with liver biopsy results, pathology and radiology correlation will be analyzed.
Results: At pre-operation, the patients showed a median age of 38 years with 63.5% female proportion and median BMI of 37.6 kg/m^2. The frequency of comorbidity such as hypertension (53.4%), diabetes (30.7%), and hyperlipidemia (38.1%) was noticed. The median preoperative AST and ALT level was 47 and 33 IU/L. According to a preliminary diagnosis of NAFLD based on radiological and laboratory abnormality, the prevalence of NAFLD was 72% showing a younger age, higher male proportion, similar BMI, higher levels of AST, ALT, hemoglobin A1C, insulin level, triglyceride, ferritin and uric acid. At 6 and 12 months of post-operation, median weight loss was 23.6 and 27.4 kg, respectively, with significantly reduced AST and ALT levels. Body composition analysis using non-contrast CT images including fatty liver, skeletal muscle mass, myosteatosis visceral and subcutaneous adiposity, has not completed yet, but will be presented at the meeting.
Conclusion: Patients who underwent bariatric surgery showed more than 70% of NAFLD prevalence based on a preliminary clinical diagnosis. 27 kg weight reduction with significant improvement of liver biochemistry was found 1 year after bariatric surgery. Detailed analysis of body composition change will be presented.

[OP-0323]

Comparison of diagnostic performance between FIB-4 and NFS in metabolic-associated fatty liver disease era

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Objectives: Fibrosis-4 index (FIB-4) and non-alcoholic fatty liver disease (NAFLD) fibrosis score (NFS) are the two most widely used non-invasive tools for screening of advanced fibrosis in subjects with NAFLD. Since metabolic dysfunction-associated fatty liver disease (MAFLD) has been proposed as a new category of fatty liver disease, we aimed to compare the diagnostic performance of FIB-4 and NFS in subjects with MAFLD and in various subgroups.
Materials and Methods: This study was designed as cross-sectional study. Data from 6,775 subjects who underwent magnetic resonance elastography (MRE) and abdominal ultrasonography at the same time during a health check-up at 13 various health check-up centers were retrospectively reviewed. Advanced fibrosis was defined as an MRE value of ≥ 3.6 kPa.
Results: The area under the receiver operating characteristic curves (AUROCs) of FIB-4 and NFS for diagnosing advanced fibrosis were similar in subjects with MAFLD. However, the AUROC of NFS was lower than that of FIB-4 in the diabetic subgroup of MAFLD (0.809 in FIB-4 vs. 0.717 in NFS, P = 0.002). The performances of both FIB-4 and NFS were poor in the subgroup of MAFLD with significant alcohol intake.
Conclusion: The overall diagnostic performance of FIB-4 and NFS for diagnosing advanced fibrosis did not differ among subjects with MAFLD. However, the performance of NFS was lower in the diabetes subgroup of MAFLD. The diagnostic performance of FIB-4 was better for fibrosis in various subgroups of MAFLD.

[OP-0339]

Diagnostic accuracy of shear wave ultrasound elastography for early detection of steatohepatitis among patients with type 2 diabetes mellitus

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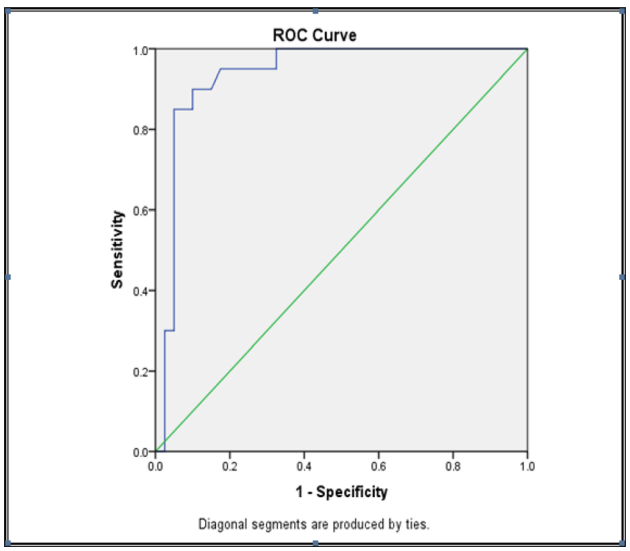
Objectives: Introduction: Metabolic (dysfunction) associated fatty liver disease (MAFLD) is a novel concept proposed in 2020 aiming to replace the term NAFLD.MAFLD is diagnosed in patients when they have both hepatic steatosis and any of the following three metabolic conditions: overweight/obesity, diabetes mellitus, or evidence of metabolic dysregulation (MD). Recently liver fibrosis staging become one of initial steps in evaluating patients with type 2 DM. Liver biopsy remains the gold standard for diagnosis of steatohepatitis. Shear wave elastography shows a stepwise increase of liver stiffness as the severity of liver inflammation increases. Aim of study: was to evaluate the diagnostic accuracy of shear wave ultrasound elastography in diagnosis of steatohepatitis in patients with type 2 DM.
Materials and Methods: a prospective study included 60 patients who visited our outpatient clinic or inpatient department at Specialized Medical Hospital, Mansoura, Egypt. These patients were adult diabetic with ultrasound showing fatty liver.Shear wave elastography was performed to all patients and stiffness of the liver was measured from different areas in kilopascal (kPa) then average stiffness by elastography was recorded. Liver biopsy was done and histopathological examination by Hematoxlin, Eosin and Masson Trichrome stains, then NAFLD activity score (NAS) was calculated.
Results: The study included 30 males and 30 females. Correlation between results of stiffness by elastography and NAS by biopsy revealed that:There was a significant positive association between average stiffness by elastography and definitive NASH (NAS 5 and 6) in patients with type 2 DM.At a level of 8.45 kPa by shear wave elastography, we can differntiate simple steatosis from steatohepatitis (Area Under Curve 0.936, senstivity 90%, specificity 90%, positive predictive value 81%, negative predictive value 49%).
Conclusion: Using shear wave elastography, we can differentiate simple steatosis from steatohepatitis in patients with type 2 DM.



[OP-0362]

Semaglutide in patients with non-alcoholic steatohepatitis: Subgroup analysis of a randomized, placebo-controlled phase 2 trial

Sven Francque[1], Mette S Kjær[2], Steen Ladelund[3], Takeshi Okanoue[4], Lyudmila Mateva[5], Ichhya Shrestha[6], Stephen A Harrison[7]

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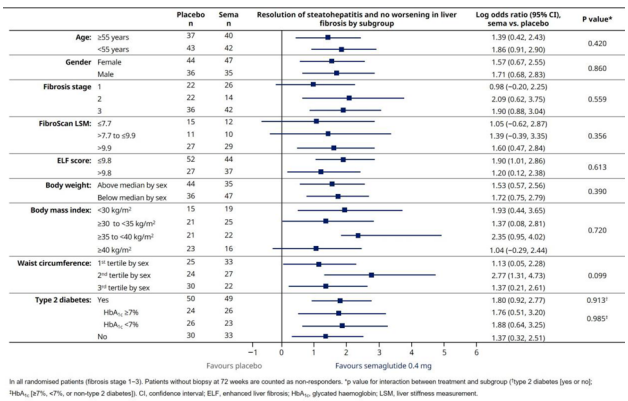
Objectives: In a phase 2 trial, significantly more patients with NASH and fibrosis (F) stage 2–3 achieved NASH resolution without worsening of fibrosis with semaglutide versus placebo. This post-hoc exploratory analysis assessed whether patient and disease characteristics influenced the effect of semaglutide on NASH resolution.
Materials and Methods: Adults with biopsy-confirmed NASH and F1–3 were randomized to once-daily subcutaneous semaglutide 0.1, 0.2, or 0.4 mg, or placebo for 72 weeks. The primary endpoint (resolution of NASH without worsening of fibrosis) was evaluated across subgroups based on gender, age, type 2 diabetes, body weight, body mass index, fibrosis stage, enhanced liver fibrosis score, and liver stiffness. Subgroups were analyzed for heterogeneity (interaction) in treatment differences for the primary endpoint.
Results: Overall, 320 patients were randomized to semaglutide 0.1 mg (n = 80), 0.2 mg (n = 78), 0.4 mg (n = 82) or placebo (n = 80). In all randomized patients (F1–3), NASH resolution without fibrosis worsening at 72 weeks was achieved by significantly more patients receiving semaglutide 0.4 mg compared with placebo (56.1% versus 20.0%; $p < 0.0001$), and a numerical benefit was seen across all subgroups (Figure). There were no significant treatment-by-subgroup interactions between semaglutide and placebo for achievement of the primary endpoint at 72 weeks. Similar results were seen with semaglutide 0.1 and 0.2 mg (data not shown).
Conclusion: A consistent beneficial effect of semaglutide on the primary endpoint of NASH resolution without fibrosis worsening was observed across a variety of subgroups based on baseline characteristics, suggesting similar efficacy across a range of patients.



In all randomised patients (fibrosis stage 1–3). Patients without biopsy at 72 weeks are counted as non-responders. *p value for interaction between treatment and subgroup (†type 2 diabetes [yes or no]; ‡HbA_{1c} [≥7%, <7%, or non-type 2 diabetes]). CI, confidence interval; ELF, enhanced liver fibrosis; HbA_{1c}, glycated haemoglobin; LSM, liver stiffness measurement.

[OP-0364]

Artificial intelligence-powered digital pathology model supports that fibrosis is reduced by semaglutide in patents with NASH

Stephen A Harrison[1], Sven Francque[2], Vanja Cejvanovic[3], Helena Cortez-Pinto[4], Niels Krarup[5], Quang Le[6], Anne-Sophie Sejling[7], Vlad Ratziu[8]

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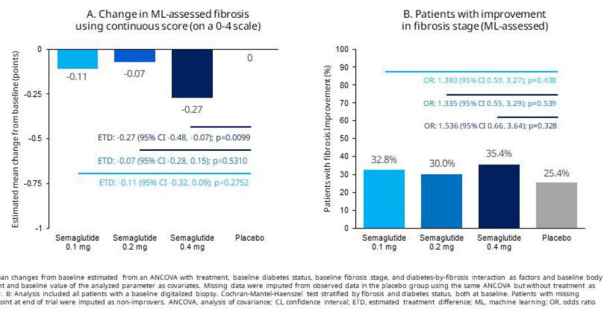
Objectives: In a phase 2 trial, semaglutide showed superior NASH resolution and numerical improvement in fibrosis stage vs placebo. Artificial intelligence (AI)-powered digital pathology may identify changes not quantifiable through manual histological evaluation. We assessed the effects of semaglutide on fibrosis using an AI pathology model.
Materials and Methods: Patients (N = 320) with NASH and fibrosis stage F1–F3 were randomized to once-daily subcutaneous semaglutide (0.1, 0.2, 0.4 mg) or placebo for 72 weeks. All biopsies were manually assessed by two independent pathologists. Digital biopsy slides, available in a subset of biopsies (n = 251 at baseline), were evaluated by PathAI machine learning model. Changes in fibrosis were evaluated by continuous fibrosis score (0–4) and categorical fibrosis stage. Changes in continuous measures and ordinal endpoints were analyzed by ANCOVA and Cochran-Mantel–Haenszel tests, respectively.
Results: Continuous AI-assessed fibrosis score showed a –0.27 treatment difference between semaglutide 0.4 mg and placebo (p = 0.0099) (Figure A). Across treatment groups, continuous fibrosis score correlated with manually assessed improvement in fibrosis stage. AI assessment found no significant improvement in categorical fibrosis stage with semaglutide vs placebo (Figure B), although there was a dose-dependent reduction in the proportion of patients with fibrosis worsening. AI tended to grade baseline fibrosis stage higher than manual assessment for stages 1–2, with low concordance between methods (weighted kappa 0.34).
Conclusion: AI-assessed continuous fibrosis score showed fibrosis was significantly reduced with semaglutide 0.4 mg vs placebo. No difference was seen using AI-assessed categorical fibrosis stage. An AI-based approach can support interpretation of histological results.



A: Mean changes from baseline estimated from an ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage, and diabetes-by-fibrosis interaction as factors and baseline body weight and baseline value of the analyzed parameter as covariates. Missing data were imputed from observed data in the placebo group using the same ANCOVA but without treatment as factor. B: Analysis included all patients with a baseline digitalized biopsy. Cochran-Mantel-Haenszel test stratified by fibrosis and diabetes status, both at baseline. Patients with missing endpoint at end of trial were imputed as non-improvers. ANCOVA, analysis of covariance; CI, confidence interval; ETD, estimated treatment difference; ML, machine learning; OR, odds ratio

[OP-0365]

The role of body weight loss as a mediator of histological efficacy of semaglutide in non-alcoholic steatohepatitis

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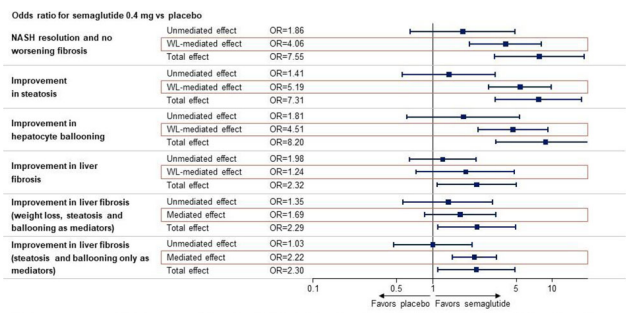
Objectives: In a phase 2 trial, significantly more semaglutide-treated patients achieved NASH resolution without worsening of fibrosis, and greater weight loss, than placebo. We assessed weight loss-mediated and non-mediated (weight loss-independent) effects of treatment on liver histology.
Materials and Methods: Adults (N = 320) with NASH and fibrosis stage F1–F3 were randomized to once-daily subcutaneous semaglutide 0.1, 0.2 or 0.4 mg, or placebo for 72 weeks. Mediation analyses using natural effects models were performed based on complete-case on-treatment measurements (N = 249) for histological parameters with a significant effect of semaglutide. Weight changes from baseline at all scheduled visits were used as mediator. The model was adjusted for baseline body weight, fibrosis stage, type 2 diabetes status, age, and gender.
Results: More semaglutide-treated patients achieved NASH resolution (67% vs 22%; $p < 0.0001$), and improvement in steatosis (73% vs 29%; $p < 0.0001$), ballooning (85% vs 43%; $p < 0.0001$), and fibrosis (53% vs 35%; p = 0.0274) vs placebo. Weight loss directly mediated 63.9% of NASH resolution without worsening of fibrosis (95% confidence interval [CI] 35.8–124.9%), 82.8% of steatosis improvement (95% CI 52.0–138.0%) and 71.6% of ballooning improvement (95% CI 38.8–132.7%). Improvement in fibrosis was not directly mediated by weight loss (25.1% [95% CI − 84.1–228.0%]); steatosis and ballooning accounted for 95.9% of total effect (95% CI 43.0–597.7%) (Figure).
Conclusion: Weight loss accounted for most, but not all, of the histological improvement with semaglutide, particularly for disease activity. Weight loss and disease activity have intricate but partly distinct contributions to fibrosis regression in NASH, which requires confirmation in future studies.



Data based on complete case on-treatment measurements. Plots are odds ratios with 95% confidence intervals. Mediators: weight loss at weeks 4, 12, 20, 28, 46, 44, 52, 62, 72. Baseline confounders: age, gender, type 2 diabetes status, fibrosis stage, body weight.

[OP-0366]

Change in FibroScan-aspartate aminotransferase (FAST) score is associated with histological improvement in non-alcoholic steatohepatitis activity

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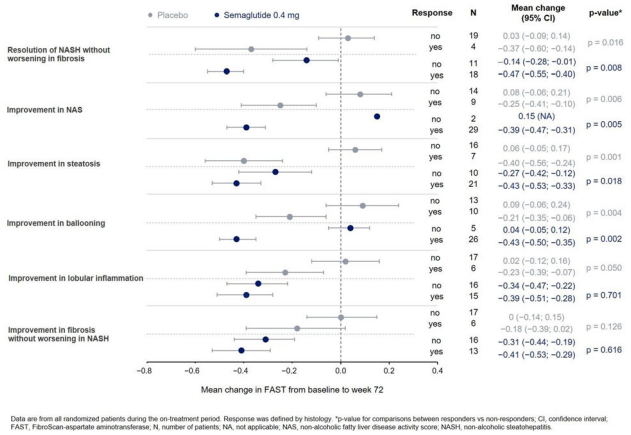
Objectives: FibroScan® liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) combined with aspartate aminotransferase (AST) – known as FibroScan-AST (FAST) – is a non-invasive method to identify risk of NASH progression. We assessed whether changes in FAST correlate with histological changes in placebo and semaglutide-treated patients with NASH.
Materials and Methods: In a randomized phase 2 trial, 320 patients with NASH and F1–F3 fibrosis received semaglutide (0.1, 0.2, 0.4 mg) or placebo. This post-hoc analysis compared changes in FAST score from baseline to week 72 with histological change in NAFLD activity score (NAS) and other clinical parameters during the on-treatment period.
Results: Overall, 161 patients had FAST scores assessed at baseline and week 72. Treatment with semaglutide for 72 weeks led to dose-dependent reductions in FAST score and individual components (LSM, CAP, AST). At week 72, mean reductions in FAST score (estimated treatment ratio vs placebo) were 0.7, 0.5, and 0.4 with semaglutide 0.1, 0.2, and 0.4 mg, respectively. Reductions in FAST scores for placebo and semaglutide 0.4 mg were associated with resolution of NASH without worsening in fibrosis, and improvements in NAS, steatosis, and ballooning (Figure). A $\geq$ 0.2 decrease in FAST score from baseline to week 72 correlated with changes in NASH activity biomarkers (ALT, cytokeratin [CK] 18 M65, CK18 M30 antigen) and fibrosis biomarkers (Fibrosis-4, AST to platelet ratio index) (range: 0.30–0.64).
Conclusion: FAST score is associated with histological improvement of NASH activity and may have potential as a non-invasive surrogate marker of disease progression.



Data are from all randomized patients during the on-treatment period. Response was defined by histology. *p-value for comparisons between responders vs non-responders; CI, confidence interval; FAST, FibroScan-aspartate aminotransferase; N, number of patients; NA, not applicable; NAS, non-alcoholic fatty liver disease activity score; NASH, non-alcoholic steatohepatitis.

[OP-0367]

Fibrosis response assessed by enhanced liver fibrosis and FibroScan liver stiffness measurement in patients with non-alcoholic steatohepatitis treated with subcutaneous semaglutide

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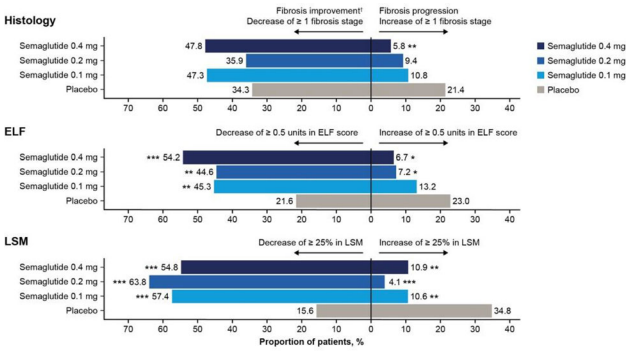
Objectives: To compare fibrosis response in semaglutide and placebo-treated patients with NASH using enhanced liver fibrosis (ELF) score, FibroScan® liver stiffness measurement (LSM), and histology.
Materials and Methods: In a 72-week phase 2 trial, 320 patients were randomized to once-daily subcutaneous semaglutide (0.1, 0.2, 0.4 mg) or placebo. In this post hoc analysis, fibrosis improvement or progression was categorized using ELF ($\geq$ 0.5 units decrease/increase), LSM ($\geq$ 25% decrease/increase), and liver histology ($\geq$ 1 stage decrease/increase) at baseline and week 72. For ELF and LSM response, proportions of subjects were compared using a logistic regression model.
Results: At baseline, a weak correlation was found between ELF and LSM (r [95% confidence interval] = 0.22 [0.13–0.31]). Histological fibrosis stage was associated with ELF ($p < 0.001$) and LSM ($p = 0.016$). At week 72, although the percentage of patients with histological improvement in fibrosis was not significantly different

between groups, the proportion of ELF and LSM responders was higher with semaglutide vs placebo (Figure). At week 72, fewer patients receiving semaglutide 0.4 mg had fibrosis progression by histology (5.8% vs 21.4%; p = 0.009), ELF (6.7% vs 23.0%; p = 0.01), and LSM (10.9% vs 34.8%; p = 0.002). For placebo and semaglutide 0.4 mg, change from baseline to week 72 in ELF and LSM correlated with biomarkers of NASH activity (AST, ALT, cytokeratin 18 M65 and M30), fibrosis (AST to platelet ratio index) and body weight.

Conclusion: Treatment with semaglutide for 72 weeks reduced fibrosis progression as measured by histology, ELF and LSM, suggesting fibrosis response is related to semaglutide use.



Data are from all randomized patients during the on-treatment period. *p < 0.05; **p < 0.01; ***p < 0.001 vs placebo; †Fibrosis improvement was defined as decrease of ≥ 1 fibrosis stage without worsening of NASH (increase of ≥ 1 point in either the lobular inflammation score or the hepatocyte ballooning score, according to the NASH Clinical Research Network criteria). ELF, enhanced liver fibrosis; LSM, liver stiffness measurement; NASH, non-alcoholic steatohepatitis.

[OP-0368]

Effect of subcutaneous semaglutide on features of the metabolic syndrome in patients with non-alcoholic steatohepatitis

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Objectives: NAFLD and NASH are closely linked to insulin resistance, visceral obesity, and features of the metabolic syndrome. We assessed the effects of semaglutide on parameters associated with metabolic syndrome in patients with NASH.

Materials and Methods: In a 72-week phase 2 trial, patients with NASH and fibrosis stage F1–F3 were randomized to once-daily subcutaneous semaglutide (0.1, 0.2, 0.4 mg) or placebo. Changes in metabolic and inflammatory parameters are reported for all randomized patients during the in-trial period; HbA_{1c} and fasting plasma glucose are reported in patients with type 2 diabetes (T2D), and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and adipose tissue insulin resistance index (Adipo-IR: fasting plasma insulin × free fatty acids) in patients untreated with insulin at baseline. Correlations with primary endpoint (NASH resolution without worsening of fibrosis) are reported in all patients on-treatment at week 72 (semaglutide 0.4 mg and placebo combined).

Results: Of 320 randomized patients, 62% had T2D and 49% were treated with insulin at baseline. Semaglutide 0.4 mg was associated with significantly greater improvements than placebo in waist circumference, HbA_{1c}, fasting plasma glucose, HOMA-IR, Adipo-IR, high-density lipoprotein (HDL) cholesterol, triglycerides, and high-sensitivity C-reactive protein (Table). Improvements in waist circumference, HbA_{1c}, fasting plasma glucose, HOMA-IR, Adipo-IR, and HDL cholesterol correlated with achieving NASH resolution without worsening of fibrosis.

Conclusion: In addition to weight loss and improved glycemic control, semaglutide 0.4 mg resulted in significant improvements in multiple features of the metabolic syndrome. Changes from baseline in metabolic parameters correlated with resolution of steatohepatitis.

		Semaglutide 0.4 mg	Placebo	ETD/ETR (95% CI)	P-value		With NASH resolution	Without NASH resolution	P-value†
Estimated change from BL at week 72*	Waist circumference, cm	−11.0	−1.3	−9.7 (−12.2, −7.3)	<0.0001	Mean ± SD change from BL (semaglutide 0.4 mg and placebo groups combined)	−8.8 ± 8.2	−3.5 ±6.6	<0.001
	HbA_{1c}, % (T2D)	−1.2	−0.01	−1.1 (−1.5, −0.8)	<0.0001		−1.2 ± 0.9	−0.5 ± 1.1	<0.001
	Fasting plasma glucose, mmol/L (T2D)	−2.1	−0.3	−1.9 (−2.7, −1.1)	<0.0001		−2.1 ± 2.3	−1.1 ± 2.7	0.006
Ratio to BL at week 72*	HDL-cholesterol, mmol/L	1.1	1.0	1.06 (1.02, 1.11)	0.0064		0.1 ± 0.1	0.0 ± 0.2	<0.001
	Non-HDL-cholesterol, mmol/L	0.9	0.9	0.97 (0.91, 1.05)	0.4514		−0.2 ± 0.7	−0.3 ± 0.9	0.981
	Triglycerides, mmol/L	0.7	1.0	0.75 (0.67, 0.84)	<0.0001		−0.4 ± 1.1	−0.2 ± 0.8	0.116
	hs-CRP, mg/L	0.4	0.9	0.46 (0.35, 0.61)	<0.0001		−1.8 ± 9.3	−1.3 ± 7.2	0.212
	HOMA-IR (no insulin at BL)	0.6	0.9	0.65 (0.52, 0.83)	0.0004		−3.0 ± 4.7	−1.7 ± 8.9	0.017
	Adipo-IR (no insulin at BL)	0.5	0.9	0.57 (0.44, 0.75)	<0.0001		−32.6 ± 55.6	−13.0 ± 68.7	0.015

*Based on ANCOVA with multiple imputation of missing data from placebo group. †P values from Wilcoxon two sample test. BL, baseline; ETD, estimated treatment difference; ETR, estimated treatment ratio.

[PP-0373]

Risk of dementia in nonalcoholic fatty liver disease subjects: A nationwide nested-case control study

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is known to be associated with metabolic syndrome in which diabetes is an important component. Diabetes is also known to be a risk factor for dementia. This study aimed to determine whether NAFLD would be a risk factor for development of dementia in an elderly population.

Materials and Methods: This study included 107,369 subjects aged ≥ 60 years in the Korea National Health Insurance Service-Senior cohort, entered in 2009 and followed up until 2016. NAFLD was diagnosed by calculating fatty liver index (FLI). Subjects were screened for dementia at baseline using a Korean Dementia Screening Questionnaire and dementia was diagnosed using ICD-10 codes. Controls were randomly selected at a ratio of 1:5 from individuals who were at risk of becoming the case subjects at the time of selection.

Results: From 107,369 subjects, 68,898 stroke and dementia free subjects without chronic hepatitis B or C or excessive alcohol drinking were evaluated. Having NAFLD, determined by FLI was associated with increased risk of dementia development (AOR [adjusted odd ratio] 1.521; 95% CI [confidence interval] 1.003–2.306). The increased risk of dementia in NAFLD subjects was independent of type 2 diabetes (AOR 1.362; 95% CI 1.067–1.739).

Conclusion: In this population based study, having NAFLD increased risk of dementia, independent of diabetes.

[OP-0379]

Text messaging intervention and weight loss in patients with non-alcoholic fatty liver disease: A randomized controlled study

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Objectives: The widespread use of mobile phone may create effective intervention for behavioral therapy. This study was performed to evaluate the effects of text messaging intervention on weight loss in patients with Non-alcoholic Fatty Liver Disease (NAFLD) to promote and maintain lifestyle modification outside of the clinical setting.
Materials and Methods: A randomizes controlled trial study in 120 well-defined NAFLD patients follow up in Phramongkutklao hospital between 2018–2020. The volunteers randomized into 3 groups: one way communication group (A), interactive group (B) and control group (C). Measurement of body weight, height, waist circumference, blood pressure and evaluation for liver function test, lipid profile, fasting plasma glucose, HbA1C before and after intervention in all volunteers was performed.
Results: Mean total cholesterol decreased 7.74 mg/dL in group A compared with increased 8.99 mg/dL in control group when follow up at 3 month (p-value = 0.029) and decreased 10.15 mg/dL compared with increased 6.03 mg/dL in control group when follow up at 6 month (p-value = 0.046). At 6-month follow up time, group B has decreased total cholesterol 17.43 mg/dL compared with increased 6.03 mg/dL in group C (p-value = 0.002) and decreased in LDL-cholesterol 16.35 mg/dL while increased 1.70 mg/dL in group C (p-value = 0.023). However, no significant change in weight between 0, 3 and 6 month of all groups.
Conclusion: Text messaging intervention can lead to decrease in total cholesterol and LDL-cholesterol in short and long term follow up.

Table 1 Summary of variables in NAFLD patients comparison between group A and B, A and C, B and C and comparison between 0, 3 and 6-month follow up time

	Group A		Group B		Group C		p-value	p-value for Bonferroni test		
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD		A vs B	A vs C	B vs C
Δ Month 0 - Month 3	-									
Body weight (kg)	37	0.35 ± 1.68	39	0.71 ± 1.91	38	0.29 ± 1.76	0.547			
WC (cm)	30	0.70 ± 1.13	37	1.07 ± 2.11	36	0.08 ± 1.00	0.024	0.985	0.314	0.021
Systolic BP (mmHg)	37	1.11 ± 14.40	39	4.03 ± 13.21	38	0.39 ± 12.17	0.448			
Diastolic BP (mmHg)	37	-0.16 ± 9.88	39	2.10 ± 8.43	38	0.55 ± 9.30	0.548			
ALT (U/L)	36	3.86 ± 14.84	38	7.84 ± 19.35	37	0.62 ± 22.81	0.273			
AST (U/L)	36	4.01 ± 10.08	38	16.46 ± 82.64	37	-0.17 ± 14.68	0.320			
Cholesterol (md/dL)	36	7.74 ± 28.75	37	6.30 ± 27.44	34	-8.99 ± 22.92	0.017	1.000	0.029	0.051
Triglyceride (md/dL)	36	1.46 ± 56.85	37	-15.38 ± 91.46	33	-21.72 ± 96.63	0.486			
HDL-chol (md/dL)	36	1.85 ± 5.90	37	1.81 ± 7.29	34	0.89 ± 6.60	0.793			
LDL-chol (md/dL)	37	5.18 ± 27.46	37	3.96 ± 27.60	36	-5.58 ± 19.32	0.141			
FPG (mg/dL)	36	2.25 ± 18.90	38	-6.56 ± 33.31	36	8.24 ± 19.86	0.042			
HbA1C	36	-0.05 ± 0.37	36	-0.11 ± 0.70	35	-0.07 ± 0.40	0.887			
Δ Month 0 - Month 6										
Body weight (kg)	37	0.47 ± 2.34	36	0.79 ± 3.49	38	0.42 ± 1.99	0.817			
WC (cm)	25	0.94 ± 1.64	25	2.06 ± 2.96	27	0.06 ± 1.08	0.003	0.164	0.361	0.002
Systolic BP (mmHg)	37	3.73 ± 13.69	35	5.4 ± 11.81	38	-0.26 ± 13.29	0.162			
Diastolic BP (mmHg)	37	2.14 ± 13.06	35	2.74 ± 8.81	38	-1.71 ± 10.56	0.171			
ALT (U/L)	35	1.39 ± 44.15	32	12.99 ± 23.48	31	3.36 ± 24.14	0.310			
AST (U/L)	35	0.83 ± 25.03	32	22.79 ± 92.59	31	-0.79 ± 15.34	0.170			
Cholesterol (md/dL)	30	10.15 ± 25.42	27	17.43 ± 31.58	30	-6.03 ± 17.76	0.002	0.844	0.046	0.002
Triglyceride (md/dL)	29	25.78 ± 54.16	27	2.36 ± 54.13	29	-5.87 ± 58.75	0.088			
HDL-chol (md/dL)	29	0.90 ± 7.71	27	1.79 ± 7.40	30	1.59 ± 6.38	0.885			
LDL-chol (md/dL)	33	9.43 ± 29.11	31	16.35 ± 30.75	34	-1.70 ± 19.15	0.026	0.907	0.273	0.023
FPG (mg/dL)	32	1.04 ± 22.43	31	0.39 ± 25.85	35	5.53 ± 22.32	0.623			
HbA1C	31	-0.08 ± 0.57	29	0.11 ± 0.94	32	0 ± 0.52	0.571			

One way ANOVA
Significant if p<0.05

[OP-0399]

Metabolic dysfunction-associated fatty liver disease criteria better identify subjects with high-risk fatty liver disease: A nationwide study

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Objectives: Clinical features of nonalcoholic fatty liver disease (NAFLD) that should constitute the diagnostic criteria of metabolic dysfunction-associated fatty liver disease (MAFLD) remain unclear. We investigated the risk of sarcopenia and cardiovascular disease (CVD) in subjects with MAFLD and non-metabolic risk (MR) NAFLD.
Materials and Methods: Subjects were selected from the Korean National Health and Nutrition Examination Surveys 2008–2011. Significant liver fibrosis was defined based on the fibrosis-4 index, categorized by age cut-offs. Sarcopenia was defined as the lowest quintile sarcopenia index. An atherosclerotic CVD (ASCVD) risk score $> 10\%$ was defined as high probability.
Results: Of the 7,248 subjects with NAFLD or MAFLD, 7,111 (98.1%) had MAFLD and 137 (1.9%) had non-MR NAFLD. In the non-MR NAFLD group, 28 (20.4%) had significant liver fibrosis. MR components were statistically similar between subjects with and without significant liver fibrosis in the non-MR NAFLD group ($P > 0.05$) but were significantly higher in the MAFLD group than in the non-MR NAFLD group ($P < 0.05$). After adjusting for confounders, the risks of sarcopenia and high ASCVD probability were similar between subjects with and without significant liver fibrosis in the non-MR NAFLD group (all $P > 0.05$); the risks were significantly higher in the MAFLD group than in the non-MR NAFLD group (odds ratio = 3.38–7.23 for sarcopenia and 3.73–6.64 for ASCVD; all $P < 0.05$).
Conclusion: The risk of sarcopenia and CVD were significantly higher in the MAFLD group but did not differ according to fibrotic burden in the non-MR NAFLD group. The MAFLD criteria might be better for identifying high-risk fatty liver disease.

Table. Adjusted risks of sarcopenia or high probability of ASCVD in MAFLD and non-MR NAFLD stratified according to fibrotic burden.

Sarcopenia	Non-MR NAFLD		MAFLD
	Without significant liver fibrosis	With significant liver fibrosis	
Model 1	1.00 (ref.)	3.84 (0.85-17.20) P=0.079	7.23 (2.67-20.63) P<0.001
Model 2	1.00 (ref.)	4.20 (0.90-19.67) P=0.069	3.56 (1.25-10.12) P=0.018
Model 3	1.00 (ref.)	4.51 (0.97-21.04) P=0.055	3.38 (1.18-9.65) P=0.023
ASCVD			
Model 1	1.00 (ref.)	1.52 (0.34-6.78) P=0.581	6.64 (2.87-15.36) P<0.001
Model 2	1.00 (ref.)	1.59 (0.36-6.98) P=0.539	5.47 (2.39-12.73) P<0.001
Model 3	1.00 (ref.)	3.01 (0.60-15.13) P=0.180	3.73 (1.52-9.13) P=0.004

Model 1: adjusted for sex and age.
Model 2: adjusted for sex, age, body mass index, and waist circumference.
Model 3: adjusted for sex, age, body mass index, waist circumference, HOMA-IR*, HDL-cholesterol*, triglycerides*, systolic blood pressure, fasting blood glucose, aspartate aminotransferase*, alanine aminotransferase*, gamma glutamyltransferase*, and fatty burden by fatty liver index.
*Log-transformed.

[OP-0411]

Metabolic dysfunction associated fatty liver disease identifies patients with cardiovascular disease risk better than nonalcoholic fatty liver disease

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Objectives: Cardiovascular disease (CVD) is the main cause of mortality in subjects with non-alcoholic fatty liver disease (NAFLD). We investigated the association between CVD risk and metabolic dysfunction associated fatty liver disease (MAFLD) or NAFLD and the influence of significant liver fibrosis on CVD risk.
Materials and Methods: Subjects who underwent a comprehensive medical check-up between 2014 and 2019 were recruited. Significant liver fibrosis was defined using NAFLD fibrosis score or BARD score. Predicted CVD risk was calculated using the 10-year atherosclerotic cardiovascular disease (ASCVD) risk calculator of 2013 ACC/AHA guidelines.
Results: Of the study population (n = 78,762), 27,047 (34.3%) and 24,036 (30.5%) subjects had MAFLD and NAFLD, respectively. A total of 1,084 (4.0%) and 921 (3.8%) subjects had previous CVD history in MAFLD and NAFLD subgroups, respectively. The prevalence of previous CVD history and high ASCVD risk score (> 15%) were significantly higher in MAFLD or NAFLD group with significant liver fibrosis than in the other groups (all $p < 0.001$). In multivariate analysis, MAFLD was independently associated with previous CVD history after adjusting for confounders (odds ratio = 1.088–1.387, all $p < 0.05$), whereas NAFLD was not (all $p > 0.05$). Adjusted odds ratios for high ASCVD risk score were significantly higher in MAFLD than in NAFLD group (all $p < 0.001$). Significant liver fibrosis was independently associated with previous CVD history and high ASCVD risk score in both MAFLD and NAFLD subgroups (all $p < 0.05$).
Conclusion: MAFLD might better identify subjects with CVD risk than NAFLD. Fibrosis assessment might be helpful for detailed prognostication in subjects with MAFLD or NAFLD.

Table. The odds ratio of prevalence of previous CVD history in subjects with MAFLD or NAFLD

Variables	Unadjusted			Model 1			Model 2			Model 3		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
MAFLD	1.387	1.281-1.502	<0.001	1.090	1.004-1.183	0.039	1.090	1.003-1.186	0.043	1.088	1.001-1.184	0.048
MAFLD without significant liver fibrosis[a]	1.000 (reference)			1.000 (reference)			1.000 (reference)			1.000 (reference)		
MAFLD with significant liver fibrosis	3.092	2.296-4.164	<0.001	3.189	2.366-4.297	<0.001	3.131	2.322-4.224	<0.001	3.007	2.227-4.060	<0.001
NAFLD	1.263	1.163-1.370	<0.001	1.014	0.932-1.103	0.747	1.028	0.944-1.119	0.528	1.011	0.928-1.101	0.802
NAFLD without significant liver fibrosis[a]	1.000 (reference)			1.000 (reference)			1.000 (reference)			1.000 (reference)		
NAFLD with significant liver fibrosis	3.754	2.727-5.169	<0.001	3.947	2.865-5.441	<0.001	3.847	2.788-5.309	<0.001	3.664	2.652-5.064	<0.001
Subgroup without significant liver fibrosis												
By NAFLD fibrosis score (>0.676)												
MAFLD	1.343	1.239-1.456	<0.001	1.103	1.015-1.199	0.021	1.091	1.003-1.188	0.043	1.064	0.978-1.158	0.147
NAFLD	1.217	1.120-1.323	<0.001	1.045	0.960-1.138	0.306	1.039	0.955-1.131	0.372	0.972	0.893-1.059	0.523
By BARD score (>2.0)												
MAFLD	1.176	1.075-1.286	<0.001	0.984	0.897-1.080	0.739	0.988	0.899-1.085	0.795	0.981	0.893-1.078	0.690
NAFLD	1.050	0.957-1.153	0.302	0.901	0.819-0.991	0.032	0.915	0.831-1.007	0.070	0.900	0.817-0.992	0.033
By FAST score[b] (>0.35)												
MAFLD	1.259	1.016-1.560	0.035	1.062	0.852-1.325	0.592	1.017	0.812-1.273	0.883	1.016	0.812-1.273	0.888
NAFLD	1.217	0.978-1.514	0.079	1.055	0.844-1.320	0.637	1.026	0.818-1.287	0.824	1.024	0.816-1.286	0.836
Subgroup with significant liver fibrosis												
By NAFLD fibrosis score (>0.676)												
MAFLD	4.153	3.090-5.581	<0.001	3.704	2.751-4.986	<0.001	3.617	2.684-4.875	<0.001	3.297	2.442-4.451	<0.001
NAFLD	4.571	3.331-6.271	<0.001	4.365	3.174-6.002	<0.001	4.287	3.116-5.897	<0.001	3.731	2.706-5.146	<0.001
By BARD score (>2.0)												
MAFLD	2.226	1.975-2.509	<0.001	1.404	1.241-1.588	<0.001	1.397	1.233-1.583	<0.001	1.389	1.226-1.574	<0.001
NAFLD	2.229	1.961-2.534	<0.001	1.392	1.220-1.589	<0.001	1.408	1.232-1.608	<0.001	1.381	1.208-1.578	<0.001
By FAST score[b] (>0.35)												
MAFLD	2.529	1.608-3.979	<0.001	2.131	1.332-3.409	0.002	1.808	1.102-2.966	0.019	1.793	1.093-2.941	0.021
NAFLD	2.654	1.636-4.307	<0.001	2.206	1.335-3.646	0.002	1.906	1.134-3.202	0.015	1.887	1.121-3.175	0.017

[a]Model 1 = age and gender.
Model 2 = model 1 + platelet, aspartate aminotransferase, alanine aminotransferase, albumin, gamma glutamyl-transferase, and serum creatinine.
Model 3 = model 3 + smoking, alcohol, and malignancy.
CVD, cardiovascular disease; MAFLD, metabolic dysfunction associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; OR, odd ratio; CI, confidence interval.
[a]Significant liver fibrosis was defined NAFLD fibrosis score >0.676.
[b]A total of 12737 subjects were analyzed due to missing transient elastography values.

[OP-0425]

Prevalence of advanced hepatic fibrosis and comorbidity in metabolic dysfunction associated fatty liver disease in Korean

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Objectives: There are several reports on the prevalence of metabolic dysfunction associated fatty liver disease (MAFLD). But prevalence of advanced hepatic fibrosis in MAFLD is largely unknown. We aimed to evaluate the prevalence of advanced fibrosis in MAFLD.
Materials and Methods: Total 6,775 subjects from nationwide 13 health check-up centers were included in this cross-sectional study. Fatty liver was evaluated using ultrasonography. Significant (≥ F2) and advanced (≥ F3) hepatic fibrosis were defined by MRE thresholds of 3.0 kPa (range: 2.99–3.65 kPa) and 3.6 kPa (range: 3.4–3.9 kPa), respectively. The sex- and age-standardized prevalence of MAFLD and hepatic fibrosis were estimated.
Results: The sex- and age-standardized prevalence of MAFLD was 33.9%. The prevalence of obesity (BMI ≥ 25 kg/m^2) in MAFLD was 71.1%, and 79.0% of obese subjects had MAFLD. The prevalence of diabetes in MAFLD was 13.3%, and 73.6% of subjects with diabetes had MAFLD. The sex- and age-standardized prevalence of significant (≥ F2) and advanced hepatic fibrosis (≥ F3) among MAFLD was 9.7% (range: 3.0–9.8%) and 3.0% (range: 2.6–4.6%), respectively. The prevalence of advanced hepatic fibrosis in overweight/obese (group I), lean (group II), and diabetic (group III) MAFLD was 2.3%, 3.1%, and 9.5%, respectively.
Conclusion: The sex- and age-standardized prevalence of advanced fibrosis was 3.0% (range: 2.6–4.6%) in subjects with MAFLD.

[PP-0434]

Metabolic stress indices including mitochondrial biomarkers for non-invasive diagnosis of hepatic steatosis and fibrosis

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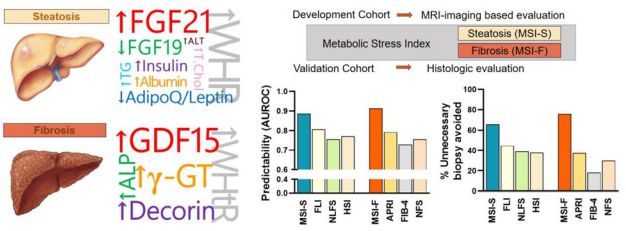
Objectives: Mitochondrial dysfunction with oxidative stress contributes to NAFLD progression. We investigated the steatosis and fibrosis predictive efficacy of a novel non-invasive diagnostic panel using stress biomarkers.
Materials and Methods: Altogether, 343 subjects who underwent magnetic resonance imaging-based liver examinations from a population-based general cohort, and 41 patients enrolled in a biopsy-evaluated NAFLD cohort, participated in the development and validation groups, respectively.
Results: Multivariate regression showed that waist-to-hip ratio, FGF21, FGF19, adiponectin-to-leptin ratio, insulin, albumin, triglyceride, total-cholesterol, and alanine-aminotransferase were independent predictors of steatosis (rank-ordered by Wald). The area under receiver-operator characteristics curve (AUROC) of the metabolic stress index for steatosis (MSI-S) was 0.886 and 0.825 in development and validation groups, respectively. MSI-S had higher diagnostic accuracy (71.7%?81.1%) than other steatosis indices. For hepatic fibrosis, growth differentiation factor 15 (GDF15) highly correlated to liver stiffness. Waist-to-height ratio, GDF15, γ-glutamyltransferase, decorin, and alkaline-phosphatase were independent predictors for fibrosis (rank-ordered). The MSI for fibrosis (MSI-F) had a higher AUROC (0.912?0.977) and better diagnostic accuracy (82.6%?92.4%) than other fibrosis indices, both in the development and validation groups. MSI-S and MSI-F differentiated steatosis and fibrosis severities, respectively, while other indices showed less discrimination.
Conclusion: Novel non-invasive indices MSI-S and MSI-F based on mitochondrial stress biomarkers FGF21 and GDF15 predicted steatosis and fibrosis. Furthermore, either MSI-S or MSI-F may increase the population that could be excluded from further evaluation, reducing unnecessary invasive investigations more effectively than other indices.



[PP-0441]

Long-term effects of the changes in hepatic steatosis status on the risk of incident type 2 diabetes mellitus: A 15-year community-based prospective cohort study

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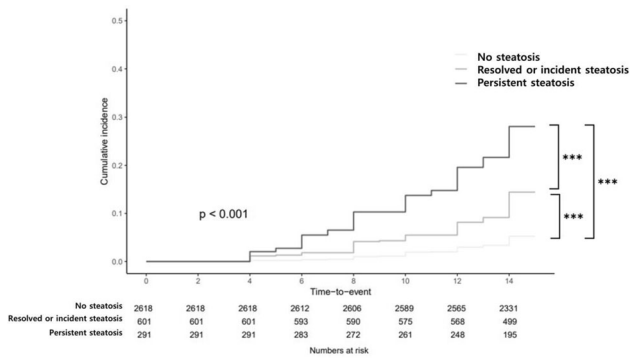
Objectives: Non-alcoholic fatty liver disease (NAFLD) is strongly associated with a risk of incident type 2 diabetes mellitus; however, the impact of changes in hepatic steatosis on the risk of developing type 2 diabetes mellitus remains unknown. We investigated the long-term effect of changes in hepatic steatosis on this risk.
Materials and Methods: We evaluated 3510 participants from the 2001–2016 Korean Genome and Epidemiology Study. Those with significant alcohol consumption (> 40 g/day for men and > 20 g/day for women) or type 2 diabetes mellitus during 2001–2004 were excluded. Steatosis was defined as NAFLD liver fat score (NAFLD-LFS) of over − 0.64, and baseline values were assessed between 2001 and 2002. Differences in NAFLD-LFS (ΔLFS) and changes in steatosis status (no, intermittent [resolved or incident], and persistent steatosis) were assessed between 2003 and 2004. Changes in the risk of diabetes status were observed until 2016.
Results: Over 52,650 person-years of follow-up, type 2 diabetes mellitus developed in 296 participants (8.4%) during year 2005-year 2016. The incidence of diabetes in those with no steatosis, intermittent steatosis, and persistent steatosis during follow-up increased by 5.1%, 14.1%, and 27.1% respectively. Multivariate-adjusted analysis (adjusted for age, sex, income, smoking status, and physical activity) revealed that the risk was higher in those with persistent steatosis than those with no steatosis and intermittent steatosis. Baseline NAFLD-LFS and ΔLFS was associated with increased risk of incident type 2 diabetes mellitus.
Conclusion: Initial severity as well as aggravation of steatosis determined by NAFLD-LFS is an independent predictor of incident type 2 diabetes mellitus. Strategies aimed at reducing liver fat may prevent future development of diabetes among patients with NAFLD.



[PP-0451]

The relationship between tobacco smoking in the past and obesity with non-alcoholic fatty liver disease among residents of Bishkek (Kyrgyzstan)

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Objectives: The study of gender differences in the risk of developing NAFLD in former smokers, taking into account the antiestorogenic properties of cigarette smoke, as well as the development of insulin resistance, will help in the development of preventive measures to prevent the development of liver pathology. The study of the relationship between tobacco smoking and obesity in patients with NAFLD will help in the fight against the development and progression of liver pathology in urban areas. The aim of the study is to study the gender characteristics of the relationship between tobacco smoking in the past and obesity in NAFLD in residents of the city of Bishkek (Kyrgyzstan).
Materials and Methods: When screening 846 patients who applied to family medicine centers in Bishkek for various reasons, 612 people were examined according to the exclusion criteria, of which men—364 (59.4%), women—248 (40.6%), aged from 25 to 70 years old. After informed consent, anthropometric data, levels of AST, ALT, history data—tobacco smoking in the past (no smoking for the previous 6 months or more) and ultrasound of the liver were examined. The data obtained were subjected to statistical processing using the Statististics SPSS 16.0 software package (T-test was used), Microsoft Excel.
Results: The data are presented in the table (table attachment).
Conclusion: In NAFLD, tobacco smoking in the past prevailed among men, who were characterized by a significant increase in waist circumference, body mass index, and the number of pack-years in history. To prevent the development of NAFLD, one of the decisive moments is to find out a clear history of previous smoking habits.

Indicator	1st group (men) (n= 364)	2nd group (women) (n= 248)	Significance
Body mass index, kg / m2	36,1±0,08	29,4±0,07	P < 0,05
Waist Size (OT), (cm)	104,8±2,07	94,2±2,1	P < 0,05
Hips, (V) (cm)	103,2±0,15	106,2±0,25	P < 0,05
OT / V ratio	1,01±0,01	0,89±0,04	P < 0,05
Pack-years of smoking in the past	16,2±2,09	10,4±1,15	P < 0,05

[PP-0452]

Stoppage of exercise during the COVID-19 pandemic results in worsening liver enzymes in patients with metabolic associated fatty liver disease

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Objectives: Worldwide, the COVID-19 pandemic has resulted in lifestyle disruptions, with lockdowns and curtailed activities. This was acutely felt in Asia from February 2020 onwards. Such drastic changes in lifestyle habits may impact negatively on metabolic related diseases. We explored these changes and their effects in patients with metabolic associated fatty liver disease (MAFLD).
Materials and Methods: The data of MAFLD patients who were prospectively enrolled from eleven Asian centres in a longitudinal cohort study were analyzed. The data from 1st January 2019 (pre-COVID-19), were compared with the data from 1st February 2020 onwards (during COVID-19). Patients were stratified by physical activity level and whether they met target recommendation of > 150 min of moderate/vigorous exercise per week.
Results: A total of 229 patients were evaluated. Mean age was 59 ± 9.6 years with 136 (59.4%) males. During the COVID-19 pandemic, 50 (21.8%) patients maintained moderate/vigorous exercise, while 28 (12.2%) and 33 (14.4%) patients started and stopped moderate/vigorous exercising respectively. 118 patients (51.5%) did not participate in moderate/vigorous exercise either before or during the pandemic. Seventy-eight (34.1%) patients achieved > 150 min moderate/vigorous exercise per week at the last visit. With the onset of COVID-19, reduction of physical activity of any kind was demonstrated in the majority (65.9%) of patients. There was a reduction of any physical activity including walking amongst those who stopped moderate/vigorous exercise and those without moderate/vigorous exercise throughout. No significant changes in BMI, waist or hip circumference were observed in any activity level group. In patients who stopped moderate/vigorous exercise, alanine transaminase and aspartate transaminase significantly increased by 18.5% and 14.8% respectively.
Conclusion: Stoppage of moderate/vigorous exercise leads to worsening of liver enzymes in patients with MAFLD and may have deleterious effects long term. As we adapt to live with COVID endemicity, novel modified healthy lifestyle habits would be needed to manage MAFLD.

	Started Exercising* (n=28, 12.2%)			Stopped Exercising* (n=33, 14.4%)			Did Not Exercise* Throughout (n=118, 51.5%)			Continue to Exercise* Throughout (n=50, 21.8%)		
	Before COVID	During COVID	P	Before COVID	During COVID	P	Before COVID	During COVID	P	Before COVID	During COVID	P
BMI	27.4 (±4.3)	27.3 (±4.2)	NS	28.9 (±5.6)	28.6 (±5.3)	NS	27.6 (±6.8)	26.9 (±8.1)	NS	27.0 (±4.2)	27.0 (±4.3)	NS
Waist Circumference (cm)	94.3 (±12.4)	95.0 (±12.1)	NS	98.5 (±14.8)	97.2 (±14.5)	NS	94.6 (±11.7)	94.6 (±11.7)	NS	92.5 (±9.8)	92.3 (±9.4)	NS
Hip Circumference (cm)	101.5 (±11.5)	101.5 (±11.1)	NS	100.9 (±15.3)	100.5 (±11.8)	NS	100.7 (±10.2)	100.4 (±9.6)	NS	97.9 (±8.5)	97.6 (±9.1)	NS
Albumin (G/L)	43.1 (±3.0)	43.7 (±2.6)	NS	40.9 (±3.4)	41.2 (±4.3)	NS	42.7 (±4.7)	43.2 (±2.9)	NS	42.6 (±3.1)	41.9 (±6.6)	NS
Bilirubin (umol/L)	15.9 (±5.2)	17.1 (±6.4)	NS	16.1 (±6.9)	15.7 (±7.5)	NS	14.4 (±6.8)	15.4 (±6.4)	NS	15.3 (±6.2)	19.9 (±27.5)	NS
ALP (U/L)	88.1 (±30.1)	84.9 (±28.1)	NS	91.9 (±34.9)	88.3 (±36.6)	NS	91.6 (±45.8)	79.1 (±25.6)	<0.05	77.8 (±20.3)	79.5 (±18.9)	NS
ALT (U/L)	46.6 (±30.9)	46.2 (±27.9)	NS	37.3 (±14.5)	44.2 (±25.9)	<0.05	44.1 (±32.6)	42.3 (±26.5)	NS	45.2 (±29.1)	45.9 (±29.7)	NS
AST (U/L)	37.9 (±37.9)	38.1 (±38.1)	NS	31.1 (±12.8)	35.7 (±16.8)	<0.05	35.4 (±19.9)	35.5 (±13.9)	NS	33.2 (±16.8)	34.6 (±17.1	NS
GGT (U/L)	51.6 (±29.6)	67.2 (±68.5)	NS	65.6 (±41.3)	46.2 (±12.3)	NS	53.5 (±29.8)	49.4 (±31.2)	NS	55.3 (±40.3	54.7 (±45.6	NS
Moderate to Vigorous Activity (min/week)	0	222.4 (±187.3)	<0.05	174 (±112.0)	0	-	0	0	-	240.8 (±205.6)	304.6 (±266.0)	<0.05
Any Physical Activity including Walking (min/week)	545.7 (±999.5)	914 (±922.7)	NS	634.6 (±437.4)	311.9 (±475.4)	<0.05	454.7 (±694.7)	322.9 (±494.0)	0.05	853.1 (±629.3)	845.7 (±540.3)	NS

* pertains to moderate/vigorous exercise

[OP-0460]

Among the liver function tests prothrombin time abnormality is frequent in type 2 diabetic patients—report from Rajshahi Medical College, Bangladesh

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Objectives: Diabetes mellitus is usually associated with obesity, coronary diseases and cerebral pathologies. However, more insights are required to evaluate a relation between DM and hepatic functions. This study assesses to what extent liver functions are modified in DM patients.
Materials and Methods: A total of 100 patients with type 2 DM and 100 normal healthy controls were enrolled in study. Different parameters of liver function tests were measured in patients in the two groups. Data were analyzed to assess the extent and magnitude of abnormal liver functions in DM.
Results: The levels of bilirubin, alanine aminotransferase (ALT), aspertate aminotransferase (AST), albumin and prothrombin time ware 0.737 ± 0.311 mg/dL, 39.00 ± 24.21 IU/L, 26.42 ± 10.40 IU/L, 4.10 ± 0.513 g/dL and 16.46 ± 2.78 s in DM and 0.506 ± 0.183 mg/dL, 28.26 ± 6.67 IU/L, 18.90 ± 4.75 IU/L, 4.12 ± 0.277 g/dL and 14.23 ± 1.04 s in control subjects. Statistical analyses revealed that most of these parameters of liver function test were significantly different in DM patients compared to control subjects ($p < 0.05$).
Conclusion: Abnormal liver functions have found in type 2 DM patients. Among the liver function tests prothrombin time abnormality (43.10%) more frequent and the impact should be considered during the management and to assess long term follow-up progress.

Frequency of LFTs abnormalities among type-2 diabetic patients and control (n=100).

Liver function tests	Type-2 diabetic patients		Control groups	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Serum bilirubin	03	5.17	00	00
ALT	18	31.03	02	02
AST	03	5.17	00	00
Serum Alkaline phosphatase	03	5.17	02	02
Prothrombin time	25	43.10	03	03
S.Albumin	06	10.34	00	00
Total :	58	99.98		

[OP-0511]

Hepatic and extrahepatic cancers in patients with non-alcoholic fatty liver disease: A multicenter registry-based cohort study

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Objectives: We aimed to study the association between non-alcoholic fatty liver disease (NAFLD) and cancers such as hepatocellular carcinoma (HCC) and extrahepatic cancers.
Materials and Methods: This was a multicenter registry-based historical cohort study. We used a database containing records of 1,398 biopsy-proven NAFLD patients from 15 hepatology centers in Japan. Information on clinical events were obtained from the patients' electronic medical records. Cancer-related data about the diagnosis using liver biopsy and recurrence post-biopsy were obtained separately. Recurrent cases were excluded.
Results: The mean age at baseline was 54.5 years, and the mean body mass index was 28.0 kg/m^2, and about half the total population were women. Data from biopsy revealed breast cancer in 20 cases with complete remission (CR) in all 20 cases, uterine, cervical, and ovarian cancer in 13 (CR in 13), HCC in 7 (CR in 2), and colon and rectal in 6 (CR in 11 cases). During a median follow-up of 4.6 years (range 0.3–21.6), 37 patients developed new occurrence of HCC (female n = 19) and 68 developed extrahepatic cancers. Specifically, 16 patients developed breast cancer (female n = 16), 10 patients developed stomach cancer (female n = 5), and 8 patients developed colon and rectal cancer (female n = 7). HCC incidence among NAFLD patients was 4.17/1,000 (95% confidence interval [CI] 3.02–5.75]).
Conclusion: The most common extrahepatic cancers at the beginning of the follow-up period (when liver biopsy was performed) were breast cancer, gynecological cancer, and colorectal cancer. With respect to new cancers that appeared during follow-up, breast cancer, stomach cancer, and colon and rectal cancer were the three most common non-hepatic cancers.

[PP-0514]

Assessment of hepatic steatosis in patients with anorexia nervosa using quantitative elastography

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Objectives: The number of patients with anorexia nervosa (AN) is increasing as society changes. Approximately 30% of patients with AN have mild liver injury. A part of patients with AN has been reported to present fatty liver change despite of their extreme low body mass index (BMI). Recently, quantification of hepatic fat content is available by FibroScan using a controlled attenuation parameter (CAP) software. In this study, we conducted the FibroScan measurement in patients with AN to assess their steatosis.
Materials and Methods: Twenty patients hospitalized with a diagnosis of AN were enrolled. Clinical parameters such as age, gender, BMI, as well as routine laboratory data were evaluated. We also assessed their hepatic steatosis by using a CAP software. We defined the level of CAP over 200 (dB/m) as cut off value for hepatic steatosis. We compared these clinical parameters among non-fatty (non-FL) group (10 patients, levels of CAP < 200) and fatty liver (FL) group (10 patients, levels of CAP > 200).
Results: All the enrolled subjects were female with a median age of 27.5 (11–62) years and BMI 13.5 ± 1.5 kg/m^2. Their mean lab data was: serum ALT 134.0 ± 328.9, γ-GTP 41.2 ± 45.3, T-chol 194.4 ± 42.1, TG 73.5 ± 31.9, the mean levels of CAP 210.2 ± 56.3, hepatic stiffness 5.7 ± 1.6 kPa. Eleven patients (55%) were positive for LK contrast. After medical treatment for 4 weeks, the levels of CAP in FL group decreased 246.6 ± 53.0 to 205.5 ± 28.3 ($p = 0.027$), and of those in non-FL group increased 169.7 ± 21.8 to 181.3 ± 39.9. The changes of serum T-chol and TG in FL group were: 176.2 ± 35.3 to 206.8 ± 37.6 ($p = 0.026$), and 65.1 ± 16.2 to 80.8 ± 33.4, whereas those in non-FL group were: 212.7 ± 40.5 to 190.4 ± 31.9, and 81.9 ± 40.4 to 63.2 ± 29.2, respectively.
Conclusion: The levels of CAP in FL group decreased, and sonographic hepatic steatosis was improved at 4 weeks after treatment. Further studies are feasible to clarity the mechanism of steatosis in patients with AN.

[PP-0519]

Non-invasive fibrosis scores—validation in Indian patients with biopsy-proven non-alcoholic fatty liver disease (NAFLD)

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Objectives: Non-invasive scores for assessing hepatic fibrosis in NAFLD have not been validated in Indian patients. We aimed to validate AST-platelet ratio index (APRI), Fibrosis-4 (FIB-4) and NAFLD fibrosis score (NFS) in biopsy-proven patients with NAFLD.
Materials and Methods: Prospectively collected data of 129 biopsy-proven NAFLD patients was reviewed retrospectively (Males—86, mean age: 40.2 ± 10.3 years). Primary objective was to assess discriminatory ability of APRI, FIB-4 and NFS scores to detect significant ($\geq$ F2) and advanced fibrosis ($\geq$ F3) on liver histology. Secondary objectives were to assess diagnostic performance of conventional cut-offs of these scores for ruling-in and ruling-out significant and advanced fibrosis and define optimal cut-offs if required. Findings were internally validated using boot-strapping.
Results: Out of 129, significant and advanced fibrosis on histology were present in 31 (24%) and 18 (14%) patients. All three scores had poor AUROCs for discriminating significant fibrosis on histology [APRI (0.61,95% CI:0.49–0.71), FIB-4 (0.62,95% CI: 0.51–0.72) and NFS (0.65, 95% CI: 0.53–0.76)]. For detecting advanced fibrosis, APRI (0.73,95% CI: 0.65–0.83) and FIB-4 (0.72, 0.64–0.83) had acceptable AUROCs but NFS fared poorly [AUROC (0.66,95% CI: 0.55–0.74)]. Conventional APRI cut-offs of < 0.5 and > 2.0 demonstrated good diagnostic performance for ruling-out (sensitivity: 0.94, specificity: 0.24, NPV: 0.96) and ruling-in (specificity: 0.91, sensitivity: 0.11, PPV: 0.17) advanced fibrosis. However, the diagnostic performance of conventional FIB-4 cut-offs of < 1.45 and > 2.67 for ruling-out (sensitivity: 0.72, specificity: 0.58, NPV: 0.92) and ruling-in (specificity: 0.88, sensitivity: 0.22, PPV:0.23) advanced fibrosis were suboptimal. Optimal FIB-4 rule-out and rule-in cut-offs in our cohort for discriminating advanced fibrosis were < 0.82 (sensitivity: 0.94, specificity: 0.28, NPV: 0.97) and > 2.81 (specificity: 0.91, sensitivity: 0.22, PPV:0.27) and performed better than the conventional cut-offs ($p = 0.02$).
Conclusion: APRI and FIB-4 have good AUROC for detecting advanced fibrosis in Indian patients with NAFLD; cut-offs however need to be recalibrated.

[OP-0553]

Correlation of serum transaminase and gamma glutamyl transferase with NAFLD activity score improvement in nonalcoholic steatohepatitis patients treated with sitagliptin and life style modification

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Objectives: Nonalcoholic steatohepatitis is the progressive form of nonalcoholic fatty liver disease which progress to cirrhosis and hepatocellular carcinoma. We aimed to evaluate the correlation of serum transaminase and gamma glutamyl transferase with NAFLD activity score improvement in NASH patients treated with sitagliptin and life style modification.
Materials and Methods: In this open label case control study, total 30 biopsy proven NASH patients irrespective of diabetes mellitus were included. 20 patients were treated with Sitagliptin and life style modification (SL) and 10 patients were treated with only life style modification (L) for one year. After one year of treatment end study liver biopsy were done. NAFLD activity score (NAS) improvement ≥ 2 was defined as histological responder. Among 20 patients of SL group 13 patients were histological responder and in L group only 2 patients among 10 were histological responders. Finally, 15 patients of histological responders and 15 patients of histological non-

responders were evaluated. ALT, AST and GGT improvement were compared between responders and non-responders after one year of treatment.
Results: Mean NAFLD activity score improvement in responders was 2.6 ± 0.73 and 0.06 ± 0.70 in non-responders. The difference of response between SL group and L group was statistically significant (P = 0.02). Mean AST improvement was 20.3 ± 26.3 U/L in responders and 4.3 ± 10.7U/L in non-responders. AST improvement was statistically significant in responders (P = 0.037). Mean ALT improvement was 43.7 ± 48.9 U/L in responders and 19.5 ± 23.6U/L in non-responders (P = 0.095). Mean GGT improvement was 29.8 ± 30.9 U/L in responders and 2.2 ± 19.2 U/L in non-responders. There was statistically significant difference of GGT improvement in responders and non-responders (P = 0.006).
Conclusion: AST and GGT improvements correlates with NAFLD activity score improvement rather than ALT. Further study in large sample is recommended to confirm these findings.

[OP-0557]

A randomized controlled trial on efficacy and safety of standardized extract of Phyllanthus niruri (Hepar-P) in treatment of non-alcoholic fatty liver disease

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Objectives: While Phyllanthus niluri is commonly used as a hepatoprotective herb, this study aimed to evaluate the efficacy and safety of its standardized extract (Hepar-P®) in the treatment of non-alcoholic fatty liver disease (NAFLD).
Materials and Methods: This was a randomized, placebo-controlled, double-blind clinical trial staged in three hospitals in Malaysia. A total of 226 NAFLD patients, who presented with a controlled attenuation parameter (CAP) score > 250db/m (S2-S3) and fibrosis score < 10 kPa (F0-F2) on transient elastography, were randomized to receive Hepar-P® (3,000 mg/day) or placebo for 12 months. The primary efficacy endpoints were the changes in the mean CAP scores and liver function test parameters, while the secondary efficacy endpoints were the changes in the mean fibrosis scores, anthropometric measurements and biochemical parameters. The safety of treatment was expressed as the incidence of adverse events (AEs). Both intention-to-treat (ITT; n = 205) and per-protocol (PP; n = 188) analyses were performed.
Results: The patients had a mean age of 50.3 ± 12.1 years and were mainly female (52.7%). Although no significant differences were detected in the changes of CAP scores between the Hepar-P® and placebo groups after 12-month treatment, the former demonstrated a greater reduction in the alanine aminotransferase level (− 6.97U/L; 95%CI: − 13.76U/L, − 0.18U/L; p = 0.044) according to the ITT analysis, as well as in the aspartate aminotransferase level (− 3.70U/L; 95%CI: − 7.40U/L, − 0.01U/L; p = 0.049) according to the PP analysis. Hepar-P® was also shown to significantly lower the liver stiffness scores after 12 months in both the ITT (− 0.70 ± 1.71 kPa vs. 0.13 ± 1.63 kPa; p = 001) and PP (− 0.65 ± 1.75 kPa vs. 0.12 ± 1.65 kPa; p = 001) analyses. The Hepar-P® and placebo groups did not considerably differ in the incidence of AEs (43 cases vs. 45 cases) and serious AEs (2 cases each).
Conclusion: Besides a good safety profile, Hepar-P® displayed a potential to improve the function and delay the damage of liver in NAFLD patients.

[OP-0561]

Association of total cholesterol to high density lipoprotein cholesterol ratio and non-alcoholic fatty liver disease in patients with chronic hepatitis B

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Objectives: To explore the association of total cholesterol to high density lipoprotein cholesterol ratio (TC/HDL-C) and non-alcoholic fatty liver disease (NAFLD) in patients with chronic hepatitis B (CHB) to identify patients who may be combined with NAFLD in the CHB patients in a convenient and cost-effective manner as soon as possible.
Materials and Methods: Retrospective analysis was performed on the CHB and CHB combined with NAFLD patients diagnosed in our hospital. They were matched by 1:1 propensity score according to gender and age, with caliper value 0.02. Both CHB group and CHB combined with NAFLD group included 186 patients.
Results: After adjusted for age, gender, body mass index (BMI), alanine aminotransferase, serum uric acid, fasting blood glucose (FBG), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), BMI (OR: 1.897, 95% CI: 1.752–2.053), FBG (OR: 1.511, 95% CI: 1.279–1.785) and TC/HDL-C ratio were risk factors for NAFLD in CHB patients, in the meanwhile, the risk of 4.03 < TC/HDL-C ratio ≤ 4.79 in CHB patients complicated with NAFLD was 3.409 times that of TC/HDL-C ratio ≤ 3.79 (95%CI: 1.844–6.301). The risk of TC/HDL-C ratio ≥ 4.79 in CHB patients complicated with NAFLD was 5.168 times that of TC/HDL-C ratio ≤ 3.79 (95%CI: 2.371–11.262) (P < 0.05). The predictive value of TC/HDL-C ratio (area under the curve was 0.726, P < 0.001) and BMI (area under the curve was 0.872, P < 0.001) for CHB complicated with NAFLD were better than FBG, TC, TG, LDL-C and HDL-C.
Conclusion: The greater the TC/HDL-C ratio, the higher the risk of NAFLD in CHB patients. The predictive value of TC/HDL-C ratio and for CHB patients complicated NAFLD was better than FBG, TC, TG, LDL-C and HDL-C.

[PP-0631]

Metabolic dysfunction-associated fatty liver disease is associated with subclinical atherosclerosis more than non-alcoholic fatty liver disease

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Objectives: A new terminology is proposed as metabolic dysfunction-associated fatty liver disease (MAFLD) from non-alcoholic fatty liver disease (NAFLD) based on its pathogenesis. However, clinical evidence of risk for cardiovascular disease (CVD) in NAFLD or MAFLD is lacking. This study is aim to evaluate association of cardiovascular risk in these two definition.
Materials and Methods: This was a cross-sectional analysis of retrospective cohorts form a single health checkup center including 2133 subjects who underwent contemporaneous ultrasound and cardiac computed tomography (CT). Fatty liver (FL) was assessed using ultrasound, and the presence of coronary artery calcification (CAC, defined as coronary artery calcium score > 0) was assessed using cardiac CT. Odds of presence of CAC were analyzed logistic regression analysis.
Results: The average age and body mass index were 57.2 years and 21.9 kg/m^2, respectively. In this cohort, 42.7% of subjects was diagnosed FL. Of these, 72.5% and 88.1% of subjects were diagnosed with NAFLD and MAFLD, respectively. Compare to subjects without FL, those with MAFLD has significant higher prevalence of CAC (33.6% vs 43.7%, $P < 0.001$) but those with NAFLD has similar prevalence of CAC (33.8% vs 37.1%, $P = 0.332$). In multivariable-adjusted analysis, MAFLD was independently associated with the presence of CAC in a sex and age-adjusted model (adjusted odd ratios (aOR) = 1.37, 95% confidence interval [CI] = 1.13–1.67, $P = 0.002$), as well as further adjusted model with use of hypertensive medicines, type 2 diabetes, and use of statin (aOR = 1.24, 95% confidence interval [CI] = 1.01–1.53, $P = 0.036$).
Conclusion: MAFLD is independently associated with presence of CAC in relatively healthy subjects. Further evaluation to indentify high-risk CVD phenotype in MAFLD is required in future.

[PP-0632]

Association between sarcopenic obesity status and NAFLD and fibrosis

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Objectives: Recently, there are several existing studies showing the association between sarcopenia and NAFLD. However, there is only one study on sarcopenic obesity, NAFLD and NAFLD-associated liver fibrosis. In this study, we aimed to investigate the relationship between sarcopenic obese status (sarcopenia only, obesity only, sarcopenic obesity) and NAFLD, and liver fibrosis in Korean adults.
Materials and Methods: 2191 subjects who performed health checkup program including abdominal ultrasonography and fibroscan at Gangnam Severance Hospital Health Promotion Center, in Seoul, Korea. Subjects were classified into the following four categories: optimal body composition (ie, nonobese and nonsarcopenic), sarcopenia only (ie, nonobese), obesity only (ie, nonsarcopenic), and sarcopenic obesity. Sarcopenic obesity was stratified by skeletal muscle mass index (SMI) and body fat using bioelectrical impedance analysis. NAFLD was diagnosed by ultrasonography and liver fibrosis was assessed by transient elastography in subjects with NAFLD.
Results: Significant differences were observed in metabolic parameters among the groups. The prevalence of NAFLD and liver fibrosis significantly increased according to sarcopenic obese status. According to the logistic regression analysis after adjusting for multiple risk factors, The odds ratio for risk of NAFLD was much higher in the sarcopenic obesity (OR, 3.68; 95% CI, 2.94–4.60) followed by in obesity only (OR, 2.25; 95% CI, 1.67–3.03), and sarcopenia only (OR, 1.92; 95% CI, 1.30–2.84) when compared with the nonobese, nonsarcopenic group and liver fibrosis was also independently associated with sarcopenic obesity status (OR, 4.69; 95% CI, 1.95–11.29, OR, 4.17; 95% CI, 1.56–11.17, OR, 3.80; 95% CI, 0.86–16.75, respectively).
Conclusion: These results demonstrated that sarcopenic obesity was independently associated with NAFLD and liver fibrosis and increased risk of NAFLD and liver fibrosis largely than visceral obesity or sarcopenia alone.

[PP-0677]

Impact of evolutionary change of nonalcoholic fatty liver disease on lung function decline

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Objectives: A relationship between fatty liver and lung function impairment has been identified, and both are independently associated with metabolic dysfunction. However, the causal relationship between changes in fatty liver status and lung function and their genome-wide association remain unclear.
Materials and Methods: A longitudinal cohort consisted of subjects who received serial health check-ups, including liver ultrasonography and spirometry, for ≥ 3 years between 2003 and 2015. Lung function decline rates were classified as 'slow' and 'accelerated' and compared among four different sonographic changes in steatosis status: 'normal', 'improved', 'worsened', and 'persistent'. A genome-wide association study was conducted between the two groups: normal/improved steatosis with a slow decline in lung function vs. worsened/persistent steatosis with an accelerated decline in lung function.
Results: Among 6,149 individuals, the annual decline rates of FVC and FEV1 were higher in the worsened/persistent steatosis group than in the normal/improved steatosis group. In multivariable analysis, improved steatosis had a lower risk of accelerated lung function decline (FVC, odds ratio [OR] = 0.81, 95% confidence interval [CI] = 0.67–0.98; FEV1, OR = 0.73, 95% CI = 0.60–0.89), while aggravated steatosis had a higher risk of accelerated lung function decline (FVC, OR = 1.29, 95% CI = 1.10–1.50; FEV1, OR = 1.23, 95% CI = 1.07–1.41). The PNPLA3 risk gene was most strongly associated with steatosis status change and accelerated declines in FVC (rs12483959, p = 2.61 × 10–7) and FEV1 (rs2294433, p = 3.69 × 10–8).
Conclusion: Regression of fatty liver alleviated the decline in lung function. Continuing efforts to improve fatty liver may preserve lung function, especially in subjects with a high genetic risk.

[PP-0678]

Association of fatty liver with incident dementia later in life among middle-aged or older adults

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Objectives: Accumulating evidence suggested the link between fatty liver and brain health. However, population-based evidence on the association of fatty liver with dementia remains unclear. This study was conducted to determine the association of fatty liver with incident dementia among middle-aged or older adults.
Materials and Methods: The study population was composed of 341,998 adults aged at least 40 who underwent health examination between 2009 and 2010 from the Korean National Health Insurance Service database. Fatty liver was assessed using the fatty liver index (FLI). Cox proportional hazards regression model was used to determine the association of fatty liver with dementia.
Results: During 2,013,299 person-years of follow-up, 4,708 participants (1.4%) developed incident dementia. Compared to intermediate FLI participants (FLI $\geq$ 30 and $<$ 60), low FLI participants (FLI $<$ 30) had decreased risk of dementia (aHR [adjusted hazard ratio], 0.90; 95% CI [confidence interval], 0.83–0.98), whereas high FLI participants (FLI $\geq$ 60) were associated with increased risk of dementia (aHR, 1.21; 95% CI, 1.08–1.35). After propensity score matching, high FLI was associated with increased overall dementia risk (aHR, 1.19; 95% CI, 1.03–1.37). The stratified analysis revealed that either alcohol consumption or current smoking deducts low FLI-associated dementia risk reduction. Among high FLI participants, subjects with advanced fibrosis were at increased risk of dementia (aHR, 1.60; 95% CI, 1.20–2.14) compared to those without advanced fibrosis.
Conclusion: Fatty liver and advanced fibrosis are associated with an increased risk of dementia. Further studies are warranted to confirm whether reversal of fatty liver may prevent the development of dementia.

[PP-0684]

Community-based participatory research leads to recruitment and retention of NASH subjects with hispanic background

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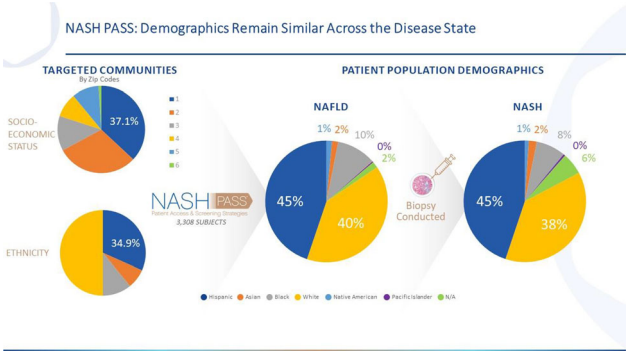
Objectives: NAFLD prevalence and mortality varies by ethnicity. Hispanics are at a higher risk of NAFLD partly because of a higher frequency of NAFLD/NASH-related genetic markers (e.g., PNPLA3 G-allele). Lack of access to clinical trials is a major health care disparity. Despite making up almost half of the US NASH populations, Hispanics only represent 12% of NASH clinical trial participants (PMID32952877). Factors such as food insecurity also increase the odds for NAFLD.
Materials and Methods: NASH-PASS is a cross-sectional diagnostic study and registry-based IRB-approved clinical research protocol with detailed and prospective data collection. It is a multicenter study primarily performed in community clinics where individuals who have clinical indicators of high risk of NAFLD are invited to participate. They are screened and assessed based on medical history, a FibroScan, a combination of circulating biomarkers, and non-invasive diagnostic algorithms. Based on algorithmic risk assessments subjects may progress to MRI and liver biopsy. Individual and composite biomarkers include Fibrosis-4, Enhanced Liver Fibrosis, PRO-C3 (marker of type III collagen formation), and FAST (FibroScan-AST) scores.
Results: Adults with T2DM or obesity were identified from at 20 community-based clinical research centers. Between April 2019 and April 2021, 1855, subjects completed their screening; 48% (889) identified as Hispanic, 13% African American (250), and 34% (631) as White. Population around NASH-PASS recruitment centers is $\sim$ 35% Hispanic, more than double the national average. Close to 50% of the subjects in NASH-PASS self-identify as Hispanic. In addition, the Adjusted Gross Income around the recruitment centers is between $1 and $50 k. Prevalence of advanced fibrosis and severe hepatic steatosis were similar amongst Hispanics and Whites and rates of consenting for further clinical trials were not significantly different.
Conclusion: Location of NASH-PASS centers facilitates identification and engagement with subjects most at risk to NAFLD/NASH because of both ethnicity and socio-economic risk factors.



[PP-0707]

Changes in serum small dense LDL levels in patients with NAFLD

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Objectives: Dyslipidemia in nonalcoholic fatty liver disease (NAFLD) is one of the common comorbid conditions, and has several other important features, one of which is the increased small dense low-density lipoprotein (sdLDL) particles, which is a subtype of LDL.. On the other hand, the relationship between the sdLDL level and NAFLD is unclear.
Materials and Methods: 51 health participant (control group) and 127 patients diagnosed with NAFLD at a single referral hospital from January 2018 to June 2021 were enrolled. The lipoprotein profile was analyzed from a blood test of NAFLD patients and health participant, and transient elastography (TE, Fibroscan®) was performed to evaluate the degree of NAFLD.
Results: Age-sex matching was performed by comparing the sdLDL of control group and NAFLD group, and the blood test results of 46 patients were compared, respectively. It was confirmed that the sdLDL value and sdLDL/LDL ratio significantly increased in the NAFLD group compared to the control group, and they increased

proportionally according to the degree of NAFLD. The sdLDL level measured in patients with NAFLD (n = 127) showed a significant positive correlation with the CAP and LS values, which indicate the degree of hepatic steatosis and fibrosis, respectively. The sdLDL/LDL ratio also showed a meaningful correlation with the degree of NAFLD, similar to sdLDL. Furthermore,in the comparison of the characteristics of the group with a normal sdLDL level and the group with a high sdLDL level, the CAP and FLI was significantly different between the two groups.
Conclusion: The sdLDL level and the sdLDL/LDL ratio have a positive correlation with the severity of NAFLD measured by TE, unlike other lipoproteins. Based on these results, the sdLDL level could be used as a new non-invasive tool to evaluate the severity of NAFLD steatosis and fibrosis, but further studies will be needed.

[PP-0725]

An mHealth Intervention (SMART-Liver) to improve self-management in patients with non-alcoholic fatty liver disease: Randomized control trial

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Objectives: Self-management for patients with non-alcoholic fatty liver disease (NAFLD) is a key to promote health outcomes. The mhealth technologies may offer the potential to provide effective and efficient healthcare to facilitate self-management behaviors. The SMART-Liver® is a personalized self-management intervention with a mobile app to coach NAFLD patients for changing lifestyles. The purposes of this study were to evaluate the SMART-Liver® intervention to improve self-management for NAFLD patients.
Materials and Methods: This study was a randomized controlled trial. The SMART-Liver® was developed the contents based on NAFLD guidelines and literature reviews. After content validity and usability test, 102 patients with NAFLD were enrolled in the hospital, and randomly assigned to SMART-Liver® intervention (N = 48) and control group (N = 56). The primary outcomes are the improvement on knowledge of NAFLD management, weight, liver fat socre, and the level of self-management using NAFLD Self-Management Questionnaire. This study is currently in progress and will finish in January 2022.
Results: SMART-Liver® consisted of education for NAFLD management, self-monitoring of diet and physical activity, coaching session based on patients' records, and feedback message for 6 months. Eighty of all participants have completed the study. The mean age of the participants was 48.6 (SD = 13.72) years, 37.5% (30/80) were females, and 66.3% (53/80) were married. The results among 80 participants were promising with a trend that participants in SMART-Liver® group (N = 32) had a mean score changes on knowledge of NAFLD management (0.28 vs − 0.48; p = 0.278), weight (− 2.0 vs − 1.7: $p < 0.001$), liver fat score (− 6.8 vs − 1.8: p = 0.243), and the level of self-management (0.4 vs 0.1; $p < 0.001$).
Conclusion: This SMART-Liver® was developed to improve self-management with personalized coaching of diet and physical activity using mobile application. The trends demonstrated that this study may be effective non-pharmacological intervention to achieve health outcomes of patients with NAFLD. Trial Registration: CRIS registry, KCT0005549, Registered on 29 October 2020.

[OP-0730]

Improvement of nonalcoholic fatty liver disease is associated with reduced risk of diabetes: A longitudinal cohort study

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is potentially reversible condition. However, whether improvement of NAFLD status leads to clinical benefit remains uncertain. We aimed to investigate whether improvement of NAFLD can decrease the risk of incident diabetes in a longitudinal way.
Materials and Methods: This is a retrospective cohort study of 12,264 adult men and women who underwent health check examinations at 1 or 2 years of interval between 2001 and 2016, and had NAFLD at baseline. NAFLD was diagnosed with ultrasonography and by excluding secondary causes. NAFLD severity was assessed by NAFLD fibrosis score at baseline.
Results: At 1–2 years from baseline visit (index visit), NAFLD was regressed in 2,809 participants (22.9%). During 55,958 person-years of follow-up after index visit (median 4 years), 1,990 participants developed diabetes. After adjusting for age, sex, alcohol intake, smoking status, physical activity, body mass index, hypertension, and hyperlipidemia at index visit, the HRs for incident diabetes in participants with regressed NAFLD compared to those with persistent NAFLD were 0.78 (95% CI 0.70–0.88) When assessed by severity of fibrosis, among participants with low NFS (< -1.455), participants with regressed NAFLD had lower risk of incident diabetes than those with persistent NAFLD (HR = 0.73,95% CI = 0.64–0.83). However, in participants with intermediate to high NFS (≥ -1.455), the risk of incident diabetes was not different between regressed and persistent NAFLD groups (HR = 1.13, 95% CI = 0.86–1.51). In other pre-specified subgroups, the negative association between regression of NAFLD and incident diabetes was consistently observed (all p-values for interaction > 0.10).
Conclusion: Regression of NAFLD was associated with reduced risk of incident diabetes. The metabolic benefit was more profound among participants without fibrosis, indicated by NFS. Thus, improvement of NAFLD may help prevent the development of diabetes among NAFLD individuals.

[PP-0731]

A sequential approach using the age-adjusted FIB-4 and VCTE for hepatic fibrosis in patients with nonalcoholic fatty liver disease

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Objectives: Vibration-controlled transient elastography (VCTE) has shown good diagnostic performance in predicting fibrosis stages in patients with non-alcoholic fatty liver disease (NAFLD). However, an optimal diagnostic approach to detect advanced fibrosis in patients with NAFLD has not been established.
Materials and Methods: We prospectively collected data from 539 subjects who underwent liver biopsy at a single center between January 2014 and December 2019. VCTE was performed using M and/or XL probes. Diagnostic performance was estimated using the area under the receiver-operating characteristic curve (AUROC). Several models combining the fibrosis 4 index (FIB-4) score and liver stiffness measurement (LSM) were analyzed to reduce the need for unnecessary liver biopsies.
Results: We observed significant fibrosis (≥ F2), advanced fibrosis (≥ F3), and cirrhosis (F4) in 173 (32.1%), 74 (13.7%), and 46 subjects (8.5%), respectively. The AUROCs (95% CI) for LSMs to diagnose ≥ F2, ≥ F3, and F4 were 0.82 (0.78–0.85), 0.92 (0.89–0.94), and 0.95 (0.93–0.97), respectively. Optimal LSM cut-off values were 6.7 (≥ F2), 8.3 (≥ F3), and 9.8 (F4) kPa. The sequential use of the age-adjusted FIB-4 and LSMs yielded the least uncertainty (5.3%) in classifying disease severity with the highest diagnostic accuracy (81%) among a variety of non-invasive test combinations.
Conclusion: The sequential approach of age-adjusted FIB-4 and VCTE could represent a practical diagnostic strategy to detect advanced fibrosis in NAFLD.

Table 4. Comparison of diagnostic performance for diagnosing advanced fibrosis among five models

	FP (%)	FN (%)	Uncertainty area (%)	Correctly classified (%)	VCTE number needed
Model A	38/93 (41)	7/322 (2.2)	52/467 (11)	370/467 (79)	467
Model B	36/85 (42)	8/238 (3.4)	144/467 (31)	279/467 (60)	0
Model C	16/59 (27)	3/211 (1.4)	197/467 (42)	251/467 (54)	467
Model D	36/93 (39)	8/323 (2.5)	51/467 (11)	372/467 (80)	467
Model E	51/109 (47)	11/333 (3.3)	25/467 (5)	380/467 (81)	144

Uncertainty area is the number (proportion) of patients who need biopsy to diagnose advanced fibrosis.

FN: false positive; FN: false negative; VCTE: vibration controlled transient elastography

A (VCTE): ruled out (LSM≤LCO); confirmed (LSM>HCO)

B (FIB-4): ruled out (FIB-4≤LCO); confirmed (FIB-4>HCO)

C (Simultaneous 1): ruled out (LSM≤LCO and FIB-4≤LCO); confirmed (LSM>HCO and FIB-4>HCO)

D (Simultaneous 2): ruled out (LSM≤HCO and FIB-4≤LCO, or LSM≤LCO and FIB-4≤HCO); confirmed (LSM>HCO and FIB-4>LCO, or LSM>LCO and FIB-4>HCO)

E (Sequential): ruled out (FIB-4≤LCO, or LCO<FIB-4≤HCO and LSM≤HCO); confirmed (FIB-4>HCO, or LCO<FIB-4≤HCO and LSM>HCO)

[PP-0740]

Serum cadmium is associated with hepatic steatosis and fibrosis: Korean national health and nutrition examination survey data IV–VII

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Objectives: Although cadmium (Cd) is correlated with elevated levels of hepatic amino transferases, its influence on the degree of liver steatosis and fibrosis are unknown yet. We aimed to investigate the associations between the serum level of Cd and degree of liver steatosis/fibrosis.
Materials and Methods: Clinical data were obtained from Korean National Health and Nutrition Examination Surveys IV–VII. Alanine aminotransferase (ALT) elevation was defined as ^{3} 33 IU/L for men and ^{3} 25 IU/L for women. Significant steatosis was defined as a hepatic steatosis index (HSI) ^{3} 36, while significant fibrosis was defined as a fibrosis index (FIB-4) ^{3} 2.67 and as an aspartate aminotransferase and platelet ratio index (APRI) ^{3} 0.7. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated after adjustment.
Results: The levels of serum Cd were assessable in 15,783 subjects. The serum cadmium concentrations were significantly associated with ALT elevation, significant liver steatosis and fibrosis. Multivariate logistic regression analysis demonstrated serum Cd level in the forth quartile had a positive correlation with ALT elevation, HSI ^{3} 36, FIB-4 ^{3} 2.67 and APRI ^{3} 0.7 using the first quartile of serum Cd level as the reference, (AOR 1.90, 1.26, 1.73 and 2.53, respectively; p values < 0.001).
Conclusion: The serum level of Cd was associated with liver steatosis and fibrosis. The evaluation of serum Cd may help for assessing an unexplained liver steatosis and fibrosis, and further prospective studies are needed to confirm our findings.

[PP-0751]

Mean platelet volume (MPV) as cardiovascularrisk factor (CVRF) in patients with acute myocardial infarction (AMI) COMORBID with non-alcoholic fatty liver (NAFLD)

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Objectives: Background: NAFLD represents most common cause of chronic liver disease in western countries and associated atherosclerosis, metabolic syndrome. MPV is a marker of platelet activation (PI) and a validated predictor of CV. The purpose of study to assess MPV in patients with AMP and NAFLD and determine relation between MPV and cardiovascular events after AMI in such patients.
Materials and Methods: Methods; We included all admitted to University Hospital (2013 to 2014) non fatal AMP patients (176).
Results: Results: Patients with NAFLD had higher MPV values. Patients who died within the first 48 h after admission, had severe liver failure, documented hepatitis B and C viruses in blood, history of alcohol intake more than 30 mg/day in men and 20 mg/day in women have not been included in the study (21 patients). The diagnosis of NAFLD was made if typical ultrasound pattern with increased echogenicity of liver, increased echogenicity compared with kidney and attenuation of echogenicity at deep parts images (15). Only grade 2 and grade 3 level of NAFLD were taken as clear diagnosis to escape misdiagnosis. Continuous variables were expressed as mean ± standard error of mean and compared using one way analysis. Categorical variables were expressed as number and percentages. Pearson chi square test was used to evaluate correlation analysis. The comparative analysis of patients with and without NAFLD showed that MPV was 10.6 ± 0.093 in patients with NAFLD and 9.5 ± 0.13 without NAFLD ($p < 0.01$) respectively.
Conclusion: Conclusions Our study suggests that MPV is significantly higher in patients with AMI who has NAFLD, which indicates increased PI in these patients. High MPV values are associated in these patients with increased predictive CV after 12 months from AMI.

[OP-0757]

Vitamin D in reducing transaminase levels in patients with non-alcoholic fatty liver disease: a systematic review and meta-analysis

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Objectives: The aim of this study is to examine the effects of Vitamin D supplementation in preventing progression of NAFLD. The primary outcome is reduction in serum ALT and AST level after Vitamin D supplementation compared to patient's baseline. The secondary outcomes include changes in hepatic steatosis and fibrosis.
Materials and Methods: A comprehensive electronic literature search from PubMed Central, Google Scholar, and Embase Cochrane Library was performed using the following search terms: Vitamin D and NAFLD. Four RCTs met the inclusion criteria and were validated using the Newcastle–Ottawa criteria. All studies included were published within the last 5 years. Trial effects were combined under the random effects model. The Cochrane Review Manager Software version 5.4 was used to analyse data.
Results: Four RCTs with a total of 520 patients were included in this systematic review and meta-analysis. Our meta-analysis analysed three RCTs to obtain a pooled estimate of the effect of Vitamin D on ALT and AST. All three studies were deemed to be homogeneous, with I^2 of less than 50%. The overall outcome rate for the effect of Vitamin D on ALT ($p = 0.25$) and AST ($p = 0.24$) revealed no significant difference between the experimental and control group. The four included RCTs reported on changes in hepatic steatosis and fibrosis through different methods hence, a systematic review was done. A reduction in hepatic steatosis was observed in 3 out of 4 trials, confirmed through biopsy, controlled attenuation parameter, liver stiffness measurement, liver ultrasound, and MRI.
Conclusion: Oral vitamin D supplementation did not show a significant difference in lowering ALT, AST. However, our systematic review showed improvement in hepatic steatosis and fibrosis in patients with NAFLD, except for those with coexisting Type II Diabetes Mellitus. Studies with a longer intervention period are warranted for exploring the effect of long time exposure to vitamin D.

[OP-0763]

Holistic approach to manage nonalcoholic steatohepatitis (NASH) with liraglutide for 24 weeks: An observational study

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Objectives: Non-alcoholic steatohepatitis (NASH) is the commonest cause of chronic liver disease that can lead to cirrhosis; where liraglutide has shown to promote weight loss, improve liver histology in obese and diabetic patients. Here we assessed the effect of liraglutide therapy on liver histology of non-alcholholic steatohepatitis patients irrespective of diabetes.
Materials and Methods: This was a 24-week prospective observational study. All the included patients (n = 42) with nonalcoholic fatty liver disease (NAFLD) Activity Score (NAS) ≥ 5, were randomized into two groups Liraglutide therapy with lifestyle modification group (L) and only lifestyle modification group (C) in 1: 1 ratio. After 24 weeks second liver biopsy was done.
Results: Liraglutide therapy improved hepatic steatosis ($P = 0.004$) and NAS ($P = 0.002$) significantly. The difference of NAS improvement between Land C group was significant ($P = 0.002$). Hepatocyte ballooning improvement in the L group was also significant ($P = 0.016$) but lobular inflammation improvement was not significant ($P = 0.667$). Fibrosis improvement in the Lgroup was also significant ($P = 0.014$) but not in Cgroup ($P = 0.773$). Liraglutide significantly reduced all the components of metabolic syndrome: BMI, blood sugar, HbA1c, HOMA-IR, fasting lipid profile, waist circumference and blood pressure. Univariate analysis explored that, (LGroup), ($P = 0.007$), improvement of BMI ($P = 0.000$), improvement of HbA1c ($P = 0.018$), and HOMA-IR ($P = 0.022$) was associated with NAS improvement without worsening of fibrosis (response). Logistic Regression analysis revealed that, only BMI improvement significantly predicted response ($p = 0.008$).
Conclusion: Liraglutide therapy holistically improves hepatic steatosis and hepatocyte ballooning, NAS and fibrosisin NASH along with reduction of metabolic factors.

[PP-0839]

Neck circumference as a screening tool for identifying NAFLD among Thai people

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Objectives: Neck circumference (NC) reflects the fat deposition in upper body and has potential to be used as a predictor of non-alcoholic fatty liver disease (NAFLD). Our objectives were to examine the association of NC with NAFLD prevalence, and to determine the optimal cut-off of NC in identifying the presence of NAFLD among the employees of an academic institution in Bangkok, Thailand.
Materials and Methods: In this cross-sectional study, 635 employees of an academic institution underwent anthropometric measurement and transient elastography following an overnight fast. NAFLD was defined as a CAP value > 238 dB/m.
Results: The NAFLD prevalence in men and women were 66.2% and 46.2%, respectively. The mean NCs for men and women with NAFLD (38.5 ± 0.3 cm and 35.8 ± 0.5 cm, respectively) were significantly higher than those without NAFLD (33.6 ± 0.2 and 31.1 ± 0.1 cm, respectively) ($p < 0.001$). Several parameters including age, weight, body mass index, waist circumference, waist to hip ratio, fasting plasma glucose and triglyceride were significantly higher among participants with NAFLD compared to those without NAFLD ($p < 0.05$). NC was independently associated with NAFLD among women with OR (95%CI) of 1.17 (1.05, 1.32). The optimal cut-offs of NC to predict NAFLD were 37 cm for men (sensitivity: 70.5%; specificity: 68.9%) and 32 cm for women (sensitivity: 70.7%; specificity: 62.1%).
Conclusion: In summary, our data demonstrate that NC can be used as a cost-effective tool to predict NAFLD among Thai people.

[OP-0852]

Risk stratification using sarcopenic obesity status in subjects with nonalcoholic fatty liver disease

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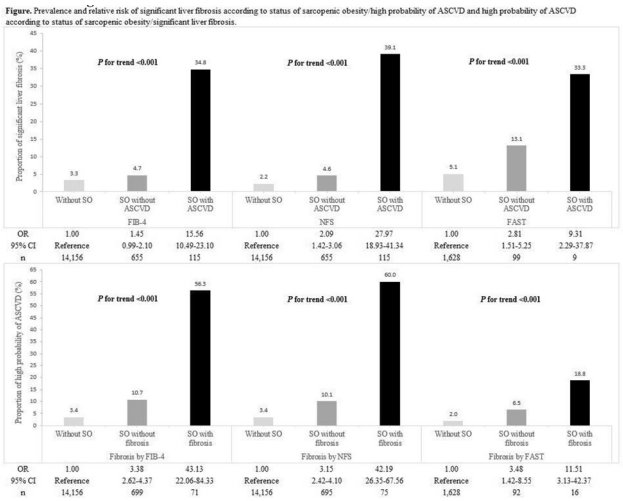
Objectives: Sarcopenic obesity (SO) is associated with an increased risk of liver dysfunction and cardiovascular disease (CVD) in general population. We investigated whether SO could identify subgroups with different risk of significant liver fibrosis and CVD in subjects with nonalcoholic fatty liver disease (NAFLD).
Materials and Methods: In this multicenter, cross-sectional study, 14,926 NAFLD subjects who underwent a health screening program between 2014 and 2020 were recruited. NAFLD was defined based ultrasound findings. Sarcopenia was defined using the sarcopenia index by multi-frequency bioelectric impedance analysis. Obesity was defined a body mass index $\geq$ 25 kg/m^2. Liver fibrosis using the fibrosis-4 (FIB-4) index (> 2.67), NAFLD fibrosis score (NFS, > 0.676), and FibroScan-AST (FAST) score (> 0.35) and CVD risk using atherosclerotic CVD (ASCVD) risk score (> 10%) were assessed.
Results: The mean age was 49.6 $\pm$ 10.8 years and 71.6% of subjects were male. After adjusting for confounders, the risk of significant fibrosis was significantly higher in SO subjects (5.2%, n = 770 of 14,926) than those without (adjusted odds ratio [aOR] = 2.06 by FIB-4, 3.20 by NFS, and 2.95 by FAST; all $P < 0.001$). The risk of high probability of ASCVD was also significantly higher in SO subjects than those without (aOR = 2.92; $P < 0.001$). In addition, the risk of significant fibrosis was significantly higher in SO subjects with high probability of ASCVD, compared with those without high probability of ASCVD (aOR = 5.29 by FIB-4, 9.37 by NFS, and 7.65 by FAST; all $P < 0.05$). Similarly, the risk of high probability of ASCVD was significantly higher in SO subjects with significant fibrosis, compared with those without significant fibrosis (aOR = 15.26 by FIB-4, 17.90 by NFS, and 5.50 by FAST; all $P < 0.05$).
Conclusion: The risks of significant liver fibrosis and CVD differed significantly according to SO status in NAFLD. Assessment of SO might be helpful in risk stratification for fibrosis and CVD risk in NAFLD subjects.



[PP-0856]

Text messaging intervention and weight loss in patients with non-alcoholic fatty liver disease

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Objectives: This study was performed to evaluate the effects of text messaging intervention on weight loss in patients with NAFLD to promote lifestyle modification outside of the clinical setting. Primary outcome is the effective of text messaging and weight reduction in NAFLD patients before and after intervention. Secondary outcome is the changing of liver enzymes and lipid profile in NAFLD patients between intervention group and control group.
Materials and Methods: A randomizes controlled trial study in 120 well-defined NAFLD patients follow up in Phramongkutklao hospital between 2018–2020. The volunteers were randomized into 3 groups: one way communication group (A), interactive group (B) and control group (C). Measurement of body weight, height, waist circumference, blood pressure and evaluation for liver function test, lipid profile, fasting plasma glucose, HbA1C before and after intervention in all volunteers was performed.
Results: Mean total cholesterol decreased 7.74 mg/dL in group A compared with increased 8.99 mg/dL in control group when follow up at 3 month (p-value = 0.029) and decreased 10.15 mg/dL compared with increased 6.03 mg/dL in control group when follow up at 6 month (p-value = 0.046). At follow up time 6 months group B has decreased total cholesterol 17.43 mg/dL compared with increased 6.03 mg/dL in group C (p-value = 0.002) and decreased in LDL-cholesterol 16.35 mg/dL while increased 1.70 mg/dL in group C (p-value = 0.023). However, no significant change in weight between 0, 3 and 6 month of all groups.
Conclusion: From this study there is no evidence to support the efficacy of text messaging intervention and weight loss in NAFLD patients at 3 and 6-month follow up time. One way communication group has decreased in total cholesterol at 3 and 6-month follow up time compared with control group. Interactive group has decreased in total cholesterol and LDL-cholesterol with statistical significant after intervention for 6 month.

[PP-0857]

Comparison of prognostic value between the advanced liver fibrosis and non-invasive test in patients with NAFLD

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Objectives: The prognosis of nonalcoholic fatty liver disease (NAFLD) is affected by histological stage 3 or higher (advanced fibrosis), and its evaluation is important. Currently, non-invasive scores (NIT) such as the FIB-4 index (FIB-4) and the NAFLD fibrosis score (NFS) are being used to evaluate patients with advanced liver fibrosis. In this study, we evaluated the usefulness of NITs for the prognostic evaluation of NAFLD.
Materials and Methods: Patients with NAFLD who underwent liver biopsy between December 1994 and November 2020 were included in this study. ROC analysis was performed for all-cause mortality, liver-related mortality, new cases of liver-related disease, and new cases of l hepatocellular carcinoma at 5 and 10 years after liver biopsy using FIB-4, NFS, and type IV collagen 7S, and cutoff values were set. Liver-related diseases were defined as hepatocellular carcinoma, esophagogastric varices, and decompensated cirrhosis. Cox proportional hazards analysis was used to predict the mortality and incidence of the above cases and compared with NITs and histological diagnosis.
Results: The results are shown in the table. The adjusted hazard ratios for all-cause mortality, liver-related mortality, new cases of liver-related disease, and new cases of l hepatocellular carcinoma were significantly higher for each NITs compared with patients with advanced liver fibrosis of stage 3 or higher.
Conclusion: NITs may be effective in predicting the prognosis of patients with NAFLD, independent of liver biopsy.

Table.

Over all death				New incident of Liver related disease			
5years after LB	/1000 person·year (95%CI)	Adjsted HR	p	5years after LB	/1000 person·year (95%CI)	Adjsted HR	p
Stage ≥ 3	6.23 (2.59-14.96)	ref	-	Stage ≥ 3	23.16 (14.59-36.77)	ref	-
FIB-4 ≥ 2.85	11.77 (6.68-20.71)	9.059	< 0.01	FIB-4 ≥ 2.84	18.67 (18.81-39.99)	14.151	< 0.01
NFS ≥ -0.168	11.97 (6.80-21.07)	10.472	< 0.01	NFS ≥ 0.064	32.18 (21.91-47.26)	31.547	< 0.01
COL4-7S ≥ 7.45	13.30 (5.53-31.94)	13.65	< 0.01	COL4-7S ≥ 6.05	24.51 (15.23-39.42)	15.583	< 0.01
10 years after LB	/1000 person·year	Adjsted HR	p	**10 years after LB**	/1000 person·year	Adjsted HR	p
Stage ≥ 3	8.13 (4.23-15.63)	ref	-	Stage ≥ 3	27.24 (18.81-39.45)	ref	-
FIB-4 ≥ 2.85	12.53 (7.89-19.88)	5.799	< 0.01	FIB-4 ≥ 2.84	30.73 (22.63-41.74)	13.945	< 0.01
NFS ≥ 0.111	11.10 (6.31-19.55)	3.507	< 0.01	NFS ≥ -0.032	32.58 (23.61-44.97)	17.175	< 0.01
COL4-7S ≥ 5.95	7.63 (3.81-15.25)	7.31	< 0.01	COL4-7S ≥ 6.05	26.52 (17.78-39.57)	12.27	< 0.01

Liver relatede death				New incident of HCC			
5years after LB	/1000 person·year (95%CI)	Adjsted HR	p	5years after LB	/1000 person·year	Adjsted HR	p
Stage ≥ 3	6.35 (2.64-15.25)	ref	-	Stage ≥ 3	11.39 (5.93-21.90)	ref	-
FIB-4 ≥ 2.85	8.08 (4.04-16.16)	13.459	< 0.01	FIB-4 ≥ 3.03	17.31 (10.43-28.71)	16.483	< 0.01
NFS ≥ 0.111	10.07 (5.03-20.13)	18.393	< 0.01	NFS ≥ 0.111	17.83 (10.56-30.11)	31.347	< 0.01
COL4-7S ≥ 8.65	19.13 (6.17-59.32)	54.387	< 0.01	COL4-7S ≥ 6.05	12.35 (6.18-24.70)	4.24	0.0504
10 years after LB	/1000 person·year	Adjsted HR	p	**10 years after LB**	/1000 person·year	Adjsted HR	p
Stage ≥ 3	7.41 (3.71-14.82)	ref	-	Stage ≥ 3	15.06 (9.22-24.58)	ref	-
FIB-4 ≥ 2.85	7.89 (4.37-14.25)	6.991	< 0.01	FIB-4 ≥ 2.68	18.02 (12.53-25.94)	23.795	< 0.01
NFS ≥ 0.111	8.39 (4.36-16.12)	8.998	< 0.01	NFS ≥ -0.032	20.12 (13.49-30.02)	26.724	< 0.01
COL4-7S ≥ 8.65	19.39 (7.28-51.68)	68.498	< 0.01	COL4-7S ≥ 5.65	14.04 (8.60-22.91)	9.306	< 0.01

LB: liver biopsy; HR: Hazard ratio; NFS: NAFLD fibrosis score; COL4-7S: Type 4 Collagen 7S

[PP-0868]

Nonalcoholic fatty liver disease in pregnant women

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is considered the commonest liver disease in the last year. The most common risk factor associated with NAFLD is the presence of the metabolic syndrome and type 2 diabetes. There are no studies of NAFLD in pregnant women in Mongolia. We aimed to investigate pregnancy outcomes in NAFLD.
Materials and Methods: Pregnant volunteers (n = 61) were referred to the obstetric medicine Clinic of Dornod Medical center, Dornod, Mongolia. All pregnant had tests for blood chemistries ALT (0–45 u/l), AST (0–35 u/l), cholesterol (349 mg/dl), triglyceride (< 453 mg/dl), HBsAg, Anti-HCV, BMI (calculator.net), gestational age and abdominal ultrasound scans using accepted criteria.
Results: The BMI in before pregnancy 2 (3%) women as underweight, 31 (51%) as normal weight, 13 (22%) as overweight and 15 (25%) as obese. During the pregnancy BMI were 25 (41%) as overweight and 27 (45%) as obese, compared to before pregnancy increased percent overweight and obese. The average of BMI before pregnancy was 26.8 ± 5.4 and during pregnancy BMI average 31.39 ± 5.1 (P value 3.5 * 10–5), this was shown to increasing obesity during pregnancy. 36 pregnant had fatty liver on ultrasound, in 32 (84.2%) increased than the weight should be, during pregnancy. Among the eleven patients that developed abnormal liver function test. Four patient with hypercholesterinemia, and another one with hyperglycemia.
Conclusion: NAFLD was high prevalence (69%) in pregnant women. Ultrasound is a noninvasive and useful diagnostic tool in the detection of NAFLD during the pregnancy. This study has shown that having are overweight and obesity increased in pregnant women is associated with increased risks for diagnosis of NAFLD.

[PP-0892]

The efficacy of ursodeoxycholic acid in liver stiffness and steatosis among ambulatory patients with non-alcoholic fatty liver disease in a tertiary hospital

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Objectives: Liver stiffness is the strongest predictor factor in non-alcoholic fatty liver disease (NAFLD) progression. Ursodeoxycholic acid (UDCA) is commonly used as the treatment of NAFLD, even though the efficacy is still disputable, it is able to improve liver function. This study aims to evaluate the effect of UDCA on liver stiffness in patients with NAFLD, as well as to evaluate its effect on liver steatosis.

Materials and Methods: A one-year retrospective cohort study using consecutive sampling technique was carried out at a tertiary health care in North Sulawesi, Indonesia. The study included 30 patients with transient elastography-diagnosed NAFLD whom liver stiffness score of F2 or more and received UDCA 250 mg every 8 h. The efficacy criteria was transient elastography liver stiffness in kPa and liver steatosis in dB/m. To evaluate statistical hypotheses, the Wilcoxon test and paired t-test were used.
Results: Among 30 patients, 60% were female, with mean age was 54.2 (SD 9.4) years old. Mean duration of UDCA treatment was 7.13 (SD 4.00) months. At the baseline, 63.33% of patients had liver stiffness score of F2, 46.67% of patients had liver steatosis score of S3. After UDCA treatment, 13.33% of patients had liver stiffness score of F2, 46.67% of patients had liver stiffness score of F1, 33.33% of patients had liver steatosis score of S3. The liver stiffness score (kPa) decreased significantly in the total sample (11.63 ± 6.04 vs 9.46 ± 4.43, $P = 0.017$). The changes in liver steatosis score (dB/m) were not significant in the total sample (284.56 ± 58.38 vs 264.16 ± 57.36, $P = 0.056$).
Conclusion: UDCA has positive effect in improving liver stiffness in patients with NAFLD. However, it has no effect in decreasing liver steatosis. UDCA may still be considered as a good choice for the treatment of NAFLD in developing countries.

[PP-0893]

Correlation between serum ferritin level and liver stiffness value among male patients with nonalcoholic fatty liver disease

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Objectives: Non-alcoholic fatty liver disease (NAFLD) is diagnosed through histology examination. However, it takes a lot of time, expensive, and causes discomfort to patients. Therefore, using other non-invasive diagnostic tools such as blood tests and vibration-controlled transient elastography (TE) is crucial. Ferritin is an acute-phase protein that is highly linked to NAFLD, and TE is known to help assess NAFLD progression by measuring liver tissue stiffness, which results are presented in kilopascals (kPa). Elevated serum ferritin is correlated to a high hepcidin level, an iron regulatory hormone that causes damaging effects to patients. The higher the number, the more severe histological derangement of the liver had happened. Considering that both ferritin and TE can be used to assess liver disease. This study aims to know whether there is any correlation between serum ferritin level and KPa value in fatty liver disease.
Materials and Methods: This research used a cross-sectional analytic retrospective study design. A total of 35 confirmed male fatty liver patient was chosen through consecutive sampling. Data analysis was done using the Spearman correlation test, with a significance level of $p < 0.05$. Serum ferritin level and kPa value were the two variables used in the research.
Results: Respondents of this study were all male, with ages ranging from 32 – 48 years old. Mean serum ferritin level and kPa values were 261.18 ± 135.98 and 6.14 ± 1.07, respectively. Based on the Spearman correlation test, there was no correlation found ($p > 0{,}05$).
Conclusion: No correlation was found between serum ferritin level and fibro scan KPa value among fatty liver patients.

[PP-0894]

Presence of diabetes but not obesity impacts the accuracy of APRI and FIB-4 for discriminating advanced fibrosis in patients with non-alcoholic fatty liver disease (NAFLD)

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Objectives: Noninvasive scores are important tools for assessing fibrosis in non-alcoholic fatty liver disease (NAFLD). Obesity and type 2 diabetes mellitus (DM) are important clinical predictors of fibrosis that are not incorporated in the commonly used noninvasive scores of APRI and FIB-4. Thus, the aim of the present study was to assess the discriminatory performance of APRI and FIB 4 for predicting the presence of advanced hepatic fibrosis ($\geq$ F3 fibrosis) on histology in patients with obesity or DM compared to patients without these co-morbidities.
Materials and Methods: We retrospectively reviewed the prospectively collected data of 129 patients [males: 86 (66.7%), age:40.2 ± 10.3 years] with biopsy proven NAFLD. Obesity was defined using Asia–Pacific cut-offs (BMI $\geq$ 25 kg/m^2). Patients were included only if they had all laboratory parameters for calculating APRI and FIB 4 scores within one month of performing liver biopsy.
Results: Advanced fibrosis on histology was present in 18 (14%) of 129 patients. In the whole cohort, both APRI (0.73, 95% CI: 0.65–0.83, $p < 0.001$) and FIB4 (0.72, 95% CI: 0.64–0.83, $p < 0.001$) showed acceptable AUROCs for detecting advanced fibrosis on histology. Eighty-seven (67.4%) patients were obese and 20 (15%) had DM. AUROCs of FIB4 [0.72 (95% CI: 0.56–0.85) vs 0.72 (95% CI: 0.61 to 0.81), $p = 0.99$] and APRI [0.74 (95% CI: 0.59–0.87) vs 0.72 (95% CI: 0.62–0.81, $p = 0.85$) for discriminating advanced fibrosis on histology were comparable in non-obese and obese patients, respectively. However, both APRI (AUROC: 0.60, 95% CI: 0.36–0.81, $p = 0.43$) and FIB4 (AUROC: 0.64, 95% CI: 0.40–0.83, $p = 0.35$) fared poorly in diabetic patients for predicting advanced fibrosis.
Conclusion: Presence of diabetes but not obesity impacts the accuracy of APRI and FIB-4 for discriminating advanced fibrosis in patients with NAFLD.

[PP-0897]

Correlation between homeostasis model assessment-estimated insulin resistance (HOMA-IR) and controlled attenuated parameter (CAP) value in non-alcoholic fatty liver disease patients

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Objectives: Non-alcoholic fatty liver Disease is a common problem in the population. Parameters to determine the degree of severity are still a challenge. Homeostasis Model Assessment-Estimated Insulin Resistance (HOMA-IR) was found to be an independent predictive factor for the development of advanced fibrosis in non-alcoholic fatty liver patients without diabetes mellitus. Controlled attenuated parameter (CAP) on FibroScan examination is used to assess the presence of steatosis in non-alcoholic fatty liver disease (NAFLD). Determine the correlation between HOMA-IR and CAP value in patients with NAFLD.
Materials and Methods: A cross sectional analytic retrospective study at a Tertiary Hospital from January to July 2021. Male respondents aged from 30–50 years old with obesity were included in the study. Patients with diabetes Mellitus were excluded.
Results: Study included 35 male respondents, with a median age of 37 years. The median value of HOMA-IR was found to be 3.55 with a minimum value of 1.28 and a maximum of 14.81. The mean CAP obtained was 314.91 ± 38.307 (95% CI 301.76 – 328.07). The correlation between HOMA-IR and CAP was analyzed using Spearman correlation test. There was a negative correlation between HOMA-IR and CAP, however it was not significant in this study (r − 0.106: p value 0.543).
Conclusion: There was no significant corelation between HOMA-IR values and CAP in patients with NAFLD.

[PP-0912]

Metabolic dysfunction-associated fatty liver disease and subsequent development of adverse pregnancy outcomes

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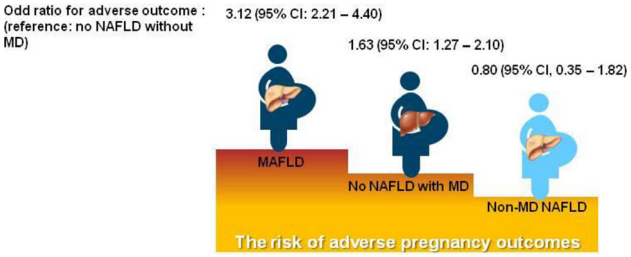
Objectives: Recently, metabolic dysfunction-associated fatty liver disease (MAFLD), rather than nonalcoholic fatty liver disease (NAFLD), was proposed to better describe liver disease associated with metabolic dysfunction (MD). In this study, we attempted to investigate the impact of MAFLD on pregnancy complications.
Materials and Methods: The current study is a secondary analysis of a multicenter prospective cohort designed to examine the risk of NAFLD during pregnancy. In the first trimester, enrolled pregnant women were evaluated for hepatic steatosis by liver ultrasonography, and blood samples were collected for biochemical measurements. The study population was divided into three groups: no NAFLD, hepatic steatosis but without metabolic dysfunction (non-MD NAFLD), and MAFLD. The primary outcome was the subsequent development of adverse pregnancy outcomes, including gestational diabetes mellitus, pregnancy-associated hypertension, preterm birth, and fetal growth abnormalities.
Results: The study population consisted of 1,744 pregnant women, including 1,523 with no NAFLD, 43 with non-MD NAFLD, and 178 with MAFLD. The risk of subsequent development of adverse pregnancy outcomes was higher in MAFLD than in non-MD NAFLD (adjusted odds ratio, 4.03; 95% CI, 1.68–9.67), whereas the risk was not significantly different between no NAFLD and non-MD NAFLD. 3) Among women with no NAFLD, the presence of MD increased the risk of adverse pregnancy outcomes. However, women with MAFLD were at higher risk for adverse pregnancy outcomes than women with no NAFLD without MD or those with no NAFLD with MD.
Conclusion: In pregnant women, MAFLD may be associated with an increased risk of subsequent adverse pregnancy outcomes.



[PP-0913]

Myosteatosis, but not sarcopenia, predisposes NAFLD subjects to early steatohepatitis and fibrosis progression

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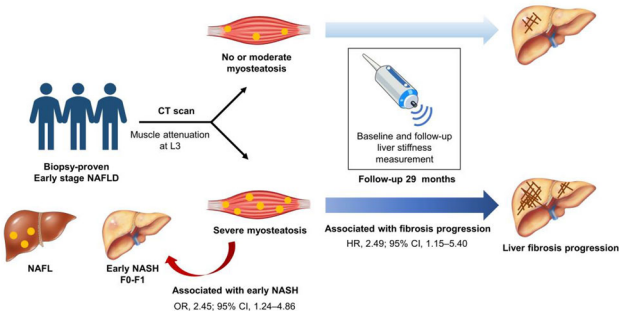
Objectives: Sarcopenia and myosteatosis are associated with advanced nonalcoholic fatty liver disease (NAFLD). However, muscle alterations in early-stage NAFLD remain unclear.
Materials and Methods: Nonalcoholic fatty liver (NAFL) or early nonalcoholic steatohepatitis (NASH) subjects without significant fibrosis were selected from a prospective biopsy-proven NAFLD cohort (n = 338). The skeletal muscle index (SMI) and mean muscle attenuation (MA) were measured using abdominal fat computed tomography at the 3rd lumbar vertebra level. Severe myosteatosis was defined as the lowest quartile of sex-stratified MA values.
Results: Early NASH subjects (n = 87) had lower MA (45.61 ± 6.45 HU vs. 47.48 ± 5.85 HU; p = 0.028) than NAFL subjects (n = 251) but a similar SMI. Subjects with more severe lobular inflammation and hepatocellular ballooning had lower MA (p = 0.003 and 0.041, respectively). The severe myosteatosis prevalence was higher in early NASH than in NAFL (33.3% vs. 21.1%; p = 0.029). Severe myosteatosis subjects were more likely to have early NASH in multivariable analysis adjusted for age, sex, and metabolic factors (OR, 2.45; 95% CI, 1.24–4.86), which was maintained after adjustment for visceral fat amount (OR, 2.44; 95% CI, 1.22–4.89). During a median 29-month follow-up, 170 subjects underwent repeated transient elastography. Fibrosis progression—an increase in liver stiffness measurement (ΔLSM) > 2 kPa or 2nd LSM ≥ 7 kPa—was found in 28 and 31 individuals. Severe myosteatosis was significantly associated with fibrosis progression after adjustment for various confounders (HR, 2.49; 95% CI, 1.15–5.40 and HR, 2.09; 95% CI, 1.01–4.34 for different fibrosis progression definitions).
Conclusion: Severe myosteatosis is significantly associated with early NASH and fibrosis progression in early-stage NAFLD.



[OP-1009]

Non-invasive tests (NITs) for predicting hepatocellular carcinoma in non-alcoholic fatty liver disease (NAFLD) patients without cirrhosis: A meta-analysis of individual patient data

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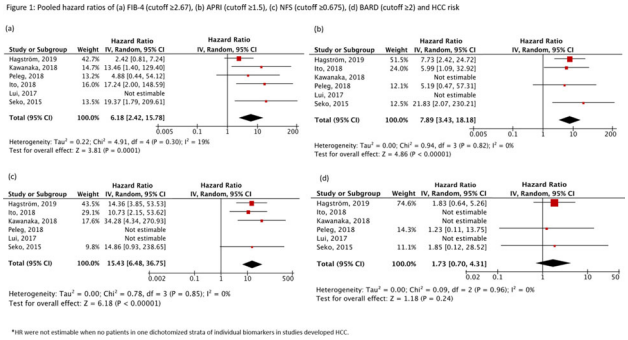
Objectives: To determine the performance of non-invasive tests (NITs) for predicting HCC development in non-cirrhotic patients with NAFLD.
Materials and Methods: Electronic reference databases (Medline, EMBASE and Scopus) were searched from inception to July 2021 for studies reporting an association between NITs and HCC development in non-cirrhotic patients with NAFLD. Pooled hazards ratios (HRs) with 95% confidence intervals for each NITs (FIB-4, APRI, NFS and BARD) were estimated using a random effects model.
Results: Of the 4,291 studies screened, 20 were included in the systematic review. Meta-analysis of individual patient data from 6 studies comprising 2,928 non-cirrhotic NAFLD patients with median follow up time ranging from 1.9 to 30.9 years showed highly significant associations with FIB-4 (cutoff $\geq$ 2.67), APRI (cutoff $\geq$ 1.5), and NFS (cutoff $\geq$ 0.675) and HCC, with pooled HRs of 6.18 (95%CI: 2.42–15.78, I^2 = 19%), 7.89 (95%CI: 3.43–18.18, I^2 = 0%) and 15.43 (95%CI: 6.48–36.75, I^2 = 0%), respectively (Fig. 1). BARD (cutoff $\geq$ 2) was not statistically significant with an increased risk (HR 1.73 (95%CI 0.7–4.31; I^2 = 0%). The pooled incidence rate difference (IRD) for those with FIB-4 $\geq$ 2.67 versus < 2.67, APRI $\geq$ 1.5 versus < 1.5, and NFS $\geq$ 0.675 versus < 0.675 as a reference, was 6.43 (p = 0.056), 1.04 (p = 0.523), and 2.14 (p = 0.483) per 1000 person-years respectively.
Conclusion: FIB-4, NFS, and APRI are strongly associated with the development of HCC in non-cirrhotic patients with NAFLD. Further studies are warranted to identify optimal cutoffs which could be useful for HCC surveillance in clinical practice.



[OP-1027]

Mid-upper arm circumference is associated liver steatosis and fibrosis in patients with MAFLD: A population based observational study

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Objectives: Metabolic associated fatty liver disease (MAFLD) was a series of liver diseases based on liver steatosis and metabolic disorders. Steatosis, as the core factor in the diagnosis of MAFLD, and fibrosis, as the major determinant of adverse outcomes of MAFLD, were needed to be estimated simply and accurately by physicians. In this study, we explored the significance of mid-upper arm circumference (MUAC) in evaluating liver steatosis and fibrosis in MAFLD patients.
Materials and Methods: We included 2239 cases with MAFLD from 2017–2018 National Health and Nutrition Examination Surveys (NHANES) database. Liver steatosis and fibrosis were measured by vibration controlled transient elastography (VCTE). Anthropometric parameters, demographic and serological test data can be obtained from NHANES database. The association between MUAC and liver steatosis and fibrosis were evaluated by multivariable linear regression model, a weighted generalized additive model and smooth curve fitting using R.
Results: MUAC was positively associated with liver steatosis in every multivariate linear regression model (model 1: β = 2.9871, 95%CI: 2.6612–3.3130; model 2: β = 3.3656, 95%CI: 3.0216–3.9079; model 3: β = 2.2781, 95%CI: 1.9148–2.6431), and this positive association was consistent in both men and women, and among different race groups (Mexican American, Other Hispanic, Non-Hispanic White, Black and Asian and other race). On the other hand, MUAC was positively associated with liver fibrosis in every multivariate linear regression model, and this positive association also was consistent in both men and women, and among Non-Hispanic population. As

MUAC ≥ 40 cm, the MACU has a better evaluation effect on liver fibrosis in MAFLD.
Conclusion: Increased MUAC was positively associated with liver steatosis and fibrosis (especially MUAC ≥ 40 cm) in MAFLD patients, which might be a simple and convenient tool in MAFLD assessment.

[OP-1064]

Develop a noninvasive nomogram model for nonalcoholic steatohepatitis significant fibrosis

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Objectives: Key issues in nonalcoholic fatty liver disease (NAFLD) patients are the differentiation of nonalcoholic steatohepatitis (NASH) from nonalcoholic fatty liver (NAFL) with significant fibrosis (≥ F2, perisinusoidal and portal/periportal).This will help to guide the subsequent management the patients. We aimed to develop a noninvasive nomogram model (LAPH) for nonalcoholic steatohepatitis with significant fibrosis.
Materials and Methods: We designed a retrospective cross-sectional study and enrolled 805 participants (405 for nomogram construction and 400 for validation). Clinical information and laboratory/imaging results of the participants were retrieved. Independent variables significantly associated with NAFLD with significant fibrosis were identified by a logistic regression model, and a NAFLD with significant fibrosis prediction LAPH model was constructed. The LAPH was then compared with three existing NAFLD-related fibrosis prediction models: liver stiffness measurement, aspartate aminotransferase (AST) to platelet ratio index (APRI) and fibrosis-4 (FIB-4). Area under the receiver operator characteristic curve (AUROC) and decision curve analysis (DCA) were performed.
Results: A total of 275/405 (67.90%) and 260/400 (65.00%) participants in the testing and validation datasets, respectively, had liver biopsy-proven NAFLD with significant fibrosis. Four variables were selected to build the LAPH: LSM, AST, platelet (PLT) and High-density lipoprotein cholesterol (HDL-C). The diagnostic accuracy of the LAPH for NAFLD significant fibrosis (AUROC 0.867, 95% CI 0.862–0.871) was significantly superior to that of the LSM (AUROC 0.834, 95% CI 0.828–0.845), the APRI (AUROC 0.670, 95% CI 0.653–0.687), the FIB-4 (AUROC 0.639, 95% CI 0.632–0.644), (all $p < 0.05$). DCA confirmed the clinical utility of the LAPH.
Conclusion: LAPH, a noninvasive nomogram model consisting of LSM, AST, PLT and HDL-C, is worthy of clinical application. This might improve the early diagnosis rate of nonalcoholic steatohepatitis with significant fibrosis.

[OP-1079]

Does Mac-2 binding protein glycosylation isomer better predict liver fibrosis in patients with metabolic associated fatty liver disease?

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Objectives: The definition of metabolic associated fatty liver disease (MAFLD) has newly been proposed. We aimed to investigate the efficacy of Mac-2 binding protein glycosylation isomer (M2BPGi), non-invasive fibrosis marker, for discriminating significant and advanced fibrosis, and cirrhosis, respectively according to MAFLD and NAFLD definitions.
Materials and Methods: Serum M2BPGi levels were collected and analyzed from 950 fatty liver patients in a tertiary hospital. Liver fibrosis was graded by transient elastography. Diagnostic efficacy of serum M2BPGi and other serum based liver fibrosis markers [fibrosis index based on four factors (FIB-4) and NAFLD fibrosis score (NFS)] was evaluated using correlation analysis and area under the ROC curve (AUC).
Results: There were 810 patients and 687 patients by the MAFLD and NAFLD definition, respectively. Serum M2BPGi level and other liver fibrosis markers showed a positive correlation with fibrosis grade. The AUC values of M2BPGi were 0.698, 0.698, and 0.828 for predicting fibrosis (F) > 1, F > 2, and F > 3, respectively in NAFLD group. The AUC values of M2BPGi were 0.706, 0.719, and 0.843 for predicting F > 1, F > 2, and F > 3, respectively in MAFLD group. The AUC values of M2BPGi for predicting severity of fibrosis were greater than those of serum based liver fibrosis markers.
Conclusion: M2BPGi showed better diagnostic efficacy for diagnosing the severity of liver fibrosis in MAFLD patients.

[OP-1107]

Assessment and comparison of cardiovascular risk factors between lean and non-lean nafld patients: A cross-sectional observational study

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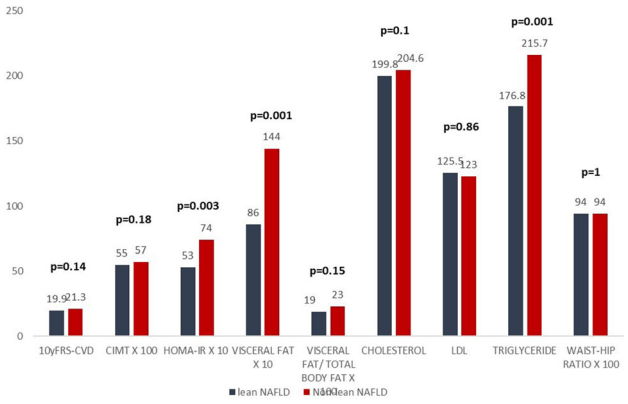
Objectives: Recent studies have shown that NAFLD is not exclusively a disease of the obese. Non-obese/ overweight can also present with NAFLD (lean NAFLD). Cardiovascular Disease (CVD) remains the most common cause of all-cause mortality in NAFLD. We tried to assess and compare the risk of atherosclerotic CVD between lean and non-lean NAFLD patients.
Materials and Methods: Cross-sectional observational study. Consecutive patients > 18 years of age with NAFLD (2016 EASL Clinical Practice Guidelines) were enrolled. Those with established CV disease were excluded. Lean NAFLD was defined as having a BMI < 23 kg/m^2 (WHO Expert Committee Recommendations, Lancet 2004). Carotid intimal medial thickness (CIMT) was measured and 10-year Framingham Risk Score (10Y-FRS) calculated using standard protocol.

Results: 110 patients of non-lean NAFLD (mean BMI 28.2) and 70 patients of lean NAFLD (BMI 21.4) were enrolled in the study. Dyslipidemia was the most common co-morbidity (41% in non-lean vs 36% in lean), followed by diabetes mellitus (40% vs 27%) and hypertension (22 vs 26%), in both groups. Age-group specific analysis (18–40 years, 41–60 years and > 60 years) of CIMT and FRS-CVD risk score, by unpaired T-test, revealed no significant difference between the two arms. Serum cholesterol and LDL did not differ significantly between the 2 groups (204.6 vs 199.8, 123 vs 125.5 respectively). HOMA-IR (7.4 vs 5.3), Serum Triglycerides (215.7 vs 176.8) and Visceral fat percentage (14.4% vs 8.6%) were significantly higher in non-lean NAFLD patients. Visceral fat-total body fat ratio did not differ significantly among the 2 groups (0.23 vs 0.19). Waist circumference was significantly high in non-lean group (98 vs 82 cms), but waist-hip ratio did not differ in the 2 groups.
Conclusion: Evaluation for atherosclerotic CV disease should be prioritised in all NAFLD patients, irrespective of body habitus, as the CV risk factors are equally high in lean and non-lean NAFLD patients, and greater than the regional average in both the groups.



[PP-1132]

Characteristics of outpatients with liver diseases (chronic viral hepatitis, hepatic steatosis, liver disease associated with diabetes mellitus and obesity) receiving essential phospholipids as an adj

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Objectives: The main goal of this study was to evaluate the profile of outpatients with diagnosed liver diseases treated with essential phospholipids (EPL) as an adjunct to standard therapy in real clinical practice.
Materials and Methods: Descriptive cross-sectional, non-interventional, multicenter study (REPAIR) was carried out in 64 sites in 5 cities of the Republic of Kazakhstan. The study was conducted in two stages: (1) the creation of a Registry, (2) the therapy compliance assessment.
Results: Among 1505 recruited patients, women were predominant (56.5%), the average age was 49.9 ± 11.1 years. The predominant liver diseases were hepatic steatosis (32.2%), disease associated with obesity (25.8%), chronic viral hepatitis (16%), liver diseases associated with type 2 diabetes mellitus [DM] (14.6%). Predominant risk factor was obesity (59.7%): the average BMI was 30.6 ± 5.6 kg/m^2 in women, and 29.9 ± 4.5 kg/m^2 in men. Other risk factors were arterial hypertension (58.8%), dyslipidemia (48.6%) and DM (24.0%). The prevalence of risk factors varied across regions ($p < 0,05$). The most frequently used diagnostic method for steatosis and steatohepatitis diagnosis was abdominal ultrasound performed in 95.3%, and the most frequent abnormalities were increased liver echogenicity (78.9%), enlarged liver size (55.9%) and the echo decay phenomenon (30.7%). Adherence to therapy varied significantly across cities ($p = 0.04$): it was higher in Almaty (86.2%), and lower in Karaganda (72.3%). The study showed that the majority of patients and doctors were satisfied with the results of treatment with EPL.
Conclusion: The profile of the recruited patients treated with EPL in routine practice, was generally represented by hepatic steatosis, liver disease associated with obesity and chronic viral hepatitis. The most common risk factors for the liver diseases were obesity, hypertension, dyslipidemia, and DM. High adherence to EPL treatment was also noted.

[OP-1197]

Assessment of liver fibrosis with transient elastography in NAFLD patients

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Objectives: To evaluate the diagnostic accuracy of transient Elastography in identifying different degrees of fibrosis in NAFLD adult patients.
Materials and Methods: A Cross-sectional study was undertaken at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre and Medical Unit II, Dow University of Health Sciences Ojha campus Karachi, Pakistan. After obtaining ethical approval, all patients above the age of 18 years, with diagnosis of NAFLD on the basis of abnormal liver function tests (LFTs) and on ultrasound abdomen consistent with fatty liver were included in the study. All patients with hepatitis, hepatic malignancies, hepatobiliary infections, and biliary tract disease were excluded from the study. Fibrosis score was calculated through Elastography as: F0-F1 (5.3–7.1 kPa, Normal); F2 (7.5–8.5 kPa, Mild/Grade-I); F3 (9.5–13.0 kPa, Moderate/Grade-II); and F4 (13.1–18.8 kPa, Severe/Grade-III). This study is an ongoing study.
Results: A total of 171 patients were enrolled in the study, from which 69 (40.35%) were male and 102 (59.64%) were female, with a mean age of 37.50 ± 9.74 years. Out of these, 112 (65.49%) belonged to the lower socioeconomic class. One hundred and twenty two (71.34%) patients had fatty liver on ultrasound and 49 (28.65%) had hepatomegaly with fatty changes. TE revealed 69 (40.35%) patients had a score of F0-F1, 62 (36.25%) F2, 29 (16.95%) F3, and only 11 (6.43%) had a score of F4.
Conclusion: The detection of liver fibrosis at early stages is crucial in preventing its progression to cirrhosis which is the irreversible process. Reversal of fibrosis is only possible if it is diagnosed as early as possible and managed with appropriate treatment.

[L-OP-1218]

Risk factors associated with NASH related cirrhosis—A case control study

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Objectives: NAFLD has emerged as a leading cause of chronic liver disease while its severe form, NASH cirrhosis, is a major cause of liver-related mortality & morbidity worldwide. We aimed to assess the risk factors of NAFLD-cirrhosis.

Materials and Methods: In this case–control study, all consecutive NASH related liver cirrhotics were enrolled as cases. The Healthy Population (Controls) were enrolled from the community who had no past or present evidence of liver disease including hepatic steatosis. A detailed pre-tested proforma was used to collect data on their lifestyle and dietary risk factors along with anthropometric measurements and biochemical assays. The diagnosis of Liver Fibrosis was done by transient Elastography with cut off values for F0 $\leq$ 6 kPa, F1 6–6.9 kPa, F2 $\geq$ 7—8.9 kPa, F3 $\geq$ 9—11.7 kPa, F4 $\geq$ 11.8 kPa. Logistic regression was done to determine the risk factors.

Results: A total of 225 subjects (NASH Cirrhosis = 103, Healthy Control = 122) were enrolled. NASH Cirrhosis patients had higher BMI (28.96 $\pm$ 4.79 vs 22.06 $\pm$ 3.81, p = $<$ 0.00), waist circumference (98.48 $\pm$ 14.95 vs 81.36 $\pm$ 10.73, p = $<$ 0.00), age (55.56 $\pm$ 9.9vs35.39 $\pm$ 13.69, p = $<$ 0.00), and comorbidities like diabetes (61.8%vs5.7%, p = $<$ 0.00), hypertension (37.6%vs7.4%, p = $<$ 0.00), dyslipidaemia (11.8%vs1%, p = $<$ 0.00) & male gender (75.5% vs. 59.8%,p = 0.02) were significantly higher among cases compared with controls. Majority of cases were sedentary. Dietary risk factors includes higher intake of non-vegetarian food, eggs and sugar compared to the controls. Lower physical activity was significantly greater among cases. On multivariate regression, the risk of liver cirrhosis remains statistically significant for age 1.12 95%CI (1.04–1.18), BMI 1.71 95% CI (1.21–2.42), Diabetes 26.72 95% CI (4.72–35.78) and T. Bilirubin 4.82 95% CI (1.23–18.87) respectively.

Conclusion: This novel study demonstrates the risk factors for NASH cirrhosis which include age, high BMI and diabetes. Sedentary lifestyle and extra intake of non-vegetarian food, egg and sugar are strongly associated with NASH cirrhosis development.

Table 1. Differences between patients with NASH cirrhosis and healthy controls

	NASH related Cirrhosis (n=103)	Healthy Controls (n=122)	p value
Age (in Yrs)	55.56±9.98	35.39±13.69	<0.00
Male n (%)	77 (75.5)	73 (59.8)	0.02
BMI (kg/m2)	28.96±4.79	22.06±3.81	<0.00
Waist Circumference (cm)	98.48±14.95	81.36±10.73	<0.00
Hb (gm/dl)	11.96±2.04	13.65±1.68	<0.00
Platelet count (pcmm)	127.24±60.92	188.13±91.19	<0.00
T. Bilirubin (mg/dL)	1.50±1.38	0.91±0.34	<0.00
S. Albumin (mg/dL)	3.7±0.66	4.56±0.38	<0.00
Hypertension n (%)	38 (37.6)	9 (7.4)	<0.00
Diabetes n (%)	63 (61.8)	7 (5.7)	<0.00
Dyslipidaemia n (%)	12 (11.8)	1	<0.00
LSM (KPa)	32.77±20.74	4.01±1.92	<0.00
CAP (db/m)	271.12±59.98	202.05±45.65	<0.00
DIETARY RISK FACTORS, n (%)			
Non-Veg Food			
Never	39 (45.3)	0	<0.00
Daily	5	1	
Less than daily, > once a week	34 (39.5)	34 (56.7)	
Once in 15 days	2	15 (25)	
Once in a month	6	10 (16.7)	
Eggs			
Never	35 (46.2)	0	<0.00
Daily	9	2	
Less than daily, > once a week	27 (34.6)	33 (67.3)	
Once in 15 days	1	8	
Once in a month	5	6	
Sugars & Jaggery			
Never	6	0	<0.00
Daily	28 (31.1)	92 (82.9)	
Less than daily, > once a week	40 (44.4)	13 (11.7)	
Once in 15 days	2	3	
Once in a month	14 (15.6)	3	
PHYSICAL ACTIVTY			
Low n (%)	65 (63.7)	86 (71.1)	<0.00
Moderate n (%)	34 (33.3)	14 (11.6)	
High n (%)	3 (2.9)	21 (17.4)	

[L-OP-1219]

Does spleen steatosis measure by transient elastography correlate with liver steatosis?

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Objectives: NAFLD is defined by presence of more than 5% steatosis in hepatocytes coupled with insulin resistance that is currently responsible for the highest number of liver related diseases worldwide. This study aims to find a novel entity of "fatty spleen" and whether it is associated with hepatic steatosis.

Materials and Methods: 64 patients were included from the outpatient department who met the criteria of NAFLD, both liver and spleen elastography were conducted via Fibroscan at the same time before treatment.

Results: Out of the 64 patients, 53 (82.8%) were males and 11 (17.2%) were females. Age ranged from 22 to 86 (mean 43.47 $\pm$ 12.15). BMI also ranged between 20.5 to 39.8 mean (28.2 $\pm$ 4.17) and Diabetes was present in 9 patients (13.6%). Steatosis values were ranged in the following order: Normal ($<$ 240), Mild (240–264), Moderate (265–294), and Severe ($>$ 295). 15 patients had (22.7%) had mild liver steatosis, 24 (37.5%) had moderate and 23 (35.9%) patients were recorded to have severe fatty liver. Similar values were also noted for spleen elastography which showed 4 (6%) had mild, 11 (16.7%) had moderate and 27 (40.9%) had severe steatosis. Bivariate correlation analysis revealed to show a significant

correlation between hepatic and splenic steatosis (p = 0.022), similarly, spleen steatosis also showed link with liver stiffness (p = 0.047), and BMI (p = 0.022). However, when corresponding between spleen steatosis and degree of liver steatosis, i.e., mild (p = 0.778), moderate (p = 0.691), and severe (p = 0.085), it failed to show a significant association.
Conclusion: Despite highlighting clear connection between hepatic and splenic steatosis, due to much overlapping of values, spleen elastography cannot differentiate mild, moderate and severe cases of spleen steatosis when compared with liver steatosis.

[L-OP-1247]

Patients with severe coronary artery disease are more likely to have advanced non-alcoholic fatty liver disease

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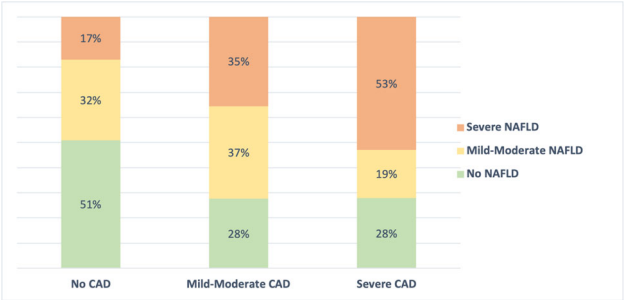
Objectives: There is increasing recognition of association of nonalcoholic fatty liver disease (NAFLD) with coronary artery disease (CAD), however, scarce data is available from India. The aim of our study was to evaluate the association between the presence and severity of CAD and NAFLD assessed by transient elastography (TE) and controlled attenuation parameter (CAP).
Materials and Methods: Patients undergoing coronary angiography, but without any known liver disease, were prospectively enrolled. Liver stiffness measurement (LSM) and CAP values were assessed using Fibroscan® (Echosens, Paris, France). Based on coronary angiography patients were categorized as: No CAD (if angiography was normal), Severe CAD (if there was triple vessel disease or left-main $\geq$ 50% stenosis), and Mild-Moderate CAD (for all other coronary angiography findings). Based on Fibroscan® values patients were categorized as: No NAFLD (if LSM $<$ 7.9 kPa and CAP $<$ 234 dB/m), Mild-Moderate NAFLD (if LSM $<$ 7.9 kPa and CAP 234–301 dB/m), Severe NAFLD (if LSM $\geq$ 7.9 and/or CAP $\geq$ 302 dB/m). Patients with congestive/right-sided heart failure and those with alternative cause of liver disease were excluded (ALD, HBV, HCV, DILI).
Results: A total of 262 patients were included (median age 61 [25–85] yrs, 81% males, median BMI 26 [17–40] kg/m^2. On coronary angiography 209 (80%) patients were found to have CAD and 53 (20%) patients had no CAD (normal coronaries). NAFLD was significantly more common in patients with CAD as compared to those without CAD (151/209, 72% vs. 26/53, 49%; p = 0.002). The frequency of severe NAFLD was highest in patients with severe CAD (36/68, 53%), as compared to patients with mild-moderate CAD (50/141, 35%) and patients with no CAD (9/53, 17%) (Figure).
Conclusion: Up to 72% of patients with CAD have undiagnosed NAFLD. The severity of NAFLD positively correlated with severity of CAD. We recommend that all patients with CAD should be investigated for NAFLD.



[L-OP-1301]

Changes of myocardial damage metrics in patients with metabolic syndrome associated with nonalcoholic fatty liver disease

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Objectives: Metabolic syndrome (MS) is a cluster of number of risk factors for the development of type 2 diabetes mellitus and cardiovascular disease. Number of MS patients are associated with nonalcoholic fatty liver disease (NAFLD), and coming together of these two conditions increases the risk of myocardial damage. Aim of the study was to evaluate the myocardial damage metrics in patients with MS associated with NAFLD.
Materials and Methods: 240 consecutive patients with MS have been enrolled in the study (aged 34–69 years, mean age 54.48 $\pm$ 15.2 years, male = 48%). Patients were divided into two groups by 120 according to the presence or absence of NAFLD in addition to the MS. Nonalcoholic fatty liver disease was diagnosed by computed tomography scanning. MS was diagnosed by International Diabetes Federation's recommendations. Baseline characteristics, anthropometry, high sensitive C reactive protein (hsCRP), plasma brain natriuretic peptide (BNP), plasma N-terminal pro-b type natriuretic peptide (NT-proBNP) were assessed. All statistical analysis was performed by SPSS 24.0 software.
Results: Patients with MS associated with NAFLD (Group I) tended to have higher level of hsCRP than those MS patients without NAFLD (Group II; P $<$ 0.05). There were not statistically significant changes with regard to BNP (P $>$ 0.05) and NT-proBNP (P $>$ 0.05) between groups. When we separately analyzed by gender there were not statistically significant changes between males and females (P $>$ 0.05). Among MS components, hypertension (1.8; 1.16–2.45; CI 95%, P $<$ 0.05), dyslipidemia (1.6; 1.15–2.24; CI 95%, P $<$ 0.05) were positively correlated with hsCRP.
Conclusion: Patients with MS associated with NAFLD might be affected by asymptomatic myocardial damage, which in terms could quickly lead to the development of the cardiovascular diseases. Further studies are needed with large amount of patients.

[L-OP-1302]

Features of characteristics of metabolic syndrome components in covid-19 patients associated with nonalcoholic fatty liver disease

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Objectives: Covid-19 was affected all over the world and caused pandemic. Compelling data suggest that Covid-19 might influence all human parts. Host of studies showed that metabolic syndrome (MetS) was associated with nonalcoholic fatty liver disease (NAFLD). Purpose of the study was to evaluate the possible impact of MetS components in the course of Covid-19 in patients with NAFLD.
Materials and Methods: 192 consecutive patients (aged 37–75 years; mean age 56.2 ± 13.2 years; male = 48%) with NAFLD and MetS who underwent Covid-19 were enrolled in this study. Patients were divided into two groups by 91 in each group according to the presence or absence of MetS. All anthropometric, laboratory and instrumental data were obtained and analyzed at baseline. All statistical analysis were performed by SPSS 24.0 software.
Results: Patients with concomitant MetS (Group I) had severe Covid-19 than those without it ($P < 0.05$). 19% out of Group I patients had severe Covid-19 whilst 12% out of Group II patients had severe course of the invective disease. Multiple regression logistic analysis showed that among MetS components having abdominal obesity (AO) (2.7; 1.6–4.4; CI 95%; $P < 0.05$), insulin resistance (IR) (2.0; 1.4–3.9' CI 95%; $P < 0.05$), hypertension (HT) (1.4; 1.3–2.4; CI 95%; $P < 0.05$) tended have a severe Covid-19 in patients with NAFLD. When we separately analyzed by gender there was not significant changes between male and female ($P > 0.05$).
Conclusion: MetS was significantly associated with severe Covid-19 in patients with NAFLD. Among MetS components AO, IR and HT independently associated with severe Covid-19 regardless of gender. Further investigations are required with large amount of participants.

[L-PP-1308]

Association with fatty liver, gastritis, and Helicobacter pylori using primary clinic

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Objectives: We investigated to determine to correlate H. pylori infection confers a higher risk of nonalcoholic fatty liver disease (NAFLD).
Materials and Methods: We retrospectively analyzed those who underwent gastroscopy and liver ultrasound at primary medical institutions. The inclusion criteria were those who performed endoscopy and CLO test with ultrasound. Cases were classified as H. pylori positive or negative according to the results of the CLO test. NAFLD was considered to have NAFLD by comparing the echo transmittance with the kidney through ultrasound due to the characteristics of a primary medical institution to determine the presence or absence of fatty liver. The risk factors for NAFLD were determined through multivariate analysis, and a P value of 0.05 or less was determined as a significant result.
Results: Of the 79 patients analyzed, 20 (25.3%) were positive for H. pylori. H. pylori infection was associated with hypertension, high ALT, and overweight, but was not significant. When H. pylori infection was diagnosed as fatty liver on ultrasound, there was a high trend, but it was not significant. (34% vs 17%, P = 0.13) However, most patients with fatty liver had gastritis, and fatty liver was strongly associated with LFT levels.
Conclusion: H. pylori infection was not significantly associated with fatty liver. However, if many studies are conducted, there may be a significant association. This study utilized data from primary medical institutions, and it is judged that it can be helpful in research on fatty liver using ultrasound.

[ABST-0340]

Study on childhood obesity and various possible causes and effects on liver in study area of Prayagraj (U.P)

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Background: Childhood obesity is one of the most serious public health challenges of twenty-first century. The problem is global and is steadily affecting many low and middle income countries, particularly in urban settings. Overweight is multifactorial condition linked to an energy imbalance and also affecting liver. India is gaining weight. Traditionally known for malnutrition Indians now report more and more frequently with overweight, obesity, and their consequences. The present study was done to analyze the overweight and obesity.
Methods: A pilot study was done on the schools in this area. A prestested questionnaire was prepared, schools in the area were approached and with informed consent of students data was collected, BMI was calculated and analysed. Total 350 students were selected in the age group of 9to12yrs. The present study found overall prevalence of overweight as 106 students of which 71 were found obese as having more BMI. It indicates that the study area (Prayagraj) has more overweight children than obese. Moreover due to COVID the reduced physical activities has created more problem.
Results: It has been found that boys are more overweight than girls as boys are more careless than girls so don't pay their attention towards their health. Children having rich family background are having high in number of overweight and obesity as compared to middle and lower class. The students attending government school were less prone than of private school students due to luxuries provided at home. Children paying more time in mobile and T.V screen and less time in physical activity along with compromising their sleep are more susceptible to obesity. Parents having obesity have more chances of having their child obese.
Conclusions: Obesity has to be controlled. Parents, teachers and peer groups have the responsibility to tackle this problem which is not so easy to solve else it would lead to an increase in liver associated diseases.

Alcoholic Liver Disease

[OP-0022]

Complement C3 activation regulates miR-451 by targeting Acsl1 in ethanol-induced liver steatosis

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Objectives: Complement plays a role in alcoholic fatty liver disease, but its mechanism is not fully understood. Meanwhile, increasing evidence shows that microRNAs play an important role in the development and pathogenesis of AFLD. The purpose of this study is to investigate the role and mechanism of miR-451 in AFLD, and to explore the regulatory effects of complement C3 activation.
Materials and Methods: miR-451 knockout and wild-type mice were used to construct an alcoholic fatty liver model to detect inflammation and fat metabolism. Cell experiments were applied to analyze the effects of miR-451 on lipid metabolism in vitro, and its target genes and transcription factors were determined by luciferase reports and ChIP. C3 deficiency mice or mice treated with CR2-Crry (a C3 inhibitor that specifically targets complement activation sites) were used to estimate its regulatory effect on transcription factor and miR-451.
Results: miR-451 was elevated in the liver tissue of ethanol-fed mice, and the expression of its target gene Acsl1 was reduced. In addition, the fatty acid degradation signal pathway is regulated, so that fat degradation in the liver of the mouse is reduced, which leads to liver fat accumulation. Interestingly, fat accumulation in miR-451 knockout mice fed with ethanol was significantly reduced, but inflammation did not change. Meanwhile, miR-451 and its transcription factor srebf1 were down-regulated in C3 deficiency and CR2-Crry treated mice.
Conclusion: C3 activation regulates miR-451 expression through Srebf1 and are involved in liver steatosis, C3 and miR-451 can be potential therapeutic targets for the treatment of alcoholic fatty liver disease in humans.

[PP-0125]

Histone deacetylase 8 is crucial for alcohol-induced steatosis and inflammation

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Objectives: Some histone deacetylase inhibitors have been investigated for treatment of alcohol-related liver disease (ALD). However, most of these are considered to be nonselective inhibitors that may lead to undesirable adverse effects. We aimed to investigate the role of newly synthesized selective histone deacetylase 8 (HDAC8) inhibitor on ALD.
Materials and Methods: A selective HDAC8 inhibitor SPA3014 (1 mg/kg and 10 mg/kg) was administered once a day intraperitoneally in chronic-plus-binge ethanol diet mouse model (NIAAA model).
Results: Hepatic HDAC8 protein expression was upregulated in ethanol-fed mice. The liver-to-body weight (%) was markedly increased in ethanol-fed mice, but that was restored in mice administered 10 mg/kg of SPA3014. H&E staining of livers revealed prominent fat accumulation and neutrophil infiltration in ethanol-fed mice and SPA3014 treatment remarkably ameliorated the hepatic steatosis and inflammations. Additionally, elevated serum AST, ALT, and hepatic TG levels were significantly attenuated by SPA3014 treatment. To determine the hepatoprotective role of SPA3014 on alcohol induced liver inflammation, mRNA levels of pro-inflammatory mediators were analyzed which were markedly upregulated in ethanol-fed group, but they were suppressed in SPA3014-treated group. Next, we evaluated the potential mechanism of SPA3014 on hepatic steatosis. Western blotting showed that the protein expression of CPT1, p-AMPKα, and PPARα was significantly downregulated in ethanol-fed mice, but restored by SPA3014 administration.
Conclusion: Selective HDAC8 inhibition may provide new therapeutic options for ALD treatment.

[PP-0237]

The Chinese herbal JianPiHuoXue formula attenuates alcoholic liver disease by repairing intestinal mucosalin mice

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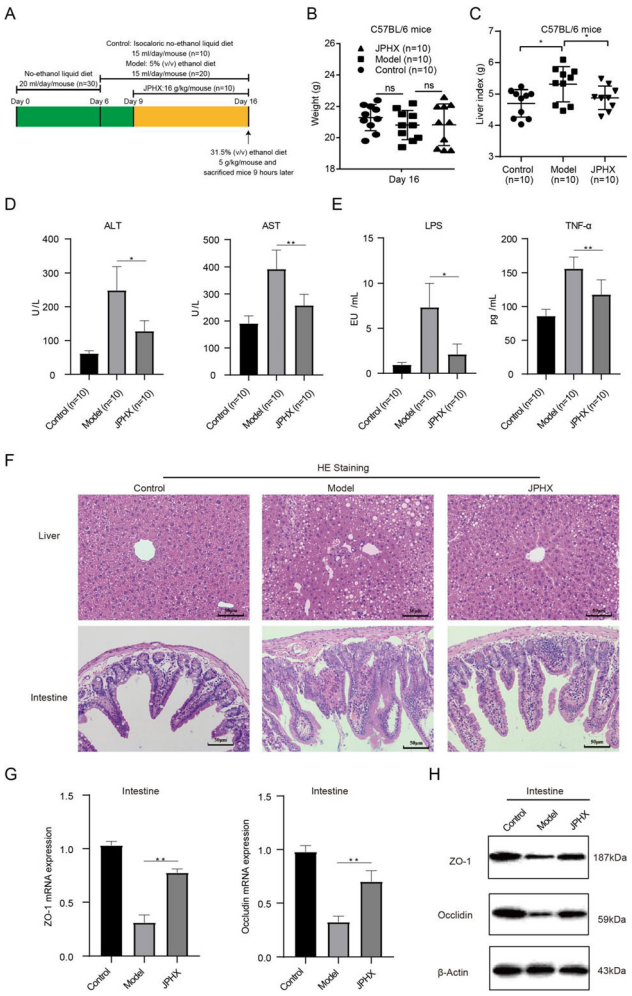
Objectives: The Chinese herbal JianPiHuoXue formula (JPHX) has been prescribed for alcoholic liver disease (ALD) in the clinic and has shown a good therapeutic effect. The study aimed to investigate the mechanisms of JPHX on the liver and intestinal mucosal repair in ALD mice model.

Materials and Methods: 6-week-old male C57BL/6 mice were fed with a 5% (v/v) ethanol liquid diet for 10 days to establish the ALD mice model. Among the mice, the control group received an all-time isocaloric no-ethanol liquid diet. In the last eight of this period, the treatment group received JPHX solution and the model group received sterile water by intragastric administration respectively. On day 16, mice were given an isocaloric or 31.5% (v/v) ethanol diet and sacrificed 9 h later. The serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), Lipopolysaccharide (LPS) and tumor necrosis factor (TNF-α) levels were measured. Then, pathological changes in the liver and intestine tissues of mice were detected by hematoxylin and eosin staining (HE). Finally, expression of tight junction proteins (TJs) included Zo-1 and Occludin were determined by Real-time quantitative polymerase chain reaction and Western blotting.

Results: Compared to the control, the HE results showed that JPHX treatment could improve hepatic steatosis, decrease liver inflammation and promote repair of the damaged intestinal mucosa. Meanwhile, JPHX treatment effectively decreased serum ALT, AST, LPS and TNF-α levels in ALD mice. Moreover, the mRNA and protein expression of Zo-1 and Occludin) were both higher in the JPHX group compared with the control group.

Conclusion: JPHX treatment could improve hepatic functions and protect the liver from damage in ALD. The mechanism of its protective effects is to increase the expression of TJs and alleviate intestinal barrier damage, and further reduce inflammation in the liver. Our study could be the basis for a subsequent prospective clinical study.



[PP-0344]

New prognostic model in hospitalized patients with non-severe alcoholic liver disease

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Objectives: Several prognostic models have been developed for patients with severe alcoholic liver disease, but few studies have yet investigated prognosis of patients with non-severe alcoholic liver disease (NSALD). In this study, we aimed to develop a new prognostic model for patients with NSALD.
Materials and Methods: We extracted 364 patients with NSALD, defined as lower than 32 of Maddrey's discriminant function score from the retrospective KACLiF cohort for the derivation of a new prognostic model (training set), and validated it in 526 patients from the prospective KACLiF cohort (validation set); These cohorts consisted of patients who had chronic liver disease and were hospitalized due to acute decompensations.
Results: Twenty-four and 36 patients died or received transplantation within 6 months in training and validation sets. In the training set, the highest area under the curve (AUC) of conventional prognostic models (e.g. MELD-Na score) was 0.744, 0.741, 0.688 for 28-, 90-, 180-days mortality. History of previous decompensation, high neutrophil proportion, presence of large ascites and overt hepatic encephalopathy, low albumin level, high sodium level, and use of vasopressor were significantly associated with the mortality of patient with NSALD. The new model consisted of past decompensation, neutrophil proportion over 70%, large ascites and use of vasopressor. It showed high predictivity for mortality in the training set as well as in the validation set (0.823 and 0.795, 0.816 and 0.784, and 0.805 and 0.755 for 28-, 90-, 180-days mortality in training and validation sets, respectively).
Conclusion: There is the high-risk group even in patients with NSALD, and a new model will help identify them. For these patients, steroid administration can be considered with close monitoring for the need for liver transplantation.

[PP-0345]

Blood concentrations of lead, cadmium, and mercury are associated with alcohol-related liver disease

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Objectives: The objectives of this study were to examine the association of the pollutants with ALD, and whether the pollutants together increased the risk of ALD.
Materials and Methods: Data were extracted from the Korea National Health and Nutrition Examination Survey (2010–2013 and 2016–2017; n = 11,993). Blood levels of lead, cadmium, and mercury were measured. ALD was defined by a combination of excessive alcohol consumption and ALD/ non-alcoholic fatty liver disease index > 0. The aspartate aminotransferase-to-platelet ratio index and fibrosis-4 score were used to evaluate ALD fibrosis.
Results: The odds ratios (ORs) of ALD for the highest versus the lowest quartiles of exposure were for lead, 7.39 (95% CI, 5.51–9.91); cadmium, 1.68 (95% CI, 1.32–2.14); and mercury, 5.03 (95% CI, 3.88–6.53). Adjusting for age, gender, smoking, occupation, education, and personal income attenuated the associations but indicated significant positive trends (all $P_{trend} < 0.001$). A positive additive interaction between cadmium and lead was observed. The relative excess OR due to the interaction was 0.96 (95% CI 0.41–1.51); synergy index = 2.92 (95% CI, 0.97–8.80). Among 951 subjects with ALD, advanced fibrosis was associated with lead and cadmium (OR = 3.46, 95% CI, 1.84–6.53; OR = 8.50, 95% CI, 2.54–28.42, respectively), but not with mercury. The effect estimates for lead and cadmium remained significant even after adjustment for daily alcohol intake.
Conclusion: Blood levels of lead, cadmium, and mercury were significantly associated not only with the risk of ALD but also with ALD fibrosis. Cadmium and lead have synergistic effects that increase the risk of ALD.

[OP-0357]

Etiology and clinical characteristics of chronic liver disease patients visiting emergency of Tribhuvan University Teaching Hospital, Nepal

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Objectives: to elucidate the etiology and clinical characteristics of CLD patients visiting emergency of Tribhuvan university teaching hospital.
Materials and Methods: From August 2017 to January 2018, patients with diagnosed with CLD were included. Patients underwent physical examination, hematological and biochemical tests and abdominal sonography and upper gastrointestinal endoscopy. Child Pugh's Score was calculated using above parameters and grading of esophageal varices was done. Data were analyzed and presented as frequency and percentage.
Results: A total of 75 patients with chronic liver disease admitted in emergency and medical wards of TUTH were studied. The mean age of CLD patient was 48 $\pm$ 9.66 years. CLD was seen maximum in age group 41- 50 years. Alcoholic liver disease was the major cause for chronic liver disease followed by chronic viral hepatitis B, Hepatitis C, Nonalcoholic steatohepatitis (NASH). 8 (10%) had Child Pugh's Class A, 22 (34%) had class B and 45 (56%) belonged to class C. 18 patients (33.3%) had small varices while 36 patients (66.6%) had large varices. A statistically significant positive correlation (p-value.
Conclusion: Alcohol is the major cause of CLD presenting to Emergency. Large varices were evident in most of the CLD patients.

[PP-0415]

Carbohydrate-deficient transferrin is a sensitive biomarker for detecting both light- and heavy-drinking

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Objectives: Although nonalcoholic fatty liver disease (NAFLD) and alcohol-associated/related liver disease (ALD) are increasing worldwide, it is often difficult to distinguish the two diseases with very similar phenotypes. Especially, it is important to correctly evaluate alcohol consumption to take appropriate therapeutic intervention. Therefore, we evaluated the ratio of carbohydrate-deficient transferrin

to total transferrin (%CDT) in patients with fatty liver disease, focusing on the correlation with metabolic factors.
Materials and Methods: In total, 120 patients with fatty liver disease including with ALD and NAFLD were screened for alcohol misuse using the Alcohol Use Disorders Identification Test. The associations of metabolic factors and hepatic steatosis/liver stiffness with drinking markers including %CDT, gamma-glutamyl transferase (GGT), and mean corpuscular volume (MCV) were assessed using multiple linear regression analyses.
Results: The %CDT increased significantly with 3–4 drinks/day. The optimal cut-off value for identifying non-to-light drinkers was 1.78% (sensitivity, 71.8%; specificity, 83.7%; AUROC, 0.851), and for identifying heavy drinkers was 2.08% (sensitivity, 65.5%; specificity, 86.8%; AUROC, 0.815), which was significantly higher than that for GGT. Multiple regression analysis revealed that this proportion was negatively correlated with body mass index, whereas GGT correlated higher liver stiffness and serum AST and TG levels, and MCV correlated with higher serum AST and HDL levels and lower serum LDL levels.
Conclusion: %CDT had a strong correlation with alcohol consumption independent of liver damage, steatosis/stiffness, or metabolic syndrome-related factors, indicating it is a useful drinking marker for accurate diagnosis of both NAFLD and ALD.

[PP-0436]

Prognosis factors associated with severe alcoholic hepatitis

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Objectives: Severe alcoholic hepatitis is defined as alcoholic hepatitis characterized by fever, hepatomegaly, decreased PT, jaundice, and leukocytosis. The prognosis for severe alcoholic hepatitis is poor. However, the prognostic factors are still unclear. The purpose of this study was to clarify the characteristics of poor prognosis among patients with severe alcoholic hepatitis seen at our department.
Materials and Methods: Twenty-five patients with severe alcoholic hepatitis (17 males and 8 females; mean age 47.6 years) who had been hospitalized between April 2010 and January 2020 were included.
Results: Twelve survived and 13 died (mortality rate 48%), and we compared the characteristics of the two groups. The outcome was also compared and examined in terms of age, PT%, T-bil, HGF, and Cre. There were no significant inter-group differences in terms of gender, age, psychiatric treatment history, and body temperature. In fatal cases, ALB was significantly lower and T-bil was higher. PT% tended to be low, Cre tended to be high, and WBC tended to be high, but the differences were not significant. HGF also tended to be high in the fatal cases, and the JAS score was significantly higher. Multivariate analysis of factors in the two groups showed that only T-bil was significant. Patients with high T-bil had a significantly lower survival rate than those with low T-bil. In the fatal cases, T-bil was high and Alb was low, which seemed to be related to nutritional status as well as liver damage. The JAS score was prognostically more useful than the MELD score or HGF.
Conclusion: In patients with severe alcoholic hepatitis, malnutrition and jaundice are predictors of poor outcome, and early multidisciplinary treatment including steroids and plasma exchange is indicated.

[PP-0746]

Lactobacillus and bifidobacterium probiotic mixture regulates alcohol and acetaldehyde metabolism in human

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Objectives: Alcohol-associated liver disease is one of the leading causes of liver related mortality and morbidity worldwide. Alcohol is oxidized to toxic and carcinogenic acetaldehyde by alcohol dehydrogenase (ADH) and further oxidized to a non-toxic acetate by aldehyde dehydrogenase (ALDH). There are two major ALDH isoforms, cytosolic and mitochondrial, encoded by ALDH1 and ALDH2 genes, respectively. Emerging evidence shows that Lactobacillus and Bifidobacterium species encode alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH) mediate alcohol and acetaldehyde metabolism, respectively.
Materials and Methods: A randomized, double-blind, placebo-controlled crossover clinical trial was designed to study the effects of Lactobacillus and Bifidobacterium probiotic mixture in humans and assessed their effects on alcohol and acetaldehyde metabolism.
Results: Twenty-seven wild types (ALDH2*1/*1) and the same number of heterozygotes (ALDH2*2/*1) were recruited for the study. The enrolled participants were randomly divided into either the probiotic or the placebo group. Each group received a probiotic or placebo capsule for 15 days with subsequent crossover. Primary outcomes were measurement of alcohol and acetaldehyde in the blood after the alcohol intake. Blood levels of alcohol and acetaldehyde were significantly downregulated by probiotic supplementation in subjects with ALDH2*2/*1 genotype, but not in those with ALDH2*1/*1 genotype. However, there were no marked improvements in hangover score parameters between test and placebo groups. No clinically significant changes were observed in safety parameters.
Conclusion: These results suggest that Lactobacillus and Bifidobacterium probiotic mixture has a potential to downregulate the alcohol and acetaldehyde concentrations, and their effects depend on the presence or absence of polymorphism on the ALDH2 gene.

[OP-0810]

The safety and effectiveness of Agrimonia eupatoria (Agrimony) extract in alcoholic liver disease: A clinical pilot study

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Objectives: Agrimonia eupatoria (Agrimony) extract has been used as a traditional medicine for the treatment of inflammatory diseases such as hemorrhagic colitis, urinary disease, and liver disease. This

study examined the safety of Agrimony extract in healthy persons and the hepatoprotective effects against alcohol-induced liver injury in alcoholic liver disease (ALD) patients.
Materials and Methods: To confirm the safety and effectiveness of the drug, the healthy group (300 mg/day) with normal liver function, the patient group diagnosed with ALD, and the patient group were divided into low-dose group (50 mg/day) and high-dose group (100 mg/day), respectively, and enrolled sequentially.
Results: A total of 6 healthy persons were administered 300 mg per day for 4 weeks. There was no person who showed adverse reactions or fatal serious adverse reactions among all the drug users. 12 patients in low dose group were treated with 50 mg per day for 4 weeks. The primary efficacy variable, AST ALT, showed a slight decrease, but it was not statistically significant (p = n.s). 11 patients in high dose group were treated with 100 mg per day for 4 weeks. The primary efficacy variable, AST ALT, showed median values ??of 86.0 IU/L (range, 57–362) and 66.0 IU/L (range, 42–116) before administration, respectively. AST 37 IU/L (range, 24–72) and ALT 31 IU/L (range, 11–59) at 2 weeks of dosing, respectively, and AST 37 IU/L (range, 25–198) at 4 weeks of dosing, respectively, ALT was 32.5 IU/L (range, 18–79). ALT was more decreased compared to AST, which was statistically significant. (p = 0.003).
Conclusion: The clinical results of agrimony extract in healthy group to verify the safety of agrimony did not show any particular side effects. Therefore, it was found that up to 300 mg can be used in clinical practice. The administration of 100 mg of Agrimony showed improvement in liver function at the 2 weeks of treatment, and it was found that the effect was maintained until the 4 weeks.

[PP-0860]

Male patients with severe alcoholic hepatitis and sarcopenia have poor prognosis

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Objectives: Sarcopenia is known as independent prognostic factor in cirrhotic patients. However, the effect of sarcopenia in patients with severe alcoholic hepatitis (SAH) has not been studied.
Materials and Methods: We included 107 patients with SAH (modified discriminant function $\geq$ 32). The total cross sectional area of skeletal muscle mass at 3rd lumbar level was measured on abdominal computed tomography, and skeletal muscle index (SMI), which was normalized to squared height, was calculated (cm^2/m^2). We used the SMI cutoff of the Japanese Society of Hepatology guideline to determine the sarcopenia (42 cm^2/m^2 for men and 38 cm^2/m^2 for women).
Results: Fifty-six patients (52.3%) had sarcopenia. Mean age was 49.6 $\pm$ 9.7 years, and 81 patients (75.7%) were male. Sarcopenia patients tended to have lower 180-day transplant-free survival than non-sarcopenic patients (P = 0.057). If analyzing by gender, sarcopenic patients had significantly lower 180-day transplant-free survival rate than non-sarcopenic patients in male (P = 0.014), but not significant in female (P = 0.849). In patients with MELD $\geq$ 24, sarcopenic patients had significantly lower survival rate (P = 0.029), but not in patients with MELD < 24 (P = 0.701).In male patients, L3-SMI showed significant negative correlation with MELD score (r = − 0.398, P < 0.001), but no significant correlation in female patients (r = 0.024, P = 0.909). In male patients, univariate analysis by Cox proportional hazard model showed that hepatic encephalopathy grade 3–4 (Hazard ratio (HR) 6.808, P < 0.001), creatinine $\geq$ 1.1 mg/dL (HR 3.995, P < 0.001), international normalized ratio $\geq$ 1.7 (HR 3.046, P = 0.009), Na $\geq$ 130 mEq/L (HR 0.397, P = 0.02), C-reactive protein $\geq$ 4.0 mg/dL (HR 4.860, P < 0.001), and sarcoepnia (HR 2.639, P = 0.019) were significant factors for 180-day transplant-free survival. However, multivariate analysis showed that sarcopenia was not significant prognostic factor.
Conclusion: SAH patients with sarcopenia had lower survival rate than patients without sarcopenia in male patients or patients with MELD $\geq$ 24. However, sarcopenia was not independent prognostic factor for 6-month transplant survival.

[OP-1046]

Effect of alcoholic hepatitis on gut microbiome: Novel findings

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Objectives: To decipher the interaction between the gut and diseased liver of AH using a metagenomics sequencing platform. Severe Alcoholic Hepatitis (AH) has high mortality and its optimal treatment remains elusive. Recent trials have targeted gut microbiome of these patients to mitigate liver inflammation with a premise that gut dysbiosis may have a significant modulatory effect on hepatic function via the gut-liver axis. However, baseline gut microbiota of patients of AH has not been adequately studied. The findings may lead us to identify the bacterial signature of liver damage in patients with severe AH which can be specifically targeted for treatment.
Materials and Methods: 16 s rDNA sequencing of bacterial DNA isolated from fecal samples [n = 18; AH (n = 12) and normal individuals (n = 6)], targeting V1–V9 region was analyzed. Annotation was analyzed on Ion-Reporter™, QIIME algorithms, MG-RAST, DESeq to identify the microbiome composition [data matched with MicroSEQ™ and Greengenes database] and taxonomic variations using reference-based Human Microbiome Project-National Centre for Biotechnology Information (HMP-NCBI) species.
Results: The mean age of AH patients was 35 (range 28–40) years, and all were males. Our data revealed lower richness and higher evenness at species level among AH than healthy controls (fig-1, 2) with a significant abundance of potential pathogens: Klebsiella pneumoniae, Klebsiella variicola, Parabacteroides distasonis, Bacteroides finegoldii, Veillonella dispar, and Bacteroides thetaiotaomicron. Among these, Bacteroides finegoldii and Veillonella dispar were earlier not reported in AH and hence a unique finding. Among phyla, Protobacteria was significantly abundant in AH which corroborates with literature.
Conclusion: Veillonella dispar alters the biosynthesis of amino acids as well the metabolism of lipopolysaccharides. On the other hand, Bacteroides finegoldii plays a major role in antibiotic-resistant. Thus, significant increased expression of these two bacteria in fecal samples of alcoholic hepatitis patients reflects a probable mechanistic pathway to predict disease progression. Our findings point towards developing gut microbiome targeted therapies as promising strategies.

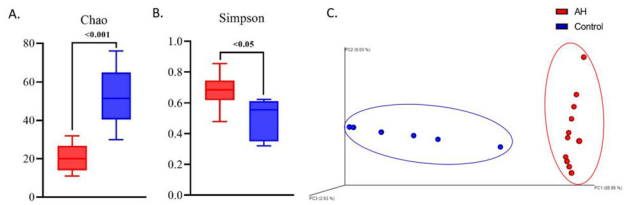

FIGURE 1. Box plot representing species-level microbial diversity in AH and Control. Diversity indices measured the alpha diversity, including the Chao (A) and Simpson index (B). * P < 0.05 (Mann-Whitney U Test). (C) β diversity Principal-coordinate analysis (PCoA), Euclidean plot at the species level of AH and control, describe similarities and dissimilarities between samples.

[OP-1048]

A correlative study of liver pathology with pancreatic pathology in alcoholics in Northern Indian population

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Objectives: To evaluate the type and severity of the liver disease with the co-existing pancreatic pathology in chronic alcoholics.
Materials and Methods: The study was carried in 390 documented chronic alcoholics who died with complications of chronic liver disease. Both the liver and pancreas were analysed by documenting the features observed both on gross and microscopic examinations. Clinical and laboratory parameters were also recorded.
Results: All the patients enrolled in the study were males and the age ranged from 22 to 65 years (mean = 45.32 years). Majority of the patients primarily had clinical features of compensated chronic liver disease at presentation and very few presented with acute abdomen due to pancreatitis. Gross examinations of liver showed 292 with micronodular cirrhosis and chronic pancreatitis in 42 cases, 8 with acute hemorrhagic pancreatitis. Chronic pancreatitis per se was frequently associated with cirrhotics and acute pancreatitis was mostly seen in non-cirrhotics.
Conclusion: The findings of frequent association between cirrhotics with chronic pancreatitis suggests a possibility common underlying pathobiology in the development of fibrosis in both the organs.

[L-PP-1276]

Effectiveness of nurse-led family intervention on stress, engagement with patient care and satisfaction among primary caregivers of chronic liver disease patients admitted in high dependency unit of I

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Objectives: To assess the effectiveness of Nurse-led Family Intervention on Stress, Engagement with patient care and Satisfaction among Primary Caregivers of Chronic Liver Disease patients admitted in High Dependency Unit of ILBS, New Delhi. To find the association of Stress with selected demographic variables among Primary Caregivers of chronic liver disease patients admitted in HDU after nurse-led family intervention in experimental group To find the association of Engagement with patient care with selected demographic variables among Primary Caregivers of chronic liver disease patients admitted in HDU in experimental group To find the association of Satisfaction with selected demographic variables among Primary Caregivers of chronic liver disease patients admitted in HDU in experimental group.
Materials and Methods: RESERCH APPROACH-Quantitative research approach RESERCH DESIGN–Quasi experimental research design (Two group pre –test and post- test design) SAMPLE SIZE – 80.
Results: Majority of the Primary Caregivers were children (25.7%) in the Experimental Group and majority were children (38%) in Camparison group.In the Experimental Group the pre-test Mean stress score was 40.94 and post-test stress score was 16.64 and pre-test of caregiver awareness was 23.86 and in the post -test 94.82 and pre-test score of Caregiver Health Engagement was 10.73 and post-test score was 25.09, whereas in the camparison group the mean pre-test stress score was 40.73 and post-test was 40.28 and mean pre-test score of caregiver awareness was 23.65 and post -test was 24.12 and mean pre-test score of Caregiver Health Engagement was 10.71 and post-test was 10.68. In the Experimental group it was found that the mean Satisfaction of the primary caregivers was 73.67 i.e. Highly Satisfied.
Conclusion: Nurse-led Family intervention was Effective in reducing the Stress of the Primary Caregivers and improving the caregiver awareness and Caregiver Health Engagement and also Nurse-led Family intervention increases the satisfaction among the parimary caregivers.

[L-OP-1316]

Management of patients with decompensated liver cirrhosis: an audit against BSG-BASL care bundle at Princess Royal University Hospital, London

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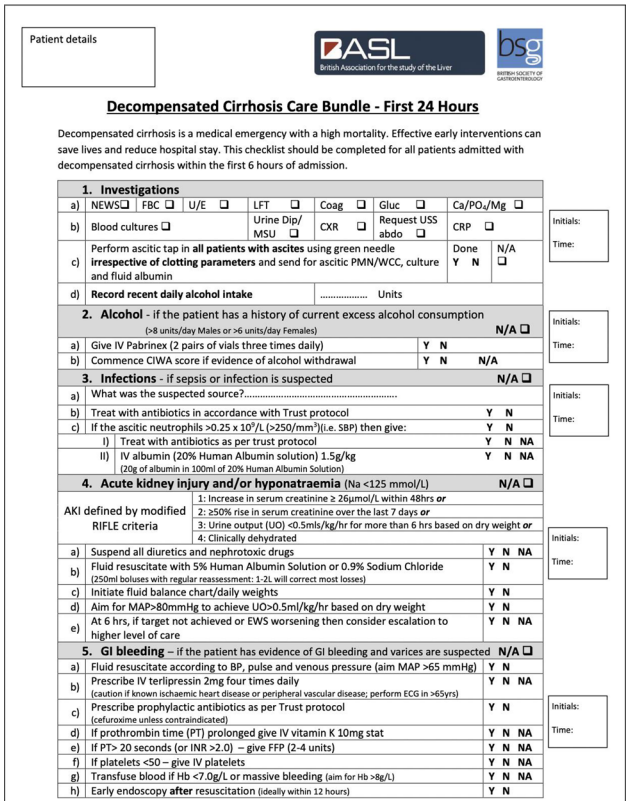
Objectives: The prevalence of chronic liver cirrhosis is rising worldwide; decompensated liver cirrhosis (DLC) is associated with significant inpatient mortality (10–20%). The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report in 2013 revealed that only 47% of patients who died from alcohol related liver disease (ARLD) received 'good care'. Consequently, the British Society of Gastroenterology and British Association for the Study of the Liver (BSG-BASL) have formulated the 'Decompensated Cirrhosis Care Bundle' for the management of patients presenting with DLC. This study aims to audit the current practice of Princess Royal University Hospital (PRUH) against the 'BSG-BASL care bundle' checklist (Fig. 1) and develop recommendations for improvement.
Materials and Methods: A retrospective audit was performed between March 2021 to October 2021 using data collected from electronic patient records (EPR). Data pertaining to the management of DLC were subsequently plotted against the BSG-BASL care bundle; analysis was conducted with R studio and Microsoft Excel.
Results: Of the 457 admissions presenting to PRUH with gastroenterological symptoms during this period, 100 were identified with DLC. The mean sample age was 57.2, with male patients (n = 71) more than females (n = 29). The average length of stay was 11.3 days and 8 patients died (8% mortality rate). Most initial investigations in the BSG-BASL bundle were completed well; chest X-ray (63%), bone profile (56%), blood cultures (43%) and urine dip (33%) had the poorest completion rate. Abdominal ultrasounds were frequently

requested late. Gastrointestinal bleeding was the main presenting complaint (36%); forty-four percent had endoscopy performed within twelve hours.

Conclusion: This study highlighted several potential areas of improvement in decompensated cirrhosis care. Greater awareness of the BSG-BASL bundle could be achieved via integration with EPR and creation of an e-learning module for new doctors.



Patient details

BASL British Association for the study of the Liver

bsg BRITISH SOCIETY OF GASTROENTEROLOGY

Decompensated Cirrhosis Care Bundle - First 24 Hours

Decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. This checklist should be completed for all patients admitted with decompensated cirrhosis within the first 6 hours of admission.

1. Investigations								
a)	NEWS❑ FBC ❑ U/E ❑		LFT ❑	Coag ❑	Gluc ❑	$Ca/PO_4/Mg$ ❑		Initials: Time:
b)	Blood cultures ❑		Urine Dip/ MSU ❑	CXR ❑	Request USS abdo ❑	CRP ❑		
c)	Perform ascitic tap in **all patients with ascites** using green needle **irrespective of clotting parameters** and send for ascitic PMN/WCC, culture and fluid albumin					Done Y N	N/A ❑	
d)	**Record recent daily alcohol intake**			..... Units				
2. Alcohol - if the patient has a history of current excess alcohol consumption (>8 units/day Males or >6 units/day Females)							N/A ❑	Initials: Time:
a)	Give IV Pabrinex (2 pairs of vials three times daily)					Y N		
b)	Commence CIWA score if evidence of alcohol withdrawal					Y N	N/A	
3. Infections - if sepsis or infection is suspected							N/A ❑	
a)	What was the suspected source?.....							Initials: Time:
b)	Treat with antibiotics in accordance with Trust protocol					Y N		
c)	If the ascitic neutrophils >0.25 x 10^9/L (>250/mm^3)(i.e. SBP) then give:					Y N		
I)	Treat with antibiotics as per trust protocol					Y N	NA	
II)	IV albumin (20% Human Albumin solution) 1.5g/kg (20g of albumin in 100ml of 20% Human Albumin Solution)					Y N	NA	
4. Acute kidney injury and/or hyponatraemia (Na <125 mmol/L)							N/A ❑	
AKI defined by modified RIFLE criteria	1: Increase in serum creatinine ≥ 26μmol/L within 48hrs *or*							
	2: ≥50% rise in serum creatinine over the last 7 days *or*							
	3: Urine output (UO) <0.5mls/kg/hr for more than 6 hrs based on dry weight *or*							Initials: Time:
	4: Clinically dehydrated							
a)	Suspend all diuretics and nephrotoxic drugs					Y N	NA	
b)	Fluid resuscitate with 5% Human Albumin Solution or 0.9% Sodium Chloride (250ml boluses with regular reassessment: 1-2L will correct most losses)					Y N		
c)	Initiate fluid balance chart/daily weights					Y N		
d)	Aim for MAP>80mmHg to achieve UO>0.5ml/kg/hr based on dry weight					Y N		
e)	At 6 hrs, if target not achieved or EWS worsening then consider escalation to higher level of care					Y N	NA	
5. GI bleeding – if the patient has evidence of GI bleeding and varices are suspected							N/A ❑	
a)	Fluid resuscitate according to BP, pulse and venous pressure (aim MAP >65 mmHg)					Y N		
b)	Prescribe IV terlipressin 2mg four times daily (caution if known ischaemic heart disease or peripheral vascular disease; perform ECG in >65yrs)					Y N	NA	
c)	Prescribe prophylactic antibiotics as per Trust protocol (cefuroxime unless contraindicated)					Y N		Initials: Time:
d)	If prothrombin time (PT) prolonged give IV vitamin K 10mg stat					Y N	NA	
e)	If PT> 20 seconds (or INR >2.0) – give FFP (2-4 units)					Y N	NA	
f)	If platelets <50 – give IV platelets					Y N	NA	
g)	Transfuse blood if Hb <7.0g/L or massive bleeding (aim for Hb >8g/L)					Y N	NA	
h)	Early endoscopy **after** resuscitation (ideally within 12 hours)					Y N		

Autoimmune and Cholestatic Disease

[OP-0158]

Clinical outcomes and validation of GLOBE, UK-PBC and UDCA response score in Korean patients with PBC

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Objectives: We evaluated clinical outcomes of primary biliary cholangitis (PBC) and validated GLOBE, UK-PBC scores, and ursodeoxycholic acid (UDCA) Response Score (URS) in Korea.

Materials and Methods: This is a retrospective cohort study performed at a tertiary medical center in Korea. We included a total of 123 patients who met the diagnostic criteria of PBC between 2007 and 2016, and started UDCA treatment. The primary outcome was liver-related events, defined as newly developed hepatic decompensation (variceal bleeding, ascites, or hepatic encephalopathy) or hepatocellular carcinoma. UDCA response was defined by normalization of alkaline phosphatase levels < 1.67 of the upper limit of normal after one year of UDCA treatment. The prognostic performance of URS, GLOBE, and UK-PBC scores was evaluated.

Results: During a median follow-up of 6.6 years (range 1.0 – 13.2 years), liver-related events were developed in 11 patients (8.9%). The area under the receiver operating characteristic curve (AUROC) of URS for prediction of UDCA treatment response was 0.87 (95% confidence interval (CI): 0.81 – 0.93). The GLOBE and UK-PBC scores showed good prognostic performance (AUROC, 0.85; 95% CI: 0.72–0.95 vs. 0.84; 95% CI: 0.66–0.96) for liver-related events, while the URS did not (AUROC, 0.58; 95% CI: 0.39 – 0.7). Baseline histological information was available for 89 patients. When patients were stratified according to histological PBC stage, the 5-years cumulative incidence rate of liver-related events was 50% for PBC stage 4 (n = 6), and was 0–4.5% for PBC stage 1–3 (n = 83). Among PBC stage 1–3, the 5-years cumulative incidence rate of liver-related events differed by URS; 0% for URS ≥ 1.04 and 10.2% for URS < 1.04 ($p = 0.034$).

Conclusion: URS showed good performance in predicting the UDCA response in Korean PBC patients, and was able to stratify clinical outcomes for non-cirrhotic PBC patients. URS can be an early biomarker for UDCA response and clinical outcomes for non-cirrhotic patients.

[PP-0271]

Factors predictive of treatment response and survival in filipino patients with autoimmune hepatitis

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Objectives: There is a dearth of data on Filipino patients with autoimmune hepatitis (AIH). We aimed to describe the demographic and clinical profiles of patients with AIH, and to characterize clinical outcomes and treatment responses.

Materials and Methods: A retrospective study involving patients from two tertiary centers diagnosed with AIH from January 1, 2007 to December 31, 2019 were included. Disease remission was defined as normalization of ALT levels while failure was defined as increase in ALT levels over baseline or clinical deterioration.

Results: A total of 48 patients were identified between 2007 to 2019. The median age at presentation was 51 (27–79 yrs.). Liver cirrhosis was already present in 37.5% (27.1% decompensated) on diagnosis. Aside from a higher histologic activity index in females ($p = 0.047$), there were no gender-specific differences. Disease remission was achieved in 88.9% of patients at 6 months while only 5.6% failed. However, at final disposition, remission rates have gone down to 58% and failure rates risen up to 12%. Treatment responses at both 6 and 12 months, along with MELD and Chip-Pugh class, influenced treatment responses at final disposition. Median overall survival was 102 weeks and was influenced by the presence of liver dysfunction and 12 months and final treatment responses.

Conclusion: Autoimmune hepatitis remain an important cause of morbidity and mortality. The results of the study highlight the need for immunosuppressive therapy to induce early remission for a higher likelihood of subsequent biochemical remission in order to reduce the risk of liver-related mortality.

Table 1. Baseline Characteristics of Patients with Autoimmune Hepatitis.

	Male n=10 (20.8%)	Female n=38 (79.2%)	Total n=48	p-value
Age	54.5 (31-79)	49.5 (27-74)	51 (27-79)	0.576
Clinical presentation				0.537
Elevated transaminases	3 (30%)	8 (21.1%)	11 (22.9%)	
Jaundice, without cirrhosis	5 (50%)	14 (36.8%)	19 (40%)	
Compensated cirrhosis	0	5 (13.2%)	5 (10.4%)	
Decompensated cirrhosis	2 (20%)	11 (29%)	13 (27.1%)	
Overlap syndrome				0.858
AIH only	9(90%)	34 (89.5%)	43 (89.6)	
AIH/PBC	1 (10%)	3 (7.9%)	4 (8.3%)	
AIH/PSC	0	1 (2.6%)	1 (2.1%)	
Child-Pugh Class (A/B/C)	4/5/1	12/19/4	16/24/5	0.945
MELD Score	12.8 (7.3-19.3)	9.1 (6-22.7)	9.97 (6-22.7)	0.223
ANA positive	7 (70%)	30 (78.9%)	37 (77.1%)	0.549
SMA positive (n=43)	5 (55.6%)	15 (44.1%)	20 (46.5%)	0.541
ANA/SMA status				0.997
Both positive	3 (30%)	11 (28.9%)	14 (29.2%)	
Either positive	6 (60%)	23 (60.5%)	29 (60.4%)	
Both negative	1 (10%)	4 (10.5%)	5 (10.4%)	
HAI total score (n=30)	12 (6-12)	13.5 (3-17)	13 (3-17)	0.047
Platelet (n=41)	199.5 (100-423)	200 (54-457)	200 (54-457)	0.800
AST	357.5 (60-901)	127.7(32-1313)	138.5(32-1313)	0.243
ALT	398 (30-1037)	96 (22.2-1968)	122.5 (22.2-1968)	0.374
ALP (n=45)	152 (109-1113)	180 (23-860)	177.8 (23-1113)	0.733
Albumin (n=35)	3.6 (2.7-4.5)	4.5 (0.9-6.5)	4.5 (0.9-0.65)	0.351
Globulin (n=35)	4.8 (2.7-5.7)	4.5 (0.9-6.5)	4.5 (0.9-6.5)	0.670
Creatinine (n=38)	0.85 (0.3-2.4)	0.69 (0.2-2.7)	0.7 (0.2-2.7)	0.222
Total bilirubin (n=35)	4.4 (1-12.1)	2.6 (0.16-26.2)	2.7 (0.16-26.2)	0.666
INR (n=26)	1.1 (0.72-1.3)	1.1 (0.85-2.2)	1.09 (0.72-2.2)	0.525

Legend: ANA Anti-nuclear antibody, AMA Anti-mitochondrial antibody, Anti-LKM1 Antibody to liver/kidney microsome type 1, FIB4 Fibrosis-4 score, PBC Primary Biliary Cholangitis, PSC Primary Sclerosing Cholangitis, - data not available

[PP-0281]

Comparison of efficacy and outcome of ursodeoxycholic acid and *S*-adenosylmethionine in patients with intrahepatic cholestasis of pregnancy: A systematic review and meta-analysis

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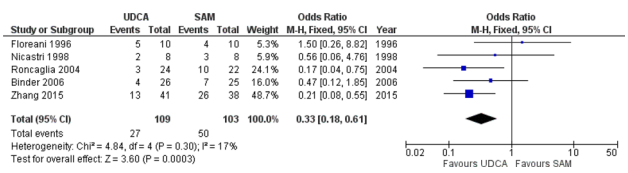
Objectives: Intrahepatic cholestasis of pregnancy (ICP) is associated with adverse maternal and fetal outcomes. However, an optimal therapeutic strategy has not been defined. This study aims to compare the efficacy and maternal and fetal outcome of ursodeoxycholic acid (UDCA) and S-adenosylmethionine (SAM) in patients with ICP.
Materials and Methods: MEDLINE, Science Direct and Cochrane Central Register of Controlled Trials were searched from 1990 to August 2021 for randomized controlled trials (RCTs) comparing the efficacy and outcome of SAM and UDCA in patients with ICP. The Risk ratios (RR) and standardized mean difference (SMD) were calculated by combining the data from the identified studies using a random effects model.
Results: A total of 5 RCTs (n = 311) were eligible for inclusion in the analysis. Incidence of preterm delivery was lower with UDCA compared to SAM (RR 0.33, 95%CI 0.18 – 0.61) without any significant heterogeneity [$\chi^2 = 4.84$, df = 4 (p = 0.30); $I^2 = 17\%$] (Fig. 1). However, there were no difference between UDCA and SAM with respect to improvement in pruritus [RR 1.72, 95%CI 0.91 – 3.23; $\chi^2 = 0.20$, df = 2(p = 0.04); $I^2 = 68\%$], rate of lower segment cesarian section (LSCS) [RR 0.86, 95%CI 0.65 – 1.13; $\chi^2 = 0.31$, df = 3(p = 0.96); $I^2 = 0\%$], rate of meconium-stained amniotic fluid [RR 0.77, 95%CI 0.40 – 1.46; $\chi^2 = 2.02$, df = 2(p = 0.36); $I^2 = 1\%$] and neonatal intensive care unit (NICU) admission [RR 0.56, 95%CI 0.26 – 1.20; $\chi^2 = 0.54$, df = 2(p = 0.76); $I^2 = 0\%$]. UDCA was found to be superior to SAM with respect to the reduction in total bile acid level (TBA) [SMD − 0.52, 95%CI − 0.81, − 0.23; $\chi^2 = 5.61$, df = 3(p = 0.13); $I^2 = 47\%$]. There was no evidence of publication bias on funnel plot.
Conclusion: UDCA is more efficacious than SAM for reduction of TBA level and rate of preterm deliveries but has no advantage over SAM for reduction of rate of LSCS, meconium-stained amniotic fluid and NICU admission.



[PP-0328]

ERRγ suppression by Sirt6 alleviates cholestatic liver injury and fibrosis

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Objectives: Orphan nuclear receptor estrogen-related receptor γ(ERRγ) stimulates bile acid production; however, the role and the regulatory mechanism of ERRγ in cholestatic liver disease are largely unknown.
Materials and Methods: This study identifies that Sirt6 is a deacetylase of ERRγ and suggests a potentially novel mechanism by which Sirt6 activation alleviates cholestatic liver damage and fibrosis through regulating ERRγ. We observed that hepatic expression of Sirt6 is repressed, whereas hepatic expression of ERRγ is upregulated in murine cholestasis models. Hepatocyte-specific Sirt6-KO mice were more severely injured after a bile duct ligation (BDL) than WT mice, and adenoviral reexpression of Sirt6 reversed liver damage and fibrosis as demonstrated by biochemical and histological analyses.
Results:. Mechanistically, Sirt6 deacetylated ERRγ, thereby destabilizing ERRγ and inhibiting its transcriptional activity. Elimination of hepatic ERRγ using Ad-shERRγ abolished the deleterious effects of Sirt6 deficiency, whereas ERRγ overexpression aggravated cholestatic liver injury. Administration of a Sirt6 deacetylase activator prevented BDL-induced liver damage and fibrosis. In patients with cholestasis, Sirt6 expression was decreased, whereas total ERRγ and acetylated ERRγ levels were increased, confirming negative regulation of ERRγ by Sirt6.
Conclusion: Sirt6 activation represents a potentially novel therapeutic strategy for treating cholestatic liver injury.

[PP-0433]

Association between NUDT15 polymorphism and thiopurine-induced leukopenia in patients with autoimmune hepatitis

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Objectives: Nudix hydrolase 15 (NUDT15) polymorphism affects to the level of thioguanine nucleotides (TGNs) that are active form of azathioprine (AZA) and major toxic material to bone marrow. Poor or intermediate metabolizer of NUDT15 polymorphism is associated with increased level of TGNs and AZA induced leukopenia. The present study aimed to investigate the incidence of NUDT15 polymorphism and whether the polymorphism is associated with AZA induced leukopenia in Korean patients with autoimmune hepatitis (AIH).
Materials and Methods: Ninety nine patients were diagnosed as AIH from March 2009 to January 2021 in Gachon University Gil Hospital, Incheon, Korea. AIH was confirmed by the criteria based on the publication of international AIH group. A total of 30 patients with NUDT15/thiopurine S-methyltransferase (TPMT) genotyping and AZA treatment were retrospectively enrolled. The genotypes of NUDT15 and TPMT, and the association of each genotypes with leukopenia (WBC count < 3,000/μl) were investigated.
Results: The median age at diagnosis of AIH was 59 (37–89) years. The ratio of female to male was 26 to 4. The genotypes of NUDT15 were wild (1*/1*, 73.3%), 1*/3*(5, 16.7%), 1*/2*(2, 6.7%), and 1*/5*(1, 3.3%). The NUDT15 genotypes of intermediate metabolizer were 1*/3* and 1*/2*. There was no poor metabolizer of NUDT15. Only 1 of 7 intermediate metabolizer showed leukopenia during AZA treatment. The genotypes of TPMT were wild (1*/1*, 93.4%), 1*/6*(1, 3.3%), and 1*/38*(1, 3.3%). There was no intermediate and poor metabolizer of TPMT. There were 4 patients who showed leukopenia during AZA treatment. Among them, only 1 patient had NUDT15 genotype of 1*/3* and stop AZA. The other 3 patients had wild type of NUDT15/TPMT and continued AZA without complication.
Conclusion: NUDT15 polymorphism was observed in 27% of patients. Most of intermediate metabolizer of NUDT15 did not induce leukopenia. Genotyping of NUDT15 is needed in case of leukopenia during AZA treatment.

[PP-0506]

CD4 + T cells in primary sclerosing cholangitis exhibit a disease-specific gene expression profile

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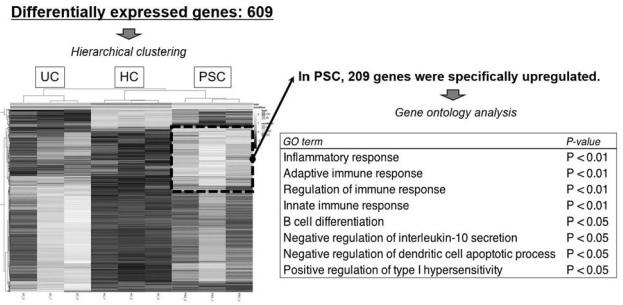
Objectives: Primary sclerosing cholangitis (PSC) is an intractable disease that has no effective treatment. The pathogenesis of PSC is thought to involve abnormal CD4 + T cell function. However, the details of their gene expression dynamics and functions remain unclear. In this study, we will analyze the gene expression in CD4 + T cells of PSC to elucidate the pathogenesis of PSC and clarify the gene profiles and functions characteristic of PSC.
Materials and Methods: Gene expression profiles in CD4 + T cells from patients with PSC were compared to the profiles in patients with UC and healthy control using RNA sequencing. To clarify functions in differentially expressed genes (DEG) in PSC, Gene Ontology (GO) analysis was performed.
Results: Among 3 groups, 609 genes were expressed with significant difference ($P < 0.01$). Profiles of 609 DEGs were clearly grouped the PSC, UC, and HC groups by hierarchical clustering. In PSC, 204 genes were specifically upregulated compared to other groups. Then 204 upregulated genes were related to immunological function (e.g. "Inflammatory response" and "Adaptive immune response") by GO analysis ($P < 0.05$)(Fig. 1).
Conclusion: Patients with PSC showed unique gene expression profiles in their CD4 + T cells. These findings are related to the immune mechanism of PSC pathogenesis and may lead to the development of new diagnostic and immunosuppressive methods.

Fig 1. Gene expression profiles in CD4⁺ T cells among PSC, UC and HC.



GO term	P-value
Inflammatory response	P < 0.01
Adaptive immune response	P < 0.01
Regulation of immune response	P < 0.01
Innate immune response	P < 0.01
B cell differentiation	P < 0.05
Negative regulation of interleukin-10 secretion	P < 0.05
Negative regulation of dendritic cell apoptotic process	P < 0.05
Positive regulation of type I hypersensitivity	P < 0.05

[PP-0601]

GLIMMER: A randomized double-blind placebo-controlled study of linerixibat, an ileal bile acid transporter inhibitor, in the treatment of cholestatic pruritus in primary biliary cholangitis (PBC)

Jidong Jia[1], Cynthia Levy[2], Stuart Kendrick[3], Christopher Bowlus[4], Atsushi Tanaka[5], David Jones[6], Andreas E Kremer[7], Marlyn Mayo[8], Nazneen Haque[9], Grace Zhang[10], Megan M. Mclaughlin[11], Gideon M. Hirschfield[12]

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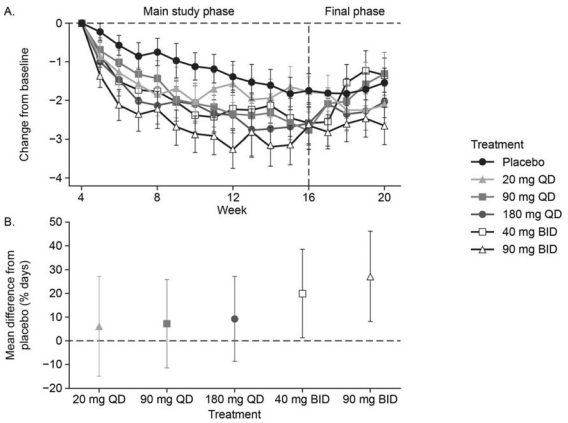
Objectives: To assess dose–response and tolerability of linerixibat in adults with cholestatic pruritus in PBC.
Materials and Methods: 147 patients were randomized to linerixibat (n = 111; 20 mg/90 mg/180 mg QD and 40 mg/90 mg BID) or placebo (n = 36) for 12 weeks, followed by single-blind placebo. Mean subject-graded worst daily itch NRS over 7 days pre-randomization/baseline were compared to the last 7 days of treatment (response: ≥ 2-point improvement).
Results: Linerixibat, particularly BID, provided rapid itch relief during treatment (Figure). Change from baseline in mean worst daily itch: 40 mg BID − 2.86 (95%CI − 3.76, − 1.95), 90 mg BID − 2.25 (− 3.19, − 1.32), with high placebo response (− 1.73 [− 2.44, − 1.01]). Itch reduction was significant (p = 0.037) with 40 mg BID vs placebo in subjects with baseline NRS ≥ 4. Percentage of itch responder days favored BID; mean increase vs placebo: 40 mg BID 20%; 90 mg BID 27% (Figure). During dosing, rapid dose–response in target engagement biomarkers was evident from Week 4 (LS mean change from baseline: 40 mg BID C4 55.39 ng/ml [95%CI 40.76,70.03], FGF19 − 73.03 pg/ml [− 121.98, − 24.07]; 90 mg BID C4 40.38 ng/ml [25.46,55.29], FGF19 − 53.60 pg/ml

[− 105.16, − 2.04]. All arms including placebo showed significant improvement in PBC-40 itch; 40 mg BID improved PBC-40 social (p = 0.0016) and emotional (p = 0.0025) domains. 10% of patients withdrew due to drug-related AEs. The only on-treatment drug-related AE in > 10% of patients was diarrhea.
Conclusion: 12 weeks linerixibat BID demonstrated rapid, significant itch improvement and improved quality-of-life with expected pharmacology. Targeting bile-acid reuptake may relieve cholestatic pruritus in PBC.
Funding: GSK (201000). Data previously presented at AASLD 2020 (Levy et al.; Presentation LP38); presented on behalf of original authors with permission.

Figure 1: Mean (+/-SE) for the observed weekly change from baseline in mean worst daily itch score (A) and mean difference (+/-SE) from placebo in percentage responder days in worst daily itch during 84 days treatment for each linerixibat dose (response defined as ≥2 point improvement in itch from baseline) (B); ITT population



BID, twice-daily; ITT, intention-to-treat; SE, standard error; QD, once-daily.

[PP-0602]

The pervasive impact of pruritus on quality of life (QOL) in patients with primary biliary cholangitis (PBC): Real world experience in TARGET-PBC

Jidong Jia[1], Elizabeth Carey[2], Helen Smith[3], Megan Mclaughlin[4], April Thompson[5], Andrea Mospan[6], Robert Sandefur[6], Richard C. Zink[6], W. Ray Kim[7], Cynthia Levy[8]

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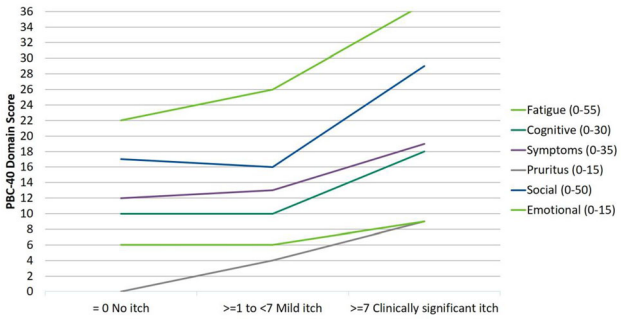
Objectives: To assess the impact of pruritus on QOL in TARGET-PBC, a longitudinal study of 667 US patients with PBC.
Materials and Methods: Participants completing ≥ 1 survey were included (n = 211). Median PBC-40 domain scores were compared between groups with clinically significant itch (CS-itch; ≥ 7 on PBC-40 itch domain), mild, or no itch, using Kruskal–Wallis tests.
Results: Median age 60 years; 92% female; 35% cirrhotic. 63 (30%) reported CS-itch, 107 (51%) mild-itch, 41 (19%) no-itch. Versus the no-itch group, the CS-itch group had more advanced PBC with more cirrhosis (37% vs 48%; p = 0.0277) and higher ALP (153 vs 177 IU/L; p = 0.0019). PBC-40 domain scores correlated with pruritus severity (Figure). The largest differences were cognitive and social domains: median scores were ~ 80% higher with CS-itch versus mild-itch; differences for fatigue, symptoms and emotional domains were smaller (42%, 46% and 50% higher, respectively). 5D itch correlated with PBC-40-defined severity (p < 0.0001). There were significant differences between the CS-itch and mild-itch group for duration, degree, disability and distribution scores (p < 0.0001). Median fatigue scores were 61 (CS-itch), 50 (mild-itch) and 50 (no-itch) (p < 0.0001 CS-itch vs mild-itch). Differences between groups remained significant in multivariable analysis when adjusting for covariates.
Conclusion: Presence and intensity of itch significantly impacts QOL; CS-itch patients fare worse than those with mild- or no-itch on fatigue, social, emotional, cognitive and other symptoms. Future interventions targeting pruritus may improve QOL.
Data previously presented at AASLD 2020; presented on behalf of original authors with permission from Wiley (Carey, et al. Hepatology 2020 72(S1):766A–7A. ©AASLD).

Figure: Median PBC-40 Domain Scores by Itch Severity



[PP-0604]

Improvement in itch correlates with improved sleep in GLIMMER, a Phase 2b trial of linerixibat for the treatment of cholestatic pruritus in primary biliary cholangitis (PBC)

Jidong Jia[1], David Jones[2], Robyn Von Maltzahn[3], Helen T. Smith[3], April Thompson[4], M. Celeste Ferreira-Cornwell[5], Megan M. Mclaughlin[6], Matthew Allinder[6], Nazneen Haque[3], Marlyn J. Mayo[7], Cynthia Levy[8]

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Corresponding author: Jidong Jia, Liver Research Center, Beijing Friendship Hospital, Beijing, China

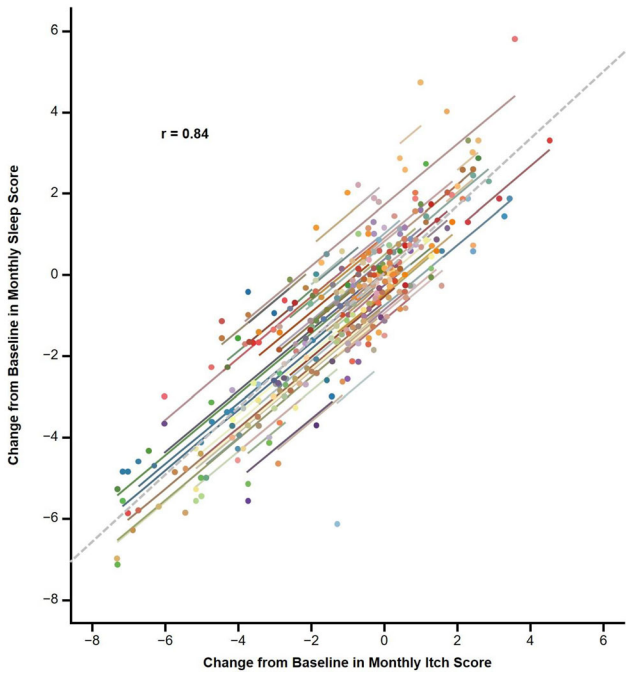
Objectives: To explore the relationship between itch severity and sleep interference in patients with PBC during the GLIMMER trial.
Materials and Methods: Patients recorded itch (twice daily) and degree of sleep interference from itch (each morning) on a 0–10 numeric rating scale. Worst daily itch and sleep interference scores were averaged over 1 week to generate weekly itch score (WIS) and weekly sleep score (WSS). Monthly itch/sleep scores (MIS/MSS) were the worst weekly score for a given month. Analyses included prespecified exploratory psychometric evaluations between WIS, WSS and other patient-reported outcomes (PROs). MIS and MSS analyses were post hoc.
Results: Analyses were conducted in the intent-to-treat population (n = 147); psychometric analyses were conducted in patients with

complete PRO data. Improvements in change in MIS and MSS from baseline were highly correlated ($r = 0.84$; $p < 0.0001$; Figure). Convergent validity analyses of WSS at baseline showed moderate correlations with the 5-D itch total ($r = 0.59$; $p < 0.0001$) and 5-D itch sleep item scores ($r = 0.58$; $p < 0.0001$).

Conclusion: Itch symptoms closely correlated with sleep interference, suggesting a possible close clinical relationship between itch and sleep; a significant correlation between 5-D itch total and WSS support this. In addition to improving the direct impact of the symptom of itch, an improvement in itch may have an impact on sleep. This is important, as sleep disturbance is common in patients with PBC and adds to disease burden.

Funding: GSK (201,000). Data previously presented at EASL 2021 (Jones et al.; Presentation 1748); presented on behalf of original authors with permission.

Figure. Bland–Altman repeated measures correlation of change from baseline using Months 1, 2 and 3 MSS and MIS, across all treatment groups (ITT population). r, correlation coefficient



[PP-0607]

Pruritus in primary biliary cholangitis (PBC) is under-treated in clinical practice: Results from TARGET-PBC

Jidong Jia[1], Marlyn J. Mayo[2], Andrea Mospan[3], Helen Smith[4], Megan Mclaughlin[5], April Thompson[6], Robert Sandefur[3], Richard C. Zink[3], Christopher Bowlus[7], Cynthia Levy[8]

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Objectives: To characterize the pruritus population and describe pruritis management in TARGET-PBC, a longitudinal study of US patients with PBC.

Materials and Methods: Participants completing ≥ 1 patient-reported outcome (n = 211) were included. Characteristics, disease severity and treatment patterns were compared between itch groups: clinically significant itch (CS-itch; ≥ 7 on PBC-40 itch domain), mild-itch, no-itch.

Results: Median age 60 years; 92% female; 35% cirrhotic. 63 (30%) reported CS-itch, 107 (51%) mild-itch, 41 (19%) no-itch (Table). CS-itch patients were younger (49 vs 52 [mild-itch] and 54 [no-itch] years; p = 0.04), had more frequent cirrhosis (48% vs 27% [mild-itch] and 36% [no-itch]; p = 0.03) and higher ALP. 97% were taking UDCA. More CS-itch patients were receiving itch treatment (51% vs 28% [mild-itch] or 27% [no-itch]); 33% with CS-itch never received itch treatment. More CS-itch patients were taking multiple PBC treatments (32% vs 22% [mild-itch] vs 22% [no-itch]) and taking fenofibrate (16% vs 1% [mild-itch] vs 5% [no-itch]). Currently treated mild-itch patients had mean 1.1 pruritus treatments; CS-itch had 1.3. The most common treatment in mild-itch was antihistamines (73%); CS-itch patients had a wider treatment range. 23% (mild-itch) and 25% (CS-itch) were taking bile acid binding resins. Mean (SD) time on-treatment was 8.0 (8.1) months in mild-itch, 6.0 (6.2) months in CS-itch.

Conclusion: Pruritus is under-treated in this real-world PBC population; many patients with CS-itch never receive treatment.

Data previously presented at AASLD 2020; presented on behalf of original authors with permission from Wiley (Mayo M, et al. Hepatology 2020;72(S1):758A–9A. ©AASLD).

Table: Patient characteristics and treatment

	Itch			P-value[1]
	No-itch	Mild-itch	CS-itch	
All participants, n (%)	41 (19)	107 (51)	63 (30)	
Female n (%)	38 (93)	97 (91)	59 (94)	0.8440
Age at diagnosis Median (IQR)	52 (17)	54 (14)	49 (17)	0.0398
Cirrhosis n (%)	15 (37)	29 (27)	30 (48)	0.0277
Decompensated[2]	5 (33)	7 (24)	18 (60)	0.0174
Most recent ALP Median (IQR)	153 (102)	143 (71)	177 (151)	0.0019
Current PBC treatment, n (%)[3]				
UDCA only	32 (78)	81 (76)	40 (63)	
UDCA and OCA	7 (17)	23 (21)	11 (17)	0.8748
UDCA and fenofibrate	2 (5)	-	8 (13)	0.0003
Other	-	3 (3)	4 (6)	
Current pruritus treatment n (%)				
Any treatment	11(27)	30 (28)	32 (51)	0.007
Current pruritus treatment n (%)				
Bile acid binding resins	-	7 (7)	8 (13)	
Antihistamines	10 (24)	22 (21)	21 (33)	
Rifampicin	-	-	4 (6)	
Sertraline	1 (2)	1 (1)	5 (8)	
Other	-	1 (1)	2 (3)	

Itch is based on the PBC-40 itch score: none (0), mild (≥1 to <7) and clinically significant (≥7).
[1] P-values are from Fisher's exact test for categorical variables or Kruskal-Wallis test for continuous variables. Comparisons were made between the 3 itch category columns (None, Mild, Clinically significant).
[2] P-value based on subset of patients with cirrhosis.
[3] Comparison of current OCA use vs. not and current fenofibrate vs. not between groups.
Alkaline phosphatase, ALP; IQR, interquartile range; obeticholic acid, OCA; UDCA, ursodeoxycholic acid.

[PP-0633]

Comparative characteristics of PBC and PBC with autoimmune hepatitis features in Kazakhstan

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Objectives: The aim of this study was to characterize the clinical, biochemical parameters and response to UDCA (Paris I criteria) in patients with PBC and PBC with autoimmune hepatitis (AIH) features in Kazakhstan.
Materials and Methods: Retrospective study (2014–2021) of 212 patients with PBC diagnosed by functional liver tests, autoantibodies spectrum, abdominal ultrasound, and liver histology.
Results: Among 212 patients 114 (53,6) were diagnosed with PBC and 98 (46,4%) – with PBC with AIH features. Most patients in both groups were Kazakh (179; 84.4%) and female (206; 97.2%). The average age was 53.0 ± 10.5 years without group difference. In both groups mild biochemical activity was predominant: 66 (57.9%) in PBC and 55 (56.1%) in PBC with AIH features. Severe disease (F3/4) was revealed in 67 (68.4%), and in 59 (53.2%) patients respectively ($p > 0.05$). PBC with AIH features had higher proportion of AMA positive cases (88; 89.8%) than PBC without AIH (83; 72.8%) ($p < 0.01$). PBC and PBC with AIH features were associated with rheumatoid arthritis in 20.4% and 12.29.7% ($p < 0,05$), autoimmune thyroiditis in 17.4% and 19.3%, vitamin D deficiency in 52% and 50%, gall stone disease in 20.8% and 27.9%, respectively ($p > 0.05$). Response to treatment according to Paris I criteria was noted in 24 out of 56 (42.9%) patients with PBC and in 9 out of 47 (19.2%) patients with PBC with AIH features ($p < 0.05$).
Conclusion: PBC and PBC with AIH features were similar regarding the age, gender, and ethnicity. PBC with AIH features compare to PBC was characterized by higher prevalence of AMA-positive cases, association with rheumatoid arthritis and lower response to UDCA.

[PP-0634]

Comparative characteristics of AMA-positive and AMA-negative primary biliary cholangitis in Kazakhstan

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Objectives: The aim of this study was to characterize the clinical, biochemical parameters and response to UDCA (Paris I criteria) PBC patients depending on AMA status in the Republic of Kazakhstan.
Materials and Methods: Retrospective study (2014–2021) of 212 patients with PBC diagnosed by functional liver tests, autoantibodies spectrum, abdominal ultrasound, and liver histology.
Results: Among 212 patients, 171 (80.7%) were AMA-positive and 41 (19,3%)—AMA-negative. Vast majority of patients in both groups were Kazakh (179; 84.4%) and female (206; 97.2%). The average age was 53.0 ± 10.5 years without differences depending on AMA-status. Mild biochemical activity in both groups was predominant (101; 59.1%—in AMA-positive and 20; 48.8%—in AMA-negative patients) without any statistical difference ($p = 0.25$). Severe disease (F3/4) was revealed in 108 (63.2%) AMA-positive and in 18 (43.9%) AMA-negative patients ($p > 0.05$). AMA positive and AMA–negative PBC were associated with autoimmune hepatitis in 88 (51.5%) and 10 (24.4%) cases ($p < 0.01$), rheumatoid arthritis in 26 (15.2% and 5 (12.2%), autoimmune thyroiditis in 35 (20.5%) and 4 (9.8%), vitamin D deficiency in 89 (52.1%) and 19 (46.3%), osteoporosis in 48 (28.1%) and 7 (17.1%), gall stone disease in 43 (25.4%) and 8 (21.2%) respectively ($p > 0.05$). Response to UDCA treatment according to Paris I criteria was noted in 24 out of 81 (29.6%) AMA-positive and in 9 out of 22 (40.9%) AMA-negative patients ($p > 0.05$).
Conclusion: AMA-positive and AMA-negative PBC did not have any statistical differences in terms of age, gender, ethnicity, biochemical profile, and disease severity, except higher prevalence of autoimmune hepatitis features in AMA-positive cases.

[OP-0705]

Serological, clinical and histologic features of autoimmune liver disease a case series

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Objectives: To evaluate the epidemiological, clinical, serological and histological features in patients presenting with autoimmune liver disease in a tertiary care hospital in Karachi, Pakistan.
Materials and Methods: A cross-sectional case series of 31 patients which were enrolled in study between a period of 45 months from January 2017 to November 2021 presenting at Jinnah Postgraduate Medical Center, Karachi. Demographic and clinical data including liver function tests, clotting profile, gamma globulin levels, autoimmune serology and liver histology were recorded on designed proforma.
Results: Mean age of patients was 28.19 ± 8.6 years. Females were 23 (74.2%) and males were 8 (25.8%). Most common symptom was fatigue (96.8%), followed by arthralgia (77.4%), anorexia and jaundice (61.3%). Type I AIH was present in 19 (61.3%), Type II AIH in 11 (35.5%) and AIH/PBC overlap in 1 (3.2%) patient respectively, however, no discrete case of PSC and PBC was reported. ANA was positive in 19 (61.3%) patients, ASMA in 7 (22.6%), anti LKM-1 in 10 (32.3%) and AMA in 1 (3.2%) patient respectively. Immunoglobulin G level was raised in all patients with mean of 1672 ± 530. Liver histology showed lymphoplasmacytic interface hepatitis in 19 (61.3%) patients and lobular hepatitis with centrilobular necrosis in 11 (35.5%) patients respectively. Steroid and azathioprine was given in 25 (80.6%) patients while 4 (12.9%) patients received only steroids and 2 (6.5%) patients did not receive any treatment. Remission was achieved in 20 (64.5%) patients.
Conclusion: In summary the most common type of autoimmune hepatitis present in our population is type I Autoimmune hepatitis which was found to be around 61% in our study. Autoimmune liver disease can occur at any age, in both sexes with favorable results on immunosuppression. It can progress to several complications like decompensated liver disease, hepatoma, osteoporosis and dyslipidemia. Liver Biopsy should be performed in all the cases.

[PP-0798]

Liver stiffness measured by transient elastography is an independent predictor for liver related events in patients with primary biliary cholangitis

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Objectives: Although liver stiffness measured by transient elastography (TE) has been shown to be predictive of liver-related events (LRE) in chronic liver diseases such as viral hepatitis, it is not clear for Primary biliary cholangitis (PBC). Therefore, we investigated prognostic value of transient elastography in patients with PBC.
Materials and Methods: 131 consecutive patients with PBC who underwent TE in three academic hospitals between 2004 and 2015 were enrolled. LRE was defined as hepatocellular carcinoma, decompensation, or orthotopic liver transplantation.
Results: The patients were predominantly female (n = 113, 86.3%) with a mean age of 53.7 years. The median liver stiffness value by TE was 7.9 kPa, and the number of patients with liver stiffness value < 7 kPa, 7–11 kPa, and > 11 kPa were 55 (42.0%), 42 (32.1%), and 34 (26.0%), respectively. During follow-up (median: 91.5 months), LRE was developed in 18 patients (13.7%). In Kaplan–Meier analysis, patients with liver stiffness value > 11 kPa were well differentiated from those with liver stiffness value < 7 kPa and 7–11 kPa in predicting the risk of LRE ($P < 0.05$, log-rank test). In univariate Cox regression, serum bilirubin and albumin levels, platelet count, and liver stiffness value by TE > 11 kPa was statistically significant (all $P < 0.05$). In multivariate Cox regression, only liver stiffness value by TE > 11 kPa was a significant predictor for LRE (hazard ratio, 5.91; 95% confidence interval 1.185–29.516; $P < 0.030$).
Conclusion: Liver stiffness value > 11 kPa measured by TE was an independent predictor for LRE in patients with PBC.

[PP-1060]

Population-based epidemiology and outcomes of primary biliary cholangitis in South Korea from 2009 to 2019

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Objectives: This study aimed to elucidate the trends of prevalence and incidence, clinical features, and outcomes of PBC in South Korea from 2009 to 2019.
Materials and Methods: The Korean National Health Service database and Rare Intractable Disease registration data on PBC, identified with the International Classification of Diseases 10 code of K74.3*, were obtained from 2009 through 2019. The age and gender-specific prevalence and incidence rates of PBC were calculated. The trends of PBC prevalence and incidence were estimated using Joinpoint regression analysis. Data on complications, comorbidities, treatment, and survival were also analyzed.
Results: A total of 4,588 patients over 20 years old were identified as an incident PBC in 2009 $\sim$ 2019 (female-to-male ratio 4.9, median age 58 years). The age and sex-adjusted incidence from 2009 to 2019 was 10.3 per million per year on average and has significantly increased from 10.3 to 11.4 with an average annual percent change (APC) of 3.9%. The age and sex-adjusted prevalence from 2009 to 2019 was 82.1 per million on average and has also significantly increased from 43.0 to 123.2 per million with an average APC of 10.9%. The prevalence of PBC showed remarkable geographic variability between 44.1 and 121.8 per million. The overall prescription rate of UDCA was 98.2%. Medication adherence to UDCA increased from 86.7% in 2009 to 92.1% in 2019. The five- and ten-year transplant-free survival rates were 86.9% and 80.6% respectively in incident PBC patients. Older age, male sex, and low adherence to UDCA were associated with lower survival rates.
Conclusion: The incidence and prevalence of PBC were 10.3 and 82.1 per million, respectively, and increased during 2009–2019 in Korea. The ten-year survival rate was 81%, which was lower with older age, male, and low adherence to UDCA. The remarkable geographic disparity of epidemiology warrants nationwide efforts for enhancing awareness and diagnosis.

[OP-1065]

Seronegative autoimmune hepatitis in children A real diagnostic challenge

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Objectives: Classical autoimmune hepatitis (AIH) is characterized by the presence of conventional autoantibodies (anti-smooth muscle, antinuclear and anti-liver-kidney-microsomal antibodies). The absence of such autoantibodies in some patients does not preclude AIH diagnosis or the need for its treatment. This group of patients was termed seronegative AIH. Whether non-conventional autoantibodies can identify this group of patients is still elusive. We aimed to study the prevalence of seronegativity of conventional autoantibodies and the occurrence of non-conventional autoantibodies in children with AIH.
Materials and Methods: in this study, 55 children with AIH were investigated for non-conventional autoantibodies (antineutrophil cytoplasmic antibodies, antibodies to soluble liver antigen, anti-tissue transglutaminase and antiplatelet antibodies). All the patients received immunosuppressive therapy and were assessed for treatment response.
Results: of the patients 44 had classical AIH (type 1, 70.09%, type 2, 9.09%) and 20% were seronegative. The four studied non-conventional autoantibodies occurred in four patients, one for each. All

nonconventional autoantibodies were exclusively associated with type 1 AIH. The clinical profile, ultrasonographic findings, liver biochemistry and histopathological findings were comparable in the classical and seronegative AIH. The majority of patients with classical (72.7%) and seronegative (54.5%) AIH were treatment responders.
Conclusion: seronegative AIH represents a substantial percentage of pediatric patients diagnosed with AIH. They were even negative for non-conventional autoantibodies. Furthermore, apart from autoantibodies, seronegative AIH is almost indistinguishable from the classical AIH and the majority of patients were treatment responders. This favorable response to immunosuppression deserves sustainable efforts for considering such a diagnosis and start therapy to halt disease progression is worthwhile.

Drug-Induced Liver Injury

[OP-0316]

Liver related adverse events reported in WHO database with use of remdesivir in COVID-19

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Objectives: Remdesivir was granted emergency approval for use in the management of COVID-19 though some studies exhibit concerns regarding its effectiveness, it is still being used for COVID-19 infection management in many parts of the globe. To date, limited data is available regarding its safety as it's a newer drug. Thus there is a need to observe and record its adverse events to aid future decisions. This study was designed with the aim of analyzing the liver-related adverse drug events (ADEs) reported in VigiBase, the WHO database for adverse event reporting.
Materials and Methods: The analysis of all suspected adverse events related to remdesivir reported in the last 5 years to VigiBase®, i.e. from January 1, 2015, to July 19, 2020, was performed. We used SOC (System Organ Class) information and PT (Preferred Terms) for analysis in the present study. We extracted three SOCs – hepatobiliary disorders, gastrointestinal disorders, and investigations. Descriptive statistics were reported in the form of frequency and percentages.
Results: The majority of ADEs were reported from males and the majority were serious in nature. A total of 1086 ADEs were reported from the 439 individuals up to July 19, 2020, in the VigiBase®, after exclusion of duplicates1004 ADE were analyzed. out of this 18.12% (182 of 1004), ADE was related to the liver from 142 subjects. The most common ADE were alternations in the liver enzymes with Alanine aminotransferase increased 4.98% (50 of 1004), 3.19% (32 pf 1004) of increase in Aspartate Aminotransferase, and increased in transaminase increased in 2. 39% (24 of 1004).
Conclusion: Deterioration of liver functions was observed with the use of remdesivir in a few patients. A thorough review of cases and proportionality analysis should be done to ascertain the causality of these adverse events as COVID-19 infection may itself leads to an increase in liver enzymes.

[PP-0333]

A case of acute liver failure due to acetaminophen overdose treated with molecular adsorbents recirculating system

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Objectives: The molecular adsorbent recirculating system (MARS) is a form of artificial extracorporeal liver support and can be used for a bridge to spontaneous recovery of hepatic function or liver transplantation in patients with acute liver failure. MARS is based on albumin dialysis principle which can be applied for patients with acute poisoning from drugs.
Materials and Methods: We report on a patient who developed acute liver failure due to acetaminophen overdose despite of intravenous N-acetyl cysteine therapy who was treated with the MARS.
Results: A 15-year-old boy presented with decreased consciousness and nausea. The patient took 35 tablets of acetaminophen (AAP) together with 10 tablets of diphenhydramine for the purpose of suicide 20 h before admission. The patient weighed 75 kg, and the ingested AAP was 303.3 mg/kg. N-acetyl cysteine ??therapy was administered, but it was ineffective. The liver function gradually deteriorated, resulting in aucte liver failure, and liver transplantation was required. The patient also had acute pneumonia, which was a contraindication to liver transplantation. We decided to apply MARS as a bridge until the liver transplantation was performed after the pneumonia had improved. MARS was applied for 8 h and laboratory findings improved and liver function gradually normalized.
Conclusion: Timely administration of N-acetyl cysteine ??is important in patients with AAP overdose. In patients with liver failure, MARS improved the laboratory data and hepatic function associated clinical characteristics. MARS not only acts as a bridge to liver transplantation, but also has therapeutic effects.

[OP-0360]

Liver related adverse events reported after the use of COVID-19 vaccines: A descriptive study

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Objectives: The present study focus on the liver-related adverse events (AEs) reported with COVID-19 vaccines in VigiBase, a database maintained by WHO for reporting adverse events.
Materials and Methods: The data of liver-related adverse events following COVID-19 vaccination was acquired on a subscription basis from VigiBase. This study included all the suspected liver-related adverse events reported in VigiBase after administering any of the three COVID-19 vaccines: Moderna, BNT162b2 Pfizer and 1222 AstraZeneca between December 15, 2020, and January 24, 2021. The MedDRA (Medical Dictionary for Regulatory Activities) and WHO-ART terminology- SOC (System Organ Class) and PT (Preferred Terms) were used for analysis. We extracted three SOCs – hepatobiliary disorders, gastrointestinal disorders and investigations. All the

SOC were further cleaned to remove all PTs other than those related to the liver. Disproportionality analysis was reported in the form of IC025, Reporting Odds Ratio and Prevalence Odds Ratio.
Results: A total of 103,954 AEs were reported for COVID-19 vaccines from 32,044 individuals, out of which only 51 (0.049%) AE from 32 patients was related to the liver. Most common liver-related AE reported were in the SOC "investigations"- increase in alanine amino transferase (0.009%) followed by increased aspartate aminotransferase and increased bilirubin (0.006%). Based on the disproportionality analysis (IC_{025} values) none of them was vaccine-related AE.
Conclusion: COVID-19 vaccines are safe for liver and there was no increase in the events were associated with the use of vaccines. As these were early data of vaccine use, analysis based on recent data need to be done to ascertain it fully.

Table 1: Liver related adverse events reported with the COVID-19 vaccine use.

System Organ Classification	Adverse Events	Frequency (%)	IC025	ROR	PRR
Investigations (36)	Alanine aminotransferase increased	9 (0.009)	-4.485	0.090	0.091
	Albumin urine present	1(0.001)	-2.937	3.074	3.074
	Aspartate aminotransferase increased	6(0.006)	-4.999	0.075	0.075
	Bilirubin urine present	1(0.001)	-2.358	19.335	19.335
	Blood albumin increased	1(0.001)	-3.516	1.363	1.363
	Blood alkaline phosphatase increased	4(0.004)	-4.774	0.110	0.110
	Blood bilirubin decreased	1(0.001)	-3.263	1.870	1.870
	Blood bilirubin increased	6(0.006)	-3.642	0.195	0.195
	Hepatic enzyme increased	2(0.002)	-7.945	0.020	0.020
	Liver function test increased	4(0.004)	-3.437	0.247	0.248
	Urine bilirubin decreased	1(0.001)	-2.372	17.494	17.493
Hepatobiliary disorders (14)	Hepatic artery embolism	1(0.001)	-2.271	52.482	52.480
	Hepatic cirrhosis	1(0.001)	-7.003	0.075	0.075
	Hepatic pain	4(0.004)	-1.801	0.951	0.951
	Hepatitis	1(0.001)	-9.363	0.014	0.014
	Jaundice	3(0.003)	-6.160	0.050	0.050
	Liver injury	1(0.001)	-7.422	0.055	0.055
	Ocular icterus	2(0.002)	-3.520	0.468	0.468
	Portal hypertension	1(0.001)	-4.466	0.530	0.530
Gastrointestinal disorders (1)	Ascites	1(0.001)	-7.652	0.047	0.047

[OP-0462]

Alteration in liver function following use of remdesivir in COVID-19 patients: A prospective study

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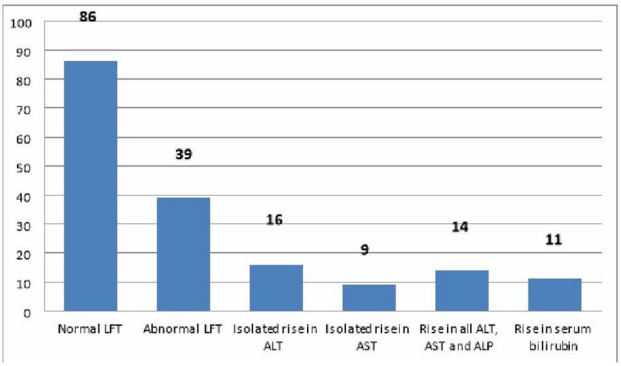
Objectives: Background: COVID-19 infection has been affecting humans globally since December, 2019 and Remdesivir was first approved by FDA for treating severe COVID-19 pneumonia in July, 2020 though its hepatic safety has not been adequately studied. Remdesivir, a nucleotide analog prodrug, has been found to create derangement in liver function. However, COVID-19 infection itself has transient implications over liver enzymes. Aims: To evaluate the effect of Remdesivir on liver function in COVID-19 in-patients with normal liver function.
Materials and Methods: This prospective study was conducted at Mediplus Hospital and Trauma Center from 1st September, 2020 to 31st May, 2021. Ethical approval was obtained and 107 PCR positive COVID-19 in-patients with normal liver function test (LFT) were included in the study. Liver enzymes (alanine and aspartate transaminases and alkaline phosphatases) and serum bilirubin were sent after 72 h of initiation of the drug. Data was entered in Microsoft excel and result studied.
Results: Out of 125 included patients, LFT became deranged in 39 (31.2%) patients. Among those 39 patients, 16 (41.0%) had isolated raised ALT, 9 (23.1%) had isolated raised AST and 14 (35.9%) had all three enzymes (AST, ALT and ALP) raised, while serum bilirubin was found to be raised in only 11 (28.2%) (Diagram1).
Conclusion: Biochemical alteration in liver function has been noted in Covid-19 patients after the Remdesivir therapy. However, that effect could also be due to hepatic implications of Covid-19 infection itself and concomitant use of other drugs.



[PP-0517]

Multi-systemic toxicity induced by amiodarone involving liver, lung, thyroid and eye: A case report

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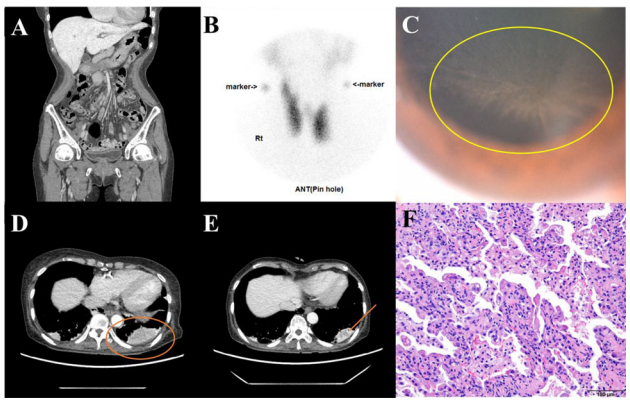
Objectives: Amiodarone is widely used for treatment of arrythmia. However, amiodarone is known to have severe toxicity regarding liver, lung, thyroid and etc. Especially amiodarone causes liver damage ranging from asymptomatic serum aminotransferase elevation to hepatic failure requiring liver transplantation. Although amiodarone toxicity has been reported, it is not well known regarding simultaneous multiple organ toxicities. Hereby, we introduce a novel case of multi-systemic toxicity of amiodarone involving liver, lung, thyroid and eye.
Materials and Methods: A 61-year-old women visited emergency room due to general weakness, nausea, visual disturbance, heat intolerance, and non-productive cough. The patient had on clopidogrel, and amiodarone due to underlying atrial fibrillation. The level of total bilirubin was 0.71 mg, aspartate aminotransferase 358 U/L, alanine aminotransferase level 177 U/L and prothrombin time 27.1 s. Computer tomography showed diffuse increased intensity of liver and scattered hyperattenuated nodular consolidations in both lungs. Via transthoracic needle biopsy of lung, fibrinoid interstitial inflammation with atypical change of type II pneumocytes and intra-alveolar foamy macrophages were revealed. Also, the level of thyroid-stimulating hormone was less than 0.008uIU/mL, and free T4 4.67 ng/dL. Thyroid scan showed diffuse homogenous intake of Technetium-99 m Pertechnetate in both thyroid lobes. At ophthalmologic exam, bilateral symmetrical corneal deposits in vortex pattern was detected. With these findings, we could diagnose the amiodarone-induced hepatic, pulmonary, thyroid and ophthalmologic toxicity.

Results: Liver function was restored after cessation of amiodarone and thyroid function was normalized with methimazole medication. However, owing to aggravation lung consolidations, systemic steroid was administered and showed improvement at 1 week follow-up exam. As her symptoms improved, she was discharged with a plan of steroid administration for 3 to 6 months.
Conclusion: This case implies the possibility of multi-systemic involvement of amiodarone toxicity. It is required to monitor the toxicity of amiodarone regarding multiple organs. Prompt cessation of the drug should be considered once diagnosis is determined.



[PP-0564]

Aminotransferase and bilirubin dynamic evolution pattern as a novel model in the prediction of acute liver failure in drug-induced liver injury (DILI)

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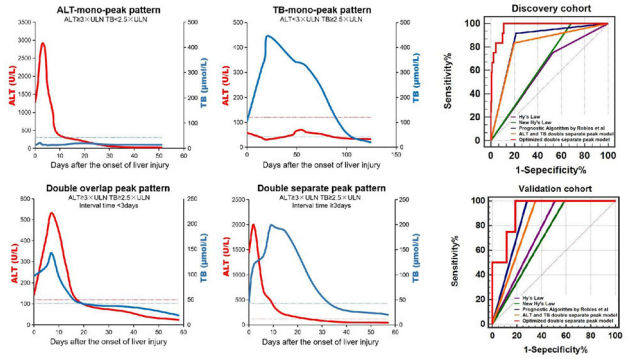
Objectives: Development, optimization and validation a new model using alanine aminotransferase (ALT) and total bilirubin (TB) dynamic evolution patterns in predicting acute liver failure (ALF) in patients with DILI.
Materials and Methods: The demographic, clinical data and outcomes of patients with DILI from 2013 to 2020 were retrospectively collected. According to the dynamic evolution of ALT and TB after DILI onset, the enrolled patients were divided into: ALT-mono-peak pattern, TB-mono-peak pattern, double overlap peak pattern, double separate peak pattern (DSP, Fig. 1.). Clinical characteristics and liver histology (if any), outcomes among different peak patterns were compared. Logistic regression was used to develop the optimized model and Bootstrap method was used to validate the model in discovery cohort and an independent validation cohort.
Results: The proportion of ALF was significantly higher in patients with the DSP pattern compared to other patterns (0.0% vs 0.0% vs 2.0% vs 14.9%, $P < 0.001$). The AUROC of the DSP model is 0.817 (95%CI: 0.768- 0.859) in discovery cohort and 0.835 (95%CI: 0.753–0.898) in validation cohort in the prediction of ALF. The prediction potency of ALF can be further improved if combined with INR and albumin (ALB) at hospital admission [discovery cohort:0.974 (95% CI: 0.949–0.989); validation cohort: 0.924 (95%CI: 0.856–0.967)], which is better than Hy's law [0.611 (95%CI: 0.553–0.667), $P < 0.001$], new Hy's law[0.657 (95%CI: 0.600–0.711), $P < 0.001$], or Prognostic Algorithm by Robles et al.[0.850 (95%CI: 0.804–0.889), $P = 0.006$]. Histopathologically, patients with the DSP pattern were predominantly cholestatic hepatitic injury pattern (70.8%, $P < 0.05$) and having higher degree of necrosis (50.0%, $P = 0.460$).
Conclusion: DILI with the DSP pattern is more likely to develop into ALF, when combined with INR and ALB at admission its predictive potency can be further improved. This novel model can identify high risk DILI patient better, so that extra care could be timely adopted to improve outcomes.



[OP-0593]

Polygoni multiflori radix praeparata inhibits anti-CTLA-4 induced liver injury in PD-1 knockout mice by inhibiting CD4 + T cells activation

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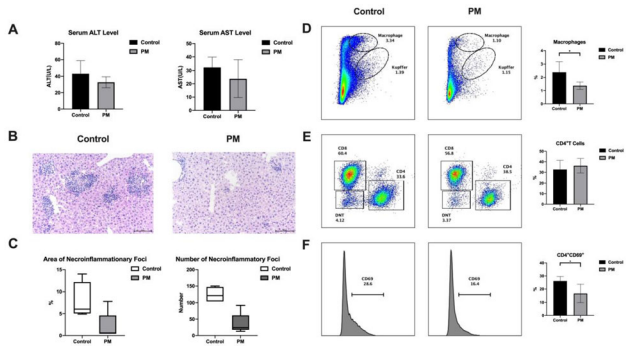
Objectives: To investigate the effects of the Polygoni Multiflori Radix Praeparata (PM) on hepatic injury induced by anti-cytotoxic-T-lymphocyte-associated protein-4 (anti-CTLA-4) in programmed-cells-death-1 (PD-1) knockout mice and its immunological mechanisms.
Materials and Methods: C57BL/6-PD-$1^{-/-}$ mice (n = 10) were divided into the control group (n = 4) and the PM group (n = 6). Anti-CTLA-4 was injected intraperitoneally − 3 day, − 1 days and weekly throughout the experiment, followed by normal saline and the PPM were given by gastric gavage for 42 days. Then the blood and liver tissues were collected on day 43. H&E, immunohistochemical stains (IHC) were performed and the infiltrated inflammatory cells from liver tissue was analyzed by flow cytometry.
Results: Compared with the control group, the levels of aminotransaminases in the PM group decreased (43.2 ± 15.5 vs 32.8 ± 6.7, $P = 0.216$). Histologically,the total number of necroinflammatory foci significantly decreased in the PM group compared with that in the control group [121.5 (104.0,147.3) vs 24 (17.5, 61.5), $P = 0.014$]. The total area of necroinflammatory foci in the PM group decreased without significant difference (7.8 ± 4.2 vs 2.1 ± 3.2%, $P = 0.103$). IHC stains revealed that the number of macrophages but not $CD4^+$ T cells reduced in the PM group. The result of flow

cytometry showed that the proportion of macrophages decreased significantly (2.39 ± 0.77% vs 1.37 ± 0.28%, P = 0.028). The proportion of $CD4^+$ T cells did not change significantly (32.7 ± 8.6% vs 36.2 ± 6.9%, P = 0.511), however $CD4^+$ T cells expressed CD69 in the PM group was significantly lower than that in the control group (26.20 ± 3.47% vs 16.74 ± 6.95%, P = 0.044).

Conclusion: Polygoni Multiflori Radix Praeparata can inhibit the progression of CTLA-4-induced PD-$1^{-/-}$ mice liver injury by inhibiting macrophages recruitment and $CD4^+$ T cells activation.



[PP-0657]

Kratom-induced cholestatic liver injury: A pandemic within a pandemic?

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Objectives: Mitragyna speciosa (commonly known as kratom) has both opioid and stimulant-like effects. Recently, Thailand decriminalized the possession and sale of kratom, led to people in many areas earned income selling Kratom at a time of widespread unemployment due to COVID-19. Here, we report a patient with post-Covid syndrome who developed mixed cholestatic-hepatocellular liver injury secondary to kratom.

Materials and Methods: A 23-year-old Thai man was seen for evaluation of fatigue and nausea, followed soon after with pruritus, dark urine and jaundice. The patient had no known underlying disease but had been treated with mild COVID-19 pneumonia in the past 2 months. He reported taking kratom recreationally for 2 weeks as a treatment for his post-COVID insomnia. Kratom was bought from his friend and used as a homemade iced cocktail called "4 × 100" that consists of Coca-Cola, tea made from boiled kratom leaves, and diphenhydramine-containing cough syrup which has been popular in Southernmost provinces of Thailand. On workup, his total bilirubin was noted to be 10.6 mg/dL, aspartate aminotransferase was 642 U/L, alanine aminotransferase 1,635 U/L. Extensive workups including viral etiologies was negative. Abdominal ultrasound revealed only fatty liver without cirrhosis.

Results: The patient had been managed conservatively for 5 days in the hospital. Urine toxicology screening confirmed the presence of only mitragynine. At two weeks later, serum total bilirubin was decreased to 1.5 mg/dL, aspartate aminotransferase was 112 U/L, alanine aminotransferase 404 U/L. He was in a stable condition and normalized liver function tests at 3 months after discharge.

Conclusion: There is growing evidence that kratom is safe if used as pure kratom products or brewed herbal decoction in small doses and for a limited period of time. However, the polydrug patterns of kratom use could lead to severe liver injury.

[OP-0673]

The use of andrographolide and effects on liver biochemistry in patients with gastrointestinal problems amid the pandemic of COVID-19

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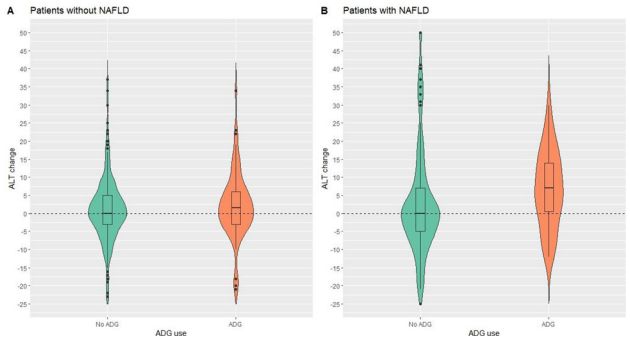
Objectives: In the situation of COVID-19 pandemic in Thailand, healthcare facility supply and access are limited. There was an announcement promoting Andrographolide (ADG) use in treatment of mild COVID-19 patients, but misconception of taking for prevention might occur. Moreover, the effect of ADG on liver function test (LFT) has not been established. We aim to study the prevalence of ADG use and effect on LFTs in patients with gastrointestinal (GI) problems.

Materials and Methods: We conducted a cross-sectional study including GI patients at our center who voluntarily filled the ADG questionnaire in Aug-Sep 2021. LFT data at that visit and at the prior visit (if available) were obtained. The changes in LFT within the same person were analyzed using Wilcoxon signed-rank test. Wilcoxon rank-sum and Chi-square test were used to compare between patients with and without ADG consumption.

Results: A total of 886 patients completed the survey, 170 patients (19.2%) took ADG within the past month. Patients who took ADG were more likely to have history of COVID-19 infection in their closed companies (5.6% vs 1.5%) compared with who did not (control group). LFT data were available in 486 (54.8%) patients, the median ALT change compared with the prior visit was higher in ADG vs control group (+ 2 vs 0, p = 0.026), and 45% had increased ALT (> 3 U/L) vs 32.2% in ADG and control group, respectively

(p = 0.023). Multivariable logistic regression analysis found that factors independently associated with an increased ALT were ADG exposure (adjusted OR [aOR] of 1.62, p = 0.042), and patients with NAFLD who gained weight (aOR of 2.37, p = 0.046).
Conclusion: One-fifth of GI patients recently took ADG, in which currently not indicated as it has no effect on preventing COVID-19 infection. Those who took ADG are more likely to experience an increase in ALT than who did not. Warning should be made regarding this issue.



[PP-0697]

A case of toxic hepatitis induced by Noni powder

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Objectives: Toxic hepatitis could be caused by hepatotoxic drugs or metabolic intermediates and that result in liver cell injury. Although toxic hepatitis of various causes was reported, there was no case of toxic hepatitis caused by noni powder. The case we will report is a rare case of toxic hepatitis caused by taking Noni powder.
Materials and Methods: This review is based on medical records including laboratory findings and results of liver biopsy reports.
Results: A 54-year-old male patient visited the hospital with jaundice and itching sensation. He has consumed daily 200 g of the Noni for four months. We performed some laboratory tests and the results are as follows; Elevated liver enzymes, total and direct bilirubin, negative markers for viral diseases and negative tumor markers. Further tests, such as a rare liver disease autoimmune hepatitis and primary biliary cirrhosis were also negative. For hepatic parenchymal evaluation, liver biopsy was performed on the right lobe. As a result, toxic hepatitis was confirmed. Patient was treated with intravenous injection of hepatotonics, such as silymarin and biphenyl dimethyl dicarboxylate. Finally, the liver enzyme is normalized, and total serum bilirubin has been recovered.
Conclusion: The etiology of toxic hepatitis is varied, one is caused by the metabolites. This case is toxic hepatitis caused by Noni powder, which has never been reported in the past. There was no other cause of toxic hepatitis and we report a case with confirmed histopathology.

[PP-0816]

Identification of magnetic resonance imaging features associated with injury type, severity and prognosis in drug-induced liver injury

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Objectives: To identify the abdominal magnetic resonance imaging (MRI) features associated with injury type, severity and prognosis in drug-induced liver injury (DILI); and to explore an MRI feature-based model to predict the likelihood of liver transplantation (LT)/liver-related death (LRD) within 6 months.
Materials and Methods: The eligible DILI patients, who had contrast abdominal MRI examination within 3 months of onset, were retrospectively enrolled from 2016 to 2020 at Beijing Friendship Hospital, Capital Medical University. The MRI features associated with type of injury, severity and prognosis were identified by c^2 test/Fisher's exact and logistic regression.
Results: The median age of 180 patients was 55.5 years with 126 (70%) women. The injury types included hepatocellular (135 cases, 75.0%), mixed (23, 12.8%), and cholestatic (22, 12.2%). Mild to moderate injury was 157 patients (87.2%) and severe-fatal/LT was 23 (12.7%). 157 patients (87.2%) fully recovered, 13 (7.2%) became chronic, and 10 (5.6%) died/underwent LT. The proportion of periportal edema in patients with hepatocellular and mixed types of injury was significantly higher than that in cholestatic injury (62.2%, 47.8% vs 18.2%, $p < 0.001$). Irregularity of liver surface [6.86 (95% CI, 1.31–35.88)], transient hepatic attenuation difference (THAD) [3.70 (95% CI, 1.26–10.90)], and splenomegaly [6.57 (95% CI, 2.14–20.16)] were independently associated with severity. THAD [8.39 (95% CI, 1.27–55.46)] and ascites [60.47 (95% CI, 6.48–564.00)] were independently associated with LT/LRD. A new model employing THAD and ascites was developed and its predictability for LT/LRD within 6 months was 0.959 (95% CI, 0.916–1.000; sensitivity 87.5%; specificity 91.9%). The internal validation yielded a C-statistic of 0.953 (95% Cl, 0.895–1.000).
Conclusion: Specific MRI features associated with types of injury (periportal edema) and severity (irregularity of liver surface, THAD, splenomegaly) were identified. The new model employing THAD and ascites may have potential clinical utility in the prediction of LT/LRD outcome in DILI patients within a 6-month period.

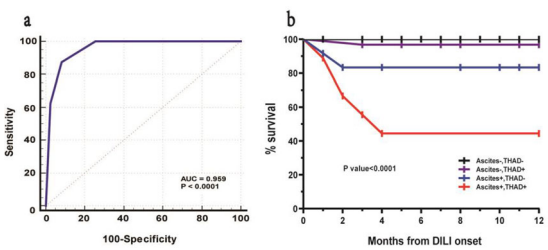

Figure 1. (A) Receiver operating characteristic (ROC) curve of the prediction model employing THAD and ascites for liver transplantation/liver-related death within 6 months. The area under ROC curve of the new model was 0.959 (95% CI, 0.917-1.000). (B) Survival of 4 groups of DILI patients with different imaging features using the Kaplan-Meier method. Abbreviation: DILI, drug-induced liver injury; THAD, transient hepatic attenuation difference; -, negative; +, positive; CI, confidence intervals.

[PP-0837]

Network pharmacology based prediction and pharmacological validation of effects of astragali radix on acetaminophen-induced liver injury

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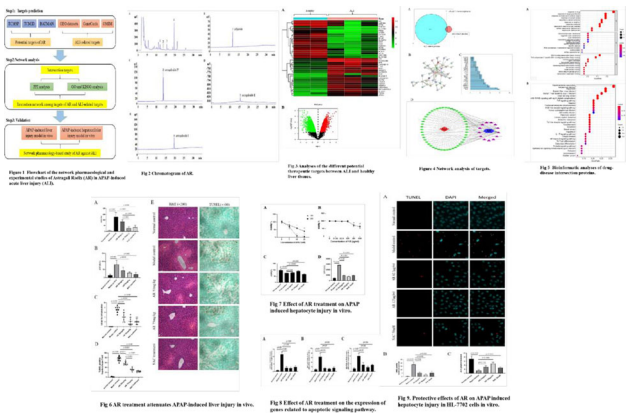
Objectives: To investigate the therapeutic effect and potential molecular mechanism of AR (Astragali Radix) in the treatment of APAP-induced acute liver injury (ALI).
Materials and Methods: Data from TCMSP were text-mined and screened to predict the target genes of the compounds in AR. Online databases (GeneCards and Online Mendelian Inheritance in Man) and Gene Expression Omnibus profiles were searched for genes related to ALI. The enriched processes, pathways, and related diseases of the target genes were analyzed by referring to the Search Tool for the Retrieval of Interacting Genes/Proteins database. A network constructed through Cytoscape was used to identify the target proteins that connect the compounds in AR with the differential genes of ALI. We used mouse models with ALI and HL-7702 cells incubated with APAP to validate the effects of AR on liver injury and their underlying mechanism by detecting liver function, hepatocyte apoptosis, and related intersection genes.
Results: A total of 49 AR–ALI crossover proteins were filtered into a protein–protein interaction network complex and designated as the potential targets of AR that determine its effects on ALI. Among the proteins, the three highest-scoring genes, MYC, MAPK8, and CXCL8, were highly associated with apoptosis in ALI. The results demonstrated that AR can exude anti-ALI effects in vivo and in vitro by improving liver function, reducing the number of terminal deoxyuridine triphosphate nick-end labeling–positive hepatocytes, and downregulating JC-1 levels.
Conclusion: Our study findings provide a new insight by predicting the mitigating effects of AR on ALI through network pharmacology. The mechanism associated with these effects is the inhibition of hepatocytes apoptosis in vivo and in vitro.



[OP-0978]

Methimazole-induced liver injury manifesting as cholestatic jaundice in an adult Filipino with Graves hyperthyroidism: A case report and review of literature

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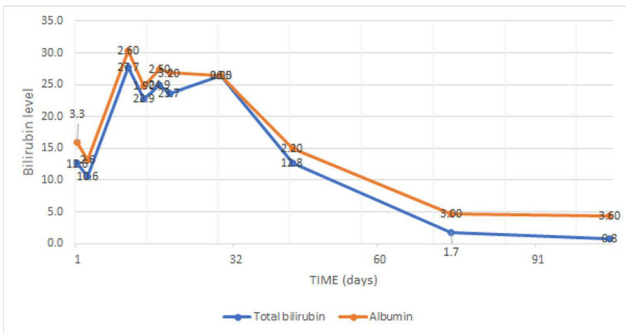
Objectives: Grave's hyperthyroidism is a prevalent global disease, mostly affecting the female and Filipino population. The most preferred, non-invasive management of Grave's hyperthyroidism is the antithyroid drug, methimazole, which is a thioamide or thyroid hormone antagonist. It is more preferred than its homologous counterpart, propylthiouracil, because it is less hepatotoxic, and only requires once daily dosing, with an uncommon effect being hepatotoxicity. This paper aims to discuss a case report of rarely seen methimazole-induced liver injury presenting as overt jaundice and its latest review of related literature.
Materials and Methods: A 56 year old female, newly diagnosed Grave's hyperthyroidism initially manifesting as bipedal edema and palpitations who developed severe cholestatic jaundice after taking methimazole (MMI) 20 mg once daily tablets for 38 days.
Results: Upon hospital admission, MMI was discontinued immediately, however, the patient's serum total bilirubin rose from 12.61 mg/dL to 27.70 mg/dL after 11 days of drug discontinuation, serum albumin dropped from 3.3 mg/dL to 1.90 mg/dL. She was worked up for causes of obstructive jaundice, acute viral hepatitis, and autoimmune hepatitis, of which had negative yield, and was managed as methimazole-induced liver injury versus thyrotoxicosis-induced cholestatic jaundice. She remained clinically and biochemically hyperthyroid, and was treated with radioactive iodine on the 11th day of admission. Her hyperthyroidism was significantly relieved, and she was started on ursodeoxycholic acid (900 mg/day) for 3.5 months, of which her serum total bilirubin count, and serum albumin reached normal levels.
Conclusion: This paper discusses the latest literature around cholestasis and its relationship with hyperthyroidism, as well as possible consequences of each treatment option for Grave's hyperthyroidism. We recommend that baseline liver function tests be taken prior the administration of oral methimazole patients.



[OP-0999]

Prednisolone therapy accelerated recovery of severe drug-induced liver injury: A prospective randomized controlled study

Bing Zhu[1], Fangjiao Song[1], Honglin Liu[1], Yin Sun[1], Tianjiao Xu[1], Dongze Li[1], Haibo Wang[1], Shaojie Xin[1], Yudong Wang[2], Gregory Cheng[2,3], George Lau[1,2], Sa Lv[1], Shaoli You[1]

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Objectives: Drug-induced liver injury (DILI) is one of the most serious adverse drug reactions and the incidence has been increasing rapidly. Accumulating evidence suggested that the immune activation and systemic inflammatory responses play a significant role in the progression of DILI. Corticosteroids are often used in DILI, but clinical usefulness remain controversial. We therefore conducted a prospective randomized controlled study to investigate whether corticosteroid therapy can accelerate recovery and reduce mortality in severe DILI (SDILI).
Materials and Methods: SDILI patients with total bilirubin (TBIL) $\geq$ 171 μmol/L presented to Fifth Medical Center of PLA General Hospital, Beijing from 1/1/2015 to 31/12/2019 were randomized into prednisolone group and control group. The primary endpoints were proportion of subjects with resolution of SDILI defined as decrease in TBIL by at least 35 μmol/L to below 171 μmol/L and overall survival at 6 months. Patients in prednisolone group received prednisolone 60 mg/day therapy for the first 7 days. Patients reaching the primary endpoint or achieved decrease in TBIL by more than 35umol/L on day 8 would continue on tapering doses of prednisolone, otherwise prednisolone would be discontinued.
Results: On day 8, 50.7% (34/67) and 26.5% (18/68) of the subjects in the prednisolone group and control group achieved the primary endpoint respectively, p = 0.002. However, there was no significant difference in overall survival at 6 months, 95.52% (64/67) vs 91.2% (62/68), p = 0.2. All deaths in both groups occurred in patients who failed to achieve SDILI resolution on day 8.
Conclusion: Prednisolone therapy may accelerate recovery of SDILI and shorten hospitalization.

[PP-1022]

A rare case of antituberculosis drug-induced liver injury with secondary sclerosing cholangitis and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: Facing treatment challenges

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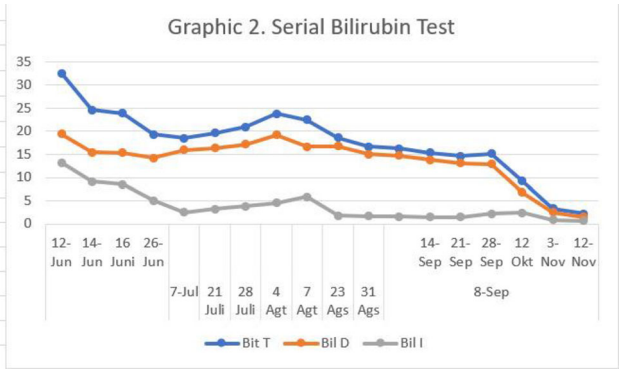
Objectives: Drug induced liver injury (DILI) can have multiple presentations, ranging from asymptomatic elevations in liver biochemistries to liver failure. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome) is a severe multiorgan hypersensitivity reaction. Secondary sclerosing cholangitis (SSC) has not been investigated in patients with drug-induced liver injury.
Materials and Methods: We present a rare case of a 28-year-old male with DILI caused by antituberculosis drug with the problem of treatment for DRESS syndrome and SSC using steroids.
Results: Patient complained of yellow skin and peeling skin after receiving antituberculosis treatment for one month, with results of AST 2050 U/L and ALT 2708 U/L, accompanied by an increase in total bilirubin of 22.40 mg/dl, with a dominant direct bilirubin of 16.80 mg/dl and an alkaline phosphatase level of 338 U/L and eosinophilia was high. Magnetic resonance imaging showed hepatomegaly with bilateral multiple intra hepatic bile duct narrowing to common bile duct with gall bladder collapse suggestive SSC. Patient received steroid therapy for the treatment of DRESS syndrome, but there was a worsening in liver function and bilirubin, so the treatment was stopped, and was given Ursodeoxycholic acid (UDCA) 3 × 500 mg and N-acetylcysteine (NAC) ??3 × 400 mg for approximately three months, currently liver function test and bilirubin close to normal and clinically improved.
Conclusion: This case illustrates clinical improvement of DILI caused by antituberculosis drug patient with DRESS syndrome and SSC using UDCA and NAC.



[PP-1041]

A case of acute hepatitis and morbilliform eruption after mRNA COVID-19 vaccination

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Corresponding author: Raymond Kwok, Gastroenterology Department Blacktown Public Hospital, Western Sydney Local Health District, Sydney, New South Wales, Australia

Objectives: A 36-year-old Caucasian woman developed acute hepatitis and morbilliform eruption arising ten days after the first dose of the mRNA BNT162b2 SARS-CoV-2 vaccine.
Materials and Methods: The patient was asymptomatic apart from the skin rash. Liver function tests showed predmoninantly severe transaminitis (AST 523 U/L, ALT 1550 U/L, GGT 151 U/L, ALP 128 U/L, bilirubin 12 umol/L). Only the ANA 1:160 was abnormal. Other serology for autoimmune and infectious diseases were negative. Multiphase computed tomography of the abdomen was unremarkable. The SARS-CoV-2 anti-spike IgG titre was 67.5 AU/mL (cut-off > 15 AU/mL).
The skin histology revealed spongiotic reaction pattern with focal interface lymphocytic inflammation. Multiple eosinophils and a few

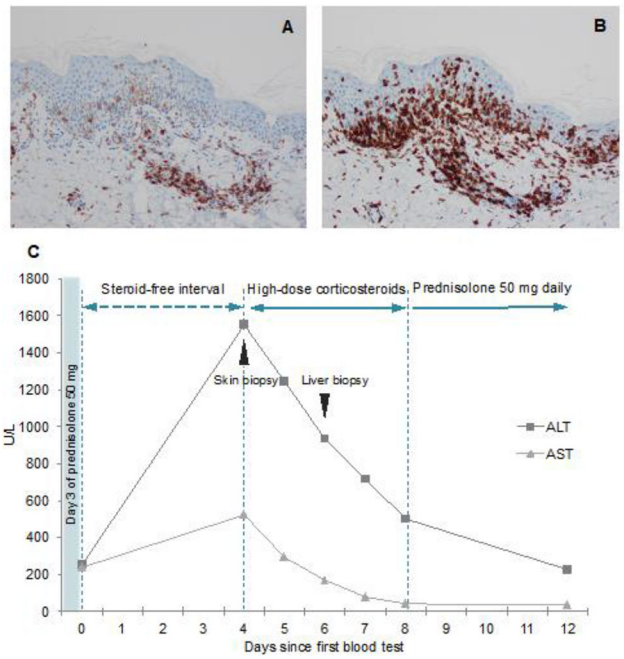
plasma cells were present. The epidermal lymphocytes were composed of CD2, CD3, C4, CD5, CD7 and CD8-positive T cells, with a CD4:CD8 ratio of 1:5. A small number stained positive with TIA1, PD1 and granzyme B. CD56 staining was negative.

A liver biopsy was performed after 2 days of steroids. Liver histology showed mild steatosis and mild inflammatory portal infiltrate comprising mainly of small lymphocytes that were CD3 positive with retained staining for CD7 and CD8. Lobular architecture was preserved with inconspicuous interface hepatitis or piecemeal necrosis.

Results: The patient was treated with intravenous hydrocortisone (400 mg/day) followed by prednisone (50 mg/day). There was rapid improvement in her liver function tests and cutaneous manifestations (Fig. 1).

Conclusion: mRNA COVID-19 vaccine induced hepatitis is a rare phenomenon that is steroid-responsive and has associations with cutaneous eruptions. Our patient's lack of hepatic histological abnormalties is most likely due to early immunosuppression. She had epidermal lymphocytosis with predominance of CD8-positive T cells that were not of cytotoxic phenotype and we are uncertain as to their significance.

There is limited guidance on the safety of SARS-CoV-2 vaccination in those who have had developed significant hepatic and cutaenous reactions. Further work is needed.



[L-OP-1335]

Sodium metabisuphite ($Na_2S_2O_5$) induced subchronic hepatic toxicity in albino mice

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Objectives: Preservatives are essential ingredients of pharmaceutical as well as food industry. The current work has been carried out to make an assessment of the effects of one of the extensively used preservatives, sodium metabisulphite $Na_2S_2O_5$ (SMB), on hepato-histological changes in mice.

Materials and Methods: Albino mice were divided into three groups, control (C) and experimental groups (G1 & G2) (n = 5). G1 & G2 were given with 1.2 mg/kg and 1.6 mg/kg of SMB, respectively, for 21 days followed by dissection to extract liver from C & G1 group while G2 group was left for another 7 days.

Results: The treatment of $Na_2S_2O_5$ induced a sub-chronic condition reflected by marked degenerative and deleterious changes in the general microarchitecture of the organ under study. With dose of 1.2 mg/kg, loss of polarity, widening of sinusoidal spaces, cellular necrosis, and mild haemorrhages with reduced compactness of the cells were noted in liver. These effects got more pronounced in sections given with 1.6 mg/kg of $Na_2S_2O_5$ and could not be reversed completely even after recovery time period of 7 days.

Conclusion: It can be concluded that the extensive use of preservative like sodium metabisulphite may be reduced or curtailed to avoid health hazards.

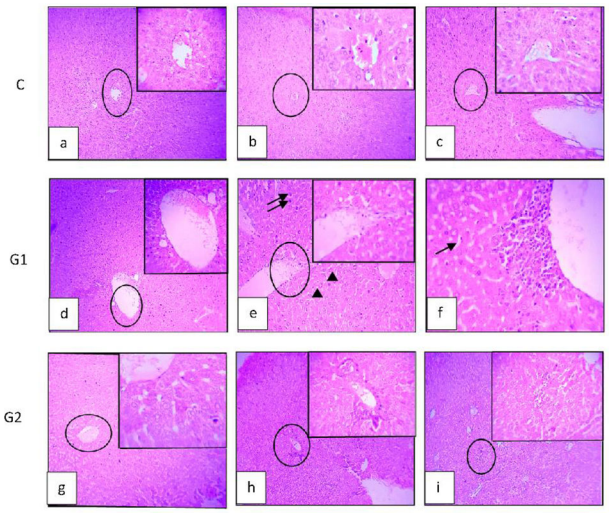

Figure: Hepato-histological comparison between sections of Control (C) and SMB induced Experimental Groups G1(dose=1.2mg/kg for 21 days) & G2(given with dose 1.6mg/kg for 21 days along with 7 days more for recovery); a,b,c=central vein; d= disruption in hepatic portal vein; e= hemorrhages inside the tissue, arrows= necrosis, arrowheads= eccentric nuclei; f= leukocyte infiltration, arrow= sinusoidal widening; g= encircled view in inset shows mitotic figures; h= damage around hepatic portal vein, i= leukocyte infiltration

Metabolic and genetic disease

[PP-0062]

Use of laminaria in the treatment of metabolic syndrome

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Objectives: to study the effectiveness of the green seaweed Laminaria in the treatment of metabolic syndrome.

Materials and Methods: 35 patients with MS were examined (23 women and 12 men).The patients were divided into 2 groups: one group received lipid-lowering (statin), antihypertensives (angiotensin converting enzyme inhibitors, calcium channel blockers) drugs to

reduce insulin resistance (metformin). Group 2, in addition to the basic treatment, received powder of Laminaria by 1 teaspoon on 1 glass of water during a meal 3 times a day for 7 days.
Results: MS is manifested by fatigue, weakness and drowsiness (87.1%), increased appetite (65.2%), polydipsia (24.3%), headache and dizziness (40.1%). The connection of the disease with obesity in 25, hypertension—in 21, diabetes mellitus – in 10 patients. In the group treated with medication only, the positive results observed on the 7th day of therapy in the form of reducing dizziness and headache (48%), reduction of polydipsia (35% patients). The rest of the complaints remained. Group treated the main treatment along with Laminaria gave positive results at 3 day in the form of reducing sleepiness and weakness (76%), reduction of polydipsia (27%), headache and dizziness (58%).
Conclusion: The combination of MS primary treatment with a reception of Laminaria manifests its effectiveness at an early stage of treatment, improves the course of the disease and reduces the risk of cardiovascular complications.

[PP-1127]

Jaundice: Including diseases caused by metabolism and human genetics

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Objectives: In general, Jaundice is caused by a disturbance in the process of formation and disposal of bilirubin. Bilirubin, which is formed due to the destruction of red blood cells, will flow in the blood and be carried to the liver to be processed and then disposed of with urine and feces. People are living with Jaundice experience failure in the process so that it does not run correctly. As a result, bilirubin accumulates in the blood and body tissues, making the sufferer's skin look yellow. The cause that is often overlooked is metabolism and genetics. This may be related to genetic inherited disorders and lack of maintenance of the body's metabolism from an early age.
Materials and Methods: In this study, we collect 10–20 articles related to the discussion, from 2016–2021 then we summarize them into a health article.
Results: A weak immune condition is caused by a weak body metabolism, which occurs due to the environment or genetics. Not a few of these cases occur. Therefore it is crucial to know the condition of the family history. If one family has a history of Jaundice, it is better to consult a doctor to get the proper treatment. Treatment of Jaundice according to dr. Tjin Willy is quoted from the Indonesian Alo Doc article, dividing the treatment into three parts, 1. Pre-hepatic treatment to prevent red blood cells 2. Intra-hepatic treatment to repair liver damage 3. Post hepatic treatment.
Conclusion: From the description of the genetic relationship and Jaundice, it can be seen that the most important thing for the prevention of this disease is to know a family history of the disease is. One way to prevent Jaundice, immediately consult a doctor regarding this disease. Transmission from genetics is the main factor that causes a person to be very quickly exposed to Jaundice.

[PP-1142]

Variation of method of producing human liver stem cells or projenitor cells by direct reprogramming

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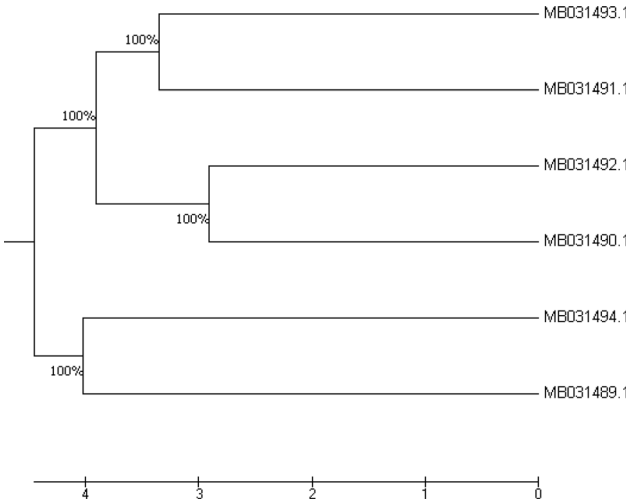
Objectives: Genetic variation is necessary in natural selection. In natural selection, organisms with environmentally selected traits are better able to adapt to the environment and pass on their genes. This study aims to evaluate the variation of method of producing human liver stem cells or projenitor cells by direct reprogramming.
Materials and Methods: Data obtained from 6 nucleotide sequences of method of producing human liver stem cells or projenitor cells by direct reprogramming sequence on secondary data form on https://www.ncbi.nlm.nih.gov/. The phylogeny analysis of variations and relationships of DNA sequences Constructed with Neighbor Joining using MEGA 7.0 software.
Results: Based on the analysis of variations, it is known that on the dendogram, 6 sequences were divided into 2 main groups, namely groups A consisting of 4 specimens and groups B consisting of 4 specimens. The optimal tree with the sum of branch length = 23.10190808 is shown. The tree is drawn to scale, with branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree. The evolutionary distances were computed using the Maximum Composite Likelihood method and are in the units of the number of base substitutions per site. The proportion of sites where at least 1 unambiguous base is present in at least 1 sequence for each descendent clade is shown next to each internal node in the tree. The analysis involved 6 nucleotide sequences. Codon positions included were 1st + 2nd + 3rd + Noncoding. All positions containing gaps and missing data were eliminated. There were a total of 2046 positions in the final dataset.
Conclusion: It can be concluded that the variation method of producing human liver stem cells or projenitor cells by direct reprogramming was quite varied. Information genetic variation can be used as an informative source to assembly of superior genes in living of human cells.



[OP-1168]

Whey protein supplement intake during resistance exercise quickly improves hepatic fat content within 2 weeks: A pilot study

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Objectives: Exercise and diet each have a positive effect on hepatic fat reduction. Additional protein intake can lower hepatic fat accumulation. However, the effect of the combination of exercise and whey protein supplementation (WPS) on hepatic fat content (HFC) is unknown. In particular, its effect in a well-controlled diet has not been studied. The objective of this study is to investigate the short-term effect of WPS on HFC and liver stiffness (LS) during resistance exercise and diet control.
Materials and Methods: A total of 12 sedentary males were recruited and assigned to two groups; Protein Supplement Group (PSG, n = 6) and Control Group (CG, n = 6). PSG took 60 g of WPS per day and CG took 60 g of carbohydrates per day for 4 weeks. All subjects were put on a calorie-controlled diet, with daily caloric intake determined by their resting metabolic rate and physical activity level. They performed resistance exercises (60–70%RM) 50 min/day, 6 days/week for 4 weeks supervised by experts. HFC was assessed by Controlled Attenuation Parameter (CAP) and Ultrasonography (US). LS assessed by transient elastography. Assessments of HFC and LS were performed pre- mid- and post-intervention after an 8-h fast.
Results: After 4 weeks of intervention, there was no significant interaction for HFC and LS between PSG and CG. However, after 2 weeks of intervention, there was a significant interaction between PSG and PG on HFC (PSG: 234.50 dB/m ± 28.02 dB/m to 187.33 dB/m ± 26.63 dB/m, CG: 222.33 dB/m ± 38.76 dB/m to 202.83 dB/m ± 30.44 dB/m, p = 0.045). Interestingly, in PSG, HFC significantly reduced by 19.5% in 2 weeks, whereas in CG, only 8.4% was significant reduced.
Conclusion: These findings demonstrate that WPS intake may improve HFC within 2 weeks during calorie-controlled diet with resistance exercise in sedentary males, although the effect seems to be insignificant after 2 weeks.

[L-OP-1231]

PNPLA-3 gene (rs738409) single nucleotide polymorphism and its affect on liver fibrosis, steatosis, and insulin resistance in patients with non-alcoholic fatty liver disease

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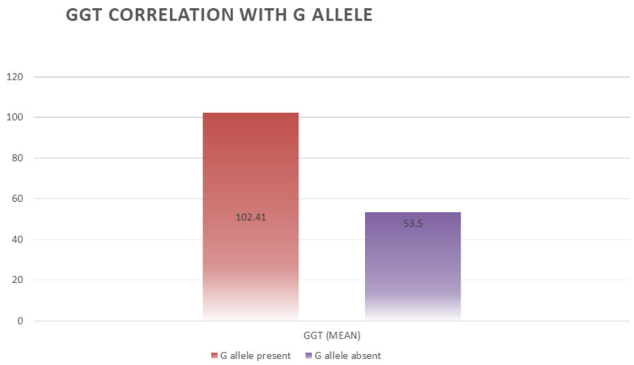
Objectives: The global burden of Nonalcoholic fatty liver disease (NAFLD) is on a rise. PNPLA3- single nucleotide polymorphism (SNP) has been associated with increased vulnerability to NAFLD. This study is aimed to determine the prevalence of PNPLA3-SNP (rs738409, encoding I148M) and its association with liver fibrosis, steatosis, insulin resistance in patients of NAFLD.
Materials and Methods: All eligible cases were identified and PNPL3 SNP (rs738409, encoding I148M) was evaluated by using amplification-refractory mutation system polymerase chain reaction (ARMS-PCR). Liver fibrosis, liver steatosis and insulin resistance were assessed as covariates.
Results: Total of 62 patients were enrolled; 47 were male. Out of 62, 22 were diabetic, 13 were hypertensive and 38 had dyslipidemia. 12/62 patients were found to have PNPLA- CC, 40 had PNPLA-CG and 10 had PNPLA-GG genotype. Patients with positive G allele were found to have elevated BMI (mean 31.41 kg/m^2) and GGT (mean 102 IU/L) with a p-value of 0.039 and 0.027 respectively. Out of 43 patients with elevated ALT, 36 were positive for G-allele (84%) whereas, 19 patients with normal ALT, 14 were positive for G-allele (74%), however, pvalue was calculated to be insignificant. HOMA was calculated in 27 patients. 23/27 patients had HOMA of 2 or more and of these 23 patients, 20 were positive for G allele (87%). 37/62 patients underwent transient elastography. Controlled attenuation parameter was mild in 10 patients, moderate in 7, and severe in 20 patients. 17 patients falling in the severe category were positive for G allele (85%). 22 patients were found to have liver stiffness of 9.6 Kpa or more. 19/22 were positive for presence of G allele.
Conclusion: PNPLA (rs738409)-CG is the most prevalent genotype among our patients with NAFLD and the presence of G allele was associated with higher body mass index and raised GGT. Further studies with a larger sample size are required.



[L-OP-1232]

Identification of novel non-HFE mutations in Chinese patients with hereditary hemochromatosis

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Objectives: Hereditary hemochromatosis (HH) is mainly caused by homozygous p.C282Y mutations in HFE in the Caucasians. We recently reported non-HFE mutations constitute the major cause of HH in Chinese. However, there is still a relatively high proportion of cases with primary iron overload from unexplained causes. We aimed

to explore novel non-HFE mutations in Chinese patients with primary iron overload.
Materials and Methods: Whole exome sequence was conducted to screen mutations in novel HH-related genes in the 9 cases with unexplained primary iron overload. Then the representative candidate genes were screened for mutations in another cohort of 18 HH cases. The biological function of the selected genes and variants were analyzed in vitro.
Results: Whole exome sequencing of 9 cases with unexplained primary iron overload identified 42 missense variants in 40 genes associated with iron metabolism pathway genes such as UBE2O p.K689R and PCSK7 p.R711W. Subsequent Sanger sequencing of the UBE2O and PCSK7 genes in the 27 cases with primary iron overload identified p.K689R in UBE2O, p.R711W and p.V143F in PCSK7 at frequency of 2/27,1/27 and 2/27 respectively. In vitro siRNA interference of UBE2O and PCSK7 resulted in down-regulated HAMP mRNA expression. Adenovirus generation of UBE2O p.K689R in cell lines resulted in increased expression of SMAD6 and SMAD7 and downregulation of p-SMAD1/5 and HAMP expression, and the reduction of hepcidin level.
Conclusion: Our study identified a series of novel candidate non-HFE mutations in Chinese patients with HH. These may provide insights into the genetic basis of unexplained primary iron overload.

[L-OP-1343]

Correlation of serum total cholesterol and liver damage status after intervention of synbiotic drink of stelechocarpus burahol with lactobacillus casei and Lactobacillus plantarum isolates: A dyslipid

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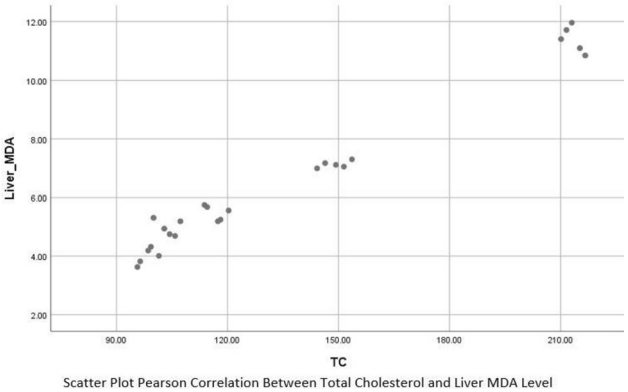
Objectives: Dyslipidemia may promote systemic oxidative stress-induced liver damage. Malondialdehyde (MDA) level is commonly known as a marker of oxidative stress. Recently, many studies revealed that synbiotic has potency as an anti-dyslipidemic agent. This study will focus on measuring total serum cholesterol (TC) and MDA level in liver dyslipidemic rats after the intervention of synbiotic drink of Stelechocarpus burahol with Lactobacillus casei and Lactobacillus plantarum isolates.
Materials and Methods: A randomized controlled group was conducted on twenty-five rats divided into five groups. The negative control group (K-) and interfered group (P1, P2, P3) were fed a high-fat diet for four weeks, while the normal group was given a standard diet. Lipid profile measurement was conducted on the rats to ensure that the rats (negative control group, P1, P2, and P3) had contracted dyslipidemia. Then, synbiotic drinks were given to the interfered group at various dosages (P1 = 1.2; P2 = 1.8; P3 = 2.4) ml/day for four weeks. At the end of the study, the rats were terminated, then serum TC was measured, and MDA level measurement was conducted on liver tissue.
Results: The mean of serum TC (mg/dL) were 98.26 ± 2.32 (normal group), 213.33 ± 2.65 (K-), 148.99 ± 3.79 (P1), 116.81 ± 2.68 (P2), 104.35 ± 2.79 (P3). Then, the liver MDA level (nmol/gram) were 3.99 ± 0.28 (normal group); 11.40 ± 0.45 (K-); 7.12 ± 0.12 (P1); 5.49 ± 0.25 (P2); 4.98 ± 0.27 (P3). One-way ANOVA with post hoc bonferroni test showed significant differences between all groups (p-value < 0.05) except the liver MDA level between P2 group and P3 group (p-value = 0.126). Bivariate Pearson correlation coefficient showed positive correlation between serum total cholesterol and liver MDA level (r = 0.98, p-value = 0.00).
Conclusion: This study suggests a positive correlation between serum total cholesterol and liver damage status with a significant linear relationship.



Scatter Plot Pearson Correlation Between Total Cholesterol and Liver MDA Level

[L-OP-1344]

Comparison effect of fermented and non-fermented yoghurt to the liver function test of the hyperlipidemia rats

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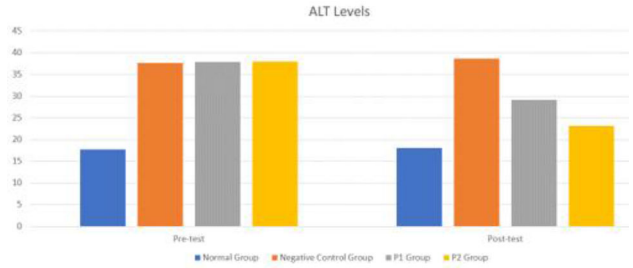
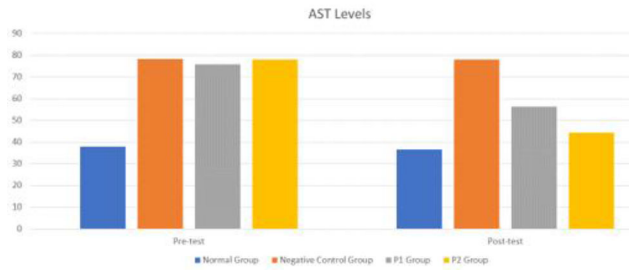
Objectives: Studies have shown that nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease and strongly associated with dyslipidemia condition. Both, ALT and AST are the common liver enzymes which together comprises liver function tests. Diet modification can be used as the one of modality to treat NAFL-associated dyslipidemia. Yoghurt in a form of fermented or non-fermented nowadays proved as an anti-dyslipidemia agent. Thus, this recent study would to compare the effect of fermented and non-fermented yoghurt to the level of ALT and AST in dyslipidemia rats.
Materials and Methods: This study utilized pre-test and post-test randomized control group design. The rats were divided into four groups. After one-week acclimatization the normal group was fed by standard diet 20 g/day, while the negative control group and interfered groups (P1 for fermented yoghurt and P2 for non-fermented yoghurt) were fed by high-fat diet for two weeks. The lipid profiles were checked to ensure the negative control group and interfered groups contracted dyslipidemia prior to receiving yoghurt 5 mL/day for four weeks. The ALT and AST were checked on day-22 and day-36 of the study.
Results: All the data were expressed as mean (u/l) of ALT and AST levels. One-way ANOVA and post-hoc Bonferroni test showed significant differences of ALT and AST level between all groups before and after given yoghurt with the p-value = 0.000 ($p < 0.05$) except between negative group, P1, and P2 in pre-test that showed no significant result. The paired sample test shown, there were significant differences in the level of ALT nor ALT before and after intervention of yoghurt in P1 and P2.
Conclusion: Both, fermented and non-fermented yoghurt can improve significantly the level of ALT and AST after two-weeks intervention without any significant differences among them.





Fibrosis and cirrhosis

[PP-0036]

FIB-4 index is not suitable for non-invasive assessment of liver fibrosis in the hospitalized type 2 diabetes patients

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Objectives: Liver fibrosis is the predictive factor for liver-related events and prognosis in patients. A liver biopsy is a gold standard for identifying fibrosis. However, it has several drawbacks, including sample error, expense, and the possibility of complications. The FIB-4 index as a non-invasive scoring system is a low-cost, noninvasive measure of hepatic fibrosis. This study aimed to the assessment of liver fibrosis among hospitalized type 2 diabetes patients.

Materials and Methods: The cross-sectional study was conducted in our study. The data from 523 medical records with T2DM patients (aged 18–85 years) were collected retrospectively in the Republican Specialized Scientific Center of Endocrinology in Tashkent and Ferghana regional Endocrinological Dispensary (n the Republic of Uzbekistan. The distribution of the FIB-4 index in the entire study sample (N = 523) and subjects with non-alcoholic fatty liver disease (NAFLD population; N = 320) was evaluated.

Results: The mean FIB-4 index in the entire study sample was 1.30 ± 0.83. FIB-4 index ≥ 2.67, which indicates a high risk of liver fibrosis. FIB-4 index ≥ 2.67 was found in 4.2% (95% CI: 3.85–4.95%) of individuals among the study sample (N = 523, Fig. 1). The prevalence of advanced fibrosis (FIB-4 > 2.67) among NAFLD patients (n = 320) was 4.4% and NAFLD patients (n = 203) was 3.9% by using the FIB-4 index (Fig. 2). The advanced fibrosis was higher among the NAFLD group (4.4%) than without the NAFLD group (3.9%), but it was not statistically significant (p = 0.965).

Conclusion: FIB-4 scores are not suitable for use in clinical practice in type 2 diabetes patients for assessment of hepatic fibrosis and require another fibrosis score.

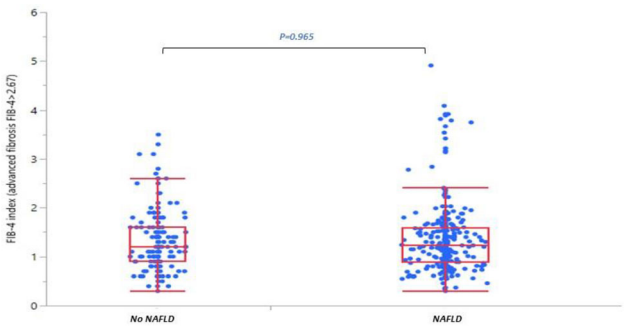

Figure 2. Distribution of advanced fibrosis (FIB-4 >2.67) in NAFLD and not NAFLD patients (N=523)

[PP-0051]

Value of the model for end-stage liver disease-GFR assessment in liver disease-sodium (MELD-GRAIL-Na) for predicting mortality in Korean patients with liver cirrhosis

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Objectives: Child–Pugh score and The Model for End-Stage Liver Disease (MELD) are classical systems for prediction of mortality in patients with liver cirrhosis (LC). The Model for End-Stage Liver Disease-GFR assessment in liver disease-Sodium (MELD-GRAIL-Na) were introduced in 2020 and was designed to reflect better renal function and therefore providing better mortality prediction. We aimed to validate the MELD-GRAIL-Na against the Child–Pugh

score and MELD for the prediction of short-term (1 month, 3 month) mortality in Korean patient with LC.
Materials and Methods: Medical records of LC patients who were admitted to Konkuk university hospital from 2015 to 2020 were retrospectively reviewed. Predictive values for 1 month mortality and 3 month mortality of Child–Pugh, MELD and MELD-GRAIL-Na score were calculated by area under the receiver operating curve (AUROC) and their comparison was performed by DeLong's test.
Results: Total of 1,249 patients were enrolled and 102 (8.2%) died in 1 month, 146 (11.7%) in 3 month. Alcohol was most common etiology of LC. The AUROCs of Child–Pugh score, MELD, MELD-GRAIL-Na for 1 month mortality were 0.831, 0.848, 0.836, and that for 3 month mortality were 0.837, 0.827, 0.815, respectively. The significant differences were found between MELD and MELD-GRAIL-Na for 1 month ($P = 0.0888$) and for 3 month ($P = 0.0395$).
Conclusion: MELD-GRAIL-Na was designed to reflect better GFR than serum creatinine in LC patients, expecting to predict better mortality rates. But in our study with Korean patients, MELD-GRAIL-Na was inferior predictor for mortality than Child–Pugh score and MELD.

[PP-0052]

Validation of the model for end-stage liver disease-lactate (MELD-La) for predicting mortality in Korean patients with liver cirrhosis

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Objectives: There were many efforts to predict mortality of patients with liver cirrhosis (LC). Child–Pugh and Model for End-Stage Liver Disease (MELD) are well known systems for prediction of mortality in patients with LC. In 2020, MELD-Lactate (La) was introduced, modifying MELD with lactate to predict better inpatient mortality. We aimed to evaluate the superiority of MELD-La over Child–Pugh, MELD for prediction of in-hospital mortality and 3 month mortality in Korean patients with LC.
Materials and Methods: Retrospective review of medical records was performed for patients with LC, who were admitted to Konkuk University Hospital from 2015 to 2020. Predictive values for In-hospital and 3 month mortality of Child–Pugh, MELD, and MELD-La score were calculated by area under the receiver operating curve (AUROC) and comparison was performed by DeLong's test.
Results: Total of 529 patients were enrolled and 60 (11.3%) died in-hospital and 92 (17.4%) died within 3 months. Alcohol was most common etiology of LC. AUROCs of Child–Pugh, MELD, MELD-La for in-hospital mortality were 0.792, 0.810, 0.801, and that for 3 month mortality were 0.806, 0.806, 0.784, respectively. MELD-La was reliable predictor of in-hospital mortality ($P < 0.0001$) and 3 month mortality ($P < 0.0001$), but it did not prove to be better predictor than Child–Pugh and MELD ($P > 0.05$).
Conclusion: As serum lactate level reflects hypoperfusion of tissues and decreased lactate clearance, MELD-La was introduced as a better predictor of mortality in LC patients. But in our study of Korean patients with LC, superiority of MELD-La was both numerically and statistically not better than predisposing tools.

[OP-0091]

A unique immune-related gene signature represents advanced liver fibrosis and reveals potential therapeutic targets

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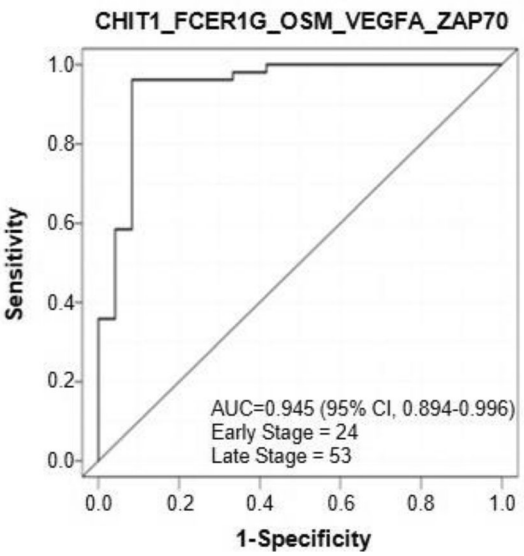
Objectives: Innate and adaptive immune responses are critically associated with fibrosis progression in chronic liver diseases. In this study, we aimed to identify a unique immune-related gene signature representing advanced liver fibrosis and to reveal potential therapeutic targets.
Materials and Methods: Seventy-seven, snap-frozen benign liver tissues with various chronic liver diseases in the different fibrosis stages (1: n = 12, 2: n = 12, 3: n = 25, 4: n = 28) were subjected to the expression analyses. Gene expression analysis was performed using the nCounter PanCancer Immune profile Panel (Nanostring Technologies, Seattle, WA, USA). Biological meta-data analysis was performed using meta-analysis program, CBS Probe PINGS^{TM} (CbsBioscience, Daejeon, KOR).
Results: Using non-tumor tissues from surgically resected specimens, we identified the immune-related, five-gene signature (CHIT1_-FCER1G_OSM_VEGFA_ZAP70) that reliably differentiates patients with low grade fibrosis (F1 and F2) and those with high grade fibrosis (F3 and F4) (accuracy = 94.8%, specificity = 91.7%, sensitivity = 96.23%). The signature was independent of all pathological and clinical features, and was independently associated with high-grade fibrosis by multivariate analysis. Among these genes, the expression of FCER1G, OSM, VEGFA, and ZAP70 was lower in high grade fibrosis than in low grade fibrosis, whereas the expression of CHIT1, which is associated with fibrogenic activity of macrophages, was higher in high grade fibrosis. Meta-data analysis revealed that STAT3, a potential druggable target, was highly interacting genes with the five gene signature.
Conclusion: Overall, we identified the immune gene signature that reliably predicts the advanced fibrosis in chronic liver diseases. This signature reveals the potential immune therapeutic targets to ameliorate liver fibrosis.



[PP-0157]

Using novel nanosensor-based microRNA detection and amplification technique, whole blood circulating microRNA levels can predict liver cirrhosis

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Objectives: Accurate prediction of liver cirrhosis is important for clinical decision making and disease management. This study aimed to evaluation the value of whole blood circulating levels of microRNA (miRNA)-A* and miRNA-B* as novel noninvasive biomarkers in prediction of cirrhosis in patient with liver disease. (*We cannot provide exact name of microRNAs before patent application.)
Materials and Methods: Total 38 patient with clinically diagnosed liver disease were analyzed. Among them, 7 patients of cirrhosis included. The whole blood circulating levels of miRNA-A and miRNA-B were quantified using nanosensor-based miRNA detection and amplification method. Receiver operating characteristic curve analysis was performed to evaluate the sensitivity and specificity of the miRNAs for prediction of cirrhosis.
Results: Compare to various qPCR-based miRNA analyses that are currently available, which generally require cDNA synthesis, the nanosensor-based miRNA detection method used in the study directly recognizes target miRNAs before amplification. By applying this method, we found that circulating miRNA-A levels were significantly downregulated in cirrhosis patients compared to those without fibrosis (Metavir stage F0) ($p = 0.009$). Likewise, circulating miRNA-B levels showed downregulated tendency in cirrhosis patients compared to those without fibrosis ($p = 0.076$). Receiver operating characteristic curve analysis revealed that both serum miRNA-A and miRNA-B levels were associated with high diagnostic accuracy for patients with cirrhosis (0.852, $p = 0.025$ and 0.815, $p = 0.045$, respectively).
Conclusion: Our results indicate that whole blood circulating levels of miRNA-A and miRNA-B by using nanosensor-based miRNA detection and amplification method might be useful non-invasive biomarker for prediction of cirrhosis in patient of liver disease.

[PP-0175]

Annexin A2 is a potential therapeutic target for liver fibrosis and hepatocellular carcinoma

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Objectives: Liver fibrosis is the main cause in the occurrence and development of hepatocellular carcinoma (HCC), however anti-fibrotic therapeutic options are still limited. Annexin A2 (ANXA2) plays an important role in inflammation and cancer development. However, the role of ANXA2 in liver fibrosis remains unknown. We sought to explore the effect of ANXA2 on liver fibrosis and HCC development.
Materials and Methods: We evaluated the association between ANXA2 expression and liver fibrosis related to hepatitis B/C virus (HBV/HCV) infection, alcohol abuse and non-alcoholic fatty liver disease (NAFLD), as well as the association between ANXA2 expression and HCC in different Ishak stages of liver fibrosis. Liver fibrogenesis mouse model induced by carbon tetrachloride (CCl_4) and bile duct ligation were used to analyze the role of ANXA2 in liver fibrogenesis and its cell localization. We also preliminarily explored the role of ANXA2 in HCC development with the background of liver fibrosis. LX-2 cells knockdown of ANXA2 were used to analyze the activation, proliferation and migration of hepatic stellata cells (HSCs).
Results: We found that ANXA2 expression were increased in HCC patients with liver fibrosis and liver fibrosis/cirrhosis patients from different etiologies, including HBV or HCV infection, alcohol abuse, and NAFLD. Moreover, ANXA2 as a predictor of poor prognosis for HCC. Furthermore, we detected expression of ANXA2 were increased in hepatic fibrosis septa and non-parenchymal cells in both liver fibrosis mouse models. Functionally, ANXA2 knockdown suppressed cell proliferation, activation and migration in LX-2 cell.
Conclusion: Our findings demonstrate ANXA2 might be a novel target for prediction and treatment of liver fibrosis and HCC because of its significance in HSCs activation and liver fibrogenesis.

[PP-0180]

Comparison of the AIMS65 to liver severity score in predicting mortality and rebleeding in liver cirrhosis patients with acute variceal bleeding

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Objectives: Acute variceal bleeding (AVB) remains a common and life-threatening complication in patients with liver cirrhosis. It remains unclear, whether measures of liver disease severity or upper gastrointestinal bleeding (UGIB) risk stratification algorithms offer superior predictive ability. We evaluated the ability of various UGIB risk stratification scores including AIMS65 and compared with liver severity as predictors of mortality and rebleeding.
Materials and Methods: We retrospectively enrolled 122 patients with liver cirrhosis and AVB at the Daejeon St. Mary's hospital from April 2014 to March 2021. We collected data at the time of acute variceal bleeding. Patients were risk stratified using AIMS65, ABC, Child–Pugh, Model for End-stage Liver Disease (MELD) scores. Primary outcomes were overall survival and rebleeding.
Results: Liver function showed child A, B, and C (32.7%, 40.9%, and 26.2% respectively). 1-month mortality showed 12.2%. Child class, MELD grade, AIMS65, and carvedilol showed significant stratification of 1Month-Mortality except ABC score ($P < 0.001$, 0.015, < 0.001, and 0.007 but $P = 0.353$). The mean OS of AIMS65 grade1, grade2, and grade3 patients were 72.9, 40.3, and 28.9 months, respectively ($P < 0.001$). The ABC, child class, and MELD also significantly showed survival difference ($P = 0.025$, $P = 0.003$, and $P = 0.000$, respectively). However, AIMS65, ABC, child class, and MELD did not predict rebleeding risk ($P = 0.655$, $P = 0.548$, $P = 0.180$, and $P = 0.160$, respectively). On the other hand, treatment of carvedilol showed survival benefit and reduced rebleeding rates ($P = 0.001$, 0.021, respectively). In a multivariate analysis, the AIMS65 and carvedilol treatment were significant predictive factors for OS ($P = 0.006$, 0.000, respectively).
Conclusion: AIMS65 is superior to established UGIB and liver disease severity risk stratification scores in predicting mortality of cirrhotic patients with AVB. In addition, carvedilol treatment reduced overall mortality and rebleeding. Therefore, application of AIMS65 score and treatment of carvedilol may show more favorable clinical outcome in patients with AVB.

[PP-0187]

Prevalence and risk factors of erectile dysfunction in male patients with cirrhosis

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Objectives: Erectile dysfunction (ED) is discouraging problem which significantly depresses quality of life of individuals. However, there are inadequate studies about ED accompanied by liver cirrhosis yet. This study aims to evaluate prevalance and risk factors of ED in male patients with liver cirrhosis.
Materials and Methods: We prospectively enrolled sexually active male cirrhotic patients from 2020 to 2021 (n = 104). Recruited patients were asked to fulfill International Index of Erectile Function (IIEF-15) questionnaire and they were classified as ED patients if their scores were < 14. Then we compared ED and non-ED group within enrolled patients. Transient elastography (TE, FibroScan(®)) was also performed to entire subjects.
Results: Mean age of total patients was 55.0 ± 8.3 years. The prevalence of ED was 37.5% (n = 39). Mean value of serum albumin level of non-ED group was 3.9 ± 0.8 g/dL and of ED group was 3.6 ± 0.8 g/dL ($p = 0.048$). Additionally, both free serum testosterone level and TE-measured liver stiffness showed statistically borderline differences between two groups (7.6 ± 2.4 ng/dL vs 6.7 ± 3.0 ng/dL, $p = 0.097$; 24.4 ± 22.6 kPa vs 32.5 ± 26.4 kPa, $p = 0.098$). However, coexistence of diabetes, hypertension, and hyperlipidemia didn't made any significant difference.
Conclusion: The prevalence of ED was 37.5% in sexually active male liver cirrhosis patients. Possible risk factors were serum albumin level, serum free testosterone level, and degree of fibrosis which was measured by TE.

[PP-0206]

The association between hepatic encephalopathy and sarcopenia after sedation endoscopy in liver cirrhosis patients and a drug to prevent hepatic encephalopathy after sedation endoscopy

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Objectives: Cirrhosis patients often show worsening of hepatic encephalopathy after sedation esophagogastroduodenoscopy (EGD). Also, Sarcopenia is associated with mortality of cirrhosis patients, sarcopenia can be predicted by measuring psoas muscle thickness per height (PMTH). The purpose of this study is to evaluate the degree of hepatic encephalopathy according to the drugs (midazolam, propofol) used during sedation EGD in cirrhosis patients and to investigate the relationship between hepatic encephalopathy and PMTH.
Materials and Methods: From April 2018 to August 2021, number connection test (NCT) was performed before and after EGD for cirrhosis patients. When performing sedation EGD, the tests were divided into three groups (propofol, midazolam, combined propofol + midazolam). In addition, by measuring the patient's PMTH, the correlation with PMTH and NCT was investigated.
Results: A total of 134 cirrhotic patients underwent EGD during the study period. The difference in NCT values before and after EGD was defined as delta NCT. Delta NCT were 4.27 ($\pm$ 14.40) seconds in propofol group (n = 50), 10.98 ($\pm$ 16.48) seconds in midazolam group (n = 32), and 12.19 ($\pm$ 16.71) seconds in combined group (n = 52), showing the worst in combined group ($P = 0.014$). In decompensated cirrhosis group, delta NCT was 3.61 ($\pm$ 14.075) seconds in propofol group, 12.76 ($\pm$ 19.448) seconds in midazolam group, and 17.58 ($\pm$ 21.311) seconds in combined group. Although there was no statistical significance, when decompensated cirrhosis group using combined drugs, delta NCT difference worsened compared to the whole group ($P = 0.077$). The average of the measured PMTH was 3.57 (mm/m), which did not show significant correlation with delta NCT ($P = 0.14$).
Conclusion: The use of propofol alone during EGD in cirrhotic patients is effective in preventing worsening of hepatic encephalopathy. In decompensated cirrhosis patients, combination of propofol and midazolam has a greater effect on exacerbation of

hepatic encephalopathy. There are limitations in predicting the degree of exacerbation of hepatic encephalopathy in EGD with PMTH.

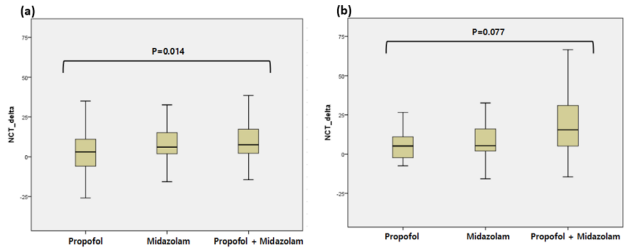

Fig 1. The difference in NCT values before and after EGD was defined as delta NCT. (a) All patients group (b) In decompensated cirrhosis patients group.

[OP-0211]

The Chinese herbal JianPiHuaZhuoXingNao formula treated minimal hepatic encephalopathy by regulating the brain-gut-peptide axis in a rat model

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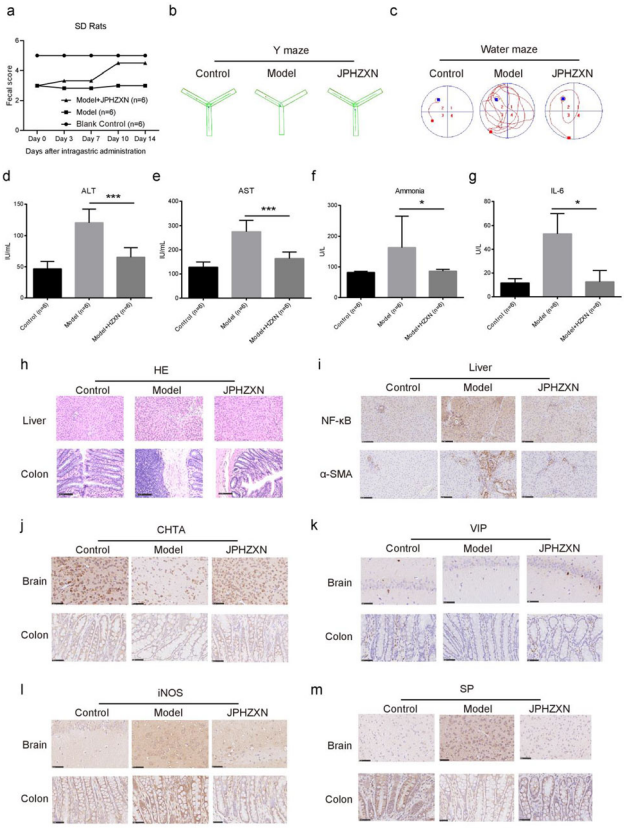
Objectives: The Chinese herbal JianPiHuaZhuoXingNao formula (JPHZXN) has been proven effective for the minimal hepatic encephalopathy (MHE) in clinical trials. Here, we evaluated the curative effect of JPHZXN on MHE rats and explored the regulating mechanism on brain-gut-peptide axis.
Materials and Methods: The MHE rat model was established by intragastric administration of 50% CCl4 and olive oil mixture with 6-week-old male Sprague Dawley rats. Then, the MHE rats were treated with JPHZXN (n = 6) for 2 weeks. The rats' behavioral changes, general situation, Bristol fecal score were recorded and evaluated. The serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), Ammonia, IL-6, and TNF-α were measured. The hematoxylin and eosin staining (HE) of liver and colon tissues were performed. and the expression of α-SMA, NF-κB, choline acetyltransferase (CHTA), vasoactive intestinal peptide (VIP), nitric oxide synthase (iNOS), and substance P (SP) in tissues were detected by immunohistochemical staining (IHC).
Results: Compared to the model group, the JPHZXN-treated rats had less time of water maze, higher scores of Y maze and fecal analysis. The serological levels of ALT, AST, Ammonia, and IL-6 significantly decreased in the JPHZXZ group. The HE and IHC results showed less inflammatory damage in liver and colon tissues and downregulated expression of α-SMA and NF-κB after JPHZXN treatment. As for the brain-gut-peptide axis related targets, with JPHZXN treatment, the expression of iNOS decreased, VIP and CHTA increased in brain and colon tissues; while SP decreased in brain tissue and increased in colon tissues.
Conclusion: Our study suggested that JPHZXN treatment could improve survival status included general conditions, spatial cognition, and memory, and reduced tissue damages of liver and colon in MHE rats. This therapeutic effect of JPHZXN on MHE relied on the regulating of the brain-gut-peptide axis. Furthermore, these results provided a basis for JPHZXN's further clinical applications.



[PP-0249]

Clinical usefulness of serum M2BPGi levels on identifying liver cirrhosis in patients with chronic liver disease

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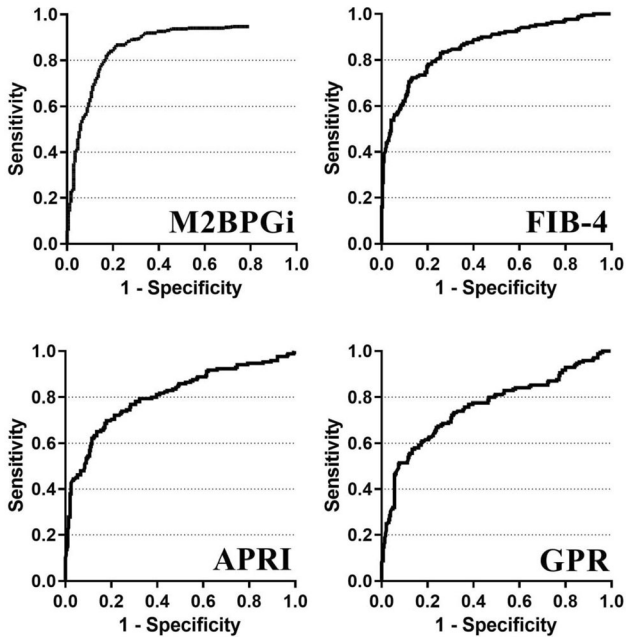
Objectives: Mac-2 Binding Protein Glycosylation isomer (M2BPGi) is a novel serological glyco-biomarker for predicting liver fibrosis. However, there was lack of data to use M2BPGi in Korean patients with chronic liver diseases. We aimed to evaluate its role of diagnosing liver cirrhosis (LC) in Korean patients.
Materials and Methods: We reviewed medical records for 258 patients that were performed serum M2BPGi in Kosin University Gospel Hospital from January 2016 to October 2018. The diagnostic accuracy of serum M2BPGi values was compared to that of other fibrosis markers, the aspartate transaminase to platelet ratio index (APRI), the fibrosis index based on four factors (FIB-4), and the gamma-glutamyltranspeptidase to platelet ratio (GPR) using receiver operating characteristic (ROC).
Results: The mean (± SD) of age of study patients was 61.2 (± 10.6) years and the proportion of male was 73.6%. 103 (39.9%) patients were positive for hepatitis B virus (HBV) and 45 (17.4%) were positive for hepatitis C virus (HCV). 178 (69.0%) patients were diagnosed LC. The mean (± SD) of serum M2BPGi level showed significant differences between LC group (5.06 ± 3.89) and non-LC group

(1.77 ± 2.64) (P < 0.001). The M2BPGi levels correlated with APRI (r = 0.444), FIB-4 (r = 0.512), GPR (r = 0.155), respectively (all P < 0.001). The area under the curve of serum M2BPGi for prediction of LC (0.798) was higher than that of APRI (0.714), FIB-4 (0.767) and GPR (0.635), respectively. The cutoff value of serum M2BPGi that maximized the sum of sensitivity (80.3%) and specificity (71.2%) was 1.72. Adjusting for sex, age, alcohol intake, HBV and HCV, M2BPGi level was an independent predictor of LC [adjusted odds ratio (OR): 1.51, 95% confidence interval (CI) 1.30–1.75, P < 0.001].
Conclusion: Serum M2BPGi could be a reliable non-invasive marker for identifying LC in Korean patients with chronic liver diseases.



[PP-0257]

The association between ALBI grade and in-hospital mortality in liver cirrhotic patients with gastroesophageal variceal bleeding

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Objectives: To evaluate the association between albumin-bilirubin (ALBI) grade and in-hospital mortality in liver cirrhotic patients with gastroesophageal variceal bleeding.
Materials and Methods: We performed a retrospective cohort study of 171 liver cirrhotic patients who were admitted with gastroesophageal variceal bleeding. The clinical and laboratory data were recorded, including the ALBI score. Univariate and multivariate logistic regression analyses were performed to identify the independent risk factors of in-hospital mortality.
Results: From 171 patients, mostly male (76%), mean age of 53 years old, with a median Child–Pugh score of 7. Fourteen patients (8,2%) died during hospitalization. The percentage of patients with ALBI grade 3 was higher in non-survivor vs. survivor (85,7% vs 37.5%). The independent risk factors of in-hospital mortality were ALBI grade 3 (versus grade 1 and 2) (adjusted OR: 9,46[1,67–53.49];p = 0.011), and age (adjusted OR: 1.1[1.04–1.19]; p = 0.002).
Conclusion: ALBI grade 3 and age were independent risk factors of in-hospital mortality in liver cirrhotic patients with gastroesophageal variceal bleeding.

[OP-0274]

The effect of sarcopenia on survival of patients with cirrhosis: A systematic review and meta-analysis

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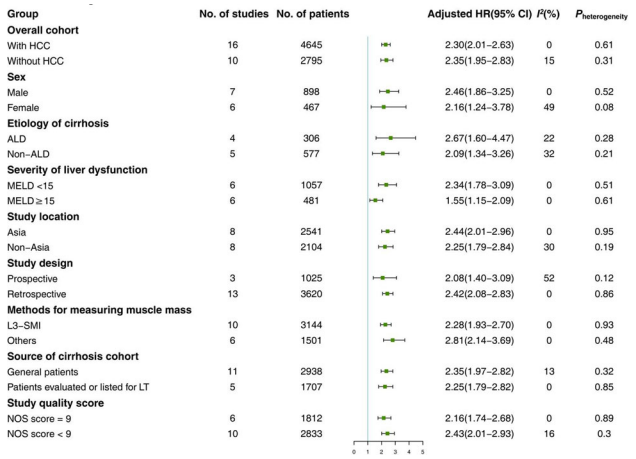
Objectives: The association between sarcopenia and prognosis in patients with cirrhosis remains to be determined. In this study, we aimed to quantify the association between sarcopenia and the risk of mortality in patients with cirrhosis, by sex, underlying liver disease etiology, and severity of hepatic dysfunction.
Materials and Methods: PubMed, Web of Science, EMBASE, and major scientific conference sessions were searched without language restriction through 13 January 2021 with additional manual search of bibliographies of relevant articles. Cohort studies of ≥ 100 patients with cirrhosis and ≥ 12 months of follow-up that evaluated the

association between sarcopenia, muscle mass and the risk of mortality were included.
Results: 22 studies with 6965 patients with cirrhosis were included. The pooled prevalence of sarcopenia in patients with cirrhosis was 37.5% overall (95%CI 32.4–42.8%), higher in male patients (41.9%), patients with alcohol associated liver disease (ALD)(49.6%), patients with CTP grade C (46.7%), and when sarcopenia was defined in patients by lumbar 3- skeletal muscle index (L3-SMI) (44.4%). Sarcopenia was associated with the increased risk of mortality in patients with cirrhosis (adjusted-hazard ratio [aHR] 2.30, 95% CI 2.01–2.63), with similar findings in sensitivity analysis of cirrhosis patients without HCC (aHR 2.35, 95% CI 1.95–2.83) and in subgroup analysis by sex, liver disease etiology, and severity of hepatic dysfunction (Fig. 1). The 1-, 3-, and 5-year cumulative probabilities of survival in patients with sarcopenia were 76.6%, 64.3%, and 45.3%, compared to 93.4%, 82.0%, and 74.2%, respectively in patients without sarcopenia (all $P < 0.001$). The association between quantitative muscle mass index and mortality further supports the poor prognosis for patients with sarcopenia (aHR 0.95, 95% CI 0.93–0.98).
Conclusion: Sarcopenia was highly and independently associated with higher risk of mortality in patients with cirrhosis.



[PP-0329]

Myostatin and decorin level decrease after treatment with direct acting antivirals

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Objectives: Myostatin is secreted from skeletal muscle cells and belong to transforming growth factor β (TGF-β) family which has been reported as a key mediator of fibrosis in several organs. It negatively works for differentiation of skeletal muscle cells, furthermore, recent study showed higher myostatin level in liver cirrhosis associated with unfavorable outcome. Decorin is small leucine-rich proteoglycan, and decorin peptide has been reported to suppress myostatin/smad signal pathway. The aim of this study to elucidate whether HCV eradication by direct acting antivirals (DAA) associate with sarcopenia in cirrhotic patient.
Materials and Methods: Patient with liver cirrhosis type C (n = 120) were enrolled in this study, and we measured serum myostatin and decorin level before DAA treatment and SVR 48 by ELISA method. We analyzed correlation between myokines and clinical parameters.
Results: Median age before treatment was 71.5 (63–92) year, the number of female patients was 71 (59%). Serum myostatin level significantly decreased after DAA treatment (before treatment 7892 pg/ml vs SVR 48 6122 pg/ml, $p < 0.001$), and decorin level also showed similar result (before treatment 12,164 pg/ml vs SVR 48 7834 pg/ml, $p < 0.001$). Multivariate analysis associated with myostatin level before treatment showed that female ($\beta = -0.193$. $p = 0.014$), BMI ($\beta = 0.194$, $p = 0.015$), M2BPGi ($\beta = 0.215$, $p = 0.014$), and decorin ($\beta = 0.221$, $p = 0.010$) were independent factor. On the other hands, multiple regression analysis showed that T-Bil ($\beta = -0.310$, $p = 0.001$), AFP ($\beta = 0.301$, $p < 0.001$), AST ($\beta = 0.247$, $p = 0.002$), and myostatin ($\beta = 0.214$, $p = 0.018$) were associated with decorin level at before treatment.
Conclusion: After DAA treatment, serum myostatin and decorin level significantly decreased. The results of multivariate analysis suggest that the decrease in decorin may reflect improvement of hepatitis. It was suggested that the reduction of myostatin by HCV eradication may contribute to the improvement of sarcopenia.

[PP-0355]

Nutritional status assessment, sarcopenia in liver cirrhosis patients

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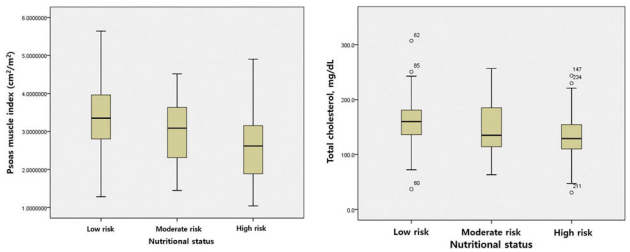
Objectives: Nutritional status assessment and Sarcopenia are important for predicting the prognosis of liver cirrhosis (LC) patients. The Royal Free Hospital Nutritional Prioritizing Tool (RFH-NPT) is a well-validated screening tool to assess the nutritional status of LC patients. Sarcopenia is a major problem related to poor prognosis of LC patients. Psoas Muscle Index is an imaging marker of sarcopenia. and Blood Total Cholesterol (TC) is classical parameters used as a marker of malnutrition. The aim of this study was to assess the nutritional status of LC patients using RFH-NPT and TC, as well as the correlation with muscle mass.
Materials and Methods: We conducted the RFH-NPT to LC patients in Kosin University Gospel Hospital from January 2020 to April 2021. The Psoas Muscle Index (PMI) was measured using abdominal CT scan performed within 3 months. The RFH-NPT were conducted in 275 LC patients. Ten patients who did not perform abdominal CT scans within the last 3 months were excluded, and then a total of 265 patients were enrolled.
Results: The mean (± SD) age of study population was 61.62 (± 10.23) years and the proportion of male was 77.7%. One hundred sixty-nine (63.8%) patients had Child–Pugh grade A, 59 (22.3%) patients had grade B, and 37 (14.0%) patients had grade C. The mean (± SD) BMI of study population was 23.60 (± 4.01) kg/m^2, the PMI was 2.94 (± 0.94) cm^2/m^2. The results of RFH-NPT showed low risk

in 126 (48.0%) patients, moderate risk in 40 (15.0%), and high risk in 99 (37.0%), respectively. PMI showed significant differences according to nutritional status of RFH-NPT ($P < 0.001$) and total cholesterol ($P < 0.001$).

Conclusion: Based on the results of RFH-NPT, 48.0% of LC patients needed nutritional support. High-risk patients were significantly associated with Sarcopenia.



[PP-0381]

Relationship between diabetes, prediabetes, and the risk of liver fibrosis

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Objectives: This study aimed to assess the risk of liver fibrosis between no glucose intolerance, prediabetes and diabetes in the general population.

Materials and Methods: A cross-sectional study was conducted based on a cohort from a health examination program which included a magnetic resonance elastography (MRE). The participants were classified into three subgroups according to glucose tolerance: no glucose intolerance, prediabetes and diabetes mellitus. Liver fibrosis was evaluated by liver stiffness measurement (LSM) value using 2-dimensional real-time MRE. The risk of liver fibrosis was compared after adjusting for confounding factors including the presence of liver disease (nonalcoholic fatty liver disease, significant alcohol consumption and viral hepatitis).

Results: A total of 2,090 subjects was included: no glucose intolerance (n = 889); prediabetes (n = 985); and diabetes (n = 216). The mean age was 50.6 years. The mean values of LSM in no glucose intolerance, prediabetes, and diabetes were 2.37 ± 0.43 kPa, 2.41 ± 0.34 kPa, and 2.65 ± 0.70 kPa, respectively ($p < 0.001$). The proportion of significant fibrosis (LSM $\geq$ 2.97 kPa) in no glucose intolerance, prediabetes, and diabetes was 3.1%, 4.4%, and 16.7%, respectively ($p < 0.001$). Compared with no glucose intolerance, the risk of significant fibrosis was higher in diabetes (adjusted odds ratio [aOR] 3.37, 95% confidence interval [CI] = 1.78–6.40, $p < 0.001$). However, there was no difference between prediabetes and no glucose intolerance (aOR 0.94, 95% CI = 0.54–1.64, p = 0.940). A subgroup analysis also showed that prediabetes is not associated with significant fibrosis unlike diabetes in subjects with or without liver disease.

Conclusion: Diabetes but not prediabetes is a risk factor for significant liver fibrosis regardless of the pressence of liver disease.

[OP-0387]

The Chinese herbal GeXiaZhuYu decoction inhibited the occurrence of liver cirrhosis by regulating the activity of hepatic stellate cells and the expression of key targets

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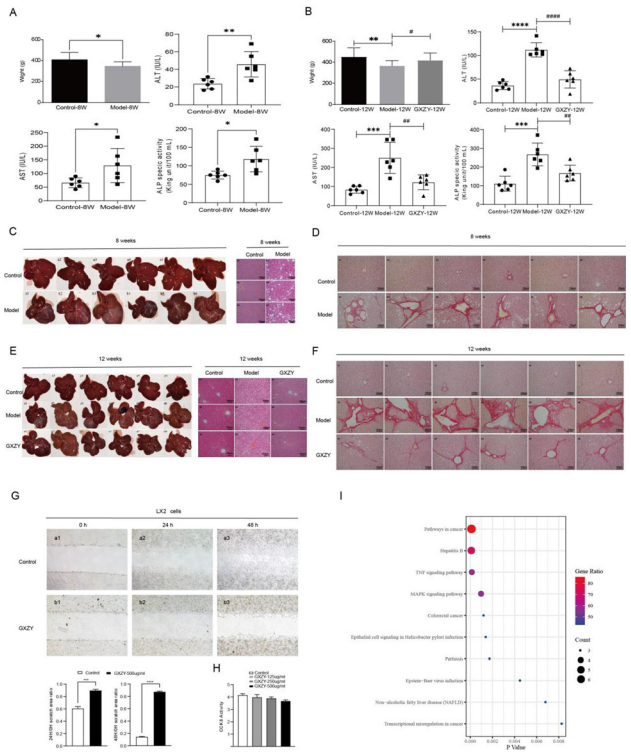
Objectives: The Chinese herbal GeXiaZhuYu Decoction (GXZY) has a therapeutic effect on liver cirrhosis (LC) in clinical trials. Here, we evaluated the curative effect of GXZY on LC rats and LX2 cells, and explored the mechanism combined network pharmacology approach.

Materials and Methods: The LC rat model was established by intraperitoneal injection of 50% CCl4 and olive oil mixture for 8 weeks with 6-week-old male Sprague Dawley rats. Then, the LC rats were treated with GXZY (n = 6) for 4 weeks. The rats' weight, liver injury, and intrahepatic collagen deposition were recorded and evaluated. The serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) were measured. The cell viability and migration capacity of LX2 cells with GXZY treatment were detected by CCK-8 and cell scratch assays. The potential targets of GXZY and LC were obtained from public databases. The Cytoscape software and pathway enrichment analysis were further performed to construct the interaction network, obtain the key targets and pathways.

Results: Compared to the model group, after treatment, the weight of GXZY-treated rats was heavier. The lower levels of serum ALT, AST, and ALP in the GXZY group were observed. The HE staining and Sirius red staining results showed less inflammatory damage and collagen deposition in liver tissues after GXZY treatment. Moreover, GXZY treatment inhibited the proliferation and migration abilities of LX2 cells. Network pharmacology analysis results suggested the key molecules of GXZY on LC were AR, JUN, MYC, CASP3, MMP9, and RELA, and mainly related to pathways in Cancer, Hepatitis B, TNF signaling pathway, and MAPK signaling pathway.

Conclusion: Our study suggested that GXZY exerted an inhibition effect on LF might by regulating the activity of hepatic stellate cells and expression of the key targets included AR, JUN, MYC, CASP3, MMP9 and, RELA.



[PP-0389]

Does altered levels of trace elements in liver cirrhosis patients correlate with severity index of the disease?

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Objectives: The present study was undertaken to evaluate the levels of trace elements in the blood of Liver Cirrhosis Patients and to assess their association with the severity of the disease.
Materials and Methods: 150 Cirrhotic subjects of either sex ranging in age from 20–70 years were included in the study and the results were compared with 50, age and sex-matched healthy control subjects. All Cirrhotic subjects were assessed for severity of disease as Mild (Child A), Moderate (Child B), and Severe (Child C) as per Child–Pugh classification. Trace elements (Cu, Zn, Se & Mg) were analyzed on Atomic Absorption Spectrophotometer.
Results: Serum level of Copper was found significantly increased in patients with liver cirrhosis as compared to the control group (Mean ± SD, 132.84 ± 12.02 v/s 100.11 ± 17.21 µg/dl, $p < 0.001$). Whereas Serum Zinc, Selenium, and Magnesium levels were significantly decreased in Cirrhotic subjects as compared to controls ($p < 0.001$). Trace elements were compared with the severity of liver cirrhosis. Serum Copper concentration was slightly increased in patients with a more severe clinical state of liver cirrhosis, however, the mean level difference of Copper among the Child–Pugh groups was statistically not significant ($p > 0.05$). Moreover, there was no significant correlation between Copper and Child–Pugh Score. Serum Zinc, Magnesium, and Selenium levels were significantly decreased with the advancement of liver disease as compared to the early stage of liver cirrhosis and showed a significant negative correlation with the Child–Pugh Score ($r = -0.86$; $p < 0.001$, $r = -0.36$; $p < 0.001$& $r = -0.35$; $p < 0.001$ respectively).
Conclusion: Trace element abnormalities may reflect the condition of liver dysfunction. Our study shows that Micronutrients status in liver cirrhosis correlates well with the severity of liver cirrhosis. Micronutrients supplementation in liver cirrhotic patients may prevent the progression of the disease and the development of complications, however, further research needs to be done.

[OP-0394]

Clinic-etiological profile of liver cirrhosis in Armenian patients

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Objectives: Background: Liver cirrhosis is a polyetiological severe disease which is associated with increased morbidity and mortality. Aims: This study focused on the clinic-etiological profile of liver cirrhosis according to the data of our clinic from 2017 to 2019.
Materials and Methods: Methods: We studied the etiology and characteristics of 420 patients presenting with cirrhosis. The diagnosis was based on biochemical, serological, virological and instrumental methods of investigations. The mean age was 52.7 ± 8.64 range from 26 to 83 with predominance of male gender 264 (62.9%), BMI-28 ± 3.4 ranging from 18 to 35.
Results: The predominant etiology was HCV 328 (78%). Following by cryptogenic cirrhosis group (probably NASH) was 39 (9,3%) patients with predominance of female 22 (56.4%); mean age was 55.9 ± 12.5; BMI –more than 25. In ethanol cirrhosis group was 26 (6.2%) patients, among them 20 (76.9%) patients were diagnosed HCV + ethanol cirrhosis. In hepatitis-B-virus (HBV) cirrhosis group were 13 (3%) patients. 14 patients (3.3%) were diagnosed with coinfected cirrhosis: HBV + HDV- 7 (50%) patients, HBV + HCV-5 (35.7%) patients, HCV + HBV + HDV and HCV + HIV- 1 patient respectively. The mean laboratory parameters: ALT-65.5 ± 8.9, albumin- 34.25 ± 7.51, INR- 1.98 ± 1.27, bilirubin 136 ± 17,2. According the severity of disease: MELD- 15,57 ± 5.8, Child Pugh A class 210 patients (50%), B class 126 patients (30%) and 84 patients C class (20%). The major complications of cirrhosis include ascites 210 (50%), hepatic encephalopathy (I grade—126 (30%), II grade- 42 (10%), III grade- 21 (5%), variceal bleeding 26 (6.2%) and hepatocellular carcinoma 54 (12.8%), hepatorenal syndrom in 13 (3.1%) cases. Acute on chronic liver failure (ACLF) was diagnosed in 19 (4.5%) of cases. According to our data, mortality rate in patients with cirrhosis was 5.35% (22 patients).The main causes of mortality were hepatorenal syndrome (36%), hepatic encephalopathy III grade (27%), variceal bleeding (13.6%) and ACLF (23.4%).
Conclusion: HCV is a leading etiological cause of liver cirrhosis in Armenian patients.

[PP-0407]

Advantage of using serum M2BPGi level to diagnose liver fibrosis among overweight and obese patients in Mongolia

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Objectives: To diagnose liver fibrosis among overweight and obese population of 40 – 65 years in Mongolia by serum M2BPGi glyco-biomarker level.
Materials and Methods: We enrolled 3315 people aged 45–60 years old who live in urban and rural areas. Questionnaires were obtained from participants, and anthropometric measurements, ultrasound, and laboratory tests were done. Serum M2BPGi level was directly measured with the chemiluminescentenzyme immune method using an automatic immunoanalyzer. Statistical analysis was performed on SPSS ver. 20.0; SPSS Inc.,Chicago, IL software. We used Pearson chi squaretest to estimate difference between parameters with percentage, and T test was used to estimate median difference. Ap value less than 0.05considered statistically significant.
Results: 3315 people participated in this study. 1955 people were recruited from Ulaanbaatar (59.0%) 1360 people were from rural areas, and 1141 (34.4%) were male and 2174 were female (65.6%). 1326 (40%) of the surveyed were overweight and 1038 (31.3%) were obese. Elevation of serum M2BPGI glyco-biomarker was significantly different from body weight, age group and sex ($p < 0.0001$).
Conclusion: From total participants, 40% were overweight and 31.3% were obese. The proportion of people with obesity increases with age.The liver fibrosis was detected 49.7% in women and 43.1% in men and it was increasing 40% to 62.4% in age group. 48.4% of people with overweight and 54.6% of obesity patients have found liver fibrosis changes.

[PP-0414]

Risk factors for progression of liver fibrosis after successful elimination of hepatitis C virus

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Objectives: to establish external factors and genetic predictors of liver fibrosis progression in patients with hepatitis C after successful therapy with direct antiviral drugs and achieving a stable virological response.
Materials and Methods: The study was carried out in the period from 2015 to 2020 in the Irkutsk region (Russia). The cross-sectional study using 126 HCV patients between year 2017–2020. Demography and genetic data were collected. Genetic studies included the determination of single nucleotide gene polymorphisms: TLR7 (rs179008); TLR7 (rs179009); TLR8 (rs3764879); TLR8 (rs3764880); IRAK1 (rs3027898); MECP2 (rs1734791); TAB3 (rs1000129516); ELK1 (rs1000619237); GPC3 (rs2267531), NAT2 (rs1495741). The degree of liver fibrosis was determined using the "Echosens FibroScan-502" (France) and evaluated using the METAVIR scale. The average age of patients was 42.1 years, the proportion of males-58.5%; structure of genotypes: GT1-51.7%; GT2-7.6%; GT3-40.7%. All patients had significant fibrosis into F2-F3 prior to treatment. Antiviral treatment was carried out with a combination of drugs ombitasvir + paritaprevir + ritonavir + dasabuvir (GT1) or sofosbuvir + daclatosvir (GT1-3). As a result of treatment, a sustained virological response was achieved in all patients. After 2–5 years of dispensary observation, 112 patients (88.9%) showed a regression of fibrosis to F0-F1; in 14 (11.1%), the degree of fibrosis did not decrease or progressed to F3-F4 or cirrhosis.
Results: In the groups of patients with regression and progress of fibrosis, the mean age was 47.8 and 48.4 years ($p > 0.05$), males 55.8% and 52.2% ($p > 0.05$), body mass index 27.2 and 25.9 ($p > 0.05$), respectively. In the recessive inheritance model in the group of patients with progression of fibrosis after successful HCV therapy, a predominance of individuals with a slow type of acetylation was noted (AA genotype rs1495741 of the NAT2 gene, OR 3.8; 95% CI: 1.6–9.1; $p = 0.002$).
Conclusion: AA genotype rs1495741 NAT2 are independent risk factors for progression of liver fibrosis in HCV patients after successful antiviral therapy with direct antiviral drugs.

[OP-0440]

Use of human serum albumin infusion for the prevention and treatment of hyponatremia in liver cirrhosis: A systematic review and meta-analysis

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Objectives: Hyponatremia is a common complication of liver cirrhosis. The effect of human serum albumin (HSA) infusion on hyponatremia in cirrhosis remains unclear.
Materials and Methods: Literature was searched in the PubMed, EMBASE, and Cochrane Library databases. If possible, a meta-analysis would be conducted. The incidence of hyponatremia was compared between cirrhotic patients treated with and without HSA. Serum sodium level after HSA infusion was evaluated. Odds ratios (ORs) or mean differences (MDs) with 95% confidence intervals (CIs) were calculated. The quality of evidence was assessed by the

Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.
Results: Twenty-eight studies were finally included. As compared to the control group, HSA group had a significantly lower incidence of hyponatremia in cirrhotic patients treated with large volume paracentesis (LVP) for tense/refractory ascites (OR = 0.52, 95%CI = 0.34–0.78, P = 0.002). HSA could significantly increase serum sodium level after LVP in cirrhosis with tense/refractory ascites (MD = 0.87, 95%CI = 0.28–1.47, P = 0.004). Only few studies regarding HSA for the treatment of hyponatremia in cirrhosis with ascites were identified. The quality of available evidence is low/very low.
Conclusion: HSA may be effective for the prevention of hyponatremia in cirrhosis. Certainly, well-designed studies should be required to clarify the effects of HSA on hyponatremia in cirrhosis.

[PP-0507]

Longitudinal assessment of fibrosis and steatosis by MR-based imaging in HCV treated with DAAs: Role of PNPLA3 variants

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Objectives: Significant fibrosis regression occurs after hepatitis C virus (HCV) therapy. However, the impact of direct-acting antivirals (DAAs) on steatosis is less clear. This study was aimed at evaluating serial fibrosis and steatosis alterations in patients with HCV genotype1, who archived sustained virological response (SVR).
Materials and Methods: We enrolled 55 HCV mono-infected and 28 HCV/HIV co-infected patients receiving elbasvir/grazoprevir from a clinical trial. Fibrosis and steatosis were assessed at baseline, follow-up week-24 (FUw24) and week-72 (FUw72) by magnetic resonance elastography (MRE) and proton density fat fraction (PDFF), respectively. Polymorphisms in PNPLA3 rs738409, TM6SF2 rs58542926 and MBOAT7 rs641738 were determined by allelic discrimination.
Results: Overall, mean MRE decreased significantly from baseline to FUw24 and FUw72. At FUw72, patients with baseline F2-F4 had higher rate of $\geq$ 30% MRE decline compared with individuals with baseline F0-F1 (30.2%vs.3.3%,P = 0.004). In multivariate analysis, significant fibrosis was associated with MRE reduction. The prevalence of steatosis (PDFF $\geq$ 5.2%) at baseline was 21.7%. Among these patients, a resolution of steatosis at FUw72 was observed in 11.1%. In patients without baseline steatosis, new onset steatosis at FUw72 was detected in 20%. Overall, mean PDFF significantly increased from baseline to FUw72. In multivariate analysis, the presence of diabetes and PNPLA3 CG + GG genotypes were significantly associated with progressive steatosis (PDFF $\geq$ 30% from baseline) after SVR. Other variants were not associated with fibrosis and steatosis alteration.
Conclusion: HCV eradication by DAAs was associated with liver stiffness improvement. In contrast, progressive steatosis was observed in a proportion of patients, particularly among individuals harboring PNPLA3 variants.

[PP-0520]

Evaluation of the iliopsoas muscle using SYNAPSE 3D

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Objectives: In recent years, the clinical importance of sarcopenia in patients with liver disease has been recognized. In addition, there are many reports on the diagnosis of sarcopenia. The guidelines for sarcopenia in Japan use the mass of the iliopsoas muscle at the third lumbar vertebra (L3) for measurement. In this study, we evaluated the correlation between the automatically calculated total iliopsoas muscle mass and iliopsoas muscle area at the L3 level and the measurement of area by a simple method using the 3D image volume analysis system SYNAPSE 3D, as well as the reproducibility of the test results and the measurement time by different measurers.
Materials and Methods: The subjects were 14 patients who were hospitalized for liver disease and underwent computed tomography (CT) of the plain from the abdomen to the pelvis.SYNAPSE 3D application "3D Fat Analysis" was used to determine the difference between the psoas muscle area (PMRAC) by automatic calculation and the psoas muscle volume (PMVAC) by automatic calculation performed by skilled and novice technicians. We evaluated the differences in psoas muscle volume (PMVAC) and the time required for each measurement, as well as the correlation between psoas muscle area, PMRAC, and PMVAC using the simplified method.
Results: The PMRAC and PMVAC at the L3 level were 13.4 $\pm$ 5.0 cm2 and 13.2 $\pm$ 3.9 cm2, 300.6 $\pm$ 87.5 cm3 and 301.4 $\pm$ 87.2 cm3, respectively. The correlation coefficients (R2) were 0.8951 and 0.9987, respectively, indicating a very strong correlation; the time to calculate PMRAC and PMVAC at the L3 level was 96.4 and 94.3 s, respectively, with no difference.
Conclusion: The measurement of PMRAC and PMVAC using SYNAPSE 3D is convenient, reproducible, and useful.

[PP-0568]

Dominant profile of patients with viral cirrhosis at different stages of providing medical care

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Objectives: Determine the dominant profile of patients with viral cirrhosis of the liver (LC) at different stages of care.
Materials and Methods: The study included 921 outpatients, 844 patients of hospital, 455 deceased of chronic viral hepatitis (CVH) and 97 cases of death caused by LC.

Results: Of the outpatients, 17% (n = 153) aged 54 ± 12 had LC and 97% patients had compensated LC without clinical manifestations. Five (5) patients had regular alcohol consumption (RAC). Most cases (93%)—chronic hepatitis C (CHC). All patients with chronic hepatitis B (CHB) had replication. Of the hospitalized patients, 633 (75%) age of 50 ± 14 (29–74) had LC and 90%—subcompensated/decompensated. RAC was seen in 60%. CHC was accounted for 30%, CHB – for 34%, and out of these, 67% had occult hepatitis B (OHB), 22%—mixed, 14%—unknown etiology. All 455-deceased aged 48 ± 12 (27–76) had LC. RAC was seen in 65%. The share of CHB was 23.7%, out of these 71%—OHB, CHC—35.2%, mixed—31.5%, 19.6%—unknown etiology. In the study of liver micropreparations from 97-deceased age 45 ± 12, only 77% of patients with subcompensated LC and 70%—with decompensated LC showed signs of completed cirrhotic transformation. In all cases of LC, the fact of multimorbidity was noted.
Conclusion: CHC dominates. There is insufficient screening OHB at the outpatient stage. Outpatient with LC are persons of working age, socially adapted and employed, without alcohol dependence, with compensated LC, with minimal clinical manifestations. Among inpatients and deceased socially maladapted individuals, and a high percentage of alcohol addicts are more common. Thirty percent (30%) of patients die from causes not related to decompensation of the underlying disease. This confirms the effect of comorbid pathology on CVH.

[OP-0569]

Frequency of sarcopenia in patients with cirrhosis and factors predicting sarcopenia

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Objectives: To determine frequency of sarcopenia in patients with cirrhosis and factors predicting sarcopenia.
Materials and Methods: A total of 386 patients with cirrhosis were enrolled. Sarcopenia was determined based on the Asian Working Group for Sarcopenia-2019. Patients' clinical and laboratory characteristics were recorded. Chi square test was applied to find out the association between sarcopenia and other demographic variables. Logistic regression analysis was performed to identify independent predictors for sarcopenia. P value of ≤ 0.05 was considered as significant.
Results: Out of 386 patients, sarcopenia was found in 314 patients (81.34%). Sarcopenia was more prevalent in females (86.8% vs 78.1%, p = 0.036). Most common etiology was chronic viral hepatitis (85.5%). 33% had hepatoma, while 32% were on statins. Mean MELD-Na score was 14.49 ± 5.543. Mean age and BMI of study participants were 52.13 with SD of 8.46. and 23.8 with SD of 4.11 respectively. On multivariate analysis, female gender (odds ratio (OR): 1.813, 95%CI 1.033 – 3.182, P = 0.038), Age > 49.5 years (OR: 2.925, 95%CI: 1.727 – 4.955, P < 0.001), and albumin > 2.45 g/dl (OR: 0.28, 95%CI: 0.129 – 0.606) were associated with sarcopenia.
Conclusion: Sarcopenia is very common in patients with cirrhosis. Special measures should be taken for patients with risk factors of sarcopenia to improve their outcomes.

[OP-0576]

Bone mineral density loss in liver cirrhosis patients

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Objectives: One of the liver cirrhosis complications is related to bone metabolism is known as hepatic osteodystrophy (HO). Pathologic fracture caused by HO can significantly affect the quality of life and life expectancy of patients. The mechanism is multifactorial. Our study was carried out to assess the prevalence of HO and to identify the factors that related to the loss of bone mineral density in liver cirrhosis patients.
Materials and Methods: Consecutive eligible patients with liver cirrhosis were recruited. Bone mineral densitometry (BMD) was evaluated by dual-energy X-ray absorptiometry (DEXA). BMD at both femoral neck and lumbar spine were collected, and the lowest T score was used. Hepatic osteodystrophy was defined as a T score of ≤ -1. Continuous variables were presented by mean or median as appropriate, and categorical variables by percentage. The univariate and multivariate analyses were performed to identify factors related to the development of hepatic osteodystrophy.
Results: Among 80 participants, 75% (n = 60) were men, 25% (n = 20) were women, and the median duration of liver disease was 3 years. The mean age and body mass index (BMI) was 48.89 ± 7.32 years old; 24.27 ± 0.06 respectively. Viral hepatitis was the most common etiology of cirrhosis (97.5%). There were 52.5% (n = 42) participants with Child-Turcotte-Pugh (CTP) score grade A, 30% (n = 24) with CTP score grade B, and 17.5% (n = 14) with CTP score grade C. The mean of lowest T score was − 1.398 ± 1.252. HO were present in 61.3% (n = 49) participants (41.3% osteopenia and 20% osteoporosis). On both univariate and multivariate analysis, BMI and duration of liver disease showed a significant association with HO (p = 0.003; p = 0.001).
Conclusion: Our study found a high prevalence (61.3%) of hepatic osteodystrophy in cirrhosis patients. Low BMI and a longer duration of liver disease were related to the development of HO in cirrhosis patients.

[PP-0581]

Combination treatment with curcumin and silibinin prevents oxidative stress and attenuates experimentally induced liver injury and fibrosis in rats

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Objectives: Hepatic fibrosis is characterized by excessive synthesis and deposition of connective tissue components, especially collagens in the extracellular matrix of the liver. Curcumin is a food additive with established antioxidant and anti-inflammatory properties. Silibinin is the active constituent of silymarin and a potent antioxidant

with proven pharmacological effects against alcoholic liver disease and non-alcoholic steatohepatitis. We studied the protective effects of curcumin and silibinin to prevent oxidative stress and attenuate experimentally induced hepatic fibrosis in rats.?

Materials and Methods: Liver injury and hepatic fibrosis was induced with intraperitoneal injections of N-nitrosodimethylamine (NDMA) in a dose of 10 mg/kg body weight daily for 10 consecutive days. Groups of animals received curcumin 200 mg/kg body weight and/or silibinin 20 mg/kg body weight everyday orally 2 h prior to the administration of NDMA and also until the end of the study. All the animals were sacrificed on day 21 from the beginning of exposure. Levels of AST, ALT, malondialdehyde, glutathione, ascorbic acid, and hyaluronan were measured either in serum, liver, or both. Immunohistochemistry was carried out for alpha-SMA, collagen type I and type III, and 4-hydroxy-2-nonenal (4-HNE). RT-PCR was performed for alpha-SMA, type I and type III collagens.

Results: Serial administrations of NDMA produced well developed fibrosis and early cirrhosis in rat liver. Combination treatment with curcumin and silibinin significantly reduced serum/hepatic levels of AST, ALT, malondialdehyde, glutathione, ascorbic acid and hyaluronan and completely prevented deposition of collagen fibers in the liver. Immunohistochemical staining and RT-PCR depicted marked decrease in the expression of alpha-SMA, 4-HNE, and collagens type I, and type III.

Conclusion: Combination treatment with curcumin and silibinin efficiently decreased oxidative stress, markedly reduced expression of collagens, and prevented hepatic fibrosis. The data demonstrated that curcumin and silibinin could be used as potent therapeutic agents to prevent liver injury and hepatic fibrosis.

[PP-0623]

Salvianolic acid A is the active compound of Salvia miltiorrhiza against the activation of NLRP3 inflammasomes on macrophages

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Objectives: Salvia Miltiorrhiza (SM) is a Chinese herbal medicine that is widely used to treat liver diseases in clinic. We previously found SM was effective in treating liver injury via inhibiting expression of NLRP3 in vivo, but the active compound of SM and the underlying mechanism remained unclearly. Here, we aimed to screen its active substances against NLRP3 inflammasomes and explore the mechanism involved.

Materials and Methods: A cell culture model was investigated to detect NLRP3-dependent IL-1β release using bone marrow-derived macrophages (BMDMs). 16 ingredients of SM, including danshensu, magnesium lithospermate B, tanshinone I, tanshinone IIA, miltirone, manool, salvianolic acid A, salvianolic acid B, salvianolic acid C, dhydrotanshinone I, dihydroisotanshinone I, caffeic acid, neocryptotanshinone, cryptotanshinone, lithospermic acid, were screened out to confirm the maximum non-toxic concentration for BMDMs by LDH and CCK8 kits, respectively. For NLRP3 inflammasome activation, BMDMs were primed with lipopolysaccharide (LPS), and subsequently were stimulated with nigericin or adenosine triphosphate (ATP). The most active substances against NLRP3 inflammasomes in SM was screened out and the underlying mechanism were explored.

Results: Maximum non-toxic concentration and IC_{50} of 16 ingredients for BMDMs were assayed. Among the ingredients, Salvianolic acid A was the most anti-inflammatory substances in SM that played a dose dependent (25, 50 and 100 μM) in alleviating the release of IL-1β on activated NLRP3 inflammasomes. Levels of mitochondrial ROS production and expression of LC3 and LC3-II in LPS (50 ng/ml)/ATP (2.5 mM)- and LPS (50 ng/ml)/nigericin (4 μM)-stimulated BMDMs were significantly reduced respectively, which revealed that Salvianolic acid A might confer mitochondrial protection via promoting autophagy pathway.

Conclusion: Salvianolic acid A might be the efficacious compound in SM against activation of NLRP3 inflammasome on macrophages in vitro. The mechanism was associated with alleviating mitochondrial oxidative stress and promoting autophagy pathway in vitro.

[OP-0625]

Neutrophillymphocyte ratio and the risk of 30-day mortality in patients with overt hepatic encephalopathy

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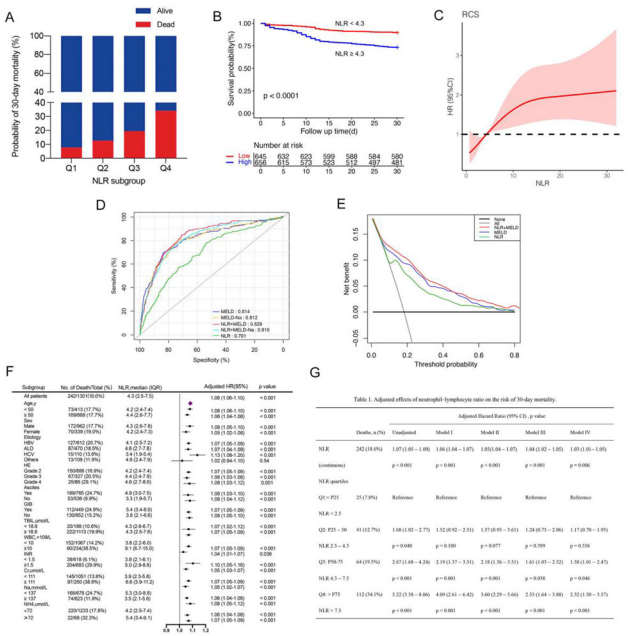
Objectives: Overt hepatic encephalopathy (OHE) is related to a risk of adverse outcomes and short survival. However, the association between different neutrophil to lymphocyte ratio (NLR) levels and the 30-day mortality risk in cirrhotic patients with OHE has not yet been well assessed.

Materials and Methods: We retrospectively included 1301 patients with OHE at Beijing Ditan Hospital between August 2008 and December 2018. By adjusting for important risk variables, we investigated the association between NLR and the 30-day mortality risk using Cox regression analysis and restricted cubic splines. The discrimination and clinical usefulness of NLR were assessed by receiver operating characteristic curves and decision curve analysis.

Results: All patients were divided into four groups according to quartiles of the baseline NLR (< 2.5, 2.5 – 4.3, 4.3 – 7.5, > 7.5). The 30-day mortality were 7.8%, 12.7%, 19.5%, and 34.1%, respectively ($p < 0.001$). Compared with the lowest quartile, increased NLR was correlated with increasing 30-day mortality after multivariable adjustment (NLR 2.5–4.3: adjusted hazard ratio [AHR], 1.17 (95% confidence interval [CI], 0.70–1.95); NLR 4.3 – 7.5: AHR, 1.58 (95% CI, 1.01 – 2.47); NLR > 7.5: AHR, 2.32 (95% CI, 1.50 – 3.57). A non-linear association between NLR and the adjusted probability of 30-day mortality was observed. There was a significant increasing 30-day mortality in the range of $4.3 < \text{NLR} < 12$. The performance of NLR + MELD (0.839) was higher than that of NLR + MELD-Na (0.829), MELD (0.814), and MELD-Na (0.812) in patients with OHE. The decision curve showed that NLR + MELD had superior standardized net benefit than MELD and NLR. Notably, elevated NLR was linked to increased incidence of 30-day mortality in the subgroup analysis of patients with OHE (HR > 1.0).

Conclusion: Elevated NLR is independently associated with 30-day mortality in cirrhotic patients with OHE.



[PP-0648]

The prediction of liver decompensation using hepatic collagen deposition assessed by computer-assisted image analysis with Masson-trichrome stain

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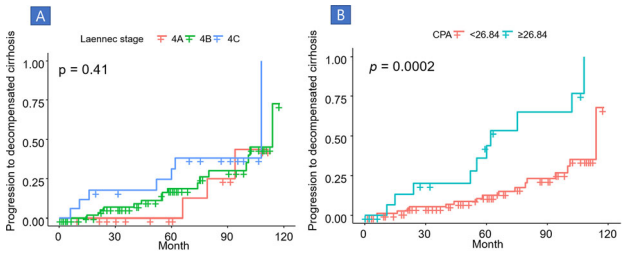
Objectives: Current pathologic system classifies structural deformation caused by hepatic fibrosis semi-quantitatively which could make a disagreement among pathologists. We measured hepatic fibrosis quantitatively using collagen proportionate area (CPA) in compensated cirrhotic patients and assessed its impact on predicting the development of liver decompensation.
Materials and Methods: During January 2010 to June 2018, we assessed 118 cirrhotic patients who got liver biopsy and computer assisted image analysis (ZEN 2.3 lite software by ZEISS) were available. Clinical and laboratory data were collected at baseline and at the time of the last follow-up or progression to liver decompensation (LD). Seventeen patients with portal vein anomaly, insufficient follow up and decompensated cirrhosis at baseline were excluded.
Results: The mean age was 50.8 ± 10.5 years, and most common etiology of liver disease was chronic hepatitis B (48.5%) and followed by alcoholic liver disease (18.8%). Median follow-up duration was 60 months during which 26 out of 101 patients experienced LD. Mean analyzed dimension of collagen was 1,025,336 ± 776,786 μm2 and included portal tract was 10.2 ± 3.8. Mean CPA was 16.91 ± 9.60%. A positive correlation between CPA and liver fibrosis stage was observed (r = 0.403, p < 0.001). Presence of diabetes at baseline (HR: 7061, p = 0.05), older age (HR: 1.18, p = 0.01), higher CPA (HR: 1.10, p = 0.05) were independent predictors of liver decompensation on multivariate Cox-regression analysis. Laennec stage did not showed significant prediction for LD progression (Fig. 1A). When dividing patients according to CPA value (26.84%), higher CPA predicts LD better than lower CPA. (Log-rank test: p < 0.001) (Fig. 1B).
Conclusion: CPA is an independent predictor of clinical outcomes in liver disease. CPA correlates well with Laennec stage in patients with LC and better predicts the LD. It is expected to be useful quantitative prognostic value for cirrhotic patients.



[OP-0661]

Acute kidney injury among hospitalized patients with cirrhosis—burden and risk factors

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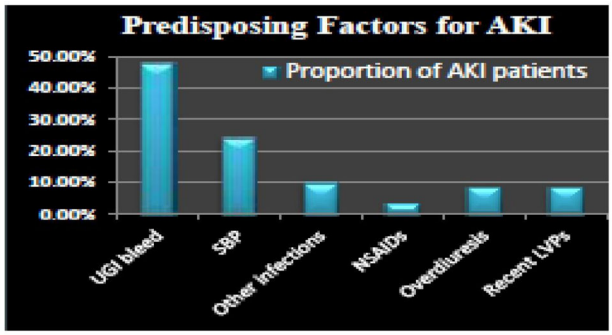
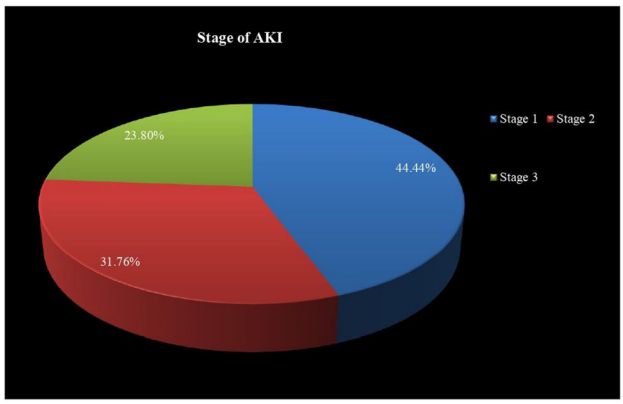
Objectives: To estimate the prevalence of AKI and its common predisposing factors in hospitalized patients with cirrhosis and its burden in terms of mortality rate.
Materials and Methods: A cross-sectional study was done in our setting including 128 patients hospitalized with cirrhosis. AKI was diagnosed and staged as per ICA-AKI criteria. Risk factors for incident AKI events was recorded and their association was tested by chi-square test. Their outcome at the end of hospital stay (in terms of survived or deceased) was recorded and mortality rate was calculated.
Results: Prevalence of AKI among patients with cirrhosis admitted to hospital was 49.2% (63/128). Majority of patients who developed AKI had advanced decompensated cirrhosis at admission (CTP-A: 8, CTP-B: 18, CTP-C: 37) and early stages of AKI (Stage-1: 28, Stage-2: 20, Stage-3: 15) predominated in our study. Most common predisposing factors for AKI among cirrhotic patients were Upper GI bleed (47.6%) and Infections (33.3%; SBP-23.8%, other infections – 9.5%), while Diuretics (7.9%), NSAIDs (3.1%) and prior large volume paracentesis (7.9%) were less common. Among patients with cirrhosis, AKI was found to be significantly associated with Upper GI bleeding (Odds ratio [95%CI]: 5.000 [2.16–11.533], p-value < 0.05) and SBP (Odds ratio [95%CI]: 6.458 [1.768–23.593], p-value < 0.05). Mortality rate among hospitalized cirrhotic patients with AKI in cirrhosis were 34.92%. Acute Kidney Injury was identified as a risk factor for mortality among patients with cirrhosis (Odds ratio [95%CI]: 3.823 [1.549–9.434], p-value < 0.05).
Conclusion: Burden of AKI (49.2% prevalence and 34.92% mortality rate) among hospitalized patients with cirrhosis is significantly high in our region. Patients with definite predisposing factors require close monitoring for early detection of renal impairment.





[PP-0676]

Bacterial pattern in adult decompensated liver cirrhosis ascitic fluid infection during first 5 months of second wave Covid-19 pandemic at tertiary hospitals in Jakarta Indonesia

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Objectives: To find out bacterial pattern of ascitic bacterial infection in adult decompensated liver cirrhosis during Covid-19 pandemic at three tertiary referral hopsitals in Jakarta.
Materials and Methods: 18 years old or more decompensated liver cirrhosis patient due to any cause with grade 2 or more ascites admitted consecutively to emergency room, inpatient and outpatient unit in Jakarta's three tertiary referral hospitals: Cipto Mangunkusumo National General Hospital, Gatot Soebroto Central Army Hospital, Fatmawati General Hospital would be performed paracentesis ascitic tap during January to May 2021. Bedsite aerobic and anaerobic bacterial blood culture bottles of 10 mL inoculation (aerobic BACT/ALERT® FA Plus and anaerobic BACT/ALERT® FN Plus bioMerieux Incorporation) were acquired under aseptic and antiseptic standards before antibiotic administration or at least 4 h after it. Diphtheroids species, Bacillus species and Staphylococcus epidermidis were considered contaminant.
Results: There were 98 ascitic culture specimens from 98 grade 2 and more ascites decompensated liver cirrhosis patients. Basic characterisitic data included: 32.6% female, 67.4% male, history of hospitalization and antibiotic admission in the last previous 3 months 76.5%, due to viral hepatitis B 38.5%. Bacterial growth was found in 11 specimens (11.1%) including 6 aerobic gram negative (54.5%): Aeromonas hydrophila, Enterobater aerogenes, Klebsiella pneumonia (2 specimens), Acinetobacter species, Pseudomonas aeruginosa and 5 aerobic gram positive (45.4%): Enterococcus faecalis, Staphylococcus cohnii ssp cohnii, Staphylococcus cohnii ssp urealyticus, Staphylococcus haemolyticus, Micrococcus luteus. There were no positive culture for Escherichia coli and anaerobic bacteria.
Conclusion: During second wave of Covid-19 pandemic in Jakarta, there were almost equal proportion of gram positive and negative bacterial in adult decompensated liver cirrhosis ascitic fluid bacterial infection patients in tertiary hospitals. This result reminds clinicians of bacterial pattern shift in ascitic fluid infection in decompensated liver cirrhosis during pandemic.

[OP-0733]

Magnetic resonance elastography predicts de novo recurrence after resection for hepatocellular carcinoma

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Objectives: Surgical resection is treatment of choice for hepatocellular carcinoma (HCC) if liver function can withstand. But, 3-year recurrence rate can be as high as 50% at 3-year after surgery. Cirrhotic liver is high risk of HCC. Recently, magnetic resonance elastography (MRE) has emerged a noninvasive method to evaluate liver fibrosis. On MRE, liver fibrosis is measured avoiding the tumor by MRI image.
Materials and Methods: Between January 2017 and December 2018, 90 patients underwent Hepatic resection (HR) for HCC. Clinical data were analyzed disease-free survival rate (DFSR) according to serum alpha-fetoprotein (AFP) level, Magnetic resonance elastography (MRE).
Results: Between January 2017 and December 2018, HR for HCC group has incidence of recurrence is 22.2% (20/90). We define MRE cut-off value 3.855 kPa by AUROC. it represent. When MRE over 3.855, Hazard ratio is 3.358 (p = 0.013).
Conclusion: Magnetic resonance elastography that measure liver fibrosis predict de novo recurrence after hepatic resection for hepatocellular carcinoma. So we consider liver transplantation in severe stiffness liver parenchyma.

[OP-0777]

Pre and post M2BPGi level can predict hepatocellular carcinoma in chronic hepatitis B patients treated with antiviral agents

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Objectives: Mac-2 binding protein glycosylation isomer (M2BPGi) is a non-invasive marker which can evaluate liver fibrosis. The aim of this study is to compare the change of M2BPGi before and after high potent antiviral treatment, and evaluate whether M2BPGi could predict hepatocellular carcinoma (HCC) development.
Materials and Methods: This retrospective study included chronic hepatitis B (CHB) patients who underwent high potent antiviral treatment and had stored serum samples at the baseline and 1–2 years after treatment initiation. Primary endpoint was HCC development evaluated by the Cox proportional hazard model.
Results: Among 268 patients, 187 (69.8%) were treated with entecavir, 81 (30.2%) were treated with tenofovir, 95 (35.4%) had initial radiologic liver cirrhosis. After follow-up, 24 (8.9%) developed HCC. The mean M2BPGi levels did not change in the liver cirrhosis group after antiviral treatment; 1.50 cut-off index (COI) at baseline and 1.55 COI after 1–2 years. However, in the chronic hepatitis group the mean M2BPGi decreased after antiviral treatment; 0.63 COI at baseline and 0.42 COI after 1–2 years. Multivariate analysis showed that the pre-M2BPGi level (adjusted hazard ratio [aHR] = 1.215, 95% confidence interval [CI] = 1.047–1.411, P = 0.010) and the post-M2BPGi level (aHR = 1.442, 95% CI = 1.126–1.710), $P < 0.001$) both predicted HCC development.
Conclusion: Both pre and post treatment M2BPGi levels can predict HCC development in chronic hepatitis B patients.

[PP-0779]

Realworld efficacy of M2BPGi on diagnosing liver fibrosis in chronic hepatitis patients

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Objectives: Mac-2 binding protein glycosylation isomer (M2BPGi) is a novel non-invasive marker for liver fibrosis, but still needs more validation. We aimed to compare the diagnostic efficacy of M2BPGi with transient elastography (TE), FIB-4, and APRI.
Materials and Methods: This retrospective study included chronic hepatitis patients who underwent M2BPGi and TE for evaluation of liver fibrosis.
Results: A total of 302 patients were included: non alcoholic fatty liver disease 135 (44.7%), fatty liver 76 (25.2%), alcoholic hepatitis 61 (20.2%). M2BPGi levels were well correlated with TE levels (r = 0.715). Clinically significant liver cirrhosis (LC) was observed in 37 (12.3%) patients. Using cut-off 1.0 and 3.0 the AUROC of M2BPGi for predicting clinical liver cirrhosis was 0.839, which was comparable with TE, FIB-4 and APRI, 0.921, 0.918 and 0.818, respectively. The sensitivity and specificity for predicting clinical LC were 97.3% and 86.8% for TE alone, however positive predictive value (PPV) was only 50.7%. Adding TE with M2BPGi increased the PPV to 80.8%.
Conclusion: A novel fibrosis marker M2BPGi well correlates with TE and other non-invasive markers, and M2BPGi can improve the diagnostic probability of TE.

[PP-0780]

Mudeng (Mu2-related death-inducing gene) overexpression accelerates liver fibrosis in carbon tetrachloride-induced cirrhosis

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Objectives: Liver fibrosis and its end-stage disease, cirrhosis, are major risk factors for hepatocellular carcinoma. MUDENG (Mu-2 related death-inducing gene, also known as AP5M1) is a gene which encodes a 490 amino acid protein initially reported to be involved in cell death of cytotoxic T cells, in tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-mediated anti-apoptotic signaling, and in trafficking of membrane vesicles. In this study, we developed a MUDENG transgenic mouse to further evaluate the role of MUDENG in inducing and potentially alleviating liver fibrosis.
Materials and Methods: Eight 8-weeks-old male MUDENG transgenic mice and C57BL/6 N male mice were injected with carbon tetrachloride (CCl4) intraperitoneally twice weekly. Livers were harvested at baseline and biweekly thereafter. The difference in the percent collagen area at baseline, 2, 4, and 6 weeks of the two groups was evaluated. Opensource software ImageJ (distributed by NIH) was used.
Results: The Ishak fibrosis grade of the MUDENG mice at baseline, week 2, 4, and 6 were 0, 1, 2, and 2, respectively. The Ishak fibrosis grade of the C57BL/6 N mice at baseline, week 2, 4, and 6 were 0, 0, 1, and 1, respectively. The collagen proportionate area (CPA) at baseline in MUDENG and C57BL/6 N mice were 0.36% and 0.38%, respectively (p = 0.77). The CPA at 2 weeks in MUDENG and C57BL/6 N mice were 0.91% and 0.67%, respectively (p = 0.03). The CPA at 4 weeks in MUDENG and C57BL/6 N mice were 2.51% and 1.29%, respectively ($p < 0.001$). The CPA at 6 weeks in MUDENG and C57BL/6 N mice were 2.86% and 1.84%, respectively ($p < 0.001$). Greater expression of TGF-β throughout the life span in MUDENG transgenic mice compared to C57BL/6 N was noticed.
Conclusion: MUDENG transgenic mice demonstrates rapid development of fibrosis compared to C57BL/6 N mice. Further studies to evaluate the pathways altered by MUDENG overexpression inducing accelerated liver fibrosis should be done.

Fig1. The collagen proportionate area between the MUDENG and C57BL/6N mice is significantly different starting at week 2 after intraperitoneal injection of CCl_4

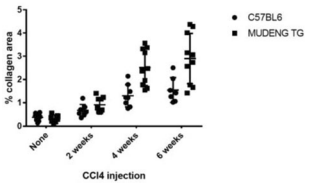
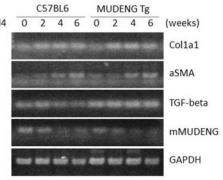


Fig 2.
Greater expression of TGF-β throughout the life span in MUDENG transgenic mice compared to C57BL/6N was noticed.



[OP-0792]

Effect of Fuzheng Huayu recipe against liver fibrosis via NLRP3/IL-1β signal pathway

Bing Da Ping[1], Shu Jing Qi[1], Kai Huang[1], Yan Yan Tao[1], Yuan Peng[1], Hai Cheng Liu[1]

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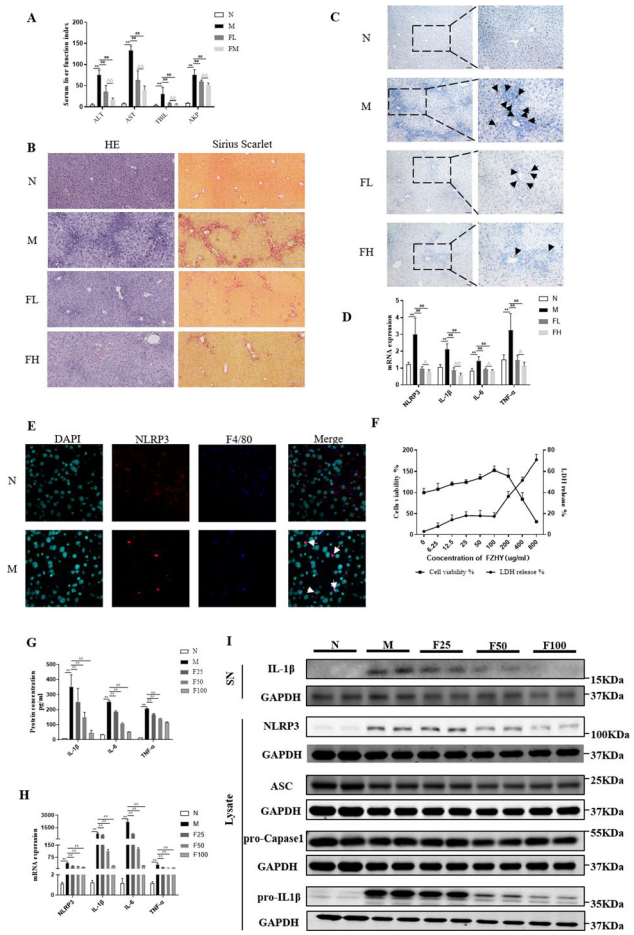
Objectives: Activation of NLRP3 inflammasomes in macrophages contributes to liver injury and fibrosis. FZHY, a Chinese herbal product, is effective in treating liver fibrosis in our previous study, but the immunological mechanism remains unclearly. Here, we tested the hypothesis that the anti-inflammatory effect of FZHY was associated with inhibiting activation of pro-inflammatory macrophages via modulating NLRP3 inflammasomes.
Materials and Methods: Liver injury was induced with 0.1% DDC diet. Primary bone marrow cells were isolated and were induced to bone marrow-derived macrophages (BMDMs). BMDMs were stimulated with lipopolysaccharide (LPS) plus adenosine triphosphate (ATP) and were synchronously incubated with FZHY. Effects of FZHY on NLRP3 signal pathway were investigated in vivo and in vitro.
Results: Compared with the normal control group, serum levels of ALT, AST, TBIL and AKP were significantly increased. More inflammatory cell infiltration and collagen fiber deposition were investigated in the liver. Expression of NLRP3 and IL-1β in liver tissue were significantly up-regulated. FZHY ameliorated the liver function, decreased the inflammation and fibrosis, and alleviated levels of NLRP3 and IL-1β on macrophages in vivo. Furthermore, FZHY played a dose dependent (25, 50 and 100 μg/ml) in alleviating the release of IL-1β on activation of NLRP3 inflammasomes in BMDMs after LPS/ATP-induction in vitro.
Conclusion: FZHY could alleviate cholestatic liver fibrosis, which is associated with the suppressing the activation of NLRP3 inflammasome on macrophages.



[OP-0795]

Fuzheng Huayu formula inhibits liver fibrosis via suppressing EGFR signal pathway

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Objectives: Fuzheng Huayu (FZHY) formula is a Chinese herbal product that is widely used to treat liver fibrosis and cirrhosis in clinic. FZHY was proved to be effective in treating liver fibrosis and cirrhosis both in animal models and patients, but the underlying mechanisms remained unknown. Here, we aimed to screen out the targets that FZHY actioned against liver fibrosis-related targets and to validate the mechanism involved.
Materials and Methods: Liver fibrosis was induced with 10% carbon tetrachloride (CCl_4) intraperitoneally for 4 weeks in C57BL/6 mice, and was treated with 2.8 g/kg or 5.6 g/kg of FZHY extract simultaneously. Liver inflammation, collagen deposition and hydroxyproline content were measured. Liver tissue was constructed for transcriptome sequencing to perform RNA sequencing observation. Target

genes for FZHY against liver fibrosis were screened out according to the GO and KEGG bioinformatics analysis, and then were validated in vivo.
Results: Compared with the normal group, levels of serum ALT, AST and TBIL were significantly increased in the model group ($P < 0.01$). A large number of inflammatory cells infiltration and collagen deposition were presented in the liver tissue. FZHY could attenuate liver inflammation and fibrosis in CCl_4 mice. The critical anti-fibrotic target genes of FZHY were screened based on bioinformatics analysis. EGFR signal pathway was of great significance according to the KEGG analysis. More positive staining of p-EGFR was investigated in model mice than that in the normal mice. FZHY treatment could significantly alleviate the levels of p-EGFR and inhibit the downstream genes, including Bax, eif4ebp1, Gas6, Jak1 of the signal pathway.
Conclusion: FZHY can effectively alleviate liver fibrosis, which is associated with the inhibition on EGFR signal pathway in vivo.

[PP-0870]

Validation of the EVendo Score for the prediction of varices in cirrhotic patients

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Objectives: Screening endoscopy for varices may be deferred when the calculated EVendo score is ≤ 3.90. This novel score has not been validated in an external cohort. This study aimed to assess the performance of the EVendo score and compare it with the Baveno VI criteria.
Materials and Methods: We identified and calculated this score in all cirrhotic patients who underwent screening endoscopy for the first time with laboratory tests and liver stiffness measurements within six months of the endoscopy date.
Results: One hundred and three patients were included. An EVendo score of ≤ 3.90 identified patients with no gastroesophageal varices (GEV) and varices needing treatment (VNT) with sensitivities of 82% and 83% and specificities of 57% and 34%, respectively. The negative predictive value for VNT was 94%. A comparison with the Baveno VI criteria in Child-Turcotte-Pugh-A patients showed spared endoscopy and missed VNT rates with EVendo score cutoffs of ≤ 3.9 and ≤ 4.5 and the Baveno VI criteria of 25%, 33%, and 16.6% and 1.7%, 1.7%, and 0%, respectively.
Conclusion: EVendo score is reliable in clinical practice for predicting GEV and VNT. The number of spared endoscopies was higher than that with the Baveno VI criteria; however, there were more missed VNT cases.

[PP-0890]

Disseminated intravascular coagulation related minor injury in decompensated alcoholic cirrhotic patients

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Objectives: At stable status, cirrhotic patients are known to maintain a coagulation balance and procoagulant tendency with increasing severity, according to Child–Pugh's staging. Therefore, an acute assessment is needed to assess to bleeding risk of cirrhotic patients. Herein, we report three cases of disseminated intravascular coagulation following minor injuries or procedures, which improved with antithrombin III supplementation with blood products.
Materials and Methods: Three cases of disseminated intravascular coagulation related minor injury in alcoholic cirrhotic patients were retrospectively analyzed from March 2010 to March 2021 originated in our hospital, including clinical manifestation, laboratory tests, and imaging examinations.
Results: Case one is a 40-year-old woman with decompensated Child Pugh B (CP-B) alcoholic cirrhosis and diabetes mellitus presented with a 1.5 cm-sized laceration on the right eyebrow. The laceration site was sutured, and she was treated with antithrombin III using blood products for three days. At baseline, she had deranged coagulation profile with platelets of 8000/uμL, prothrombin time of 23 s, activated partial thromboplastin time of 32 s and fibrinogen of 310 mg/dL. Case two is a 50-year-old man with decompensated CP-C alcoholic cirrhosis presented with right thigh hematoma and contusion. He was treated with antithrombin III using blood products for five days. Case three is a 52-year-old man with decompensated CP-B alcoholic cirrhosis and diabetes mellitus who presented with bleeding after an electric cauterization of a bleeding site. The bleeding occurred after a bite on the buccal mucosa. He was treated with antithrombin III using blood products for three days.
Conclusion: Antithrombin III supplementation with blood products (red blood cell, fresh frozen plasma, and platelet) transfusion may help improve coagulation status in decompensated alcoholic cirrhotic patients with disseminated intravascular coagulation related to minor injuries.

[PP-0902]

Combination of tartaric acid, homoserine, formic acid and EPA was a predictor for histological respond in entecavir treatment-naive hepatitis B cirrhosis

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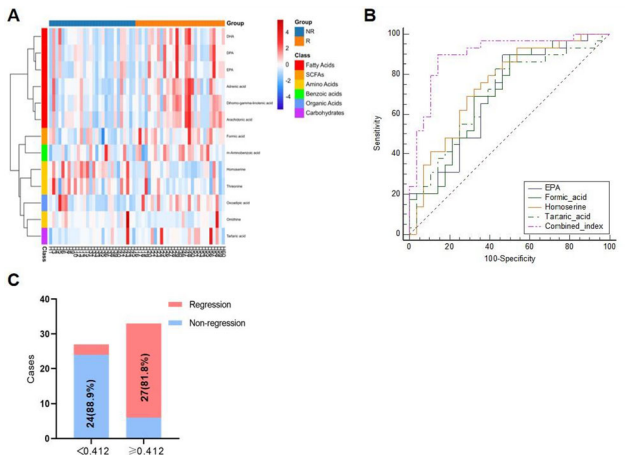
Objectives: Antiviral therapy such as entecavivir can reverse hepatitis B liver fibrosis or cirrhosis. However, only 35–39% would

obtain histological respond. This study aims to discover the serum metabolites biomarkers in hepatitis B cirrhosis that may predict histological respond to entecavir-based antiviral therapy.

Materials and Methods: Sixty patients with hepatitis B cirrhosis, balanced by clinical characters, were selected from clinical cohort (NCT 0,224,159). After 48-week entecavir treatment, patients were divided into regression group (Ishak score decreased by $\geq$ 1 point, n = 30) and non-regression group (Ishak score unchanged or increased by 1 point, n = 30) according to liver biopsy. The serum samples at baseline were tested by UPLC-MS/MS, and the data were analyzed by multivariate principal component analysis and orthogonal partial least-squares-discriminant analysis to discover differential metabolites. The potential clinical values of these metabolites were evaluated by receiver operator characteristic curve (ROC) analysis. We applied logistic regression to reveal combination of biomarkers.

Results: Thirteen differential metabolites, mainly classified into fatty acids, amino acids and organic acids were selected (Fig. 1A). Compared with the non-regression group, levels of 10 metabolites such as arachidonic acid, EPA, DHA were higher in regression group at baseline, while the levels of homoserine, ornithine and threonine were lower. A combined index including tartaric acid, homoserine, formic acid and EPA, of which the sensitivity was 80% and specifity was 90%. The AUC of the combined index was 0.878 (95% CI 0.787–0.969). Among patients with score < 0.412, the regression rate was 11.1%, much lower than 81.8% of those ≥ 0.412 ($P < 0.001$, Fig. 1 B,C).

Conclusion: Patients with better histological response to entecavir treatment showed differences in metabolite levels at baseline. An index combined with four metabolites was an ideal predictor for histological respond in hepatitis B cirrhosis. A cut-off value of 0.412 distinguished patients who had a better respond to therapy.



[PP-0917]

Liver fibrosis by fibroscan in chronic hepatitis B patients during tenofovir disoproxil fumarate in Mongolia

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Objectives: We aimed to assess the performances of liver fibrosis during antiviral treatment by liver stiffness (LS) measurement using Fibroscan in chronic hepatitis B (CHB) patients.

Materials and Methods: We followed and evaluated treatment outcome of fifty six patients with chronic hepatitis B, initiating their TDF regimen at the Mongolian National University of Medical Sciences and Happy Veritas Clinic and Diagnostic Center. Each patient underwent transientelastography measurements, HBV quantification and serum liver marker assays before treatment with TDF, orally, once daily.

Results: The mean age of the patients (27 men, 29 women) was 45 $\pm$ 11. Before treatment LS measurement results indicated fibrosis stage F0 in 18 patients (32.1%), F1 in 6 (10.7%), F2 in 19 (33.9%), F3 in 18 (16.1%), and F4 in 4 patients (7.1%). After SVR12-SVR24 months the mean stiffness score of F1 increased from 7.8 to 8.3, F2 increased from 9.38 to 10.3, F3 decreased from 13.3 to 12.3, F4 increased from 23.8 to 28.4. In table 1 shows the changes of liver stiffness by Fibroscan after treatment. There was a significant negative correlation between platelet count and liver stiffness score.

Conclusion: In CHB patients who is receiving TDF regimen, annual LS measurement revealed that significant advanced fibrosis improvement slows but continues during treatment.

Table 1. The changes of liver stiffness by Fibroscan after TDF treatment

		Liver fibrosis stage before treatment				
		F0	F1	F2	F3	F4
After treatment	n	18	6	19	18	4
	FO	16 (88.9%)	3 (50%)	4 (21.1%)	4 (22.2%)	
	F1		1 (16.7%)	4 (21.1%)		
	F2	1 (5.6%)	1 (16.7%)	4 (21.1%)		
	F3		1 (16.7%)	7 (36.8%)	12 (67.7%)	1 (25%)
	F4	1 (5.6%)			2 (11.1%)	3 (75%)

[PP-0942]

Comparision of methods that evaluate the prognosis of liver cirrhosis

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Objectives: To compare the new method that evaluate prognosis of liver failure with the traditional method.

Materials and Methods: The 23th October 2019 our study was approved by meeting of biochemical principles (notary in 47) in MNUMS. 322 patients with liver cirrhosis who had been in department of Gastroenterology of the Third State Central hospital were evaluated. Before treatment we took the sample of hematology, biochemistry and coagulation. Laboratory examination performed by Sysmex-KX 21, Biochemistry by Humalizer 2000, for the coagulation we used Humaclot apparatus. All statistical analysis were conducted with the SPSS 21.0.

Results: Among all cases 39.3% of patients were in group A, 50.8% in group B, 9.8% in group C according to the Child Pugh classification. For the MELD score 10.9% of patients were in up to 10 score, 73.2% were in 10–19, 13.7% were in 20–29, 2.2% were in 30–39 score and there was no patients who had over 40 score. In the MELD classification total bilirubin or liver functional test indicate jaundice, INR point to coagulation, creatinine shows renal function thus it is more sensitive than the Child Pugh. Therefore we have some idea other researchers. PLT was 119.2 ± 6.2 in A group according to the Child Pugh whereas PLT was 132.3 ± 16.7*109/l in 0–9 score group in the MELD, PLT% was 26.9 ± 1.3 in A group and 26.7 ± 2.3 in 0–9 score of MELD, prothrombin time was 17.3 ± 0.4 in A group and 16.4 ± 0.9 in 0–9 score of MELD. The splenic length was 12.1 ± 0.2 in A group whereas 11.8 ± 0.5 in 0–9 score of MELD. This shows MELD classification enable to make early diagnosis and evaluate the prognosis therefore appropriate other researchers.
Conclusion: The MELD score more sensitively than Child Pugh (CTP) score. 13.7% of studied patients requires urgent liver transplantation.

[PP-0943]

The comparative study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection in Mongolia

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Objectives: Comparative study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection in Mongolia.
Materials and Methods: Our study continued from January 2018 to March 2020 and we measured liver fibrosis stage in patients with HBV infection and HBV/HDV co-infection using a FibroScan (kPa). In our study, in random sampling cases are selected 354 patients with HBV single infection and HBV/HDV co-infection. 177 of all patients have HBV/HDV co-infection. We selected parameters from patient medical histories in our study, such as serologic markers of HBV,quantification of HBV and HDV in serum samples, blood test, liver function test and liver fibrosis stage. Summary statistics were performed using SPSS 22.0 software.
Results: 354 patients (169 men (47.7%) and 185 females (52.3%); range (18–75)) are participated in our study. According to the comparative study in laboratory tests, ALT level was HBV—44 (36; 51.5) and HBV/HDV—61 (39.8; 97.55). AST level was HBV—39.1 (30; 83) and HBV/HDV—50 (33.1; 77.8). The Platelet count was HBV—193 ± 66 and HBV/HDV 181 ± 62.8. When we compared, liver fibrosis stages were HBV—F0 67 (37.9%), HBV/HDV—F0 57 (32.2%), HBV—F1 22 (12.4%), HBV/HDV—F1 17 (9.6%), HBV—F2 39 (22%), HBV/HDV F2 39 (22%), HBV—F3 29 (16.4%), HBV/HDV—F3 41 (23.2%),HBV—F4 20 (11.3%) and HBV/HDV—F4 23 (13%). In table 1 shows the difference of liver fibrosis by age group.
Conclusion: 65.5% of all patients with HBV/HDV co-infection are from 31 to 50 years old. Liver fibrosis of patients with HBV/HDV co-infection is a higher 1.88 kPa than patients with HBV infection.Aging can also increase the risks of liver cirrhosis. Our study shows that, the hepatitis is more severe in patients with HBV/HDV co-infection and the platelet count is more decreased.

[PP-0946]

Functional and morphological abnormality of liver among diabetic patients with viral hepatitis/ M2BPGI and elastography changes comparative results

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Objectives: To indentify viral infection, viral hepatitis in patients with diabetes and to compare liver function and diabetes control for diabetic patients with liver disease.
Materials and Methods: Biochemistry test, coagulation, immunology test are evaluated in 117 patients in clinical laboratory of National university hospital. We are used FIBROSCAN TOUCH 502 elastograpy in Mungun guur hospital. We studied the liver biopsies of 10 consecutive patients in clinical pathology division of Bio-Medical school of MNUMS. Therefore Place paraffin infiltrated tissue in a mold with a small volume of liquid paraffin. Based Paints Hemtoksilin Eozin all cases (H & E) determined by contrast, forms a good examination of a light microscope, fabrication and PAS stain on glycogen accumulation cell cytoplasmic and nuclear levels.
Results: There were 117 patients and by average of ages 51–52 aged patient. The following up study diabetic patients type 2 n = 78, diabetic patients with HCV n = 39 two groups. Diabetic patients group in biochemistry test total cholesterol4.78 ± 1.16; triglyceride2.62 ± 1.54;HbA1c 9.46 ± 4.37; in immunology tests M2BPGi (COI) counted 2.24 ± 2.19 and fibroscan's fibrosis 7.38 ± 2.37, steatosis 290.6 ± 50.5.BMI 31.6 ± 4.5.6 case possessed so-called glycogen nuclei of hepatocytes, 6% had PAS-positive thickening of blood vessels in the portal tracts. Diabetic patients with HCV patients group in biochemistry test total cholesterol 4.4 ± 1.09; triglyceride 2.01 ± 1.08;HbA1c in immunology testsM2BPGi (COI) counted 3.23 ± 1.58and fibroscan's fibrosis 11.8 ± 7.4, steatosis 290.6 ± 50.5.BMI 29.8 ± 4.9. Liver biopsy had central vein fibrosis, and sinusoidal fibrosis.
Conclusion: Diabetic patients group in immunology tests M2BPGi (COI) counted 2.24 ± 2.19 and fibroscan's fibrosis 7.38 ± 2.37, 6 cases possessed so-called glycogen nuclei of hepatocytes, 6% had PAS-positive thickening of blood vessels in the portal tracts. in liver biopsy fibrosis F_{1-2}. Diabetic patients with HCV patients group in immunology tests M2BPGi (COI) counted 3.23 ± 1.58and fibroscan's fibrosis 11.8 ± 7.4. Liver biopsy had central vein fibrosis, and sinusoidal fibrosis.

[OP-0971]

Role of plasma osteopontin level as a predictor of hepatic fibrosis regression and response to antiviral treatment in patients with chronic HBV or chronic HCV infection

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Objectives: Hepatitis B virus and Hepatitis C virus infection is one of the public health problems in Egypt. So we aimed to evaluate the efficacy of serum osteopontin as predictor of hepatic fibrosis regression and virological response in patients with chronic HBV or HCV infection.
Materials and Methods: This study has been conducted on 74 HBeAg + ve chronic HBV infection, 74 chronic HCV infection and 74 healthy controls. HBV patients treated with Entecavir. HCV patients treated with sofosbuvir, daclatasvir with or without ribavirin. One year post HBeAg seroconversion and 3 months after end of regular antiviral treatment for patients with chronic HBV and chronic HCV infection respectively, hepatic condition was reevaluated.
Results: 14.9% of patients with HBV, failed to achieve undetectable HBV DNA or HBeAg seroconversion and 2.7% of patients with HCV infection, failed to achieve SVR. In chronic HBV, pretreatment high serum osteopontin predict failure of virological response and hepatic fibrosis regression at a cutoff > 115.5, with 90.91% sensitivity, 82.54% specificity. Also high degree of liver stiffness predicts failure of hepatic fibrosis regression at a cutoff > 8.7, with 81.8% sensitivity, 73% specificity.
Conclusion: In chronic HBV infection low osteopontin predicts good virological response and hepatic fibrosis regression. But it has no role in predicting SVR or hepatic fibrosis regression in chronic HCV infected patients.

[PP-0994]

Diagnostic efficacy of Serum Asialo α1-acid glycoprotein levels for liver fibrosis and cirrhosis in CHB compared to healthy subjects: A prospective study

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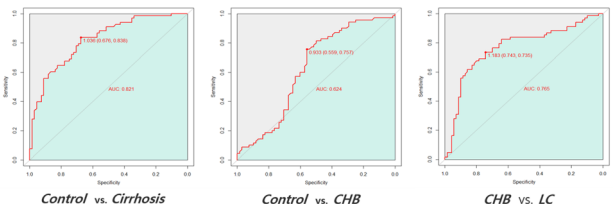
Objectives: Serum Asialo α1-Acid Glycoprotein (AsAGP) is a novel biomarker specific for liver fibrosis. However, there is no prospective study to investigate diagnostic performance of AsAGP for fibrosis burden compared with healthy control. The aim of this study to evaluate the diagnostic efficacy of serum AsAGP level in differentiating chronic hepatitis and cirrhosis.
Materials and Methods: A total of 206 subjects were prospectively enrolled. Liver cirrhosis was classified based on liver stiffness levels (> 11 kilopascal) measured by transient elastography (FibroScan). Only the cases that satisfies all the following criteria were enrolled as healthy control; absence of fatty liver in sonography, HTN, DM We compared serum AsAGP level between the three groups and evaluated diagnostic performance differentiating chronic hepatitis and cirrhosis.
Results: Serum AsAGP level was significantly different between heathy control, chronic hepatitis and liver cirrhosis (1.04 ± 0.31 μg/ml, 1.12 ± 0.34 μg/ml, 1.51 ± 0.43 μg/ml respectively; $p < 0.001$). Serum AsAGP level was positively correlated with liver stiffness ($r = 0.46$, p-value < 0.001). We performed area under the receiver operating characteristics (AUROC) for evaluating diagnostic efficacy of AsAGP between three group. AUROC of Healthy control versus cirrhosis was 0.821 ($P < 0.001$). AUROC of Healthy control versus chronic hepatitis was 0.624 ($P < 0.001$). AUROC of chronic hepatitis versus cirrhosis was 0.765, $P < 0.001$). In multivariate analysis, serum AsAGP level was the independent predictor of cirrhosis (odds ratio 129.36, p-value < 0.0007).
Conclusion: Serum AsAGP level in patients with cirrhosis was significantly higher than healthy controls and chronic hepatitis. AsAGP level showed a good diagnostic performance in predicting liver cirrhosis and chronic hepatitis which suggests a potential role as a biomarker for liver fibrosis.



[PP-1083]

Changing landscape of liver cirrhosis in multi-racial Asian country: A decade comparison

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Objectives: Viral hepatitis B was a commonest cause of cirrhosis in Asian countries, however with the rising prevalence of obesity and prevention strategy for viral hepatitis B, we predict that there is a change in the epidemiology of cirrhosis. Our aim is to determine the change of aetiology of cirrhosis and hepatocellular carcinoma in our centre.
Materials and Methods: A cross sectional study was conducted where we recruited all cirrhosis patients who were attending inpatient and outpatient service in our centre from July 2019 to July 2021. Baseline demography and clinical characteristics were collected via electronic medical record system. Data collected was analyzed and compared with historical data from our centre that was collected approximately a decade ago, from April 2006 to May 2009.
Results: A total of 354 patients were recruited into this study consisting of 198 male (55.9%) and 156 female (44.1%) with mean age of 63.36 year-old (20–90). The aetiologies of cirrhosis were NASH,

n = 144, (40.7%); viral hepatitis B, n = 78, (22%); viral hepatitis C, n = 31, (8.8%); alcohol, n = 29, (8.2%); hepatitis B + NASH, n = 16, (4.5%); cryptogenic, n = 23, (6.5%) and autoimmune hepatitis, n = 11, (3.1%). NASH was the leading aetiology among Malays (50.4%) compared to Indians (46.3%) and Chinese (32%). Hepatitis B was the main aetiology among Chinese (33.3%) compared to Malays (16%) and Indians (6.3%). Alcohol was the predominant aetiology among Indians (25%) compared to Chinese (4.8%) and Malays (0%). 48 patients (13.6%) had HCC with viral hepatitis B being the dominant cause (45.8%) followed by NASH (18.8%) and alcohol (6.3%).

Conclusion: Our study showed that there was a drastic change in epidemiology of cirrhosis where the predominant aetiology have changed from viral hepatitis B to NASH. However, viral hepatitis B remained the commonest cause of HCC followed by NASH.

Table 1

Duration of study	July 2019 - July 2021	April 2006 - May 2009
Number of subjects, n	354	460
Mean age, year(range)	63.36 (20-90)	58.8 (15-87)
Gender, n (%)		
Male	198 (55.9%)	317 (68.9%)
Female	156 (44.1%)	143 (31.1%)
Race n (%)		
Malay	119 (33.6%)	96 (20.69%)
Chinese	147 (41.5%)	274 (59.6%)
Indian	80 (22.6%)	90 (19.6%)
Others	8 (2.3%)	0%
Child Pugh classification, n (%)		
A	231 (65.3%)	Not available
B	66 (18.6%)	Not available
C	30 (8.5%)	Not available
Not available	27 (7.6%)	Not available
Liver cirrhosis Aetiology, n (%)		
NASH	144 (40.7%)	0
Viral hepatitis B	78 (22.0%)	212 (46.1%)
Viral hepatitis C	31 (8.8%)	85 (18.5%)
Viral hepatitis B and NASH	16 (4.5%)	0
Viral hepatitis B and alcohol	0	5 (1.1%)
Viral hepatitis C and NASH	6 (1.7%)	0

[L-PP-1254]

Notoginsenoside R1 ameliorates liver fibrosis induced by carbon tetrachloride via regulating PPAR-γ/TGF-β1/Smad2/3 pathway

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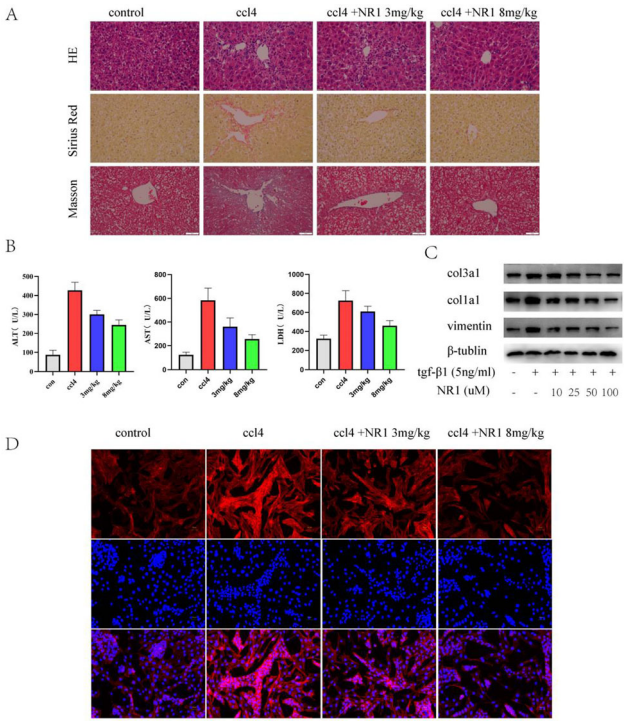
Objectives: Notoginsenoside R1 (NR1), an extract of the traditional Chinese medicine Panax notoginseng, has been reported to be beneficial to cardiovascular and cerebrovascular diseases. The current research aims to investigate the mechanism of NR1 alleviating carbon tetrachloride (CCl4) induced hepatic fibrosis in mice.

Materials and Methods: C57 mice were injected three times per week with 1:9 CCl4 in olive oil or olive oil alone (vehicle control mice) by intraperitoneal (ip) injection (2 mL/kg body weight) for 12 weeks. The mice were randomly divided into 4 groups (n = 6): vehicle control group, CCl4 group, and CCl4 plus different doses of NR1 (3 or 8 mg/kg, i.p.) groups.

Results: Histopathological changes and elevation in serum transaminase activity, inflammation levels indicated aggravated hepatic injuries induced by 12-week of CCl4 intraperitoneal injection. Treatment of NR1 significantly decreased serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), inflammatory cytokines tumor necrosis factor (TNF)-α and interferon (IFN)-γ. Hematoxylin–eosin staining (HE), Sirius red and Masson staining suggests that NR1 robustly ameliorated liver inflammation and fibrosis. The anti-fibrotic effect of NR1 was demonstrated by reductions in mRNA and protein expression of α-smooth muscle actin (α-SMA), and collagen in both liver tissue and hepatic stellate cell (HSCs). NR1 inhibited the activation of nuclear factor kappa-B (NF-κB) and TNF-α in vitro. Furthermore, peroxisome proliferator-activated receptor (PPAR)-γ upregulation and transforming growth factor-β1 (TGF-β1) and phosphorylation of Smad2/3 downregulation on both mRNA and protein levels were observed by NR1 treatment compared to CCl4 group in JS-1 and LX-2, which were reversed by T0070907, a selective PPAR-γ inhibitor.

Conclusion: This study demonstrated that NR1 possesses anti-inflammatory and anti-fibrotic effects via regulating PPAR-γ signaling to inhibit TGF-β1/Smad2/3 pathways in HSCs.



[L-OP-1259]

Study of thyroid function in patients of chronic liver disease and correlation with severity of chronic liver disease

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Objectives: To determine thyroid hormone levels in the liver cirrhosis patients and to study possible correlation between hypothyroidism and liver cirrhosis.
Materials and Methods: Overall 66 patients with cirrhosis and 19 controls were recruited, and they underwent detailed evaluation including blood sugar, lipid profile, LFTs, RFTs, CBC, PT/INR, thyroid profile, ultrasonography of abdomen, upper GI endoscopy and stool for occult blood testing.
Results: Fall in serum free T3 was the commonest thyroid abnormality seen in 87.9% cases. Fall in free T4 was seen in 7.6% cases and rise in thyroid stimulating hormone was observed in only 6.1% cases. Mean FT3 in cases was seen to be significantly less in cases than in controls (2.38 ± 1.29 vs 5.16 ± 0.74). For markers of severity, FT3 level was also found to be low in patients with decreased serum albumin level (p value = 0.002). FT3 level was low in patients with high Child–Pugh-Turcott score (p value-0.011). Mean T3 was seen to fall with rise in PT/INR and fall in platelet count. No significant correlation was found between low free T3 levels and srum bilirubin, severity of ascites and variceal grading.
Conclusion: The most common thyroid function abnormality in chronic liver disease patient was Low FT3, normal FT4 and normal TSH. Free triiodothyronine levels are the most sensitive predictors of decompensated liver disease. Positive correlation between FT3 and serum albumin and an inverse correlation between FT3 level and CPT score was found. As serum albumin and CPT are used as an indicator of severity of liver disease, FT3 may also be used as a marker in grading the severity of liver disease.

[L-OP-1331]

Post-trancriptional regulation of HAS2 by miR-200c in the pathogenesis of liver fibrosis

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Objectives: microRNAs (miRNAs), a class of small noncoding RNAs, are often dysregulated in liver diseases and contribute to liver pathology via post-transcriptional regulation. Previously, we identified hyaluroan synthase 2 (HAS2) as a driver of liver fibrosis. During liver fibrogenesis, HAS2 was overexpressed in activated hepatic stellate cells (HSCs). The purpose of this study is to elucidate the regulatory mechanism of HAS2 expression by miRNA(s) and to determine the role of HAS2/hyaluronan (HA) in liver injury, inflammation, and fibrosis.
Materials and Methods: Acute CCl_4-induced liver injury and chronic CCl_4-induced liver fibrosis models using HSC-specific Has2 knockout mice were used. Liver samples from 65 liver fibrosis patients with chronic hepatitis B virus infection were analyzed.
Results: We found that miR-200c was commonly downregulated in human and murine liver fibrosis among miRNAs which can putatively target HAS2. TGF-β treatment also decreased miR-200c expression in LX-2 cells. Through miTarget 3'UTR luciferase assay, we demonstrated that HAS2 is a direct target of miR-200c. miR-200c repressed not only HAS2 but also mRNA expression levels of fibrogenic genes and chemokines. We found that hyaluronidase 2 (HYAL2), but not HYAL1, was significantly increased in the advanced stage of liver fibrosis. Another cohort from GEO database (GSE84044, liver fibrosis patients with chronic hepatitis B virus infection) also supported our results. HYAL2 catalyzes the cleavage of high molecular weight-hyaluronan to low molecular weight-hyaluronan (LMW-HA). LWM-HA treatment stimulated chemokine production, such as CCL3 and CCL4, which play an important role in liver inflammation and fibrosis. Loss of Has2 in HSCs attenuated acute CCl_4-induced macrophage infiltration as well as chronic CCl_4-induced liver inflammation and fibrosis.
Conclusion: We demonstrate that downregulation of miR-200c in fibrotic livers increased HAS2 expression, which allows the secretion of chemokines and perpetuation of inflammation. This suggests that HAS2 can be a potential therapeutic target for liver inflammation and fibrosis.

[L-OP-1337]

Antifibrotic potential of quercetin against thioacetamide-induced hepatocellular fibrosis by regulating iron homeostasis

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Objectives: Aberrational iron regulatory pathway leads to disturbance in iron homeostasis, resulting in many health complications especially chronic hepatic disorders. Key mediators of the iron regulatory pathway are not only associated with but also affect the progression of hepatic fibrosis. The purpose of this experimental work is to scrutinize the potential of quercetin for amelioration and prevention of hepatic fibrosis by regulating key mediators of iron homeostasis.
Materials and Methods: Progressive hepatic fibrosis was induced by intraperitoneal injection of thioacetamide (200 mg/kg) twice a week for 6 weeks followed by daily oral intake of quercetin (50 mg/kg) and silymarin (50 mg/kg) respectively for 4 weeks, substantially to probe into the therapeutic efficacy of quercetin; preventive groups received concurrently intraperitoneal injection of thioacetamide (200 mg/kg) twice a week and daily oral intake of quercetin (50 mg/kg) and silymarin (50 mg/kg) respectively for 6 weeks, to investigate preventive potential of quercetin.
Results: Serological results demonstrated that thioacetamide significantly changed the total serum iron levels and catalase activity (P-value < 0.05). These changes were significantly restored and prevented by treatment with quercetin and silymarin respectively when compared with hepatotoxic group. The mRNA expression of iron regulatory key mediators; transferrin, hepcidin, ferritin, heme oxygenase-1, were significantly (P-value < 0.001) upregulated after the use of thioacetamide, while quercetin and silymarin treatment caused a significant decline in the expression of these genes as compared to the hepatic injury group. Findings from Prussian blue staining also elucidated striking recovery from hemosiderin deposition within hepatocytes and thus hepatic fibrosis.

Conclusion: From the current study, it can be concluded that quercetin has the potential to inhibit hepatic fibrosis by regulating iron homeostasis.

Portal Hypertension and its complications

[OP-0048]

Frequency of post banding ulcers- single center study, Karachi, Pakistan

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Objectives: 1. To determine the frequency of post esophageal band ligation ulcers in patients undergoing esophageal band ligation in a tertiary care centre. 2. To determine the risk factors associated with developmentof post esophageal band ligation ulcers.
Materials and Methods: Cross sectional study was conducted at Endoscopy Suite, Section of Gastroenterology, Aga Khan University Hospital (AKUH), Karachi. Data was prospectively collected from patients. Patients were enrolled after endoscopic band ligation. Oesophageal variceal band ligation was performed by occluding the protruding variceal column with elastic rubber rings, using a transparent cap attached to the distal end of the endoscope (using a 6 shooter Saeed multiband ligator, Cook Medical Endoscopy, Limerick, Ireland) and followed for 4 weeks for development of post-banding ulcers. Demographic data was presented as simple descriptive statistics giving mean and standard deviation and qualitative variables was presented as frequency and percentages. Effect modifiers were controlled through stratification. Post stratification chi square test was applied taking p-value of ≤ 0.05 as significant.
Results: A total of 138 patients were included in this study. Mean age, 52.04, mean hemoglobin level, platelet count and prothrombin time was 9.60 $\pm$ 2.02 g/dl, 116,070 $\pm$ 58,500 mcl and 13.7 $\pm$ 1.82 s respectively. 85 (61.6%) were male and 53 (38.4%) were female. Out of 138 patients, 14 (10.1%) developed post band ulcers and 8 developed (5.8%) bleeding.
Conclusion: Post banding ulcers and post-banding ulcer bleeding is an uncommon but severe complication of esophageal banding. Patients with advanced Child Pugh Class and prior history of esophageal variceal band ligation have higher risk of developing post band ulcers.

[PP-0053]

Early hospital readmissions in patients with cirrhosis: A retrospective review of causes and predictive factors

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Objectives: Hospital readmissions not only put financial burden on patients and their families but employ significant amount of healthcare resources, physician consultations and economic as well as social burden on the society. We aimed to evaluate the causes and predictive factors in our population to avoid the early readmissions.
Materials and Methods: This is a retrospective descriptive cross-sectional study conducted at Aga khan university hospital Karachi, Pakistan in which we have reviewed the records of patients admitted from 1st October 2020 to 31st Dec 2020 and early readmissions of patients within 30 days.
Results: From the total of 124 patients, 36 got readmitted within 30 days of their index admission. Mean age of the patients was 55.2 ($\pm$ 6.54), 67 (54%) were male and 57 (46%) were females. The most common etiology of cirrhosis was hepatitis C i.e. 57 (46%) followed by NAFLD 43 (34.7%) and hepatitis B 18 (14.5%). The cause of admission, Child Pugh score and MELD-Na on index and readmission is shown in Table 1. UTI is found to be the most common source of infection in index admission as well as in readmission. Patients with higher MELD-Na and Child Pugh score B and C were found be the predictive factors for readmissions.
Conclusion: We concluded that high Child Pugh and Meld-Na was seen in patients who got readmitted. Variceal bleed, ascites and encephalopathy led to higher readmission rates. Improvement is needed in the management of sepsis and portal hypertension especially in patients with high Child Pugh and Meld-Na scores to avoid readmissions.

Table 1 Description of causes and prognostic markers at index and re-admission.

Frequencies/ Mean(±SD)	Index Admission (n=124)	Re-admission (n=36)
Child Pugh Score (%)		
A	8(6.5)	0
B	62(50)	12(33.3)
C	54(43.5)	24(66.6)
MELD-Na	19.9(±6.25)	23.0(±5.7)
Causes (%)		
Variceal Bleed	34(27.4)	2(5.55)
Encephalopathy	34(27.4)	18(50)
SBP	10(8.1)	1(2.7)
Ascites	32(25.8)	13(36.1)
AKI	6(4.8)	2(5.55)
Other	8(6.5)	0
Infection (%)		
URTI	3(2.4)	0
LRTI	4(3.2)	3(8.3)
UTI	20(16.1)	15(41.6)
None	97(78.2)	18(50)

SBP = Spontaneous Bacterial Peritionitis; AKI= Acute Kidney Injury;
URTI= Upper Respiratory Tract Infection; LRTI= Lower Respiratory Tract Infection;
UTI= Urinary Tract Infection

[PP-0112]

Initial treatment response and survival outcome of spontaneous bacterial peritonitis in cirrhotic patients with hepatocellular carcinoma

Chang Hun Lee[1,2], Hyeonseok Baek[1,2], Seok Hyun Seo[1,2], Seung Young Seo[1,2], Seong-Hun Kim[1,2], Sang Wook Kim[1,2], Seung Ok Lee[1,2], Soo Teik Lee[1,2], In Hee Kim[1,2]

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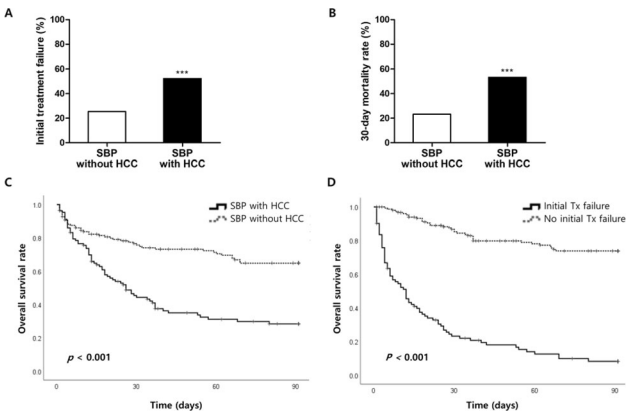
Objectives: To compare the initial treatment responses and short-term mortality of spontaneous bacterial peritonitis (SBP) in cirrhotic

patients with hepatocellular carcinoma (HCC) versus those without HCC and to analyze factors associated with initial treatment failure and short-term mortality of SBP.
Materials and Methods: We retrospectively reviewed data from SBP with liver cirrhosis (LC) patients between 2004 and 2020 at Jeonbuk national university hospital. A total of 245 cases were included and 107 cases (43.7%) were combined with HCC.
Results: Overall, the rate of initial treatment failure, 7-day and 30-day mortality were 91 (37.1%), 42 (17.1%), and 89 (36.3%), respectively. Baseline CTP score, MELD score, culture positive rate, and rates of antibiotic resistance were not different regarding presence of HCC. However, patients combined with HCC showed higher rate of initial treatment failure compared to non-HCC patients (52.3% vs. 25.4%, $P < 0.001$). In similar, 30-day mortality was also significantly higher in patients with HCC compared to non-HCC patients (53.3% vs. 23.2%, $P < 0.001$). In multivariate analysis, HCC, renal impairment, CTP grade C, and antibiotic resistance were independent factors for initial treatment failure. Furthermore, HCC, hepatic encephalopathy, MELD score, and initial treatment failure were independent factors for 30-day mortality. Kaplan–Meier survival analysis showed statistically significant poor survival outcome in HCC and initial treatment failure group with log-rank test ($P < 0.001$ and $P < 0.001$, respectively).
Conclusion: HCC is an independent risk factor for initial treatment failure and high short-term mortality in cirrhotic patients with SBP.



[PP-0114]

A comparison of endoscopic variceal obliteration and retrograde transvenous obliteration in patients with gastric variceal bleeding

Chang Hun Lee[1,2], Jun Tae Park[1,2], Hee Jin Moon[1,2], Byung Chul Jin[1,2], Seung Young Seo[1,2], Seong-Hun Kim[1,2], Sang Wook Kim[1,2], Seung Ok Lee[1,2], Soo Teik Lee[1,2], In Hee Kim[1,2]

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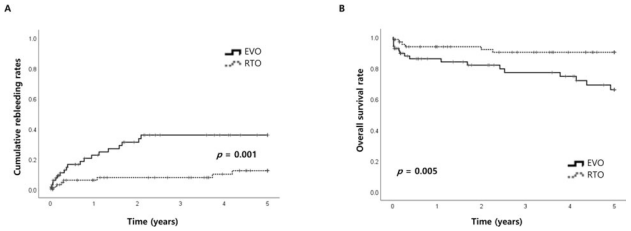
Objectives: Gastric variceal bleeding (GVB) is one of the severe complications of liver cirrhosis. However, optimal treatment strategy is not still determined. We compared clinical outcomes of endoscopic variceal obliteration (EVO) and retrograde transvenous obliteration (RTO) in patients with GVB.
Materials and Methods: We reviewed data from GVB patients who were admitted from 2005 Jan to 2020 Dec in Jeonbuk National University Hospital. First, we selected eligible RTO patients, then age-and-sex-matched EVO patients were selected using propensity score matching analysis. Clinical parameters were compared between the two groups.
Results: Totally 142 patients (71 of each group) were included. In baseline clinical characteristics, EVO group revealed more frequent previous bleeding history and concomitant esophageal varices. CTP and MELD score were more severe in EVO group. Endoscopic findings represented that IGV1 was more common in RTO group and size of varices was larger. We compared procedural results and time leading up to the procedure was significantly lower in EVO group. Procedural success was more than 90% in both groups and showed no difference. Laboratory results after 1-year of treatment for GVB also showed no significant difference. Kaplan–Meier analysis was performed and re-bleeding rate was lower in RTO group. In overall survival rate, RTO group also showed better survival outcome compared with EVO group ($P = 0.005$).
Conclusion: EVO and RTO both showed considerably high success rates with tolerable adverse events. RTO group revealed lower re-bleeding rate and better survival outcome compared with EVO group in patients with GVB.



[PP-0118]

A comparison of endoscopic variceal ligation and endoscopic variceal obliteration in patients with gastric cardia variceal bleeding

Hye Jin Kang[1,2], Chang Hun Lee[1,2], Hee Jin Moon[1,2], Byung Chul Jin[1,2], Seung Young Seo[1,2], Seong-Hun Kim[1,2], Sang Wook Kim[1,2], Seung Ok Lee[1,2], Soo Teik Lee[1,2], In Hee Kim[1,2]

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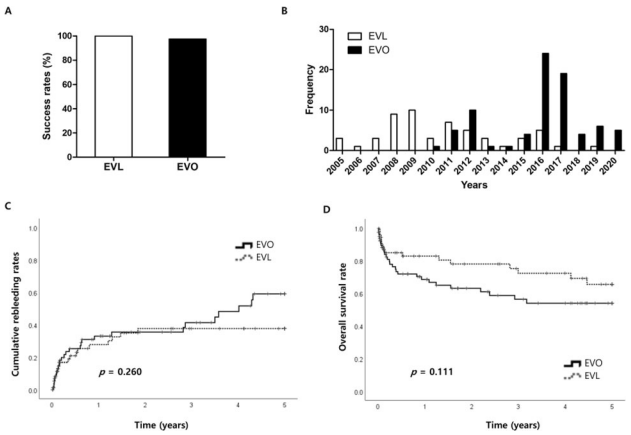
Objectives: The purpose of the study is to evaluate the treatment efficacy of endoscopic variceal ligation (EVL) and endoscopic variceal obliteration (EVO) in patients with type 1 gastroesophageal varices (GOV1) bleeding around the esophagogastric junction.
Materials and Methods: From January 2005 to December 2020, the data of patients with GOV1 variceal bleeding who underwent endoscopic management (EVL or EVO) at Jeonbuk National University Hospital was retrospectively reviewed. Clinical parameters were compared between the two groups.
Results: A total of 133 patients (55 in EVL 80 in EVO) were included. In baseline clinical characteristics, EVO group showed a significantly larger size of esophageal varices and gastric varices. Baseline CTP and MELD scores did not differ between groups. EVL

was mainly implemented before 2010 and tended to be replaced by EVO after 2010. We evaluated the procedural success rate and the result was almost 100% in both groups. Kaplan–Meier analysis was performed and there was no difference in re-bleeding rate between groups. There were also no statistical differences between groups in overall survival rates.

Conclusion: EVL and EVO showed considerably high success rates in GOV1 variceal bleeding patients. In terms of re-bleeding and overall survival, there was no significant difference between EVL and EVO.



[PP-0156]

Spontaneous iliopsoas muscle hematoma mimicking avascular necrosis in alcoholic liver cirrhosis: A case report

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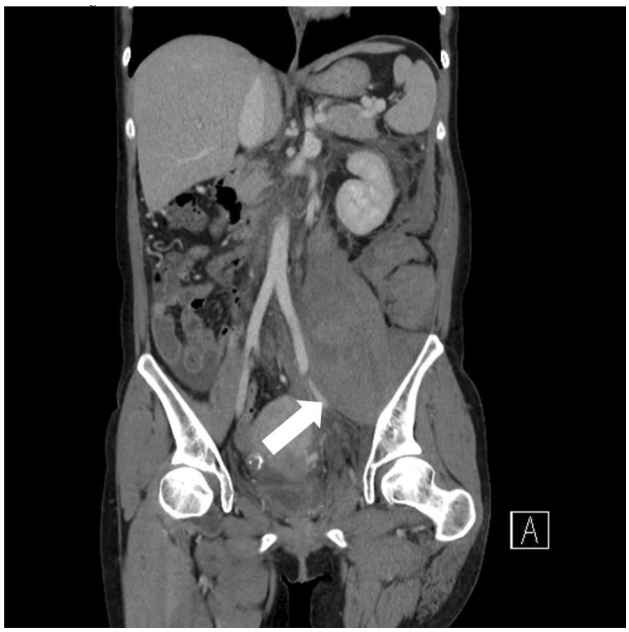
Objectives: Spontaneous hematoma of the iliopsoas muscle in patients with alcoholic liver cirrhosis is rare. We report a rare case of spontaneous iliopsoas hematoma that caused a positive Patrick's sign and mimicked avascular necrosis in a patient with alcoholic liver cirrhosis.

Materials and Methods: A 35-year-old female presented with left inguinal pain and limitation of motion. She had a history of alcoholic liver cirrhosis.

Results: On physical examination, Patrick's sign was positive, suggestive of hip joint pathology. Computed tomography scan of the abdomen indicated a 20-cm-sized hematoma along the left iliopsoas muscle. Because the patient's liver function was poor and there was no evidence of active bleeding, a conservative treatment option was taken. On follow-up computed tomography one month later, the size of the hematoma decreased to 3.3 cm.

Conclusion: Although avascular necrosis occurs frequently in patients with chronic alcohol intake, a rare but fatal iliopsoas muscle hematoma mimicking avascular necrosis should be considered in alcoholic liver cirrhosis.



[PP-0297]

Efficacy of contrast-enhanced computed tomography on the management of gastroesophageal varices in patients with hepatocellular carcinoma

Takayuki Kondo[1], Kisako Fujiwara[1], Sae Yumita[1], Miyuki Nakagawa[1], Keita Ogawa[1], Hidemi Unozawa[1], Terunao Iwanaga[1], Naoto Fujita[1], Hiroaki Kanzaki[1], Keisuke Koroki[1], Kazufumi Kobayashi[1,2], Soichiro Kiyono[1], Masato Nakamura[1], Naoya Kanogawa[1], Tomoko Saito[1], Sadahisa Ogasawara[1,2], Shingo Nakamoto[1], Tetsuhiro Chiba[1], Jun Kato[1], Naoya Kato[1]

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Objectives: Prevention of variceal bleeding and screening of gastroesophageal varices is critical in the management of hepatocellular carcinoma (HCC). However, it is inefficient to perform the endoscopic screening every year in a crowded treatment schedule. Contrast-enhanced computed tomography (CECT) is often performed for HCC screening. Therefore, we examined whether CECT can be used to screen for gastroesophageal varices and whether it is effective in predicting variceal bleeding.

Materials and Methods: This retrospective study enrolled 312 patients initially diagnosed with HCC between 2011 and 2014. We measured the maximal short-axis diameter of vessels in the lower esophagus/fundus on CECT, and examined the changes between the time of diagnosis and 1/2/3 years later, and verified the relationship with variceal bleeding. We also compared the finding on CECT and endoscopic findings in 231 patients who underwent endoscopy within 3 months from CECT.

Results: Diameter of vessels in esophagus/fundus subdivided on the basis of endoscopic variceal classification was no varices (F0): $1.1 \pm 1.3/0.1 \pm 0.5$ mm, small varices (F1): $4.1 \pm 0.8/3.7 \pm 1.5$ mm, medium varices (F2): $7.3 \pm 1.2/8.7 \pm 2.1$ mm, large

varices (F3): 9.2 ± 3.0/12.0 ± 2.4 mm. Best cutoff value was F1:3.1/3.4 mm (AUC = 0.986/0.972) F2: 5.5/5.7 mm (AUC = 0.995/0.999). Esophageal vessel diameter (EVD) worsened significantly after 2/3 years (P = 0.026/0.012). Gastric vessel diameter (GVD) showed worsening at both 1/2 and 3 years (P = 0.047/0.012/0.004). In cases of cirrhosis with EVD > 3 mm, there was a significant change in EVD over time. Cumulative esophageal variceal bleeding rates were 3.7/6.2/10 at 1/3/5 years. The deterioration in EVD of 0.3/0.7/2.3 mm or more at 1/2/3 years (AUC = 0.883/0.842/0.961) correlated with variceal bleeding. HCC staging, portal vein tumor thrombosis, and treatment for HCC were not significantly associated with variceal bleeding.
Conclusion: The EVD/GVD on CECT correlates well with endoscopic findings. The screening of varices should be conducted in case with EVD > 5.5 mm or EVD > 3 mm with cirrhosis. If deterioration is observed in EVD, treatment should be considered because of the high risk of esophageal variceal bleeding.

[PP-0309]

Prognostic impacts of the change in muscle mass on patients with cirrhosis according to sex

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Objectives: It is known that sarcopenia is significantly associated with the mortality and occurrence of complications of patients with cirrhosis. However, muscle mass can change, and it is not yet known how these changes affect the clinical course of patients with cirrhosis.
Materials and Methods: Among prospective cohort of patients with cirrhosis who had received the abdomen CT annually for HCC surveillance, those who underwent two or more CT scans were included. L3 skeletal muscle index (SMI) was adopted as a proxy of skeletal muscle mass, and we calculated a change of SMI between baseline and one-year (delta SMI/yr). Cirrhotic complications included ascites aggravation, spontaneous bacterial peritonitis, overt encephalopathy and variceal bleeding.
Results: In a total of 306 patients, 78 and 36 had sarcopenia and Child–Pugh class B/C decompensation, respectively. During a median follow-up of 36 months, 23 patients died and 32 had undergone complications of cirrhosis. Multivariate Cox regression analyses showed only Child–Pugh score and MELD score at 1-year were associated with survival. However, delta SMI/yr was associated with complication occurrence even after adjusted for Child–Pugh or MELD score at 1-year. The effect differed according to sex, and 1% decrease in delta SMI/yr accelerated 1.05 and 1.27-fold occurrence of complication in male and female, respectively. In addition, delta SMI/yr showed good prediction of occurrence of complication, with a cut-off of − 2.62% (sensitivity 73.9%, specificity 76.3%).
Conclusion: Delta SMI/yr was significantly associated with the occurrence of cirrhotic complications of patients with cirrhosis, independently with Child–Pugh and MELD scores at 1-year.

[PP-0418]

Outcome of intermittent thoracentesis versus pigtail catheter drainage for hepatic hydrothorax

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Objectives: Management of hepatic hydrothorax (HH) remains a challenging clinical scenario with suboptimal options. Therapeutic thoracentesis is simple drainage management that can provide rapid relief of symptoms, though its effects are temporary, and the procedure needs repeating. Recently introduced pigtail catheterization may be a promising alternative treatment for HH, though it has not been well studied. Is pigtail catheter drainage effective and safe compared to intermittent thoracentesis?
Materials and Methods: This multicenter, retrospective study included 164 cirrhotic patients with pleural effusion, treated at participating institutions from March 2012 to June 2017. Patients with neoplasms, cardiopulmonary disease, and infectious conditions were excluded. We compared the clinical outcomes including complications related to procedures, overall survival, and re-admission rates of pigtail catheter drainage versus thoracentesis.
Results: A total of 164 patients were divided into pigtail catheter (n = 115) and thoracentesis (n = 49) groups. During the follow-up period of 6.93 months after discharge, 98 patients died (pigtail; n = 47 vs. thoracentesis; n = 51). The overall survival (p = 0.61) and 30-day mortality (p = 0.77) were similar between the pigtail catheter and thoracentesis group. Only MELD scores were associated with overall survival (adjusted HR, 1.08; p < 0.01) in patients with HH. Spontaneous pleurodesis occurred in 59 patients (51.3%) in the pigtail catheter group. Re-admission rates did not differ between the pigtail catheter and thoracentesis groups (13.2% vs 19.6% p = 0.7). A total of five complications occurred, including four total cases of bleeding (one patient in the pigtail catheter group and three in the thoracentesis group) and one case of empyema in the pigtail catheter group.
Conclusion: Pigtail catheter drainage is not inferior to that of intermittent thoracentesis for the management of HH, proving it may be an effective and safe clinical option.

[PP-0420]

Subclinical diabetes confirmed by 75gm-OGTT influence on the prognosis of decompensated cirrhosis

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Objectives: Disorders of glucose metabolism, such as impaired glucose intolerance (IGT) and diabetes mellitus (DM), frequently occur in cirrhosis. However, it has been underestimated when fasting plasma glucose (FPG) levels are considered. We aimed to evaluate who needs to be undertaken a 75-g oral glucose tolerance test (OGTT) to find underlying subclinical diabetes.
Materials and Methods: This prospective study included 713 patients with either compensated (Child–Turcotte–Pugh [CTP] class A) or decompensated cirrhosis (CTP class B/C) without previous DM history. All patients underwent a 75-g OGTT. The patients were divided into three groups: normal glucose tolerance (NGT), IGT, and newly diagnosed DM (subclinical DM).
Results: Among 713 patients, NGT was diagnosed in 139 (19.5%), IGT in 252 (35.3%), and subclinical DM in 322 (45.2%) patients, respectively. During a median follow-up period of 42.0 months, the cumulative survival rates of patients were as follows: NGT, 75.6%; IGT, 57.6%; and subclinical DM, 54.8%. Overall, IGT (adjusted hazard ratio [aHR], 1.669; 95% CI = 1.050–2.653; P = 0.03) and subclinical DM (aHR, 1.723; 95% CI = 1.101–2.698; P = 0.017) were identified as independent predictors of mortality. In patients with compensated cirrhosis (n = 415), neither IGT nor subclinical DM conferred a higher risk of mortality. However, among patients with decompensated cirrhosis (n = 298), those with IGT (aHR, 2.279; P = 0.022) and subclinical DM (aHR, 2.211; P = 0.022) showed a survival rate worse than those with NGT. In addition, subclinical DM was identified as an independent risk factor for infection (aHR, 2.801; P = 0.034).
Conclusion: IGT and subclinical diabetes by OGTT are associated with an unfavorable prognosis in cirrhosis, and the effect is pronounced in the decompensated state.

[PP-0445]

A novel strategy for the management ofgastroesophageal varices during molecular targeted therapy for hepatocellularcarcinoma

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Objectives: Bleeding from gastroesophageal varices (GOV) is one of the lethal complications managing advanced hepatocellular carcinoma. It is controversial how to reduce the endoscopic screening for varices and how to provide a prophylactic treatment. In this study, we examined whether contrast-enhanced computed tomography (CECT), which is frequently used for HCC screening, can be used to screen for GOV, and also investigated factors related to GOV bleeding and exacerbation during molecular targeted therapy.
Materials and Methods: This retrospective study included 494 patients who received molecular targeted therapy as first-line therapy for HCC between 2009 and 2019 and conducted the following analyses: (1) comparison between the endoscopic finding and the diameter of GOV measured by CECT, (2) GOV bleeding rate and predictive factors for bleeding after treatment, (3) GOV exacerbation rate and predictive factors for exacerbation on CECT 3 months after treatment.
Results: (1) Diameter of lower esophageal and gastric fundus vessels on contrast-enhanced CT correlated well with endoscopic variceal findings. (2) Cumulative bleeding rate from GOV was 7.4% at 1 year and 12.4% at 3 years. The presence of portal vein tumor thrombosis (PVTT), a diameter of lower esophageal vessels > 5.7 mm, and diameter of gastric fundus vessels > 3.8 mm were the predictive factors for GOV bleeding. (3) 221 patients were examined by CECT 3 months after treatment. There was no significant change in the diameter of the gastric fundus vessels. However, the diameter of the esophageal vessels was significantly worsened in 20 patients with F0 equivalent (N = 142), 18 with F1 equivalent (N = 61), and 3 with F2 equivalent (N = 18). Even if the esophageal varices are equivalent to F0 on CECT, patients with esophageal vessel diameter > 1.9 mm or PVTT were shown to have an exacerbation of esophageal varices after three months.
Conclusion: CECT evaluation of GOV during molecular-targeted therapy may help reduce unnecessary EGD and identify patients who need preventive treatment.

[OP-0556]

Segmental portal hypertension with bleeding isolated gastric varix as pancreatic neuroendocrine carcinoma presentation: A case report

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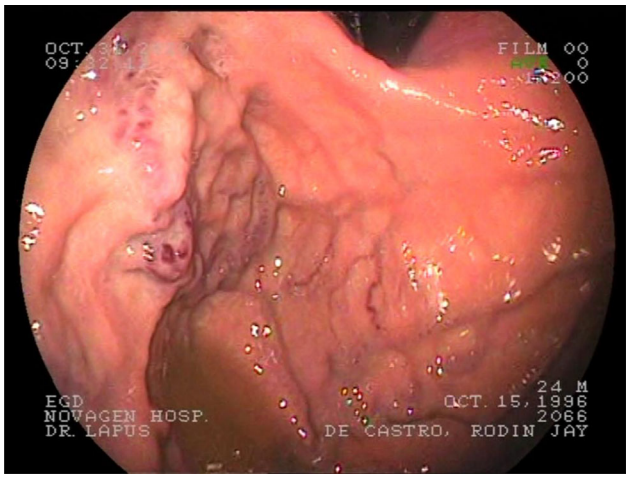
Objectives: Pancreatic neuroendocrine tumors (PNETs) are rare and often indolent neoplasms representing only about 2% of pancreatic neoplasms. Segmental portal hypertension (SPH) is reported as a local complication of PNET burden from splenic vein occlusion by mass effect or splenic vein tumor thrombus. Left-sided portal hypertension as a result of splenic vein occlusion constitutes only about 5% of all cases of portal hypertension. In this case, we discuss a case of pancreatic neuroendocrine carcinoma presenting as a case of a bleeding isolated gastric varix.
Materials and Methods: This is a case of a 23-year old male with no known comorbidities presenting with four-month history of intermittent episodes of hematemesis and weight loss. Esophagogastroduodenoscopy revealed an isolated gastric varix noted at the fundus with signs of recent bleed. Magnetic resonance imaging (MRI) of the upper abdomen revealed a lobulated heterogeneously enhancing mass arising from the distal pancreatic tail measuring 5.5 × 4.9x4.8 cm, which abuts the splenic hilum with apparent encasement of the vessels. Multiple enhancing hepatic nodules were seen on both lobes.
Results: The patient had undergone distal pancreatectomy, splenectomy, omentectomy and liver biopsy, and noted that the distal pancreas measuring 8.0 × 5.4 and 4.8 cm was almost entirely occupied by an irregular, solid mass. Histopathological findings revealed well – differentiated pancreatic neuroendocrine carcinoma with perineural invasion and metastatic tumor to peripancreatic lymph nodes and liver. The patient recovered from the operation uneventfully and was discharged stable. Patient was advised chemotherapy, however was lost to follow up.
Conclusion: In patients presenting with bleeding isolated gastric varices without signs of liver disease, diagnostic work-up for underlying pancreatic tumors must be done since it can be the only manifestation of a malignant tumor, as seen in this case.



[PP-0651]

The therapeutic effect of dabigatran in the liver cirrhosis patients with portal vein thrombosis

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Objectives: Portal vein thrombosis (PVT) develops in 10–25% of liver cirrhotic (LC) patients and may aggravate portal hypertension. The standard therapy for PVT in the LC patients were known as vitamin K antagonist. But nowadays, direct oral anticoagulant (DOAC) is more popular than vitamin K antagonist, and it can be used without monitoring. The aim of study is to find out the effect and safety of DOAC in PVT.
Materials and Methods: Patients with LC and non-malignant PVT were prospectively enrolled and randomized into two groups (dabigatran vs. warfarin). The baseline clinical and laboratory variables were collected, The size of the thrombus were evaluated at the baseline, 3 months and 6 months after treatment with abdominal CT scan.
Results: 10 patients were enrolled in the study during the period between Oct 2017 and Dec 2020. 5 patients were allotted in each group and one patient in each group was dropped out because of death without treatment complication and other hospital reference. Only one patient in warfarin group showed recanalization at the CT scan 6 months after treatment. All others except one failed to achieve the goal. There was no bleeding complication in all patients.
Conclusion: 1) Both dabigatran and warfarin showed limited therapeutic effect, only one patient in warfarin group had showed a resolution, but right portal vein thrombosis occurred again 6 months after the end of warfarin treatment. 2) Thrombolytic therapy is effective in only acute thrombosis. The patient are eligible if there are no thrombosis in the image study during recent two years. But two patients with cavernous transformation were included in each study group. it may cause worse results than expected. 3) The larger scale study is needed to find out that the DOACs is more effective than warfarin, and which DOAC has better treatment response.

[PP-0738]

Clinical characteristics in cirrhotic patients with non-forward flow of superior mesenteric vein

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Objectives: Non-forward or reversed flow is exclusively found in the portal vein system. Our previous reported that non-forward or hepatofugal flow of splenic vein was associated with gastric varices bleeding. However, the influence of non-forward flow of superior mesenteric vein (NFSMV) has not been determined. Thus we retrospectively examined the clinical characteristics of NFSMV in patients with chronic liver disease.
Materials and Methods: From March 2012 to June 2018, 380 patients with chronic liver disease had Doppler ultrasound examination for hemodynamics in portal vein system. Flow direction was judged using reference of color Doppler findings. The cases of bidirectional blood flow were also included to NFSMV cases.
Results: Among the candidate patients, 96 cases were included, including 18 cases of NFSMV and 78 cases of non-forward flow of splenic vein. NFSMV was detected at the main level of SMV in 13 cases, of which 8 were continuous reversed flow and 5 were bidirectional. Occlusion of portal vein system was found because of thrombus in 7 cases and tumor invasion in 4 cases. Of the 17 cases with NFSMV and liver cirrhosis, 1 case was Child–Pugh classification A, 9 cases for B, and 7 for C. Hepatic encephalopathy was observed in 8 cases, of which 3 cases had difficulty in treating. Moderate ascites was observed in 4 cases.
Conclusion: Patients with reversed, non-forward flow of superior mesenteric vein were accompanied by severe decompensated liver symptoms. Deep attention in the treatment of chronic liver disease is required.

[PP-0791]

Clinical outcome of endoscopic variceal obliteration compared with plug-assisted retrograde transvenous obliteration in cirrhotic patients with gastric varix

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Objectives: Endoscopic variceal obliteration (EVO) and balloon-occluded retrograde transvenous obliteration (BRTO) are used to manage gastric variceal bleeding. We compared the rebleeding and survival rate of patients with gastric varix treated with EVO or BRTO.
Materials and Methods: A retrospective study enrolled 234 patients with gastric variceal bleeding between July 2005 and May 2020. For the management of gastric variceal bleeding, 96 patients underwent EVO and 138 patients underwent BRTO. Rebleeding was defined as new-onset hematemesis, hematochezia, melena, or endoscopically proven bleeding. Time-to-rebleeding and survival time were examined by Kaplan-Meyer analysis.
Results: There were no significant differences in baseline characteristics among the two groups. There was also no difference with respect to endoscopic features of gastric varices including F-component and location. No long-term mortality difference was observed (Hazard ratio (HR) 1.107, P = 0.651). Lower rates of rebleeding were found with BRTO (HR 0.407, P = 0.012) compared to EVO. No difference was seen in the rate of new portal hypertensive complications (P = 464). But, esophageal varix bleeding with emergency EVL after BRTO is significantly higher than after EVO (p = 0.038).
Conclusion: BRTO is associated with a lower rate of rebleeding but there were no significant differences in survival time.

[OP-0811]

Correlate severity of thrombocytopenia with different grades of esophageal varices in chronic liver disease patients undergoing EGD in a tertiary care hospital

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Objectives: The aim of this study is to correlate severity of thrombocytopenia with different grades of esophageal varices in chronic liver disease patients undergoing EGD in a tertiary care hospital.
Materials and Methods: Material and methods: Study design: Cross sectional study. Setting: This study was conducted in Gastroenterology and Hepatology department of Liaquat National Hospital Karachi. Duration of study: Six months from. Subjects and methods: Seventy six patients were included who fulfilled the inclusion criteria after taking the informed consent. The SPSS version 17 was applied to the data.
Results: There were 55 (72.4%) males and 21 (27.6%) females. The mean age was 45.6 ± 14.7 years. 10 (13.2%) had Hepatitis B, 58 (76.3%) Hepatitis C, 01 (1.3%) Wilson's disease, 03 (3.9%) Autoimmune disease and 04 (5.3%) Alcoholic liver disease. 09 (11.8%) had Child–Pugh Class A, 41 (53.9%) Class B and 26 (34.2%) had Class C. The mean platelet count was 85/?l ± 40.2/?l. Out of 76 patients 70 (92.1%) had esophageal varices. 23 (30.3%) had grade III varices, 19 (25%) had grade II, 14 (18.4%) each had grade I & IV and 06 (7.9%) had grade 0 varices.
Conclusion: We concluded that thrombocytopenia can be used to stratify risk for occurrence of esophageal varices in cirrhotic patients and gastroscopy will have a high yield for varices when platelet count is 100/?l.

[PP-0817]

Esophageal variceal rebleeding in cirrhotic patients: Risk factors and mortality

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Objectives: Rebleeding from esophageal varices occurs within the first 2 year after the initial bleeding episode in approximately 60% of portal hypertensive patients, which results in serious bleeding-related consequences. The aims of the present study were to identify risk factors of esophageal variceal rebleeding and to analyze bleeding-related mortality in cirrhotic patients with portal hypertension.
Materials and Methods: Eighty-four patients with a previous history of esophageal variceal bleeding were retrospectively recruited and allocated to the following each group; rebleeding or non-rebleeding group. To find out independent risk factors for recurrent bleeding after initial cessation of first esophageal variceal bleeding, follow-up adherence of endoscopic and pharmacologic intervention as well as clinicodemographic, endoscopic, and radiologic findings were compared between the two groups.
Results: Fourty-three patients (51.2%) were assigned to the rebleeding group. Their median rebleeding period is 22 month and 1-, 2-, and 3-year rebleeding rates were 37%, 59%, and 65%, respectively. Among the clinical parameters analyzed, the initial location of esophageal varices ($p < 0.01$) and the regularity of elective endoscopic variceal ligation ($p < 0.01$) for the prophylaxis of rebleeding were significant factors affecting variceal rebleeding. The compliance of taking β-blocker was tended to be worse in rebleeding group than non-rebleeding group, but not significant. One-, two-, and three-year overall mortality rates of rebleeding group were 5%, 18%, and 29%, while those of non-rebleeding group were 2%, 2%, 2%, respectively, being significantly higher in rebleeding group than non-rebleeding group (p = 0.049). One-, two-, and three-year bleeding-related mortality rates of rebleeding group were significantly higher than those of non-rebleeding group (5%, 18%, 26% vs 0%, 0%, 0%, respectively, p = 0.006).
Conclusion: The significant bleeding-related mortality showed in cirrhotic patients with esophageal variceal rebleeding that was associated with the location of varices and regularity of applying elective endoscopic variceal ligation after initial cessation of first bleeding episode.

[PP-0820]

Portal hypertensive colopathy in cirrhotic patients: Clinical presentation and implication

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Objectives: Portal hypertensive colopathy (PHC) is known to be presented as mucosal/submucosal abnormalities of colon not rarely observed in patients with liver cirrhosis. However, no general consensus is established in aspects of the definition of these colonic lesions and its clinical relevance. This study was performed to

identify the pattern and frequency of colonic mucosal/submucosal changes and to evaluate their clinical implication in cirrhotic patients.
Materials and Methods: One hundred-thirty nine patients with liver cirrhosis who underwent diagnostic colonoscopy with simultaneous esophagogastroduodenoscopy, after excluding the patients with a previous history of any gastrointestinal intervention, were enrolled in the present study. Medical records with endoscopic findings of enrolled cirrhotic subjects were compared with those of age- and sex-matched health examinees (control).
Results: PHC indicated as mucosal/submucosal abnormalities of colon (hemorrhoid/anorectal varices, angiodysplasia, diffuse erythema/hyperemia, edema, granularity/atrophy, friability/spontaneous bleeding) were more frequent in cirrhotic patients than age- and sex-matched controls (38.8% vs. 3.6%, $p < 0.05$). The most frequent colonic abnormalities were hemorrhoids/anorectal varices (20.9%), the next was angiodysplasia (10.1%). Cirrhotic patients with colonic abnormalities were more likely to have high grade esophageal varices than cirrhotics without colonic abnormalities (44.4% vs. 25.9%, $p = 0.012$). However, no significant difference was noted in age, sex, etiology of cirrhosis, Child–Pugh classification, MELD score, presence of portal hypertensive gastropathy between the patients with or without colonic abnormalities. During follow-up period, gastrointestinal bleeding occurred in 7 patients (5%) in whom 6 patients had colonic abnormality. One-, three-, and five-year gastrointestinal bleeding rates of cirrhotic patients with colonic abnormalities were higher than those of patients without colonic abnormalities (3.7%, 7.4%, and 11.1% vs. 0%, 1.2%, and 1.2%, respectively, $p < 0.05$).
Conclusion: Mucosal/submucosal abnormalities of PHC including vascular lesions with varices, angiodysplasia, non-specific inflammation, and mucosal friability were frequent in cirrhotic patients, implicating to be a risk parameter of gastrointestinal bleeding.

[OP-0863]

A Comparison of prognostic models for predicting 6-week mortality in patients with acute variceal bleeding

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Objectives: Acute variceal bleeding (AVB) in patients with cirrhosis continues to have high mortality. Predicting 6-week mortality from baseline variables is essential for optimal focused management of patients who are at higher risk of mortality. Many models have been used for predicting 6-week mortality, but most of them lack precision and require further validation. We aimed to find out significant baseline predictors of 6-week mortality, develop a prognostic model using baseline variables, and compare the new model with the existing prognostic models using AUROC..
Materials and Methods: We prospectively included cirrhotic patients presenting with AVB admitted at our hospital from January 2019 to September 2021. Patients with malignancy or with significant cardio-respiratory comorbidity were excluded. They were treated as per standard guidelines using vasoactive drugs and endotherapy. They were followed for 6 weeks and baseline predictors of 6-week mortality were determined.
Results: A total of 112 patients were included in study (median age 49) [range 22–76], 87% males. Etiologies of cirrhosis were alcohol (66%), NASH (24%), HBV (4%), and others (5%). The baseline median (range) CTP, MELD and MELD-Na scores were 9 (5–15), 16 (6–40), and 18 (6–40), respectively. Eighteen percent patients had active bleeding during initial endoscopy. Twenty-three (20%) patients died within 6 weeks of admission. Most patients died of progressive liver failure following AVB. On Cox regression analysis the independent baseline predictors of 6-week mortality were: hepatic encephalopathy, inotropic requirement, platelet count, creatinine, and albumin levels. Using these variables, a prognostic model was created (DELHI Model), which was compared with other existing models (CTP, MELD, MELD-Na, MELD-E, MELD-Na-E, CP-Cr, and AIMS65) in predicting 6-week mortality. The DELHI Model and MELD-E model were found to have highest AUROC (Figure).
Conclusion: In cirrhotic patients with AVB, the MELD-E model and our novel DELHI model predicts 6 weeks' mortality with higher accuracy than the existing prognostic models.

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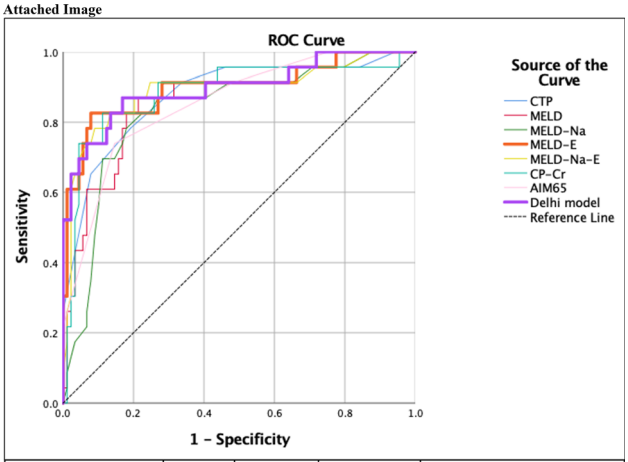

Models	AUROC	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CTP	.876	.044	.000	.789	.964
MELD	.861	.045	.000	.772	.949
MELD-Na	.833	.049	.000	.737	.929
MELD-E	.897	.044	.000	.810	.984
MELD-Na-E	.890	.047	.000	.799	.981
CP-Cr	.885	.046	.000	.795	.976
AIM65	.853	.044	.000	.768	.939
Delhi model	.897	.043	.000	.812	.982

[PP-0885]

Platelet count spleen diameter ratio to predict esophageal varices in mongolian patients with liver cirrhosis

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Objectives: Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of esophageal varices is one of the major complications of portal hypertension. To validate whether the platelet count/spleen size ratio can be used to predict the presence of esophageal varices in Mongolian patients with hepatic cirrhosis.
Materials and Methods: This was a cross-sectional study to validate the diagnostic test for hepatic cirrhosis and was performed between 2017 to 2020. Only stable patients were included in the study. Patients with active gastrointestinal bleeding at the time of admission were excluded. All patients underwent screening upper gastrointestinal endoscopy. Biochemical parameters were evaluated, and ultrasound was used to measure the longest diameter of the spleen. The platelet count/spleen diameter ratio was calculated and analyzed to determine whether it can predict the presence of esophageal varices.

Results: A total of 62 patients were included. The mean age was 53.23 ± 14 years; 34 (55%) were men, and 28 (45.0%) women. Child–Pugh classification, 36 (58%) patients were classified as class A, 22 (37%) as class B, and 4 (5%) as class C. The platelet count/spleen diameter ratio to detect esophageal varices independent of the grade showed using a cutoff value of ≤ 884.3, had 84% sensitivity, 72% specificity, and positive and negative predictive values of 93% and 42%, respectively.
Conclusion: The platelet count to spleen diameter ratio may be a useful tool for diagnosing EVs in liver cirrhosis noninvasively when endoscopy facilities are not available.

[OP-0906]

Timing of endoscopy in patients with cirrhosis and acute variceal bleeding: A single-center retrospective study

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Objectives: Endoscopy plays an important role in the management of liver cirrhosis with acute variceal bleeding (AVB). However, the optimal timing of endoscopy remains controversial in current guidelines and studies.
Materials and Methods: Patients with cirrhosis and AVB consecutively admitted from January 2010 to June 2014 were retrospectively analyzed. The timing of endoscopy was calculated as the interval from the last presentation of AVB or the admission to endoscopy. Early endoscopy was defined as the interval < 12 h, < 24 h, or < 48 h. Propensity score matching (PSM) analysis was performed. Rate of failure to control bleeding and in-hospital mortality were evaluated.
Results: A total of 353 patients were included. When the timing of endoscopy was calculated from the last presentation of AVB, overall analysis demonstrated that early endoscopy group had higher rate of failure to control bleeding (< 12 h: 8.0% versus 4.9%, P = 0.320; < 24 h: 13.8% versus 3.3%, P = 0.001; < 48 h: 9.9% versus 2.9%, P = 0.021) and in-hospital mortality (< 12 h: 8.0% versus 1.9%, P = 0.037; < 24 h: 5.3% versus 2.4%, P = 0.182; < 48 h: 4.1% versus 2.9%, P = 0.760); PSM analysis demonstrated that early endoscopy group had higher rate of failure to control bleeding (< 12 h: 8.1% versus 2.7%, P = 0.615; < 24 h: 15.6% versus 1.6%, P = 0.009; < 48 h: 7.1% versus 4.7%, P = 0.746), but not in-hospital mortality. When the timing of endoscopy was calculated from the admission, both overall and PSM analyses did not demonstrate any significant difference in rate of failure to control bleeding or in-hospital mortality between the two groups.
Conclusion: Early endoscopy might not be beneficial for the outcomes of patients with cirrhosis and AVB.

[PP-0928]

Prognostic Value of Sarcopenia on the Recurrence of Hepatic Encephalopathy

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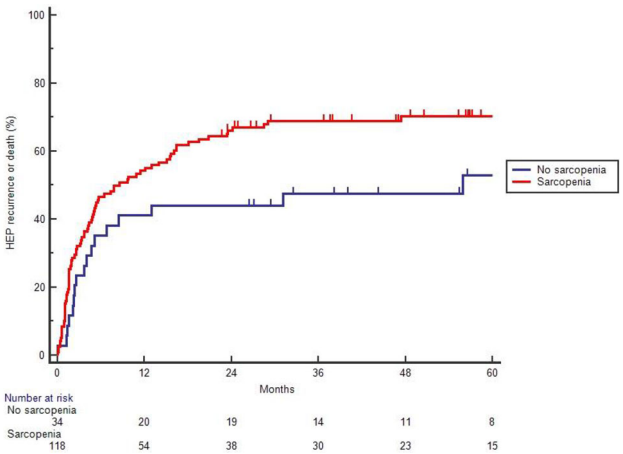
Objectives: The presence of sarcopenia in patient with cirrhosis is a risk factor for the development of hepatic encephalopathy (HEP). However, the impact of sarcopenia on the recurrence of HEP have not been investigated. We aimed to investigate the prognostic value of sarcopenia on the recurrence of HEP.
Materials and Methods: We included 152 patients who experienced the first episode of HEP between 2009 and 2019 in our hospital. Sarcopenia was defined as and L3 skeletal muscle index of < 50 cm^2/m^2 for men and < 39 cm^2/m^2 for women. The occurrence of HEP recurrence or mortality between the patients with and without sarcopenia was compared by log-rank test. Cox regression analysis was performed to investigate independent predictors of the recurrence of HEP.
Results: The median age of the study population (97 men and 55 women) was 60 years. Approximately three-quarters of the study population (118/152. 77.6%) had sarcopenia at the time of the first episode of HEP. During the study period, the patients with and without sarcopenia experienced HEP recurrence in 86 (86/118, 72.9%) patients and 18 (18/34, 52.9%) patients, respectively. The cumulative incidence rates of HEP recurrence were significantly different between patients with and without sarcopenia (log-rank P = 0.03; Fig. 1). The presence of sarcopenia was an independent predictor of HEP recurrence (adjusted hazard ratio = 1.93, 95% confidence interval 1.14–3.26, P = 0.02).
Conclusion: Sarcopenia can be a useful predictor of the recurrence of HEP.



[OP-0959]

The Efficiency of clinical evaluation in predicting varices and variceal bleeding in Cirrhosis

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Objectives: In our study, we aimed to obtain scores that will allow us to predict varices, variceal bleeding, and high-risk varices in cirrhotic patients.
Materials and Methods: Between 1 July 2020–2021, endoscopies of 139 cirrhotic patients were performed in our unit. We classified F1 and F2 esophageal varices as low-risk varices, F3 esophageal varices, F1 or F2 esophageal varices with red spots signs, and all gastric varices as high-risk varices. Patients who were diagnosed with hepatocellular cancer at the time of enrollment, and younger than 16 years of age were not included in the study. We used binary logistic regression analysis, the Youden Index, and ROC analysis as statistics.
Results: In our cohort (n:139; female 50.3%, mean age 53.35 ± 15.58, Child-Turcotte-Pugh A: 66/ B:57/ C:16), varices were found in 108 (77.6%) and high-risk varices in 49 (35.2%) of our cohorts. It was observed that 33 (30.5%) of those with varices had a history of variceal bleeding, and 12 (11.1%) had variceal bleeding in a 1-year follow-up. According to the scores obtained in our study [(-parameters used in the formula), threshold value, Area Under the Curve (AUC), sensitivity, specificity, positive and negative likelihood ratio, p value]; varices score [(Charlson Comorbidity Index (CCI), presence of hepatic encephalopathy, PC/SD (Platelet count/Spleen diameter ratio)), 10.612, AUC 0.776 (0.678—0.874), 75.9%, 71.0%, 2.62, 0.34, $p < 0.001$]; variceal bleeding score [(presence of ascites, age, spleen size (mm), presence of high-risk varices), -9.85, AUC 0.832 (0.750–0.919), 81.8%, 69.3%, 2.67, 0.26, 0.4, $p < 0.001$]; high risk varices score [(presence of ascites, PC/SD),—7.949, AUC 0.727 (0.642—0.812), 75.5%, 64.4%, 2.12, 0.38, $p < 0.001$] were revealed.
Conclusion: We think that the varices, variceal bleeding, and high-risk varices scores obtained in our study can be used in clinical practice.

[PP-1038]

Non-invasive assessment of portal hypertension using MR Elastography: Does it predict the clinically relevant change of HVPG?

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Objectives: Hepatic venous pressure gradient (HVPG) measurement is a validated method, which accurately evaluates changes in portal hypertension (PH). Magnetic resonance elastography (MRE) is a well-established method for liver fibrosis staging. We investigated the correlation between MRE-assessed stiffness of the liver and spleen and HVPG values. Furthermore, we evaluated whether MRE values reflected changes in PH after the administration of β-blockers.
Materials and Methods: From January 2018 to September 2019, we enrolled 47 consecutive patients with cirrhosis requiring prophylactic treatment of esophageal varices according to the Baveno VI criteria were prospectively included. At enrollment, patients were initiated on carvedilol starting at a dose of 6.25 mg/day, which was up-titrated to 12.5 mg/day. Patients underwent HVPG measurement and multifrequency MRE at baseline and 6 weeks.
Results: The median HVPG and MELD score of the patients was 15.0 mmHg (Interquartile range [IQR], 12.0–20.0) and 11.0, respectively. Median baseline values of MRE-assessed liver (LS), spleen stiffness (SS), and hepatic T1 values were 6.4 kPa (IQR, 5.0–7.4), 8.8 kPa (IQR, 7.1–9.6), and 1051.4 ms, respectively. There was significant correlation between LS ($r = 0.409$, $P = 0.007$), hepatic T1 values ($r = 0.390$, $P = 0.027$) and HVPG, whereas SS did not correlate with HVPG ($r = -0.043$, $P = 0.779$). Median 6-week changes in MRE-assessed LS (Δliver), SS (Δspleen), hepatic T1 values (ΔT1), and HVPG (ΔHVPG) were − 0.2 kPa, − 0.1 kPa, -2.4 ms, and − 1.5 mmHg, respectively. Overall, Δliver ($\gamma = 0.212$, $p = 0.245$), Δspleen ($\gamma = -0.124$, $p = 0.484$) nor ΔT1 ($\gamma = -0.054$, $p = 0.808$) were correlated with ΔHVPG. However, using categorized stage of HVPG, MRE-assessed Δliver significantly correlated with ΔHVPG in patients with low-HVPG ≤ 16 mmHg ($\gamma = 0.522$, $p = 0.026$), though not in patients with high-HVPG > 16 mmHg ($\gamma = 0.140$, $p = 0.634$).
Conclusion: MR parameters related to liver stiffness provide excellent accuracy for diagnosing PH, and reflect changes in HVPG following administration of β blockers for less severe PH.

[PP-1062]

Diagnostic value of two-dimensional shear wave elastography in cirrhotic portal hypertension

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Objectives: The gold-standard methods for the diagnosis of portal hypertension(PH) in cirrhosis is the measurement of hepatic venous pressure gradient(HVPG), but it is invasive and not available at all centers. Two-dimensional shear wave elastography (2D-SWE) has been validated as a noninvasive diagnostic technology for liver stiffness(LS) and spleen stiffness(SS) measurement, but their value for severe portal hypertension (SPH) diagnosis are not well known.
Materials and Methods: The patients with chronic liver disease who underwent HVPG measurements were consecutively enrolled in this study from November 2020 to October 2021 in Beijing Friendship Hospital. The diagnostic performance of 2D-SWE for predicting the presence of HVPG ≥ 12 mmHg and HVPG ≥ 20 mmHg was evaluated using the receiver operating characteristics (ROC) curves.
Results: A total of 25 patients (mean age: 54.8, 60.0% male) with cirrhosis who underwent liver and spleen stiffness measurements using 2D-SWE were included eventually. Twenty-one patients were found HVPG ≥ 12 mmHg, diagnosed as SPH, which patients were at increased risk of variceal bleeding. The ability to record at least 3 LS or SS measurements by 2D-SWE and IQR < 30% were the features associated with reliable results. Liver stiffness and spleen stiffness were correlated well with HVPG($r = 0.662$ and $r = 0.479$, $P < 0.05$). In addition, for diagnosing HVPG ≥ 12 mmHg, 2D-SWE-LS and 2D-SWE-SS had similar diagnostic performance (AUC: 0.705 vs. 0.909, $P = 0.254$), and their optimal cut-off values were 14.5 kPa (sensitivity 90.91%, specificity 50.0%), and 43.7 kPa (sensitivity 91.67%, specificity 50.0%) respectively. For diagnosing HVPG ≥ 20 mmHg, the area under the receiver operating characteristic curves of 2D-SWE-LS and2D-SWE-SS were 0.709 and 0.744, so when LS was > 24.4 kPa (sensitivity 83.3%, specificity 85.71%), or SS was > 48.4 kPa (sensitivity 48.4%, specificity 91.67%), patients were at increased risk of treatment failure and mortality in acute variceal bleeding.
Conclusion: 2D-SWE measurement of liver and spleen stiffness are reliable and shows promise as a noninvasive assessment of portal hypertension in cirrhosis.

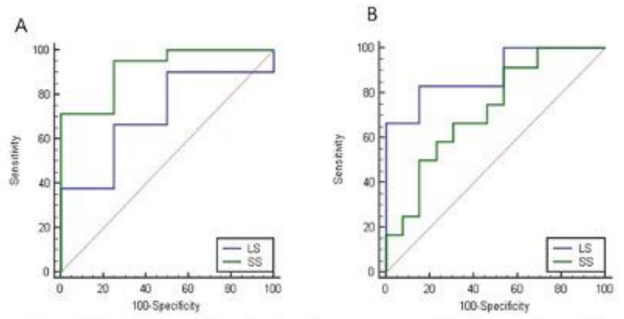

Figure. ROC curves for liver stiffness and spleen stiffness measurement with 2D shear wave elastography for diagnosis of different HVPG levels. A, HVPG≥12mmHg; B, HVPG ≥20mmHg.

[PP-1073]

Efficacy of rifaximin against covert hepatic encephalopathy in the Japanese population

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Objectives: Covert hepatic encephalopathy (CHE) impairs quality of life and occurs in approximately 30% of liver cirrhosis cases. Rifaximin is recommended as a therapeutic agent for overt hepatic encephalopathy (OHE) in Japanese clinical practice guidelines. However, the usefulness of rifaximin against CHE has not yet been thoroughly investigated in Japan. Herein, we examined the efficacy of rifaximin against hyperammonemia and CHE.
Materials and Methods: We observed 102 patients with hepatic encephalopathy with hyperammonemia secondary to chronic liver disease and examined any changes in ammonia levels following rifaximin treatment. A neuropsychological test (NPT) was performed before treatment initiation and at 4 and 12 weeks following treatment. We investigated whether the enrolled patients would recover from CHE. CHE was diagnosed when the patients had two or more abnormalities according to the four tests in the NPT while any symptoms indicating OHE were absent.
Results: Among the 102 cases, a significant therapeutic effect of rifaximin was observed on hyperammonemia from 2 to 48 weeks after starting treatment. Excluding 10 cases diagnosed with OHE while starting rifaximin treatment, 12 of the total 92 cases (11.8%) transitioned to OHE within 1 year. The NPT was performed before starting rifaximin treatment in 45 non-OHE cases, of which 29 (64.4%) were diagnosed with CHE by the NPT criteria. Among 24 patients whose NPT could be evaluated at 4 and 12 weeks after starting treatment, 10 (41.6%) patients recovered from CHE at 12 weeks.
Conclusion: Rifaximin is significantly effective against both hyperammonemia and CHE in the Japanese population.

[OP-1074]

Efficacy and safety of rivaroxban in the treatment of portal vein thrombosis in decompensated cirrhosis: A single ceners observational study

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Objectives: The use of rivaroxaban for portal vein thrombosis (PVT) indecompensated cirrhosis remains controversial. Here, we aimed to evaluate the efficacy and safety of rivaroxaban for PVT in decompensated cirrhotic patients in our center.
Materials and Methods: We analysed the data of rivaroxaban with initial dose of 10 mg daily for PVT in decompensated cirrhotic patients between April 2018 and July 2021 in our center. Regular imaging (abdominal CT or MRI) was performed to monitor the recanalization of PVT. Adverse events including bleeding episodes were recorded during anticoagulation treatment, and as well as the reoccurrence of PVT after anticoaguation.
Results: 1. A total of seventeen patients with decompensated cirrhosis enrolled. All patients had a history of hepatic decompensation, and 13(76.5%) had advanced liver dysfunction (Child–pugh B).The median follow-up under anticoagulation therapy was 32 weeks (rang 12–131 weeks). Recanalization was achieved in 12 patients (70.5%) with a median time of 14.5 weeks, including one patients with Chilpugh A for complete recanalization. However, two patients developed thrombosis progression at 48 weeks. One patient with newly-developed thrombosis (Child–pugh Class A) achieved complete recanalization within 3 months, unfortunately the thrombosis recurred half a year after stopping the drug. 2.During the follow-up period, five bleeding events were observed (29.4%, including 2 major gastrointestinal bleeding, 2 minor gastrointestinal bleeding, and 1gingival bleeding), of which 3 cases (60%) were associated with portal hypertension. One patient (5.9%) with Child–pugh B8 died of bleeding complications. Two hepatic encephalopathy was observed (grade II or above, 11.8%). Two patients (5.9%) had a significant decrease in platelets. No liver damage was observed during anticoagulation. No significant difference of bleeding and wosened liver dysfuntion were found between patients with Child–pugh A and Child–pugh B.
Conclusion: Rivaroxaban (10 mg/d) may provide a promising benefit for PVT in decompensated cirrhosis, but needed to be further studied.

[OP-1088]

To determine the frequency, etiology and outcome of upper gastrointestinal bleeding; An experience of a tertiary care hospital in Karachi

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Objectives: Upper gastrointestinal bleeding (UGIB) is a common medical illness that leads to hospitalization The etiology of a disease for acute UGIB can be broadly separated into variceal and non-variceal causesThis study done to determine the frequency, etiologies and outcome of upper Gastrointestinal bleeding (UGIB) in patients presenting to a tertiary care hospital in Karachi.Pakistan.
Materials and Methods: Study design: Prospective, observational. Location: Gastroenterology department, Jinnah Post-graduate Medical Center,Karachi.Pakistan. Duration: 1st October 2019 to 30th September 2020. Patients aged 18 years or above of either gender who were presented to us with complain of hemetemesis, melena or hematochezia were included in the study. All patients underwent

Esophago-gastro-duodenoscopy(EGD) to determine the etiology of UGIB.
Results: A total of 536 patients were enrolled in the study, 311 (58%) were male and 225 (42%) were female. Mean age was 49 ± 13.6 years. Hematemesis 506 (94.4%) was the most frequent presenting symptom. The mean hospital stay was 2 ± 0.7 days. Among 536, 320 (59.7%) patients had Hepatitis C, 61 (11.4%) had Hepatitis B, 48 (09%) had diabetes, 33 (6.2%) had hypertension and 14 (2.6%) had ischemic heart disease (IHD). Variceal bleeding 388 (71%) was seen as the main reason for UGIB. The total 38 (7.1%) patients became died within 30 days of UGIB after intervention. Among death 34 (24.4%) patients were aged > 60 years.
Conclusion: Variceal bleeding was the most common cause of UGIB among our population with male predominance. Mortality is greater in the elderly population with co-morbid as compared to the young population.So it is necessary to screen every chronic liver disease patient for upper GI endoscopy to decrease the mortality and burden of hospitalization.

The Etiology Of Upper Gastrointestinal Bleeding In Patients Presenting to a Tertiary Care Hospital, Karachi, Pakistan.
Syed Shayan Ali[1], Nazish Butt[1], Hafiz Haris[1].

Endoscopic findings (N=536)

		Frequency	Percentage (%)
Esophageal varices	Small	53	9.7
	Large	322	59.2
Gastric varices	OGV-I	5	0.9
	OGV-II	9	1.7
	IGV-I	32	5.9
	IGV-II	1	0.2
Peptic ulcer	Forest class Ib	1	0.2
	Forest class II-a	4	0.7
	Forest class II-b	2	0.4
	Forest class III	67	12.3
Mass	Esophageal	5	1
	Gastric	5	1
	Duodenal	5	1
Polyp	Gastric	3	0.6
	Duodenal	2	0.4
Esophagitis	LA-A	6	1.1
	LA-B	6	1.1
	LA-C	10	1.8
	LA-D	3	0.6

[OP-1092]

Hepatorenal syndrome-acute kidney injury in decompensated cirrhosis versus acute on chronic liver failure: A comparison of response rates and predictors of response to terlipressin and albumin

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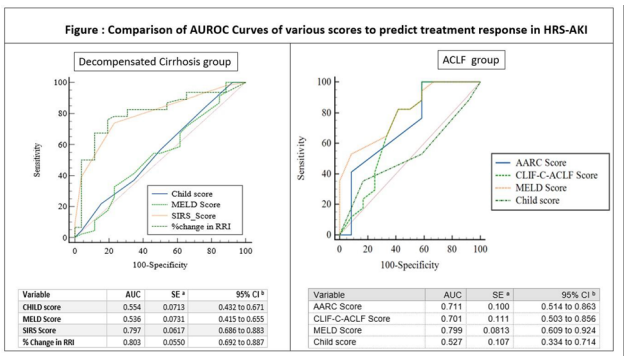
Objectives: A combination of terlipressin and albumin is the first-line pharmacologic treatment for Hepatorenal Syndrome-Acute Kidney Injury(HRS-AKI). There is limited data on the use of vasoconstrictors for HRS-AKI in ACLF. We compared the response rates to terlipressin-albumin therapy in decompensated chronic liver disease (DCLD) and ACLF and determined the early predictors of treatment response.
Materials and Methods: Patients with HRS-AKI treated with terlipressin and albumin were included. ACLF was determined by the APASL definition. Univariate and multivariate logistic regression analysis was used to determine parameters that were predictive of HRS reversal.
Results: 122 patients with HRS-AKI—84 DCLD and 38 ACLF were included. In DCLD patients, there was complete response (CR) to treatment in 54.8%, partial response in 14.3%, and no response in 31%. The independent predictors of CR were presence of systemic inflammatory response syndrome (SIRS) at baseline (p = 0.016, OR-6.19(CI:1.40–27)) and reduction in renal resistive index (delta-RRI) > 5% by day-3 (p = 0.001, OR = 24.2(CI:3.4–168.6)). Other factors associated with CR were baseline creatinine < 2.5 mg/dL (p < 0.001) and a rise in mean arterial pressure (MAP) > 5 mmHg by day 3 (p < 0.001). Non-responders had significantly higher mortality at 1 month (27% vs 9.5%, p = 0.04) and 6 months (74% vs 45%,p = 0.025). ACLF patients had CR in 57.9%, partial response in 10.5% and no response in 31.6%. APASL grades 1,2,3 had response rates of 75%, 62.5% and 40% respectively. Factors associated with CR were bilirubin < 10 mg/dL(p = 0.03), baseline creatinine < 2.5 mg/dL(p = 0.017), resolution of SIRS by day-3(p = 0.004), RRI reduction > 5% by day-3(p < 0.001), MELD < 30(p = 0.002) and AARC score < 10(p = 0.032) but no independent predictor was identified. Non-responders had higher 28-day mortality (66.6% vs 27.2% p = 0.02) and 90-day mortality (83.3% vs 36.3% p = 0.004).
Conclusion: SIRS and delta-RRI are simple parameters to predict treatment response in decompensated cirrhosis patients with HRS-AKI. In DCLD and ACLF, non-responders have higher mortality and should be identified early to expedite liver transplantation.



[PP-1105]

Nutritional therapy in massive esophageal varices bleeding in cirrhosis patient with severe portal hypertension: A case report

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Objectives: This report aims to describe nutritional therapy as a component of management in patients with esophageal varices bleeding in liver cirrhosis.
Materials and Methods: We present a case of a 32-year-old male with a history of chronic hepatitis B and cirrhosis with hematemesis melena. He had 5 prior episodes of upper GI bleeding started 25 years ago with the latest one being 5 months ago. He underwent esophageal varices ligation and was admitted to intensive care unit (ICU) with hypovolemic shock due to massive bleeding and mechanically ventilated. Massive bleeding after ligation and failed to insert naso-gastric tube left the patient nil per os and required total parenteral nutrition (TPN). TPN was initiated with 16 kcal/kg/day and 0.9 g/kg/day protein. After 10 days, naso-gastric tube was successfully inserted as the bleeding stopped and enteral nutrition (EN) was

initiated. Nutrition was gradually increased to 20 kcal/kg/day and 1 g/kg/day protein as tolerated hemodynamically.
Results: After three weeks of hospitalization, the patient exhibited improvement in his clinical condition and was successfully extubated. The patient showed a negative nitrogen balance (18.86 g N/24 h) and body composition analysis (BIA) examination revealed low muscle mass. Furthermore, protein administration was targeted to 1.3 g/kg/day and supplemented with ketoacid analog considering the impaired renal function. To date, the patient is still being treated in ICU and prepared to undergo procedure partial splenic embolization and splenorenal shunt. We intend to re-assess the nitrogen balance and BIA to evaluate the outcome of subsequent nutritional therapy.
Conclusion: Despite the improvement of clinical condition, protein administration up to 1 g/kg/day was insufficient to cover the catabolism occurred in this patient. TPN supply was inadequate to meet the elevated nutritional demand. Nonetheless, continuous care of nutrition support team enabled satisfactory EN which led to improvement in patient outcomes.

[OP-1110]

Intra-abdominal pressure (IAP) as a short-term predictor of Hepatorenal Syndrome (HRS) in NASH and non-NASH decompensated cirrhosis

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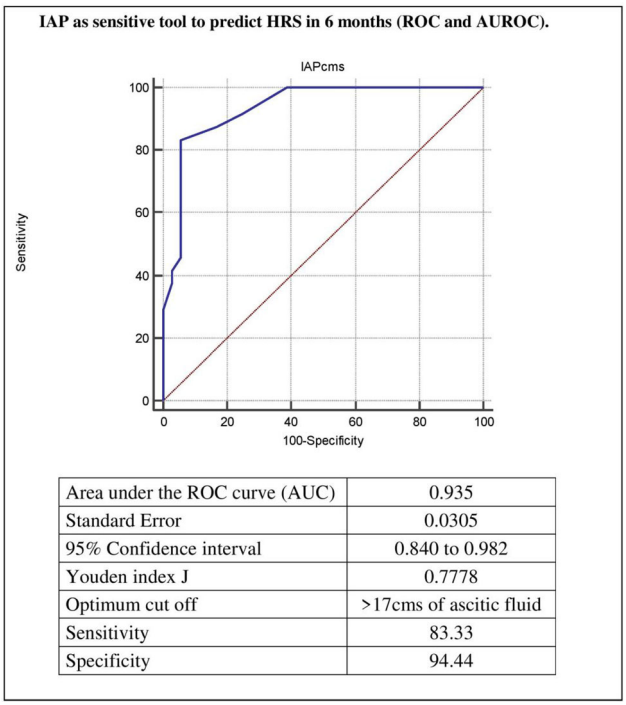
Objectives: Hepatorenal Syndrome(HRS) is characterized by renal arterial vasoconstriction which preceeds clinically manifest renal dysfunction. The primary aim of our study was to obtain the best cut-off value of Intra-abdominal pressure (IAP) in predicting HRS over 6 months, in patients with decompensated chronic liver disease (DCLD). We also tried to determine other factors associated with the development of HRS.
Materials and Methods: In a prospective follow-up study of 60 decompensated cirrhotics with tense ascites, IAP was measured using a simple Direct method, during ascitic tapping, at initial admission. Baseline parameters were obtained and then followed up for 6 months to look for the development of HRS and mortality.
Results: IAP measured in 60 patients with tense ascites showed values from 10–25 cms of ascitic fluid (Mean 17.12 cms; Median 16 cms). ROC plot derived a cut-off of IAP $>$ 17cms (AUROC: 0.935; Sensitivity 83.33%; Specificity 94.44%) for predicting the occurrence of HRS. Among other variables, Renal Resistive Index (RRI) demonstrated significant correlation with IAP ($r = 0.617$, $p < 0.001$). When we compared the 2 groups (IAP $>$ 17 vs $\leq$ 17)(n = 22 vs 38), higher levels of Blood Urea, S.Creatinine and RRI were more in patients with IAP $>$ 17 ($p = 0.05$). On subgroup analysis, there was significant difference between NASH and Non-NASH etiology($p = 0.01$). Majority of NASH etiology had IAP $>$ 17. In multivariate analysis, IAP $>$ 17 cms of ascitic fluid ($\equiv$ 12.5 mm of Hg) was a significant predictor of HRS and mortality over a period of 6 months ($p < 0.005$).
Conclusion: Direct measurement of IAP is a simple, non-invasive, sustainable, diagnostic screening tool to predict the short-term development of HRS and mortality in patients with DCLD. Majority of NASH etiology had higher IAP. This translated to a prediction of NASH-related cirrhosis to have greater RRI and higher IAP with greater propensity to develop HRS and mortality over 6 months follow-up.



Area under the ROC curve (AUC)	0.935
Standard Error	0.0305
95% Confidence interval	0.840 to 0.982
Youden index J	0.7778
Optimum cut off	>17cms of ascitic fluid
Sensitivity	83.33
Specificity	94.44

[PP-1146]

Platelets count/Spleen diameter ratio: A predictive factor for esophageal varices recurrence after eradication by endoscopic ligation

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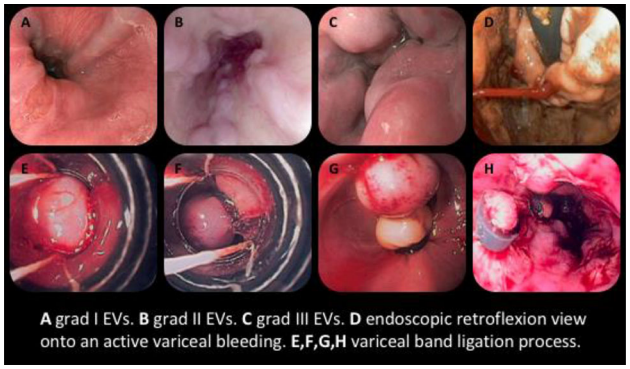
Objectives: Esophageal varices(EV) are a severe complication of portal hypertension(PH), which puts them at risk of rupture. Esophageal varices ligation(EVL) is currently the standard endoscopic treatment for hemostasis. Our study aims to assess the effectiveness of EVL by determining the rate of eradication and to look for predictive factors of EV recurrence(EVR).
Materials and Methods: This is a retrospective, monocentric study of patients with PH treated with EVL over a period of 6 years(2012–2018) with a minimum follow-up of 24 months. The non-invasive scores: APRI, FIB-4, King's score, Cirrhosis Discriminant Score(CDS), Goteborg University Cirrhosis Index(GUCI), ASAT/ALAT ratio, platelet count/splenic diameter ratio(PSD) were calculated during the first EVL session. EVR was defined as the reappearance of grade I(or higher) EVs after their initial eradication.
Results: 53 patients were included with an M/F sex-ratio of 1.04 and a mean age of 52.23. Viral cirrhosis was the main etiology of PH(88%). A total of 115 EVL sessions were performed (average = 2sessions/patient (range 1–4)). EVL was performed for hemostatic/primary prevention in 56% of cases and secondary in 44% of cases. The overall eradication rate was 72.2% with an average delay of 12 weeks. EVR occurred in 68% of patients, statistically

correlated in univariate analysis with secondary prevention(p = 0.019), hypertensive gastropathy(p = 0.013), persistence of cardial varices(p = 0.046), splenic size(p = 0.002), portal thrombosis (p = 0.07), and non-invasive scores: APRI(p = 0.03), FIB-4(p = 0.015), CDS(p = 0.013), ASAT/ALAT ratio(p = 0.019), GUCI(p = 0.07), King's score(p = 0.041) all high, as well as the low PSD ratio($p < 0.0001$). The area under the ROC curve of the PSD ratio in the prediction of EV recurrence was 0.794 (95% CI: 0.669–0.890,$p < 0.0001$). A cut-off of the PSD ratio at 521 was defined to predict recurrence(sensitivity 78.4%, specificity 70.5%).
Conclusion: To our knowledge, this study would be the first to have studied the predictive value of non-invasive scores in the risk of EVR. PSD ratio would be a reliable and easy tool for predicting EVR.



[OP-1158]

Prevalence and risk factors associated with non-malignant portal venous thrombosis in patients with decompensated cirrhosis

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Objectives: Portal vein thrombosis (PVT) due to portal flow stasis, complex thrombophilic disorders and factors leading to endothelial dysfunction, is an increasingly recognized complication in patients with cirrhosis. We tried to assess the prevalence and risk factors associated with PVT in decompensated cirrhotics without hepatocellular carcinoma (HCC).
Materials and Methods: We prospectively enrolled 245 patients with decompensated cirrhosis. All patients underwent detailed clinical history, evaluation, baseline investigation and ultrasonography (USG). PVT was confirmed by CECT Abdomen in patients with USG evidence of PVT or alteration in portal flow dynamics.
Results: 35 patients with HCC or malignant PVT were excluded. Of the 210 patients included, 30 had PVT (12.3%). Factors significantly associated with PVT were NASH related cirrhosis(OR-8.13, p = 0.001), duration of cirrhosis > 4 years, poorly controlled ascites, first decompensation as upper gastrointestinal bleed (UGIB), > 1 prior UGIB, > 1 prior endoscopic variceal band ligation (EVL), low platelet count(< 64,000), Serum Ascitic Albumin Gradient (SAAG) > 1.9, Ascitic fluid Albumin < 0.7 g%, PV diameter (PVD) > 13.7 mm, PV velocity (PVV) < 12 cm/sec and Spleen size > 13.6 cm. ROC showed that ascitic fluid albumin < 0.7 g% was more predictive than other parameters (sensitivity 95.65%, specificity 80.18%). There was no difference between CHILD B/C status or MELD Na among both groups. Logistic regression analysis showed Ascitic fluid albumin < 0.7 g% (OR-140), SAAG > 1.9(OR-11.2), > 1 EVL sessions(OR-20.1), PV diameter > 13.7cms(OR-63.6) were significant risk factors for the development of PVT in DCLD ($p < 0.001$).
Conclusion: In our study, the association of high SAAG, low Ascitic fluid Albumin and low Platelet count as markers of extent of cirrhosis, dilated PV and low PVV indicating sluggish portal flow and multiple EVL sessions that trigger thrombosis in the spleno-portal axis, were significantly associated with PVT in DCLD. Patients with NASH related cirrhosis are at higher risk of PVT and should be carefully evaluated.

Table: Comparison of variables

Variables		DCLD and no PVT		DCLD With PVT		Total		p value
		n	%	n	%	n	%	
NASH related cirrhosis	No	149	82.8	17	56.7	166	79	**0.001**
	Yes	31	17.2	13	43.3	44	21	
Duration of cirrhosis (in years)	≤ 4	136	75.6	13	43.3	149	71	**<0.001**
	>4	44	24.4	17	56.7	61	29	
Poorly controlled ascites	No	81	45	20	66.7	101	48.1	**0.028**
	Yes	99	55	10	33.3	109	51.9	
Platelet count	≥64000	118	72.4	15	50	133	68.9	**0.015**
	< 64000	45	27.6	15	50	60	31.1	
Ascitic Fluid Albumin	≥0.70	95	85.6	3	13	98	73.1	**<0.001**
	< 0 .70	16	14.4	20	87	36	26.9	
SAAG	≤ 1.90	60	54.1	5	21.7	65	48.5	**0.005**
	>1.90	51	45.9	18	78.3	69	51.5	
1st decompensation as UGIB	Yes	50	27.8	20	66.7	70	33.3	**0.006**
	No	130	72.2	10	33.3	140	66.7	
Prior number of UGIB	≤1	140	77.8	13	43.3	153	72.9	**<0.001**
	>1	40	22.2	17	56.7	57	27.1	
Prior number of EVL	≤ 1	149	82.8	12	40	161	76.7	**<0.001**
	>1	31	17.2	18	60	49	23.3	
Portal vein diameter	≤ 13.7	120	78.9	9	30	129	70.9	**<0.001**
	>13.7	32	21.1	21	70	53	29.1	
Portal vein velocity	≥12.00	130	86.1	8	26.7	138	76.2	**<0.001**
	< 12.00	21	13.9	22	73.3	43	23.8	
Spleen size	≤13.6	89	57.1	6	20.7	95	51.4	**<0.001**
	>13.6	67	42.9	23	79.3	90	48.6	

[PP-1170]

The relationship between blood ammonia level and degree of portosystemic shunts and HVPG

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Objectives: The portosystemic shunt is one of the reasons for the increase of blood ammonia, so the blood ammonia level may be

related to the degree of portal hypertension (PH). This study aims to explore the relationship between the level of blood ammonia and the degree of portosystemic shunt and hepatic vein pressure gradient (HVPG) in patients with PH.
Materials and Methods: Patients with PH who attended in Beijing Friendship Hospital from January 2018 to November 2021 were collected, and their blood ammonia levels were tested before intervention. Endoscopy and imaging were applied to screen the presence of gastroesophageal varices (GEV) and other collateral circulations, and the degree of PH was measured by HVPG.
Results: 1) 53 patients with PH were enrolled. There was no difference in blood ammonia levels among patients without portosystemic shunt, only with GEV, with GEV and other collateral circulations ($P = 0.172$). In patients with GEV and other shunts, ammonia level was correlated with the degree of GEV when the liver function was classified as Child–Pugh A ($r = 0.769$, $P = 0.006$). 2) Among the 30 patients with liver cirrhosis who underwent HVPG measurement, no difference was found in blood ammonia level between HVPG < 20 mmHg (median NH4 = 71umol/L, n = 15) and HVPG ≥ 20 mmHg (median NH4 = 67umol/L, n = 15) ($P = 0.983$). and there was no correlation between blood ammonia level and HVPG at different Child–Pugh levels.
Conclusion: Under Child–Pugh A, patients only with GEV have a correlation between blood ammonia level and its severity, but the relationship between blood ammonia level and HVPG needs to be further studied.

[PP-1171]

Spleen stiffness measurement by FibroScan630 predicts the presence esophageal varices and of high-risk esophageal varices

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Objectives: Liver stiffness (LS) and spleen stiffness (SS) are two most widely accessible non-invasive parameters for predicting esophageal varices (EV), but the reported accuracy of the two predictors have been inconsistent across studies. Fibroscan 630 is a novel spleen dedicated examination to detect (LS) and spleen stiffness (SS) by different vibration frequency. The aim of the study was to test the feasibility of spleen stiffness measurement (SSM) by FibroScan® (SSM@100 Hz) on its screening and diagnostical use for esophageal varices.
Materials and Methods: A total of 28 patients were included in this study (14 patients were NCPH,18 patients were NCPH). All the patients underwent ultrasonography including LSM and SSM by FibroScan 630. All patients underwent upper gastrointestinal endoscopy to assess the presence and severity of esophageal varices.
Results: The UGE examination verified that 5 patients without EV,5 patients with low-risk EV, and 18 with high-risk EV. Patients with EV had a median SSM@100 Hz of 50.85 ± 27.73 kPa which was significantly higher ($P < 0$ 0.005) than that of patients without EV (20.12 ± 5.58 kPa). Among patients with EV, SSM@100 Hz values of high-risk EV (62.1 ± 26.04 kPa were significantly higher ($P < 0.005$) than low-risk EV (38.28 ± 28.10 kPa). The AUC of SSM@100 Hz for EV presence was 0.887 (95% CI: 0.710?0.975), and the cut -off value was 26.9 Kpa. The AUC of high-risk EV was 0.700 (0.498?0.857) and the cut-off value was 38.4kpa. The LSM measurement by @50 Hz differentiate the presence of EV($P = 0.039$, the AUC of LSM@50 Hz for EV presence was 0.867 (95% CI: 0.676?0.967), and the cut-off value was 7.1 Kpa. But the LSM@50 Hz can not differentiated the high-risk EV.
Conclusion: SSM@100 Hz is a new performant non-invasive marker for EV and HRV providing a higher accuracy the LSM.

[OP-1183]

Prevention and treatment of esophageal and gastric variceal bleeding in real practice in the Republic of Kazakhstan

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Objectives: To evaluate approaches in the prevention and treatment of esophageal and gastric variceal bleeding in real clinical practice in the Republic of Kazakhstan.
Materials and Methods: Analysis of routine practices on management cirrhotic patient with esophageal and gastric variceal bleeding with the use online questionnaire. 40 gastroenterologists, 20 endoscopists and other related specialists were covered.
Results: According to the data obtained through the questionnaire, endoscopic ligation was the most common method in the instrumental prevention of bleeding from esophageal variceal bleeding. Endoscopic band ligation was used 4.5 times more often than sclerosant injection. Balloon tamponade with sengstaken-blackmore tube remained the main and most common method of hemostasis for esophageal variceal bleeding. In real practice, only 28% of patients were adherent recommendations for treatment with NSSB/carvedilol (in terms of self-monitoring of heart rate and blood pressure) and 11% reach the target heart rate.
Conclusion: The management of portal hypertension related bleeding requires a multidisciplinary approach involving hepatology, gastroenterology, endoscopist, interventional radiology and surgery. For hemostasis and prophylaxis against initial and recurrent bleeding, endoscopic therapy is a critical modality. A variety of techniques, including band ligation, sclerosant injection, tissue adhesive injection, and coil embolization, are available for endoscopic therapy.

[L-OP-1246]

A survival model of decompensated liver cirrhosis patients with left ventricular diastolic dysfunction

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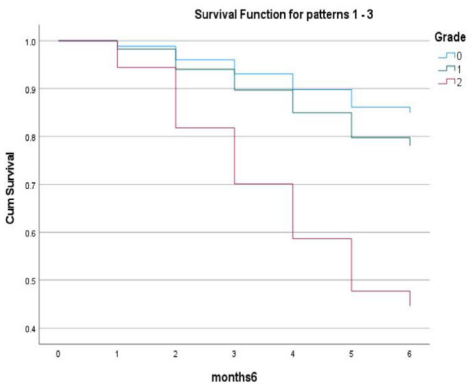
Objectives: The cardiac function is presumed to decrease with the progression of liver cirrhosis (LC) and its attendant complications. We aimed to study the impact of Left ventricular diastolic dysfunction (LVDD) on the survival of patients with decompensated LC.
Materials and Methods: 2D echocardiography with tissue Doppler imaging was done in patients with LC from August 2020 to October 2021 in Government Medical College,Thiruvananthapuram, with follow-up of 6 months.
Results: 121 patients were enrolled. Mean age was 52.5 ± 9.5 years. 85(70.2%) had LVDD(43% grade-1; 27.2% grade-2) and 36(29.8%) had no LVDD. The majority were males(85.9%). However, females had more tendency to develop LVDD(76.5% vs 69.2%). The main etiology was Alcohol(65.2%) followed by NASH(16.5%) and HBV(12.4%). NASH had a higher tendency to develop LVDD vs Alcohol (85% vs 67%). Child–Pugh class (CTP) was not associated significantly with LVDD ($p = 0.143$). The association between LVDD vs MELD score ($p < 0.001$) and MELD ≥ 15 was significant ($p = 0.017$). LVDD and its severity were significantly associated with 6 months survival, with higher grades showing higher mortality; 12.19% (no LVDD) vs 18.7% (Grade-1) vs 38.89% (Grade-2)($p = 0.007$). In our study also, short-term survival had significant association with CHILD score (< 0.001), MELD score (0.017), grades of Ascites (< 0.001), multiple Large Volume Paracentesis(LVP) (< 0.001), prior Spontaneous bacterial peritonitis(SBP)($p = 0.01$), Acute Kidney Injury(AKI)($p = 0.07$), Hepatic encephalopathy(HE)($p = 0.025$) and higher Ascitic fluid Protein > 1 g/dl($p = 0.013$). However, on multivariate analysis, grades of LVDD were shown to be an independent predictor of survival (< 0.001). In Cox regression analysis, LVDD was an independent predictor of survival, with hazard risk 1.4 for Grade-1 and 4.7 for Grade-2. Kaplan–Meier analysis demonstrated lower survival for Grade-2 compared to Grade-1 and No LVDD.
Conclusion: LVDD and its severity is an independent predictor of short-term survival in decompensated LC and should be diligently looked for in patients with high SAAG high protein ascites above > 1.0 g/dl.

Figure: Cox regression survival analysis in patients with different grades of LVDD



[L-PP-1282]

Effectiveness of caregiver empowerment program on hepatic encephalopathy in terms of knowledge, preparedness and skills among the caregivers of liver cirrhotic patients at ILBS, New Delhi

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Objectives: Providing structured information for the understanding of hepatic encephalopathy (HE) might be relevant to the prevention and management of the syndrome. Awareness of previous hepatic encephalopathy (HE) and compliance with treatment can probably reduce HE recurrence. This study aimed to design a brief, structured educational intervention and evaluate its usefulness in terms of Knowledge, Preparedness, and Skills among the Caregivers of Liver Cirrhotic Patients in the care of HE patients.
Materials and Methods: Eighty cirrhotic patients' caregivers were enrolled and randomly allocated in the Experimental (group A; n = 40) and Comparison group(group B; n = 40). Caregivers underwent a Structured questionnaire for knowledge assessment (20 items questionnaire for the assessment of caregivers' knowledge about hepatic encephalopathy), The Preparedness for Caregiving Scale (8 items scale to assess the preparedness of the caregivers), and a Structured questionnaire for skill assessment (14 items questionnaire for the assessment of caregivers' skill for hepatic encephalopathy). A 45 min one-on-one educational session was then provided to caregivers in group A, including basic information on the pathophysiology, hygienic and medical management of HE.
Results: No demographic/clinical differences were observed at baseline between the two groups. Similarly, there were no significant differences in HE-related Knowledge, Preparedness, and Skills available at baseline between the two groups. After the posttest, The intervention was highly effective in increasing caregivers' Knowledge, Preparedness, and Skills in the care of HE patients.
Conclusion: The study concludes that the caregiver empowerment program was effective in improving the caregivers' of HE patients' knowledge, preparedness, and skill in care HE and there is no statistically significant difference were found in the knowledge, preparedness, and skill of the caregivers of HE with their sociodemographic variable and clinical variable of HE patient.

Acute Liver Failure and ACLF

[PP-0113]

HDL-related biomarker apolipoprotein A-I may predict poor outcome in patients with chronic liver failure

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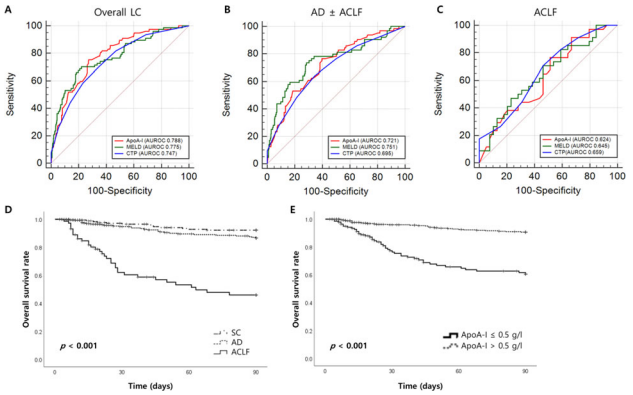
Objectives: The aim of this study was to investigate the prognostic performance of serum apolipoprotein A-I (Apo A1) in patients with advanced liver disease.
Materials and Methods: We reviewed data from patients with liver cirrhosis who were admitted to Jeonbuk National University Hospital from 2009 to 2020. Three groups—stable cirrhosis (SC), acute decompensation (AD) of cirrhosis, and acute-on-chronic liver failure (ACLF)—were classified and compared. Prognostic performance of Apo A1 was determined by the area under the receiver operating characteristic (AUROC) compared to the MELD, CTP, and CLIF-AD or CLIF-ACLF scores.

Results: A total of 563 patients (429 men and 134 women) with liver cirrhosis were included in this study. The proportion of patients with SC, AD, and ACLF was 197 (35.0%), 293 (52.0%), and 73 (13.0%), respectively, and mean serum Apo A1 level was decreased in ACLF group. There were 77 (13.7%) non-survivors during the 90-day follow-up, and serum Apo A1 levels were significantly lower in this group (0.70 ± 0.42 vs 0.91 ± 0.41, $p < 0.001$). The AUROC of Apo A1 for 90-day mortality was 0.788 which was as high as that of MELD scores. In addition, 90-day survival rate assessed by the Kaplan–Meier survival analysis with the log-rank test was significantly higher in the low Apo A1 group ($p < 0.001$).
Conclusion: HDL related biomarker Apo A1 could be a useful predictor of short-term (90-day) prognosis in patients with chronic liver failure.



[OP-0265]

Etiology and clinical features of end-stage liver disease of Central China

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Objectives: This current study aims to investigate profiles and clinical manifestations of ESLD in a multicenter cohort from Central China.
Materials and Methods: A total of 1425 cirrhotic patients diagnosed of ESLD from sixteen tertiary hospitals in January 2013 to December 2018 were enrolled. The enrolled pateints included acute-on-chronic liver failure (ACLF), acute decompensation of cirrhosis (ADC) and chronic liver failure (CLF). All pateints recieved comparable internal medications. The etiology and clinical manifestations of each phenotype were evaluated.
Results: Of all 1425 patients, 328 were ACLF, 908 were ADC and 190 were CLF. Hepatitis B virus infection was the most common etiology (51.52%, 49.89% and 38.95%, respectively) among all the groups. Hepatitis C virus infection (8.54% and 8.23%) and alcohol assumption (10.57% and 7.05%) were the second and third etiologies of ACLF and ADC, while alcohol assumption (17.37%) was the second in CLF. A combined etiologies, HBV infection combined alcohol assumption, were common in CLF (7.89%). Patients with ACLF were more likely to occur in male individuals. Compared to the ADC and CLF, these pateints also possessed higher levels of ALT, TBIL, Cr, INR, PCT, Ferritin and occurring of bacterial or fungal infection, hepatorenal syndrome, hepatic encephalopathy, upper gastrointestinal bleeding, and MELD score, Child–Pugh score and SOFA score, but with a lower serum sodium and PLT. Significant differences were observed in the 28-day and 90-day transplant-free mortality rate (ACLF, 29.71%, 51.23%; ADC, 9.66%, 17.97%; CLF, 8.16%, 24.49%) among all entities ($p < 0.0001$). In addition, patients with CLF showed a higher incidence of primary hepatic carcinoma compared to ACLF and ADC (24.21% vs 15.24%/17.17%).
Conclusion: ESLD exhibited heterogenous etiology profiles and clinical phenotypes, in which ACLF manifested higher incidence of SIRS, complications or extrahepatic organ failures, and lower transplant-free short term survival.

[OP-0540]

The impact of the acute insults on the mortality rate of 81 patients with acute-on-chronic liver failure (2018-2021yy)

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Objectives: Background Acute-on-chronic liver failure (ACLF) is a syndrome characterized by acute decompensation of chronic liver disease associated with organ failures and high short-term mortality. There is some consensus that the outcome of hepatic decompensation could vary depending on the nature of acute insult. This study was aimed to assess mortality rate according to acute insults in Armenian ACLF patients.
Materials and Methods: Methods 81 patients (27 retrospectively and 54 prospectively) fulfilling the criteria of ACLF based on the APASL 2020 consensus recommendations were screened. Biochemical, serological, virological and instrumental parameters were investigated.

Results: Results Mean age was 47 ± 16 years with a predominance of males (n = 57[70%]). According to our data the predominant acute insult was active alcohol consumption [31(38%)], followed by hepatitis B-virus (HBV) [19(24%)], drug-induced-liver-injury (DILI) [16(20%)], autoimmune-hepatitis (AIH) flare [5(6%)],hepatitis A, E and D viruses [2 (2.5%)] respectively and unknown [4(5%)]. Patients with 1 and ≥ 2 organ failures were [14(17%)] and [67(83%)] respectively. Baseline laboratory values: ALT 710.9 ± 1127/ 17–6612/ U/L, WBC 10.4 ± 5.2 /3.54–20/ × 103 cells/mm3, Platelets 156.2 ± 99.1 /19–462/ × 103 cells/mm3, Serum sodium 134.7 ± 9.4/100–146/ mmol/l, INR 2.1 ± 0.6/1–3/, Serum albumin 3.2 ± 0.7 /2–5/g/dL, Serum creatinine 2.1 ± 2.4 /1–8/ mg/dL. The assessment of severity of disease was 22.1 ± 5 /16–34/ according MELD and 12.6 ± 1.2 according CTP score. The overall mortality rate was 32% (26 patients), who had ≥ 2 organ failures. The most frequent causes of death were hepatorenal syndrome and hepatic encephalopathy with severe ascites.. The mortality in the AIH-ACLF group was the highest [4 (80%)], followed by HBV-ACLF [9 (47%)], DILI-ACLF [5 (31%)], alcohol-ACLF [8 (26%)].
Conclusion: Conclusion · According to our data active alcohol consumption was and remains prevalent among acute insults in ACLF patients. · The most common complications were hepatorenal syndrome and hepatic encephalopathy with severe ascites. · AIH-ACLF and HBV-reactivation are associated with highest mortality rate.

[OP-0620]

SARS-CoV-2 infection in patients with underlying chronic liver disease is associated with significantly greater risk of liver decompensation and acute on chronic liver failure

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Objectives: Chronic liver disease (CLD) patients are hypothesized to have greater risks of liver decompensation following SARS-CoV-2 infection. Data evaluating COVID-19 in CLD patients remains sparse. We aim to evaluate whether SARS-CoV-2 infection in CLD patients is associated with increased risks of liver decompensation or acute on chronic liver failure (ACLF).
Materials and Methods: Using the Common Data Schema from COVID-19 Research Database, a large U.S. database containing over 72 million linked patients with both electronic health records and claims data, we evaluated CLD patients with (CLD + COVID-19) vs. without COVID-19 (CLD without COVID-19). Patients had minimum 6-months follow-up until censoring event or end of study period (August 31, 2021) to evaluate incident liver decompensation (i.e. ascites, hepatic encephalopathy, variceal bleeding, hepatorenal syndrome, liver failure) and incident ACLF (EASL-CLIF definition). Outcomes were evaluated using adjusted multivariate Cox proportional hazards models.
Results: Among 923,671 adults with CLD (44.7% women, 12.4% cirrhosis), 3.8% had CLD + COVID-19 and 96.3% had CLD without COVID-19. Over a median follow-up of 242–267 days, when compared to CLD without COVID-19, CLD + COVID-19 patients had significantly greater risk of liver decompensation (HR 1.22, 95% CI 1.13–1.32, $p < 0.001$) and ACLF (HR 1.54, 95% CI 1.17–2.03, $p < 0.01$). Among CLD patients with cirrhosis at baseline, COVID-19 was similarly associated with higher risk of ACLF (HR 1.66, 95% CI 1.26–2.19, $p < 0.001$). When evaluating individual organ failures in patients with ACLF, CLD + COVID-19 vs. CLD without COVID-19 was associated with significantly greater risks of cardiovascular failure (HR 4.75, $p < 0.001$), respiratory failure (HR 5.80, $p < 0.001$), and renal failure (HR 3.93, $p < 0.001$).
Conclusion: Among a large U.S. cohort evaluating COVID-19 in CLD patients, SARS-CoV-2 infection was associated with significantly greater risks of liver decompensation and ACLF in patients with underlying CLD. The primary drivers of ACLF were the increased risks of cardiovascular failure, respiratory failure, and renal failure associated with COVID-19.

[OP-0675]

Prognosticating acutely decompensated cirrhosis patients at index presentation in real world setting

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Objectives: The development of acute-on-chronic liver failure (ACLF) in patients of cirrhosis with acute decompensation (AD) increases mortality; ACLF more commonly develops in patients with previous decompensation. There is paucity of studies regarding development of ACLF and mortality in patients presenting with index episode of AD. We aimed to investigate the short-term outcomes in cirrhosis patients with index AD episode.
Materials and Methods: Consecutive cirrhosis patients with first episode of AD seen in between January 2018- June 2019 at GIPMER, New Delhi were evaluated. Patients with hepato-cellular carcinoma (HCC), pregnancy and age > 65 years and < 18 years were excluded. The patients were followed up for 90 days and divided into three subgroups at time of presentation: ACLF (ACLF at presentation), pre-ACLF (AD who develops ACLF on follow-up), and AD without ACLF (AD who do not develop ACLF on follow up) for comparison. The outcomes noted were death and development of ACLF.
Results: Total of 124 AD patients were seen; 88 patients were included, mean age was 44.65 ± 11.37 years and 61(69.3%) were males. Overall, 31(35.2%) patients had ACLF at presentation, 11(12.5%) patients developed ACLF on follow up and 46(52.3%) patients had AD without ACLF on follow up. Baseline MELD-Na and Child–Pugh score was significantly higher in ACLF group (26.19 ± 4.63, 11.39 ± 1.68) as compared to pre-ACLF (18.91 ± 5.52, 9.73 ± 1.49) and AD (16.2 ± 5.04, 8.72 ± 1.90) groups. Inflammatory markers like white blood count and IL-6 were significantly higher in ACLF (8.3 × 109/L [5.6–10.6, × 109/L], 37 pg/mL [17.1–79 pg/mL]) and pre-ACLF (9.6, × 109/L [4.6–13.0, × 109/L], 21.1 pg/mL[10.5–56.1 pg/mL]) groups. Total of 21(23.9%) patients died; 12(38.7%) patients in ACLF, 7(63.6%) patients in pre-ACLF and 2(4.3%) patients in AD group died.
Conclusion: One-third of AD patients had ACLF at presentation; ACLF increases mortality in AD. The aggressive treatment and prevention of ACLF will be helpful in reducing mortality.

Baseline Characteristics of Study Groups and Outcomes

	AD(n=46)	Pre-ACLF(n=11)	ACLF (n=31)	p value
Age, years (mean ±SD)	45.91±11.02	48.36±10.96	41.45±11.60	0.145
Male sex, n (%)	28 (60.9%)	9 (81.8%)	24 (77.4%)	0.191
Decompensation, n (%):				
Ascites	34 (73.9%)	10 (90.9%)	28 (90.3%)	0.132
HE	1 (2.2%)	1 (9.1%)	14 (45.2%)	**<0.001**
GI Bleed	24 (52.2%)	4 (36.4%)	5 (16.1%)	**0.006**
Comorbidities, n (%):				
DM	1 (2.2%)	3 (27.3%)	0	**0.001**
HTN	1 (2.2%)	1 (9.1%)	0	0.220
Hypothyroid	2 (4.3%)	2 (18.2%)	0	**0.045**
MAP (mm Hg) (mean ±SD)	74.46±5.95	73.18±4.40	71.29±7.29	0.212
Etiology, n (%):				
Alcohol	13 (28.3%)	4 (36.4%)	21 (67.7%)	**0.002**
HBV	8 (17.4%)	2 (18.2%)	2 (6.5%)	0.349
HCV	11 (23.9%)	2 (18.2%)	2 (6.5%)	0.135
NASH	2 (4.3%)	3 (27.3%)	3 (9.7%)	0.059
AIH	1 (2.2%)	0	2 (6.5%)	0.479
BCS	0	0	1 (3.2%)	0.395
PBC	1 (2.2%)	0	0	0.630
HBV+HCV coinfection	2 (4.3%)	0	0	0.393
Cryptogenic	8 (17.4%)	0	0	**0.018**
Bilirubin, mg/dL median (IQR)	1.7 (0.8-4.15)	2.13 (1.2-9.2)	16 (6.3-21.26)	**<0.001**
AST, U/L median (IQR)	68 (35.75-107.5)	60 (50-78)	124 (72-163)	**0.002**
ALT, U/L median (IQR)	46.5 (25-86.25)	43 (26-86)	47 (32-111)	0.577
Albumin, g/dL (mean ±SD)	2.88±0.49	2.60±0.60	2.74±0.53	0.284
Total Protein, g/dL (mean ±SD)	6.74±0.70	6.32±0.75	6.62±0.84	0.575
INR (mean ±SD)	1.38±0.25	1.52±0.38	2.0±0.72	**<0.001**
Blood Urea, mg/dL median(IQR)	30 (21.75-42)	32 (29-42)	30 (20-43)	0.822
Creatinine, mg/dL (mean ±SD)	0.87±0.25	0.91±0.18	0.89±0.25	0.833
Na, mEq/L (mean ±SD)	135.24±5.99	133.64±5.55	130.58±4.52	**0.001**
White blood count, x 10^9/L median (IQR)	5.0(4.0-9.1)	9.6 (4.6-13.0)	8.3 (5.6-10.6)	**0.014**
Platelet count, x 10^3/uL median (IQR)	86 (58.25-122.25)	104 (75-134)	96 (76-140)	0.26
SBP, n (%)	3 (8.8%)	1 (10.0%)	7 (28.0%)	0.119
MELD-Na (mean ±SD)	16.2±5.04	18.91±5.52	26.19±4.63	**<0.001**
Child-Pugh Score (mean ±SD)	8.72±1.90	9.73±1.49	11.39±1.68	**<0.001**
Cystatin-C, mg/L (mean ±SD)	1.22±0.45	1.81±0.55	1.71±0.60	**<0.001**
IL-6, pg/mL median(IQR)	10.8 (7.15-17.25)	21.1 (10.5-56.1)	37 (17.1-79)	**<0.001**
Mortality, n (%)	2 (4.3%)	7 (63.6%)	12 (38.7%)	**<0.001**

Abbreviations: ACLF, acute-on-chronic liver failure; AD, acute decompensation; AIH, Autoimmune hepatitis; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BCS, Budd-Chiari Syndrome; DM, Diabetes Mellitus; GI Bleed, Gastrointestinal bleed; HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; HE, Hepatic encephalopathy; HTN, hypertension; IL-6, Interleukin-6; INR, International Normalized Ratio; IQR, interquartile range; MAP, Mean arterial pressure; MELD, model of end stage liver disease; Na, Sodium; NASH, Non-alcoholic steatohepatitis; PBC, Primary Biliary Cholangitis; SBP, Spontaneous bacterial peritonitis; SD, standard deviation;

[PP-0702]

The relationship between Zinc deficiency and infection in patients with hepatitis B virus related acute-on-chronic liver failure

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Objectives: Hepatitis B virus (HBV) related acute-on-chronic liver failure (ACLF) has a high mortality rate. This study aimed to imply a correlation between zinc (Zn) deficiency and infection in patients with HBV related ACLF.

Materials and Methods: Patients with HBV related ACLF were enrolled in this study retrospectively. Their demographic, clinical and laboratory data, including age, sex, blood cell count, biochemical parameters, coagulation parameters, viral parameters of HBV, pre-existing chronic liver diseases, complications and treatment outcome were collected.

Results: A total of 284 patients were included in this study, including 205 patients with liver cirrhosis and 79 patients with non-cirrhosis. Zn deficiency occurred most frequently (84.51%), followed by subclinical zinc deficiency (14.08%) and normal Zn (1.42%). Compared to the subclinical Zn deficiency or normal Zn group, the patients in Zn deficiency group had a higher model for end-stage of liver disease (MELD) score ($P < 0.05$). Hepatic encephalopathy, infection and MELD score were found as independent factors influencing prognosis ($P < 0.05$). Further, age, total bilirubin and serum Zn were independent factors for infection ($P < 0.05$) (Table 1). The level of serum Zn in patients without complications at admission was significantly higher than those with complications ($P = 0.004$). Moreover, there was a significant decrease in serum Zn level in patients with prothrombin time activity less than 20% ($P < 0.001$).

Conclusion: Zn deficiency is common in patients with HBV related ACLF. Most notably, Zn deficiency is closely associated with infection and the severity of the disease in patients with HBV related ACLF.

Table 1 Univariate and multivariate logistic regression analyses of infection

	Univariate analysis OR (95%CI)	P value	Multivariate analysis OR (95%CI)	P value
Age	1.033 (1.007-1.059)	0.012	1.035 (1.008-1.063)	0.010
ALB	0.951 (0.907-0.997)	0.036		
AST	1.000 (0.999-1.000)	0.210		
TBIL	1.003 (1.001-1.005)	0.009	1.003 (1.001-1.005)	0.009
GGT	0.998 (0.994-1.002)	0.240		
PT	1.038 (1.002-1.075)	0.038		
WBC	1.063 (0.987-1.145)	0.106		
PLT	0.998 (0.994-1.001)	0.217		
Ferritin	1.000 (1.000-1.000)	0.374		
Mg	0.236 (0.019-2.872)	0.257		
Cu	0.999 (0.947-1.053)	0.958		
Zn	0.838 (0.736-0.953)	0.007	0.865 (0.755-0.990)	0.035

[PP-0748]

Distribution of patients with in ACLF in Kazakhstan

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Objectives: Acute-on-chronic liver failure (ACLF) is a serious problem worldwide, with a prevalence among at-risk groups of about 20–35%. Asia has not seen significant reductions in mortality in ACLF patients over the past two decades, with mortality in the nationwide sample approaching 50% The events that trigger ACLFs differ depending on the geographic region. Reactivation of chronic HBV, acute hepatitis A virus or hepatitis E viral infection, acute alcoholic hepatitis, and acute bacterial infection are the most common provoking ACLF events in Asia. Currently, there is no data on ACLF in Kazakhstan in the literature available to us. Starting from 2020, we performed an analysis of patient records aimed at assessing the prevalence, etiology of acute liver disease against the background of chronic liver damage, disease outcomes and mortality rates.

Materials and Methods: This study was aimed to assess mortality rate according to acute insults in Kazakh ACLF patients. 15 patients (retrospectively) fulfilling the criteria of ACLF based on the APASL 2020 consensus recommendations were screened. Biochemical, serological, virological and instrumental parameters were investigated.

Results: Results In the period from 2020 to 2021, 15 cases of patients with ACLF were registered in Nur-Sultan. The age of the patients varied from 20 to 67 years, the average age was 49 years, the male gender prevailed over the female -73%. According to our data, the predominant etiological factor was alcohol consumption (53%), followed by hepatitis B virus (23.5%), then hepatitis C virus (15.6%) and primary biliary cholangitis (7.9%). The mortality rate was 13% (2 patients), 13 patients (87%) were discharged with improvement.

Conclusion: · According to our data active alcohol consumption was and remains prevalent among acute insults in ACLF patients. · The most common complications were hepatorenal syndrome and hepatic encephalopathy with severe ascites. AIH-ACLF and HBV-reactivation are associated with highest mortality rate.

[PP-0989]

Quick sequential organ failure assessment in acute-on-chronic liver failure patients

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Objectives: Quick Sequential Organ Failure Assessment (qSOFA) has been suggested to screen for sepsis. In this study, we aimed to evaluate the ability of qSOFA in patients with acute-on-chronic liver failure (ACLF).
Materials and Methods: We prospectively collected data of chronic liver disease (CLD) patients who admitted due to acute deterioration (AD). ACLF was defined according to Asian Pacific Association for the Study of the Liver ACLF Research Consortium (AARC) and European Association for the Study of the Liver Chronic Liver Failure Consortium (EASL-CLIF) definitions.
Results: Among 1497 patients, 1114 patients (74.4%) were male and 151 patients (10.1%) had bacterial infection (BI). Mean age was 54.7 ± 11.5 years. The area under receiver operating characteristics (AUROC) values of qSOFA for 28-day and 90-day mortality were 0.809 and 0.730 in patients with BI and 0.583 and 0.567 in patients without BI, respectively. The AUROC for 28-day and 90-day mortality were 0.557 and 0.581 in patients with AARC-ACLF, and 0.670 and 0.603 in patients with EASL-CLIF-ACLF. By Kaplan–Meier analysis, patients with qSOFA ≥ 2 showed significantly lower 28-day and 90-day survival rate than those with qSOFA < 2 in total patients and in patients with EASL-CLIF-ACLF regardless of the presence of BI (all $P < 0.01$). In patients with AARC-ACLF, patients with qSOFA ≥ 2 showed significantly lower 28-day and 90-day survival rate in those with BI ($P = 0.042$ and $P = 0.034$), but not in those without BI ($P = 0.871$ and $P = 0.337$). The qSOFA ≥ 2 was independent prognostic factor for 28-day and 90-day survival ($P = 0.001$ and $P < 0.001$) by Cox proportional hazard model.
Conclusion: qSOFA was useful tool to assess the short-term mortality in CLD patients with AD and BI. Patients with qSOFA ≥ 2 have high short-term mortality rate in ACLF patients, especially those with BI. qSOFA ≥ 2 was independent prognostic factor in CLD patients with AD.

[OP-1002]

Comparative analysis of acute on chronic liver failure related to herbs and anti-tubercular drugs

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Objectives: Liver injury precipitated by drugs and herbal medicines(DHMs) can have variable presentations and outcomes. In Indian subcontinent, drug induced liver injury due to Anti-tubercular drugs(ATDs) and inadvertent herbs induced liver injury (HILI) are common. Comparative natural history and outcome of acute-on-chronic liver failure(ACLF) due to common DHMs is largely unknown.
Materials and Methods: Consecutive in-patients with ACLF precipitated by herbs or ATDs(year 2010–2021) were compared for baseline clinical profile, disease severity, histological features and organ failures. Treatment outcomes and predictors of in-hospital mortality were also analyzed.
Results: 529 patients presented with ACLF related to HILI(ACLF-H, n = 430) and ATDs(ACLF-D, n = 99) [Mean Age-47.6 + 14 years, mean MELD score and HVPG were $29.1 + 5.4$ and $15.5 + 3.4$ mmHg respectively]. 61.4% patients had underlying histological cirrhosis. 21.2% patients had additional superadded acute insult [severe alcoholic hepatitis(n = 66), acute hepatitis E or A(n = 24/15)]. Twelve percent ACLF_H patients presented with clinical cholestasis, autoimmune hepatitis(n = 18) and hypersensitivity reactions(n = 4). Most common recognizable agent associated with ACLF-H was Tinospora cordifolia (n = 35,8.1%), inadvertently used in Indian households during the COVID-19 pandemics. Patients with ACLF-H as compared to ACLF-D had higher male preponderance (70.9% vs. 54.5%;p-0.002) and peripheral eosinophilia (6.4% vs. 1%;p-0.03), clinical cholestasis (19.6% vs 10.8%;p-0.05) and acute kidney injury (44.4% vs. 28.3%;p-0.003) at presentation. Use of plasma exchange(18.5%) had no impact on outcomes. None of the patients underwent liver transplantation. In-hospital mortality(19.2%) was higher in ACLF-D compared to HILI ACLF-H (31.3% vs. 17.2%;p-0.002). Presence of AKI [HR:5.5 (95%CI:2.78 to 11.1)], hepatic encephalopathy[HR:4.4(95%CI:1.76 to 11)] and pneumonia[HR:7.2(95%CI: 3.59 to 14.65)] were independent predictors of mortality.
Conclusion: Herbs and anti-tubercular drugs are common precipitants of ACLF in India and have high in-hospital mortality resulting from sepsis and organ(s) failure. In the absence of specific treatment options, prevention and early and careful monitoring of liver functions is of utmost importance.

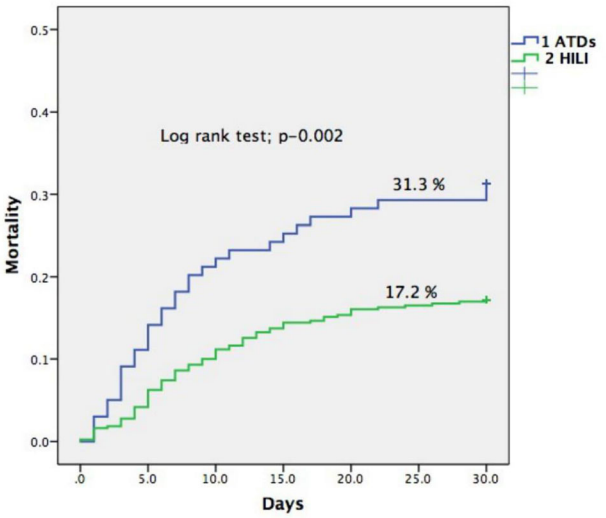

Figure. Mortality at 1-months in patients with ATDs ACLF vs. ACLF related to herbs.

[PP-1133]

Clinical relevance of CLIF-C acute decompensation score in patients with alcoholic hepatitis

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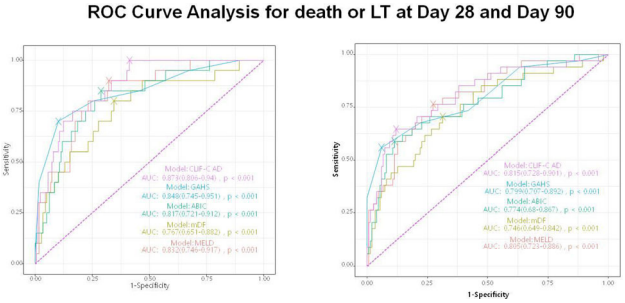
Objectives: Acute-on-chronic liver failure (ACLF) is associated with poor prognosis in patients with alcoholic hepatitis (AH). However, clinical relevance of CLIF-C acute decompensation score (CLIF-C ADs) in patients with alcoholic hepatitis is unknown. We analyzed prognostic value of ACLF ADs and traditional prognostic models in patients with AH.

Materials and Methods: This was a longitudinal analysis of prospective observational cohorts from nationwide multicenter including 1733 episodes in 1497 patients with AD of chronic liver disease. Of these, 212 episodes in 200 patients clinically diagnosed AH were included. The predictive values of 28- and 90-day overall mortality and liver transplantation (LT)-free survival were analyzed using CLIF-C ADs and traditional prognostic models including Maddrey's discriminant function (mDF), model for end-stage liver disease (MELD), Glascow alcoholic hepatitis score (GAHS), and age-bilirubin-INR-creatinine (ABIC).

Results: In this cohort, 129 episodes (60.8%) were diagnosed severe AH (SAH) defined as mDF $\geq$ 32, and 33 episodes (25.6%) treated with steroid among patients with SAH. For prediction of the 28-day mortality or LT, area under curve (AUC) of CLIF-C ADs, mDF, MELD, GAHS, and ABIC is 0.872, 0.767, 0.832, 0.848, and 0.817, respectively. For prediction of the 90-day mortality or LT, AUC of CLIF-C ADs, mDF, MELD, GAHS, and ABIC is 0.815, 0.774, 0.805, 0.799, and 0.774, respectively. In patients with SAH, CLIF-C ADs $\geq$ 56 and GAHS $\geq$ 9 were good predictors for 28- (P = 0.003 − 0.001 and P = 0.017 − 0.004, respectively), 90-day (P = 0.003 − 0.001 and P = 0.001 − < 0.001, respectively) mortality or LT, but MELD $\geq$ 21 and ABIC $\geq$ 6.71 is not irrespective of steroid treatment.

Conclusion: Conclusions: CLIF-C ADs is good predictor for 28- and 90-day overall mortality or LT in patients with AH. In patients with severe AH, CLIF-C ADs $\geq$ 56 and GAHS $\geq$ 9 provides additional value to predict prognosis irrespective of steroid treatment.



[OP-1186]

Assessment of severity of Acute Liver Injury and its outcome in patients with Dengue Fever in Lahore and Rawalpindi

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Objectives: To evaluate the impact of Dengue Virus infections on liver by measuring aminotransferase levels of the patients suffering from DF during epidemic in Lahore in 2011 and in Rawalpindi in 2015.

Materials and Methods: It is a multi-centered retrospective analysis of 1700 patients (1000 from LGH Lahore and 700 from HFH, Rawalpindi in 2011 & 2015 respectively. Data was analyzed in SPSS 19 with 16 variables on which relevant details were noted.

Results: The patients were classified in to classical DF, DHF and DSS (77.6%, 20.6% and 1.8% respectively. The degree of rise in aminotransferases indicating liver injury observed in LGH, Lahore was 34.9% (Grade A), 48.5% (Grade B), 14.8% (Grade C) and 1.8% (Grade D). However, in BBH, Rawalpindi, it was observed as 43.8% (Grade A), 49.3% (Grade B), 6.6% (Grade C) and 0.3% (Grade D). In classic DF patients, (5% vs 2.8%) were having grade C & D liver damage and (95% vs 97.2%) have no significant liver injury in LGH and HFH respectively. In DHF, aminotransferases were high in (83.2% vs 68.6%) of which (71.3% vs 54.8% patients have Grade C and (31.8% vs 17.3%) have Grade D Liver injury. In patients with DSS, (10% vs 3.1%) have Grade C and 90% vs 83.2%) with Grade D (Highest mortality and long term morbidity) in LGH and HFH respectively.

Conclusion: In Dengue outbreaks in Lahore (2011) and Rawalpindi (2015), majority of patients suffered from DF and a rise in liver enzymes was observed in majority of patients though a significant rise of liver enzymes (Grade D) was observed in patients suffering from DHS and DSS patients only. However, there is significant rise in liver enzymes in 2011 epidemic as compared to 2015 in comparative analysis of two Divisions of Punjab.

[OP-1199]

Fulminant hepatic failure etiology, clinical manifestations, and outcome: An experience of tertiary care hospital of Karachi, Pakistan

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Objectives: The study was aimed to determine the etiology, clinical manifestations, and outcome associated with Fulminant hepatic failure (FHF).
Materials and Methods: A cross-sectional study was conducted at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan from January 2018 till to date. All patients of both gender $\geq$ 16 years were recruited and investigated for acute viral serology, complete blood count, liver function tests, renal function tests, serum creatinine, MELD score parameters and King's college criteria (KCC) parameters.
Results: Total 91 patients were enrolled, out of which 46 (50.54%) were males and 45 (49.45%) were females with a mean age of 29.04 $\pm$ 8.15 years. Hepatitis E was found to be the most common cause of FHF 53 (58.24%). Seventy one (78.02%) of patients died and 20 (21.97%) patients recovered and were discharged symptom free. Variables i.e. presence of viral hepatitis E, serum creatinine $>$ 2.5 mg/dl, and sepsis were found to have significant association with mortality on linear correlation. Only serum creatinine more than 2.5 mg/dl and development of sepsis were found to predict the outcome after multivariate analysis. The KCC criteria cut off point was reached in a total of 77 (84.61%) patients (out of 91) of which 71 (92.20%) patients died.
Conclusion: The mortality rate of FHF is very high which can be reduced to some extent in a non-liver transplant areas by controlling the risk factors associated with poor outcome.

[OP-1200]

Fulminant hepatic failure in pregnancy: challenges, etiology, management and its aassociated mortality

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Objectives: The study was aimed to determine the challenges, etiology, management and its associated mortality in pregnant Fulminant hepatic failure (FHF) patients.
Materials and Methods: A cross-sectional study at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan from January 2018 till to date. All pregnant patients with FHF, having age $\geq$ 16 years were recruited and investigated for acute viral serology, complete blood count, liver function tests, renal function tests, serum creatinine, MELD score parameters and King's college criteria (KCC) parameters.
Results: We have enrolled 47 patients up till now with the mean age of 25.14 $\pm$ 8.32 years. Hepatitis E was found to be the most common cause of FHF in 41 (87.23%). Thirty-three (70.21%) of patients died and 14 (29.78%) patients recovered and were discharged symptom free. Variables i.e. presence of viral hepatitis E, serum creatinine $>$ 2.5 mg/dl, and sepsis were found to have significant association with mortality on linear correlation. Only serum creatinine more than 2.5 mg/dl and development of sepsis were found to predict the outcome after multivariate analysis. The KCC criteria cut off point was reached in a total of 40 (85.10%) patients (out of 47) of which 30 (75%) patients died. Prevention/treatment of cerebral oedema, timely pregnancy termination, running N acetylcysteine, giving mechanical ventilation in indicated patients, ssurveillance for infections and prompt antimicrobial treatment, correction of coagulopathy, maintenance of optimum haemodynamic, volume replacement, vasopressor support, renal perfusion, preventing hypoglycemia and providing nutritional supplementation were found to have mortality benefits and early recovery.
Conclusion: We conclude that hepatitis E is the usual cause of FHF in our pregnant women, the diagnosis should be considered early with consultation regarding termination of the pregnancy. Management protocols need to be individualised for each case keeping in mind the risk versus benefit to both the mother and the foetus.

[OP-1201]

Transient elastography in chronic hepatitis B patients

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Objectives: To determine the degree of fibrosis via transient elastography (TE) in treatment naïve patients of chronic hepatitis B
Materials and Methods: An observational, cross-sectional study was conducted at the gastroenterology department, JPMC, Karachi, during the period from 1st December 2019 to 31st October 2020. Patients of either gender with age $\geq$ 18 years, with documentation of chronic hepatitis B infection were eligible for inclusion in the study.
Results: A total of 87 patients were enrolled in our study. The mean age was 33 $\pm$ 12 years. 54 (62%) were male and 33 (38%) patients were female. Among 87 patients, fifty five patients had F0-F1 fibrosis, in which 35 (40%) were in carrier state16 (18%) were in immune tolerant state, 03(3.5%) patients were HbeAg –ve (CHB) and 01 (01%) was HbAg + ve (CHB). Among patients with F2 fibrosis, 14 (16%) were CHB carrier, 2 (2%) were in immune-tolerant state and 02 (02%) were HbeAg –ve (CHB) patients. Patients with F3 fibrosis 3 (3.3%) patients were HBeAg –ve (CHB), 6 (07) HbeAg + ve (CHB). Among patients with F4 fibrosis 1 (01%) was HbeAg-ve and 04 (4.5%) were HbeAg + ve.
Conclusion: Transient elastography is a good tool for determining fibrosis in CHB patients. All patients with the diagnosis of CHB

should be evaluated with TE regardless of viral load, especially in HBeAg positive patients.

[L-OP-1210]

Serum prealbumin is a valuable biomarker for the prediction of the occurrence and prognosis of HBV related ACLF

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Objectives: Early prediction of the occurrence and precise assessment of the prognosis of acute-on-chronic liver failure may offer individualized management thereby improve the clinical outcomes.
Materials and Methods: Clinical and laboratory data were collected from chronic hepatitis B patients admitted to the Fifth Medical Center of Chinese PLA General Hospital between 2010 and 2018. Patients in the retrospective case control study were also obtained from Third Affiliated Hospital of Sun Yat-sen University and Beijing Friendship Hospital. ROC curves, univariate, multivariate and competing survival analysis were carried out to evaluate the value of serum prealbumin (PA) for predicting the occurrence and prognosis of HBV related ACLF patients.
Results: HBV-ACLF patients had lowest level of serum prealbumin compare to other HBV related liver disease patients including chronic hepatitis B (CHB), compensated and decompensated cirrhosis($P < 0.001$). Serum PA could predict the occurrence of HBV-ACLF in patients with CHB and patients with decompensated cirrhosis, with the area under ROC curves being 0.994(0.891, 1.000) and 0.901(0.789, 0.966), respectively (Fig. 1E-G). Serum PA was also an independent biomarker for the prognostication of HBV-ACLF, with a HR of 0.697(0.562, 0.863) at the cutoff value of 28 mg/L. In the CHB-ACLF patients as a single marker PA perform better in the prognostic prediction than the multifactor MELD score (Fig. 1. I, L). By adding PA into the MELD score system, mMELD were built and the C-index (SE) for the predicting accuracy of 1 year survival of mMELD, MELD, MELD-Na and Child–Pugh were 0.677(0.021), 0.628(0.022), 0.615(0.022) and 0.614(0.021) respectively.
Conclusion: This study demonstrated the potential of serum PA as a biomarker for the prediction of occurrence and clinical outcomes of HBV-ACLF; and the mMELD score system with serum PA integration seems to superior to those widely reported ones for the prognostication of HBV-ACLF patients.

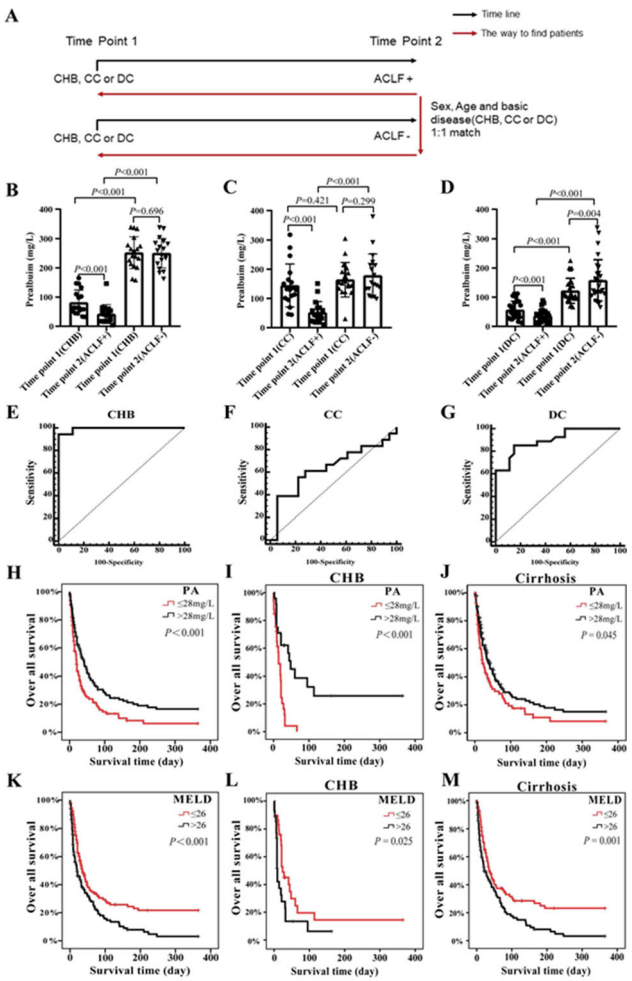

Figure 1. Serum PA can be used as a potential predictor and prognosis prediction marker of ACLF. (A) Design of the retrospective case control study; (B) Serum PA level of CHB patients who progressed to ACLF or not (n=18); (C) Serum PA level of CC patients who progressed to ACLF or not (n=18); (D) Serum PA level of DC patients who progressed to ACLF or not (n=27); (E) ROC curves of PA for predicting ACLF in CHB patient; (F) ROC curves of PA for the predicting ACLF in CC patient; (G) ROC curves of PA for predicting ACLF in DC patient. (H) Mortality was significantly higher in HBV-ACLF patients with PA ≤28 mg/L; (I) Mortality was significantly higher in CHB related ACLF patients with PA ≤28 mg/L; (J) Mortality was significantly higher in cirrhosis related ACLF patients with PA ≤28 mg/L; (K) Mortality was significantly higher in HBV-ACLF patients with MELD >26; (L) Mortality was significantly higher in CHB related ACLF patients with MELD >26; (M) Mortality was significantly higher in cirrhosis related ACLF patients

[L-OP-1220]

The rapidity of decline in kidney functions in the first two weeks predicts worse outcomes in alcohol associated acute on chronic liver failure—A prospective multicentric study from AARC

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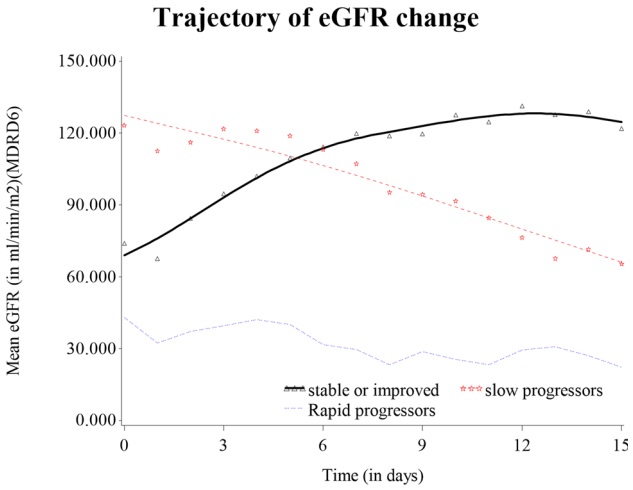
Objectives: The rate of decline in renal functions in patients with acute on chronic liver failure (ACLF) has not been studied. We aimed to investigate in ACLF patients; the rate of decline in eGFR in alcohol-associated ACLF (A-ACLF) compared to other etiologies, predictors of decline and its impact on clinical outcomes.
Materials and Methods: Rapid progressors (RP) were defined as decline in renal functions leading to dialysis in first two weeks, those with gradual decline as slow progressors (SP) and remaining as non-progressors.
Results: Prospective cohort of ACLF (n = 1514, A-ACLF = 722, other etiologies-792) from the AARC database, (age 42.3 ± 9.6 years, MELD 29.7 ± 7.0, 98% males, 48% with sepsis, 67% with grade 3 ascites, baseline eGFR 84.4 ± 57.9 ml/min/m^2, NGAL of 1301.2 ± 1573.7 ng/ml and Cys (n = 376) of 2.1 ± 1.1 mg/L were followed for median of 67 (17–94)days. There were 50% NP, 38% were SP and 12% RP. Patients with A-ACLF had higher proportion of RP compared to other etiologies [12% vs. 6%; $p < 0.001$]. The instantaneous risk of mortality was significantly higher in RP versus SP and NP (as ref.) [HR 8.45 (6.12–11.66) vs 1.71 (1.22–2.40) vs. 1] and independently predicted higher 90-day mortality. Grade 3 ascites, hepatic encephalopathy, AARC score and sepsis were independent predictors of rapid progression in A-ACLF. In the subset of patients, renal biomarkers, higher NGAL(n = 229) (log transformed) [OR 1.71, 1.24–2.37) and Cys(n = 376)[OR 2.30, 1.58–3.37] predicted rapid decline in renal functions in A-ACLF patients along with the AARC score [OR 1.38, 1.08–1.70].
Conclusion: The rapidity of renal functional decline towards dialysis in the first two weeks is greater A-ACLF patients. Severity of liver failure, ascites, and sepsis determine rapid progression in A-ACLF patients. NGAL and Cystatin C can help stratify patients at risk of rapid decline and need of early dialysis.



Footnote: MDRD6 stands for Modification of Diet in Renal Disease

[L-OP-1240]

Platelet-to-white blood cell ratio is associated with long-term adverse outcomes in patients with acute deterioration of chronic liver disease

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Objectives: Acute deterioration (AD) of chronic liver diseases (CLD), including cirrhosis and non-cirrhotic liver disease has known that it was closely associated with short-term and long-term adverse outcomes including death or liver transplantation by the organ failure severity and underlying liver function. The platelet-to-white blood cell ratio (PWR) is recently suggested to be a predictor of adverse outcomes in patients with hepatitis B virus associated liver failure. However, the role of PWR in CLD patients with AD is unclear. Therefore, we aimed to investigate whether PWR is a predictive marker for adverse outcomes in these patients.

Materials and Methods: The multicenter, prospective, observational Korean acute-on-chronic liver failure (KaCliF) study included 1,772 non-electively hospitalized patients with ACLF from October 2015 to May 2019 at 31 university hospitals. We grouped the patients according to the PWR and analyzed the short-term and long-term adverse outcomes (death or liver transplantation).
Results: The mean follow-up duration was 11.57 ± 10.88 months. The cumulative overall survival (OS) rate was lower in the patients with low PWR than in those with high PWR (log-rank $P < 0.001$). In univariate analysis at 28-day, 90-day, and 1-year adverse outcome, low PWR was a risk factor for that. However, in multivariate analysis, low PWR was not significantly associated with adverse outcome. Interestingly, in cox regression multivariate analysis low PWR was identified as a significant prognostic factor for adverse outcomes in CLD patients with AD (hazard ratio [HR], 1.573; 95% confidence interval [CI], 1.055–2.344; P = 0.026) as well as model for end-stage liver disease (MELD) score 3.0 and serum albumin level (HR 1.101; CI 1.063–1.141; $P < 0.001$ and HR 0.583; CI 0.421–0.808; P = 0.001, respectively).
Conclusion: PWR was associated with a higher incidence of long term adverse outcomes in chronic liver disease patients with AD along with underlying liver function. PWR may be a useful predictor for long-term outcome.

[L-OP-1241]

Thrombocytopenia was associated with long-term poor outcomes in acute deterioration of chronic liver disease

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Objectives: Acute deterioration (AD) of chronic liver diseases, including cirrhosis and non-cirrhotic liver disease has known that it was highly associated with short-term and long-term mortality by the organ failure severity and underlying liver function. Platelet count is a clinically accessible and affordable prognostic factors. The present study aimed to investigate association of thrombocytopenia with adverse outcomes including liver transplantation and death in patients with AD.
Materials and Methods: The multicenter, prospective, observational Korean acute-on-chronic liver failure (KaCliF) study included 1,772 non-electively hospitalized patients with ACLF from October 2015 to May 2019 at 31 university hospitals. We grouped the patients according to the platelet count and analyzed the short-term and long-term adverse outcomes (death or liver transplantation).
Results: Among a total of 1,772 patients, 1,351 patients without SIRS were analyzed because SIRS affect to platelet. The mean follow-up duration was 11.96 ± 10.85 months. The cumulative overall survival (OS) rate was lower in the patients with thrombocytopenia (platelet count $< 50 \times 10^9$/L, $< 100 \times 10^9$/L) than in those without (log-rank P = 0.013, P = 0.002). In univariate analysis at 28-day, 1 year adverse outcome, thrombocytopenia ($< 100 \times 10^9$/L) was a risk factor for that. However, in multivariate analysis, thrombocytopenia ($< 100 \times 10^9$/L) was associated with 1-year adverse outcome (Odds ratio 1.285; 95% confidence interval [CI] 1.025–1.611, P = 0.03), not in analysis of 28-day adverse outcome. Interestingly, thrombocytopenia ($< 50 \times 10^9$/L) was identified as a significant prognostic factor in patients with AD (hazard ratio [HR], 1.718; 95% CI, 1.049–1.2.814; P = 0.032).
Conclusion: Lower platelet count was associated with a higher incidence of short-term and long term adverse outcomes in chronic liver disease patients with AD along with underlying liver function.

[L-PP-1253]

Acute liver failure as a consequence of mushroom ingestion: A case report

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Objectives: Acute liver failure (ALF) is a life-threatening condition that may lead to fulminant hepatic failure requiring liver transplantation. Ingestion of toxic mushroom is scarcely reported as a cause of acute liver failure in Indonesia. We reported a case of ALF in patient with history of mushroom ingestion, that gradually improved after supportive therapy.
Materials and Methods: A 36-year-old male without any history of liver diseases is admitted to the hospital with gradual loss of consciousness after having profuse diarrhea and vomiting for 5 days. 10 h before onset of diarrhea, he ingested wild mushroom while he was on a mountaineriing activities. The patient was somnolent, icteric, moderately dehydrated, with mild epigastric pain and increased bowel sound. Laboratory examination revealed liver AST 1804 U/L, ALT 4139 U/L, INR 3.34, total bilirubin 14.434 mg/dL, with negative antiHAV, HbsAg, and antiHCV. Liver ultrasound shows no abonrmalities.
Results: Patient was admitted to intensive care unit and was given normal saline rehydration, intravenous l-ornithine-l-aspartate, intravenous formulation of glycrrhizin-glycine-l-cysteine hydrochloride, and intravenous vitamin K. His consciousness returned gradually. Liver function improve after 1 week and returned to normal after 3-weeks.
Conclusion: Mushroom poisoning is an important etiology of ALF. According to current literature, there's no blood work that can point out mushroom poisoning, so a thorough history taking and clinical examination play an important role in diagnosing these cases. Therapy is mainly supportive, and restoration of liver function normally occurs without sequelae.

[L-OP-1285]

Neutrophil specific degranulation genes ELANE, MPO and CD177 are associated with short-term mortality in Acute-on-Chronic Liver Failure

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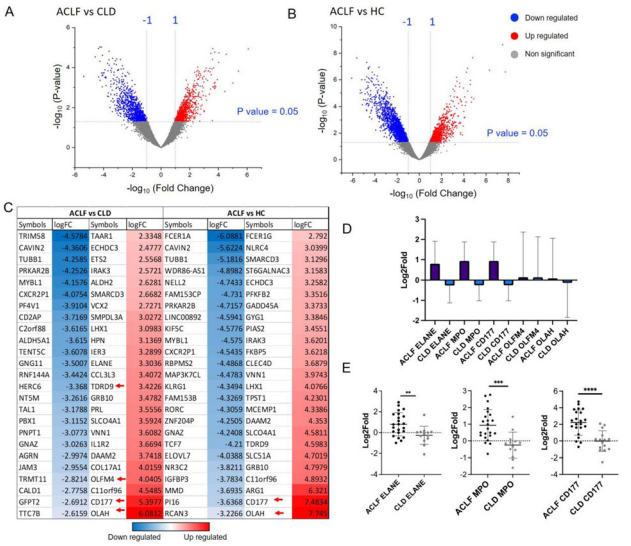
Objectives: Acute-on-Chronic Liver Failure (ACLF) is associated with high short-term mortality believed to be driven by innate immune dysfunction. The neutrophil-to-lymphocyte ratio (NLR) is an important predictor of mortality in ACLF and studies show altered functionality of ACLF neutrophils. However, molecular understanding of neutrophil dysfunction in ACLF is poor. We hypothesize that the neutrophil dysfunction observed in ACLF will be reflected in their transcriptome profile and will be different from the underlying chronic liver disease. Our objectives are: (i) To describe the transcriptomic differences in ACLF vs.CLD neutrophils (ii) Understand the pathways based on this transcriptomic analysis, and (iii) Validate observed differentially expressed genes and to understand their relevance in ACLF outcome.
Materials and Methods: Microarray-based total gene expression analysis was carried out using the Agilent SurePrint G3 Human gene expression v3 Platform, in neutrophils isolated from ACLF (n = 10), chronic liver disease (CLD) (n = 5) and healthy controls (HC; n = 4). Statistical analyses were performed using GeneSpring and pathways analysis was performed using NetworkAnalyst and Enrichr. Results were validated for a subset of genes by quantitative RT-PCR, in ACLF (n = 30), CLD (n = 15) and HC (n = 15). The protein expression of selected neutrophil genes was confirmed using flow cytometry.
Results: Gene expression analysis showed 2068 genes in ACLF vs CLD and 3177 genes in ACLF vs HC were differentially expressed. Significant upregulation of neutrophilic inflammatory signatures were found in ACLF compared to CLD and HC. Neutrophil-specific genes ELANE, MPO and CD177 were highly upregulated in ACLF and their expression was higher in ACLF 28-day non-survivors. Elevated expression of CD177 protein on neutrophil surface in ACLF was confirmed by flow cytometry.
Conclusion: Overall, our results show a predisposition for degranulation and reduced transmigration in ACLF neutrophils. The neutrophil specific genes ELANE, MPO and CD177, which are important components of the degranulation pathway, are associated with short-term survival outcomes in ACLF.



[L-OP-1312]

Choices for the treatment of graves disease with severe liver dysfunction: A retrospective cohort study

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Objectives: For graves' disease (GD) with severe liver dysfunction (LD) management, reliable treatment methods are essential. The prevailing study aimed to appraise the clinical role of radioiodine (^{131}I) and radioiodine combination with artificial liver support system (ALSS) for hyperthyroid with severe LD.
Materials and Methods: The study included 48 patients with GD complicated by severe LD, who were grouped in accordance with whether or not received with ALSS therapy: group A(34 cases) received single radioiodine (^{131}I), but group B(14 cases) received radioiodine (^{131}I) in combination with ALSS and subjected to a 6-month follow up. Clinical values, containing liver function parameters, thyroid hormone levels, therapeutic efficacy and coagulation function were calculated. The cost—effectiveness of two treatment methods was also analyzed in the study.
Results: The therapeutic efficacy of GD of group A and B were 91.18% and 78.57% (P = 0.471) in six months after treatment. The therapeutic efficacy of severe liver dysfunction were 97.06% and 85.71% (P = 0.126). The mortality of group A and B were 2.9% and 14.3%, respectively. The average length of stay in hospital of the two groups were 28.8 ± 13.01 and 42 ± 13.86 days (P = 0.003). The total cost and daily average cost of group A were less than those of group B (P < 0.01).
Conclusion: ^{131}I therapy for GD combined with severe LD was effective and safe. No deterioration of liver function was found due to the change of thyroid hormone level after ^{131}I treatment. The role of ALSS was not as great as expected, but ALSS combined with iodine ^{131}I was still an effective means to manage severe LD complicated with GD.

Table2 Comparation thyroid function efficacy in two groups

	Time	Cases	Cured	Improved	No response	Effective rate
	discharge	34	11	19	4	88.24%
	Follow-up	34				
	In two months		14	16	4	88.24%
Group A	Follow-up	34				
	In six months		20	11	3	91.18%
	discharge	14	8	6	0	100.00%
	Follow-up	14				
	In two months		8	4	2	85.71%
Group B	Follow-up	14				
	In six months		10	1	3	78.57%

The effective rate between two groups do not show a significant difference (χ^2=1.797,0..519, P=0.307,1.000,0.471)

Table3 Comparation liver function efficacy in two groups

	Time	Cases	Cured	Improved	No response	Effective rate
	discharge	34	0	28	6	82.35%
	Follow-up	34				
	In two months		0	33	1	97.06%
Group A	Follow-up	34				
	In six months		10	23	1	97.06%
	discharge	14	0	10	4	71.43%
	Follow-up	14				
	In two months		1	11	2	85.71%
Group B	Follow-up	14				
	In six months		3	9	2	85.71%

The effective rate between two groups do not show a significant difference (χ^2=0.208, 0.672, 2.347, P=0.648,0.412, 0.126)

Liver Cancer—Basic

[OP-0059]

Association of genetic polymorphisms of OATP with susceptibility to hepatocellular carcinoma in Hepatitis C patients who achieved SVR by direct acting antivirals

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Objectives: Simeprevir, daclatasvir, ledipasvir, paritaprevir and ritonavir are all substrates and inhibitors of the organic anion transporting polypeptide (OATP1B1 transporter, whereas sofosbuvir, ombitasvir and dasabuvir are not substrates. The purpose of this study is to evaluate the association of organic anion transporting polypeptide (OATP) gene polymorphism and hepatocellular carcinoma in Hepatitis C patients who achieved SVR by direct acting antivirals.
Materials and Methods: Four single-nucleotide polymorphisms (SNPs) (388 A > G, 521 T > C, 334 T > G, and 699 G > A) of the OATP gene were genotyped by PCR–RFLP in 200 patients with chronic HCV infection (CHC) treated with DAAs, Laboratory work up and abdominal ultrasound was performed at baseline, at 12 weeks after end of treatment and then at every 6 months of follow up (FU).
Results: The overall SVR12 rate was 99.5%. The SVR12 rate was similar between the patients with HCC and without HCC (100% vs 99.4%, p = 0.49). HCC developed in 10 (5%) of the patients, approximately 11 months (6–36 months) after the end of the treatment. No significant differences were found regarding OATP gene polymorphisms among the case groups (including CHC and HCC) and no matter in comparisons of alleles, genotypes, or haplotypes. Similar insignificant results were also observed when subgroup analyses were performed in different gender.
Conclusion: Our observation suggests that SNPs 388 A > G, 521 T > C, 334 T > G, and 699 G > A of OATP gene might not contribute to the development of HCC in Hepatitis C patients who achieved SVR by direct acting antivirals.

[PP-0085]

Synergistic effects of sorafenib and mesenchymal stem cells carrying cytosine deaminase gene with 5-fluorocytosine combination therapy on hepatocellular carcinoma

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Objectives: Mesenchymal stem cells (MSCs) are emerging cell therapeutic agent with a cancer-cell targeting property, and cytosine deaminase (CD) have been considered a promising enzyme in cancer gene therapy by converting prodrug 5-Fluorocytosine (5-FC) to anti-cancer drug 5-Fluorouracil (5-FU). This study aimed to investigate combination effect MSC/CD with 5-FC and sorafenib to enhance therapeutic efficacy in hepatocellular carcinoma (HCC).
Materials and Methods: The therapeutic efficacy of MSC/CD with 5-FC and combination effect of sorafenib was evaluated in vitro co-culture system with MSC/CDs., survival rates of the cells were measured using the CCK-8 assay.
Results: In vitro experiments showed successful anti-tumor effect of MSC/CD with 5-FC to Huh-7/GFP cells and Hep3B/GFP cells. Sequential therapy of MSC/CD with 5-FC and following sorafenib administration demonstrated synergistic anti-cancer effect in both cell lines than sorafenib alone.
Conclusion: The combination treatment of MSC/CD transplantation followed by the sequential 5-FC and sorafenib administration could be a new therapeutic approach for HCC to enhance anti-cancer efficacy in HCC.

[PP-0111]

SORT1 with oncogenic potential promotes tumor progression by enhancing the interaction between cancer-associated fibroblasts and cancer cells in hepatocellular carcinoma

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Objectives: Cancer-associated fibroblasts (CAFs) play an important role in the tumor microenvironment. The objectives of this study were to identify the aggressive phenotype of CAF-derived SORT1 in HCC.
Materials and Methods: In vitro experiments were performed to validate the function of CAF-derived SORT1 on the cell growth and proliferation of HCC cells. First, co-culture was performed to confirm the interaction between CAF and HCC. HCC cell lines were seeded on the bottom of six-well plates. Then CAFs were seeded on the upper insert membrane with 0.4 μm pore size of the Transwell chamber.
Results: We found that co-culture with CAF increased cell growth and cell proliferation in HCC cell lines. SORT1 knockdown decreased the cell growth and proliferation of HCC cells.
Conclusion: Since the role of CAF-derived SORT1 in the phenotype of HCC remains largely unclear, our study provides a CAF-derived SORT1 inhibitory effect in the tumor microenvironment.

[PP-0115]

Cancer-associated fibroblast-specific gene signature is a potential biomarker for predicting prognosis and immune infiltration in hepatocellular carcinoma

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Objectives: Cancer-associated fibroblast (CAF) is one of the base components in the tumor micro-environment, promoting the proliferation and invasion of cancer cells. This study aimed to identify and investigate CAF-specific signature associated with immunosuppression in hepatocellular carcinoma (HCC).
Materials and Methods: Whole Transcriptome Sequencing (WTS) and Small RNA Sequencing (SRS) datasets from eight pars of CAFs and para-cancer fibroblasts (PAFs) were produced and analyzed. and we performed target prediction and network analysis using TargetSCAN 7.2 and Ingenuity Pathway Analysis.
Results: A total of 7 miRNA-target gene pairs, in 47 genes and 20 miRNAs, with statistically significant negative correlation were identified, and the high expression level of CAFs-specific 5 genes was an independent risk factor for predicting poor overall survival in TCGA LIHC.
Conclusion: CAF-specific signatures potentially contribute to tumor immunosuppression and would be a promising biomarker for predicting prognosis and immune infiltration in HCC.

[PP-0166]

Characterization of tumor-infiltrating MAIT cells in hepatocellular carcinoma

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Objectives: Mucosal-associated invariant T (MAIT) cells are human liver-enriched unconventional T cells, which primarily recognize vitamin B2 metabolites from bacteria or fungi presented by MHC-class I-related (MR1) protein. In addition to the anti-bacterial or anti-fungal function, their role in various viral infection including HBV, HCV, or HDV is previously described, but their role in anti-tumor immunity, as well as in the hepatocellular carcinoma (HCC) is unclear.
Materials and Methods: We defined MAIT cells by MR1-tetramer + T cells, because of the significant downregulation of CD161 which is a representative marker in addition to the TCR-Valpha-7.2 in the liver or tumor tissues. Using MAIT cells from HCC and background liver tissues, we performed RNA sequencing to characterize intratumoral MAIT cells. Using flow cytometry, we characterized MAIT cells in protein level. Functional assays were performed using co-culture of hepatoma-cell lines and MAIT cells.
Results: In RNA sequencing, intratumoral MAIT cells had a distinct gene signature, which is associated with T cell activation. In protein level, these intratumoral MAIT cells showed overexpression of activation markers, suggesting MAIT cells are activated in tumor environment. In vitro co-culture assay showed MAIT cells are activated by hepatoma cells, and they can secrete IFN-γ and express cytotoxic molecules. Mechanistically, MAIT cell activation by tumor cells was dependent on cytokines, but not on MR1. However, due to the activation, intratumoral MAIT cells were depleted, and this depletion was associated with poor outcome. Furthermore, gene signature of intratumoral MAIT cells were also associated with T cell exhaustion, which was validated by functional assay. MAIT cell exhaustion was also associated with poor outcome.
Conclusion: Our results indicate that MAIT cells are potential immunotherapeutic target, and the strategy for the qualitative and quantitative expansion of MAIT cells is needed.

[OP-0253]

Association of ACRBP gene polymorphism (+26A/G) to Liver Cancer leads to novel biomarker discovery for Cancer diagnosis

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Objectives: Liver cancer (LC) involves many genes which may stake to an increased prospect of becoming LC. Despite intense efforts there are still many specific biomarkers need to be identified for specific disease risk assessment. Several studies have shown statistical evidence of linkage between ACRBP gene and Liver cancer. It might therefore be considered as a candidate gene for liver cancer research.
Materials and Methods: This study investigated the relationship between the ACRBP gene and the risk for liver cancer. The study was carried out with dry and wet lab approaches to identify the most deleterious SNP (Single nucleotide polymorphism) and their association for the diagnosis of LC as novel biomarker. With an array of available SNP data on dbSNP we sorted out functional SNPs in ACRBP gene by implementing different authentic computational tools for functional and structural assessment, molecular dynamics, and energy minimization studies. Thereafter we have employed 42 samples of LC pateints in Bangladesh and healthy control to observe the association with our identified nsSNP by experimental validation (extraction, amplification, digestion and sequencing method).
Results: Out of a total 1008 SNPs in ACRBP, we investigated 198 coding nonsynonymous SNPs (nsSNPs) and observed that 8 of them could be expected to alter the protein's function based on the predictions of both sequence homology–based and structural homology–based algorithms. By analyzing multiple tools having different perspectives an aggregate result were produced where rs11545745 (Q26R) nsSNP was found to be most likely to exert deleterious effect. 3D model of mutated protein was generated to determine the functional and structural effect of the mutations on ACRBP.
Conclusion: Our findings indicate that rs11545745 could be a novel biomarker in LC patients diagnosis though detailed study on more. LC patients need to be performed.

[OP-0256]

Digital aging and mental health deteriorations: Risk mitigation in the older people with liver disease in Indonesia

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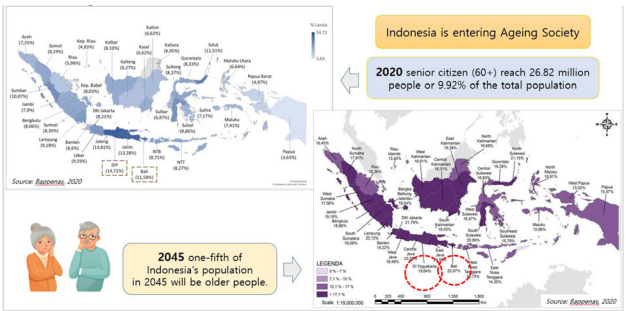
Objectives: Indonesia is entering an aging society with an older people population reaching 26.82 million people or 9.92% of the total population in 2020 and it is predicted that around one-fifth of Indonesia's population in 2045 will be older people. The senior citizen is the covid-19 most at risk due to comorbidities and low digital literacy. In Indonesia, the liver is one of the highest comorbid factors in increasing the risk of death by 13.5 times and increasing to 16.8 times in the elderly due to COVID-19. This condition increases the aging market in Indonesia but low digital literacy will affect the lower QoL.
Materials and Methods: Using data from the 2014 Indonesia Family Life Survey (IFLS), this study aims to analyze mental health problems and mobile phone ownership in older adults (60 +) with Liver disease.
Results: The analysis shows that the proportion of older people with liver disease reaches 4,07% and 59,18% are male. 57,5% of them experienced mental health problems and the percentage is higher in men. However, the percentage of elderly with liver disease experiencing mental health problems will decrease by 6,78% when they have a cellphone. The elderly SES in Indonesia has a fairly diverse distribution between provinces and 55,8% of them are still working. Nearly half of older people's education attainment is elementary school, which reaches 46.05 percent. In general, the elderly with higher digital literacy prefer to seek treatment at a formal health facility than traditional practitioners such as shamans. They tend to seek outpatient care treatment at a community health center or Puskesmas (44,11%), specialist (29,41%), and private hospital (11,76%).
Conclusion: Increasing digital aging encourages elderly health literacy, as well as decreases mental health problems. Mainstreaming the digital aging issue can help various information and services needed by the elderly to be healthier, independent, and with dignity.



[OP-0279]

YAP/TAZ expression in hepatocellular carcinoma (HCC) and the effects of YAP/TAZ inhibition on HCC

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Objectives: To assess the expression levels of YAP and TAZ in patient-derived HCC tissue and identify the effects of YAP/TAZ inhibition depending on the baseline YAP/TAZ expression when combined with sorafenib using patient-derived multicellular tumor spheroid (MCTS) model.
Materials and Methods: Primary HCC cell lines were established from patient-derived tissue. Six patient-derived HCC cell lines were selected according to YAP/TAZ expression on western blot: high, medium, low. Then, MCTS was generated by mixing patient-derived HCC cells and stroma cells (LX2, WI38, and HUVECs) and YAP/TAZ expression was assessed using Western blot. Cell viability of MCTS upon 48 h of drug treatment (sorafenib, sorafenib with CA3 0.1 μM, and CA3 (novel YAP1 inhibitor)) was analyzed.
Results: TAZ expression was major in monolayer HCCs and YAP expression shown from tissue western blot reappeared in MCTS. Out of six patient-derived HCC cell lines, cell lines with high YAP/TAZ expression at MCTS level responded more sensitively to the combination therapy (Sorafenib + CA3 0.1 μM) despite potent cytotoxic effect of CA3 exhibited in all of the patient-derived HCCs. MCTS with medium or low YAP/TAZ expression did not show difference in drug sensitivity: sorafenib vs. sorafenib combined with CA3 0.1 μM.
Conclusion: Targeting YAP/TAZ inhibition using novel YAP1 inhibitor CA3 could be a promising therapeutic strategy to enhance sensitivity to sorafenib especially in HCCs with high YAP/TAZ expression in MCTS.

[OP-0314]

Cytokine Change in Hepatocellular Carcinoma after Radiotherapy

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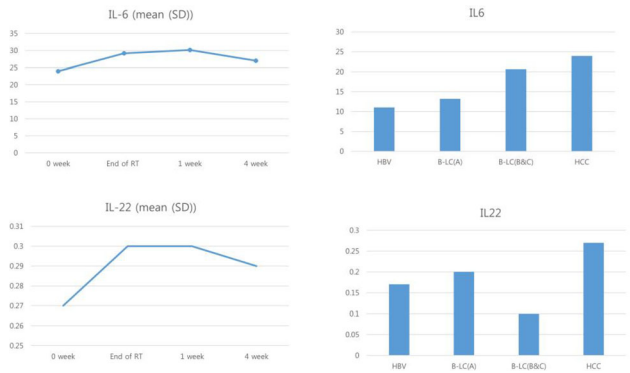
Objectives: Radiotherapy (RT) can enhance tumor immunogenicity and increases production of cytokines. Prior studies have examined change of cytokine level in cancer patients after radiotherapy, but study on hepatocellular carcinoma (HCC) is lacking. This study investigated the effects of radiotherapy on serum levels of interleukin-2 (IL-2), IL-10, IL-22 and tumor necrosis factor alpha (TNF-a) with HCC.
Materials and Methods: Data of HCC patients who underwent radiotherapy at one tertiary referral hospitals between March 2016 and December 2019 for the prospective study. This study included 20 hepatitis B virus (HBV) patients with HCC undergoing RT and 69 HBV controls. The control group was classified into three groups as follows: chronic hepatitis B (CHB) (n = 20), liver cirrhosis (LC) (n = 21), decompensated LC (DLC) (n = 20). Cytokines were serially monitored at pre-RT, end of RT, 1 week and 4 weeks after RT.
Results: At baseline, serum mean levels of IL-6 and IL-22 were higher in patients with HCC than in controls. In control group. serum mean levels of IL-6 and IL-22 were highest in DLC group and lowest in CHB group. The mean levels of IL-6 and IL-22 were increasing early after RT. Levels of TNF-a and aminotransferase (AST) had a positive correlation over time after RT (1 week: r = 0.622 (p = 0.004), 4 week: r = 0.523 (p = 0.022)).
Conclusion: RT induces changes in levels of IL-6 and IL-22 in HCC patients. Expression of IL-6 and IL-22 level is correlated with liver disease severity.



[PP-0318]

Prospero homeobox-1 overexpression is associated with the invasive and oncogenic phenotypes of human hepatocellular carcinoma cells

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Objectives: The transcriptional factor prospero homeobox-1 (PROX-1) is crucial for embryonic development of various organs and cell fate specification. Also, it exhibits either oncogenic or tumor suppressive activity, depending on cancer types. However, the relationship between PROX-1 and hepatocellular carcinoma (HCC) remains still obscure. The aims of current study were to investigate the impact of PROX1 on invasive and oncogenic phenotypes of human HCC cells.
Materials and Methods: We investigated the impact of PROX-1 on tumor cell behavior by using the pcDNA-myc vector and small interfering RNA in HepG2 and Huh7 human HCC cell lines. The flow cytometry, migration, invasion, proliferation, and tube formation assays were performed. The expression of PROX-1 by western blotting was investigated in human HCC cells.
Results: PROX-1 overexpression enhanced tumor cell proliferation, and inhibited apoptosis and cell cycle arrest via the modulation of activities of caspase-3 and PARP, and cyclin dependent kinase inhibitors including p21, p27, and p57 in HCC cells. The number of migrating and invading HCC cells was significantly increased after PROX-1 overexpression. The expression of N-cadherin and ZO1 was increased in HCC cells after PROX-1 overexpression. PROX-1 overexpression enhanced the angiogenesis through the increased expression of VEGF-A and -C, and decreased expression of angiostatin. The glycogen synthase kinase-3β (GSK-3β) and forkhead box O1 (FOXO1) phosphorylation were increased by PROX-1 overexpression in HCC cells. They were reversed after PROX-1 knockdown.
Conclusion: Our results indicate that PROX-1 overexpression is associated with the invasive and oncogenic phenotypes of human HCC cells via the phosphorylation of GSK-3β and FOXO1.

[OP-0348]

Overexpression of SCY1 Like Pseudokinase 3 (SCYL3) promotes tumor growth and metastasis via regulation of ROCK2 stability in hepatocellular carcinoma

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Objectives: SCY1 Like Pseudokinase 3 (SCYL3) is termed PACE-1 (Protein- associating with the carboxyl-terminal domain of Ezrin) because it physically interacts with the C- terminal domain of ezrin in lamellipodia, implicating its role in regulation of invasiveness of cancer cells.?However, the clinical relevance and functional role of SCYL3 in cancer remain unknown and uncharacterized. In this study, we investigated its clinical relevance, functional role, and underlying mechanisms in hepatocellular carcinoma (HCC).
Materials and Methods: We examined the expression and clinical relevance of SCYL3 in HCC by qPCR analysis and immunohistochemistry as well as analysing the TCGA dataset. Functional characterization was performed by lentiviral- based overexpression activation and knockdown approaches. Functional roles and mechanistic insights of SCYL3 in HCC were investigated by invasion/migration assay, i n vivo in orthotopic implantation,?reciprocal immunoprecipitation, protein expression assays, protein stability assay.
Results: We showed that SCYL3 was overexpressed in HCC, with preferential expression in metastatic human HCC tumors. Functional analyses showed that SCYL3 was found to be critical in migration, invasion and in vivo tumor growth and metastasis and significantly impact patients' clinical outcome. ROCK2, a crucial regulator of cytoskeletal reorganization, was first identified as the direct protein

binding partner of SCYL3. Through physical interaction with ROCK2, SCYL3 regulates its protein expression post- transcriptionally via altering protein stability. By inhibiting the degradation of ROCK2, SCYL3 increases formation of actin stress fibers and focal adhesions and thus promotes HCC metastasis.
Conclusion: We showed that SCYL3 plays a novel metastatic role in HCC by regulating ROCK2 stability.

[PP-0374]

Kruppel-like factor 10 deletion and hepatocellular carcinoma development

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Objectives: Kruppel-Like Factor10(KLF10) is originally identified as an early response gene following Transforming growth factor(TGF) β treatment of osteoblasts. It is known to serve as a positive feedback loop for regulating TGFβ signaling. Since TGF-β signaling is reported to play an important role at various stages of liver diseases, from initial liver injury toward liver fibrosis, cirrhosis and cancer, we investigated whether deleting KLF10 would affect the formation of liver fibrosis and hepatocellular carcinoma(HCC).
Materials and Methods: We used KLF10 deleted C57BL/6 mice and compared them with the wild type mice. Liver fibrosis was induced by feeding high fat diet(HFD) for 24 weeks. Chemically induced HCC was generated by injecting diethylnitrosamine(DEN) intra-peritoneally to 2-week-old mice for 8 weeks, and KLF10 expression was evaluated in human HCC specimens.
Results: Although KLF10 deletion resulted in increased TGFb and downstream signaling SMAD2, the inhibitory SMAD7 expression was also upregulated. When HFD was given, liver fibrosis was induced in both the wild type and KLF10 KO mice liver, and KLF10 deletion did not alter the level of liver fibrosis. However, incidence of HCC was increased in KLF10 KO mice. DEN treated KLF10 KO mice also demonstrated increased mesenchymal marker, N-cadherin and matrix metalloproteinase(MMP) 2. As for the epithelial markers, MMP7 was suppressed and E-cadherin showed no difference in KLF10 KO, DEN treated mice, as compared with that of the wild type mice. When KLF10 expression was immunohistochemically assessed in resected HCC human specimens, low KLF10 expression at tumor sites was associated with poor survival rate and lower recurrence free survival rate.
Conclusion: Although deleting KLF10 did not show any effect on HFD induced liver fibrosis, KLF10 deletion resulted in higher HCC incidence. In accordance with the animal study results, low KLF10 expression in HCC tumor sites was associated with poor prognosis after curative HCC resection.

[OP-0444]

Regulatory T cells induce suppressive immune milieu in intrahepatic cholangiocarcinoma and promote lymph node metastasis

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Objectives: Background: Emerging evidence indicates that immunogenicity plays an important role in intrahepatic cholangiocarcinoma (ICC). Herein, we systematically evaluated immunogenicity and their clinical relevance in ICC.
Materials and Methods: Methods: Highly immunogenic ICCs were identified by public dataset and the Cancer Immunome Atlas (TCIA). Then, we assessed the prognostic impact of highly immunogenic ICCs and key components after curative resection. Finally, we revealed the clinical relevance of immune milieu in ICCs.
Results: Results: Using Gene Expression Omnibus (GEO) dataset (GSE 89,749) and TCIA, we identified CD8 + and forkhead box p3 (Foxp3) + TILs, T-cell immunoglobulin and mucin domain 3 (TIM-3), and human leukocyte antigen-A (HLA-A), as highly immunogenic ICCs. Immunohistochemical analysis in in-house cohort showed that Foxp3 + TILs correlated with CD8 + TILs ($P = 0.045$) in intra-tumor, and high Foxp3 + /CD8 + ratio (FCR) emerged as an important factor for poor survival ($P < 0.001$). Furthermore, FCR in tumor-free lymph node in ICCs with lymph node metastasis was higher than those without lymph node metastasis ($P = 0.003$).
Conclusion: Conclusions: FCR can be an important biomarker that potentially represents the immune environment in ICCs, which plays an important role in tumor progression, especially lymph node metastasis.

[OP-0473]

Genomic profile of hepatocellular carcinoma after sustained virologic response

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Objectives: With the advent of direct acting antivirals (DAAs), many cases of chronic hepatitis C have achieved sustained virologic response (SVR), and hepatocellular carcinoma (HCC) has been decreasing. However, HCC after SVR has been reported. It is unclear whether HCC after SVR is multicentric origin (MO) or intrahepatic metastasis (IM). In this study, we analyzed the genomic profiles of synchronous and metachronous HCC occurred before and after DAA treatment to clarify the carcinogenesis patterns.
Materials and Methods: We prospectively followed up 612 consecutive patients who achieved SVR after DAA treatment at our hospital from July 2013 to June 2020 to investigate the presence of HCC. DNA was extracted from HCC, and genomic analysis was performed using a 72-gene panel of 285,470 nucleotides related to HCC generated internally. Detected mutations were annotated by OncoKB to identify oncogenic and actionable mutations.

Carcinogenesis patterns were diagnosed by comparing the obtained genomic profiles.
Results: Of the 612 patients, 48 (8%) had HCC. Of the 48 patients with HCC after DAA treatment, we studied 8 nodules in 3 patients who had HCC before DAA treatment and 16 nodules in 7 patients who did not have HCC before DAA treatment. In the genomic analysis of those 24 nodules in 10 cases, 454 mutations were detected. Of 454 mutations, 51 were oncogenic, and TP53 was the most common (n = 20). In addition, 7 actionable mutations were detected. Only 2 nodules in 1 patient which occurred before DAA treatment were IM, but the remaining 22 nodules in 9 patients which occurred after DAA treatment were MC, regardless of whether it was synchronous and metachronous.
Conclusion: Analysis of carcinogenesis patterns by genomic profiling showed that all HCC after DAA treatment was MO. In addition, actionable mutations can be detected, suggesting the possibility of a therapeutic strategy based on genomic profiles.

[PP-0482]

Exosomal miR-125b exerts anti-metastatic properties and predicts early metastasis of hepatocellular carcinoma

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Objectives: Cancer metastasis is responsible for the majority of cancer-related deaths. Exosomal miRNAs have emerged as promising biomarkers for cancer, serving as signaling molecules that can regulate tumor growth and metastasis. The aim of this study was to explore exosomal miRNAs that could predict extrahepatic metastasis in patients with HCC.
Materials and Methods: This study examined serum samples from 239 HCC patients and 45 non-HCC patients. Exosomal miRNA was measured by quantitative real-time PCR (qRT-PCR) in a large set of patients. To investigate the role of exosomal miRNA in HCC, we performed a series of in vitro tests such as exosome labeling, qRT-PCR, reverse transcription PCR, wound healing assay, transwell assay, and western blot assay.
Results: Exosomal miR-125b was drastically downregulated in HCC patients with metastasis than in those without metastasis. In vitro, we observed the uptake of miR-125b by exosome in recipient cells. Exosome-mediated miR-125b significantly inhibited migration and invasion abilities and downregulated the mRNA expressions of MMP-2, MMP-9, and MMP-14 in recipient cells via intercellular communication. Further investigation revealed that miR-125b suppressed SMAD2 protein expression in recipient cells by binding to its 3' untranslated regions. Exosome-mediated miR-125b transfer also disrupted TGF-β1-induced epithelial-mesenchymal transition and TGF-β1/SMAD signaling pathway in recipient cells by leading to a decrease of SMAD2 protein expression. Moreover, exosomal miR-125b was downregulated after metastasis compared to that at baseline in patients with serial measurements before and after metastasis.
Conclusion: The results imply that exosome-mediated miR-125b exerts anti-metastatic properties in HCC. These findings highlight that circulating exosomal miR-125b might represent a reliable biomarker with diagnostic and therapeutic implications for extrahepatic metastasis from HCC.

[PP-0483]

Significance of TERT genetic alterations and telomere length in hepatocellular carcinoma

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Objectives: Telomerase reverse transcriptase (TERT) mutations are reportedly the most frequent somatic genetic alterations in hepatocellular carcinoma (HCC). An integrative analysis of TERT telomere signaling during hepatocarcinogenesis is lacking. This study aimed to investigate the clinicopathological association and prognostic value of TERT gene alterations and telomere length in HCC patients undergoing hepatectomy as well as transarterial chemotherapy (TACE).
Materials and Methods: TERT promoter mutation, expression, and telomere length were analyzed by Sanger sequencing and real-time PCR in 305 tissue samples. Protein–protein interaction (PPI) analysis was performed to identify a set of genes that physically interact with TERT.
Results: The PPI analysis identified eight key TERT-interacting genes, namely CCT5, TUBA1B, mTOR, RPS6KB1, AKT1, WHAZ, YWHAQ, and TERT. Among these, TERT was the most strongly differentially expressed gene. TERT promoter mutations were more frequent, TERT expression was significantly higher, and telomere length was longer in tumors versus non-tumors. TERT promoter mutations were most frequent in HCV-related HCCs and less frequent in HBV-related HCCs. TERT promoter mutations were associated with higher TERT levels and longer telomere length and were an independent predictor of worse overall survival after hepatectomy. TERT expression was positively correlated with tumor differentiation and stage progression, and independently predicted shorter time to progression after TACE.
Conclusion: The TERT-telomere network may have a crucial role in the development and progression of HCC. TERT-telomere abnormalities might serve as useful biomarkers for HCC, but the prognostic values may differ with tumor characteristics and treatment.

[OP-0492]

The characterisation of tumour self-seeded cells in liver cancer progression

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Objectives: Recent studies indicated a multi-directional seeding of circulating tumour cells (CTCs). Apart from seeding to distant tissues

(metastases), CTCs can also reinfiltrate and colonise already established tumours. This process of "tumour self-seeding" provides new insights into the dynamics of tumour progression, and has been indicated to promote tumour growth, angiogenesis and invasion. However, tumour self-seeded cells (TSCs) have not been well identified and characterised due to unsuitable animal models. Therefore, this study aims to develop a novel animal model to recapitulate the process of tumour self-seeding and characterise the transcriptional and functional profiles of TSCs in liver cancer.

Materials and Methods: Kikume Green–Red (KikGR) is an irreversibly photoconvertible protein that changes fluorescence from green (KikGreen) to red (KikRed) upon violet light irradiation. Human tumour cell lines were knocked-in with KikGR plasmid and injected into mouse liver. After tumour formation, KikGreen$^+$ CTCs in the blood vessels were photoconverted to KikRed$^+$ CTCs. KikRed$^+$ CTCs that recolonised the primary tumour were identified as KikRed$^+$ TSCs, which could be distinguished from non-photoconverted KikGreen$^+$ primary tumour cells (PCs). KikRed$^+$ TSCs and KikGreen$^+$ PCs were isolated by fluorescence-activated cell sorting (FACS) and analysed by RNA sequencing and functional assays. Potential TSC population in cancer patients was investigated using single-cell RNA sequencing data.

Results: A novel animal model was successfully developed to fully recapitulate the process of tumour self-seeding. 114 genes were significantly and differentially expressed between TSCs and PCs, with potential TSC markers identified (TM4SF1, EMP1, SH3BGRL3). Further analysis showed TSCs were enriched with gene ontology relating to metastases and cell proliferation. Functional assays demonstrated that TSCs were more invasive and tumorigenic than PCs. Moreover, potential TSC population was identified in cancer patients.

Conclusion: TSCs present as a cell subpopulation within the primary tumour with enhanced invasiveness and tumorigenesis, which may provide novel cell targets with diagnostic, prognostic or therapeutic potential.

[PP-0498]

miR-23b-3p suppresses EMT, migration, and invasion by downregulating c-MET in hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) is the most commonly diagnosed malignancy of the liver. Epithelial-mesenchymal transition (EMT) with a switch from E-cadherin to N-cadherin has strongly promoted cell migration, invasion, and metastasis in most cancers. c-MET overexpression leads to metastasis through the promotion of EMT, migration, and invasion in HCC. miR-23b-3p was downregulated during HCC progression. This study aimed to investigate the role of c-MET regulating the EMT, migration, and invasion by targeting miR-23b-3p in HCC cell lines.

Materials and Methods: We measured c-MET and miR-23b-3p expression in tissues of patients with HCC. Also, miR-23b-3p mimic, inhibitor, and c-MET siRNA were transfected into HCC cell lines. The expression of EMT-related mRNA and protein was detected by quantitative real-time PCR and western blot. Also, EMT characteristics were analyzed with cell migration and invasion assay.

Results: The protein levels of c-MET were substantially increased in HCC tissues than in adjacent non-tumor tissues. Western blot and real-time PCR showed that knockdown of c-MET increased the epithelial marker claudin1 and decreased the levels of the mesenchymal markers (N-cadherin, Snail, Slug, and twist) and stemness markers (CD44, nanog, and KLF4). In addition, c-MET knockdown suppressed cell migration and invasion. The mRNA expression of miR-23b-3p decreased in HCC tissues. In vitro, the inhibition of miR-23b-3p promoted EMT, cell migration, and invasion. In contrast, overexpression of miR-23b-3p suppressed EMT, cell migration, and invasion. In addition, TGF-β1 stimulation after miR-23b-3p overexpression induced neither the mesenchymal phenotype nor cell migration. Also, transfection with miR-23b-3p inhibitor led to induced EMT. However, the co-transfected with c-MET knockdown, such effect was blocked.

Conclusion: Knockdown of c-MET suppressed EMT, cell migration, and invasion by targeting miR-23b-3p. These results suggest that c-MET/miR-23b-3p may serve as specific biomarkers and therapeutic targets for HCC.

[OP-0510]

Differential proto-oncogenic response to sorafenib of various liver cancer cell populations

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Objectives: Sorafenib is first-line systemic therapy for advanced hepatocellular carcinoma (HCC). However, its efficacy seems to be influenced by cellular heterogeneity. This study aims to investigate the effect of sorafenib treatment among various HCC cell populations.

Materials and Methods: In vitro study was performed using different HCC cell lines representing epithelial–mesenchymal transition (EMT)-transformed cells (JHH6, HLE, and HLF), and progenitor cells (HepG2 and Huh7), and immortalized hepatocytes (IHH). Cellular immunophenotype was profiled by flow cytometry using HCC stemness biomarkers. Cells were subjected to sorafenib treatment (between 1 and 80 μM), and lethal concentration (LC_{50}) of sorafenib was determined. In silico analysis of protein–protein interaction (PPI) network was performed to identify several proto-oncogenes as common targets followed by the analysis of gene expression modulation.

Results: Flow cytometer analysis using EpCAM, CD133, CD13, CD24, and CD90 confirmed the heterogeneity of cell lines used in the study. The LC_{50} values of sorafenib were found to be variable ranging from 18.3 to 47.4 μM. In silico PPI network analysis identified at least 10 proto-oncogenes candidates subjected to mRNA analysis following 50 μM sorafenib treatment. Gene analysis showed a significant decrease of AurKA, FGR, HGFR, YES1, FOS, and FYN in at

least two cell lines with the FOS decrease as the most significant (around 80% in HLE, HLF, Huh7, and HepG2 ($p < 0.05$). Notably, the downregulation of these proto-oncogene targets was most marked in progenitor cell lines (8/10 and 4/10 for HepG2 and Huh7, respectively).
Conclusion: This study indicates the relevance of cellular heterogeneity in response to sorafenib. Further modulation of target proto-oncogenes can be beneficial to increase the efficacy of sorafenib, in particular for progenitor subtypes of HCC.

[OP-0512]

Silencing of programmed death ligand 1 affects the stemness markers of liver cancer cells

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Objectives: Immune checkpoint therapies anti-PD-1/PD-L1 were shown to be highly effective compared to chemotherapy or systemic therapy. However, despite the success of anti-PD-1/PD-L1 in other cancers, a substantial proportion of liver cancer patients fails to respond. This project investigates the heterogeneity of liver cancer cells against anti-PD-L1 therapy, in focus to the cancer stem cells (CSC) markers.
Materials and Methods: To assess the dynamics of PD-1/PD-L1, hepatic samples were taken from HBV-transgenic mouse C57BL/6 J-TG(ALB1HBV)44BRI/J with age: 3 (inflammation), 6 and 9 (dysplasia and pre-tumoral), 12 and $\geq$ 15 months (tumor) together with its wild type (C57BL/6 J) counterpart. Transgenic mouse showed a progressive increase of CSC markers during hepatocarcinogenesis. PD-L1 RNA silencing was performed by siRNA in various human liver cancer cell lines: progenitor lines (HepG2 and Huh7) and epithelial–mesenchymal transition (EMT)-transformed lines (HLE, HLF, and JHH6). Dysregulation of CSC markers was examined by gene expression analysis.
Results: From 112 tissue samples of in vivo model, Pdcd1 (PD-1) was increased along hepatocarcinogenesis, from inflammation until tumor development. Pdcd1l1 (PD-L1) expression was already significantly up-regulated also at early injury ($p < 0.01$). High expressions of both Pdcd1 and Pdcd1l1 was detected in pre-tumoral stage nodule in 9-month-old mice. No difference was noticed for Pdcd1lg2 (PD-L2). From in vitro models, EpCAM was noticed in progenitor whereas CD44 in EMT-transformed lines. RNA silencing down-regulated the PD-L1 mRNA expression in all cell lines up to 90% ($p < 0.05$ to all lines). Except for JHH6, PD-L1 downregulation was accompanied by dysregulation of stemness marker EpCAM in progenitor lines (around 50%) and CD13/ANPEP in both progenitor (around 50%) and EMT-transformed lines (60% and 40% for HLE and HLF, respectively) ($p < 0.05$ vs mock). However, the extent of down-regulation was depended on siRNA concentration.
Conclusion: Targeting PD-1/PD-L1 checkpoints is a promising approach for liver cancer therapy. However, understanding cellular heterogeneity is essential to define its efficacy.

[PP-0542]

Genetic features of hepatocellular carcinoma according to the serum biomarkers

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Objectives: Serum a-fetoprotein (AFP), Lens culinaris agglutinin − reactive AFP (AFP-L3), and des-g-carboxyprothrombin (DCP) are useful biomarkers of hepatocellular carcinoma (HCC). However, associations among molecular characteristics and serum biomarkers are unclear.
Materials and Methods: We analyzed RNA expression and DNA variant data from The Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA-LIHC) to examine their associations with serum biomarker levels and clinical data. From 371 TCGA-LIHC patients, we selected 91 seen at 3 institutions in Korea and the United States and measured AFP, AFP-L3, and DCP from preoperatively obtained serum. We conducted an integrative clinical and molecular analysis, focusing on biomarkers, and validated the findings with the remaining 280 patients in the TCGA-LIHC cohort.
Results: Patients were categorized into 4 subgroups: elevated AFP or AFP-L3 alone (↑AFP&L3), elevated DCP alone (↑DCP), elevation of all 3 biomarkers (↑All), and reference range values for all biomarkers (RR). CTNNB1 variants were frequently observed in ↑DCP patients (n = 7 [53.8%]) and RR patients (n = 10 [38.5%]), but ↑DCP patients with a CTNNB1 variant had worse survival than RR patients. TP53 sequence variants were associated with ↑AFP (n = 8 [30.8%]) and ↑DCP (n = 4 [30.8%]). The Wnt − b-catenin signaling pathway was activated in the ↑AFP&L3, whereas liver-related Wnt signaling was activated in the RR. TGF-b and VEGF signaling are activated in high AFP&L3, while dysregulated bile acid and fatty acid metabolism were dominant in ↑DCP. We validated these finding using the remainder of the TCGA-LIHC cohort and showed similar results to the test cohort.
Conclusion: Serum AFP, AFP-L3, and DCP levels can help predict variants in the genetic profile of HCC, especially for TP53 and CTNNB1. These findings may facilitate development of an evidence-based approach to treatment.

[OP-0563]

Decreased expression of ST6GAL1 in hepatocellular carcinoma is correlated to poor prognosis and lower immune infiltrating level

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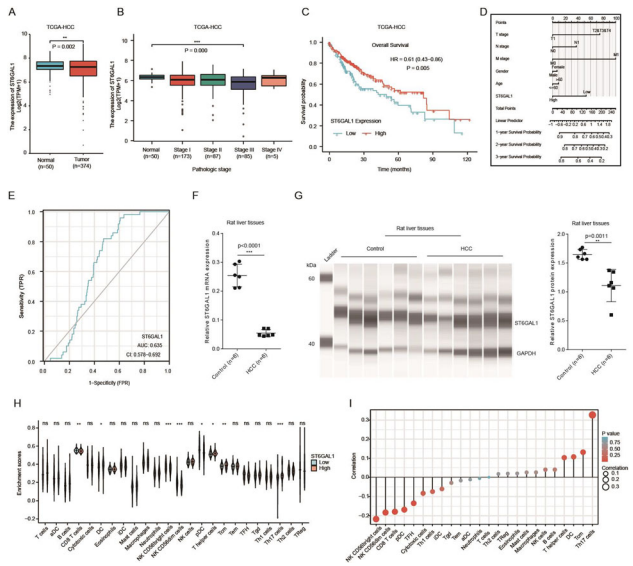
Objectives: Hepatocellular carcinoma (HCC) is one of the most malignant tumors over the world. The ST6 β-galactside α-2,6-sialyltransferase 1 (ST6GAL1) gene was found aberrantly expressed in a variety of cancers, but its function and mechanism are still unclear. The aim of this study was to explore the role of ST6GAL1 in HCC.
Materials and Methods: The HCC dataset was downloaded from The Cancer Genome Atlas database (TCGA). The ST6GAL1 expression of tumor tissues and normal tissues, and the relationship between ST6GAL1 expression and prognosis was analyzed by R language software. The diagnostic efficacy of ST6GAL1 was evaluated using pROC package. The HCC rat model was constructed by intraperitoneal injection of diethylnitrosamine, and the expression of ST6GAL1 mRNA and protein levels were detected by Real-Time quantitative PCR and Western Blotting. The correlation between ST6GAL1 expression and tumor immune infiltration was explored utilizing GSVA package.
Results: The ST6GAL1 expression was significantly lower of HCC tissues than in normal tissues, and its downregulation was associated with poor prognosis of HCC patients. The COX regression analysis showed that upregulation of ST6GAL1 was an independent prognostic factor for good prognosis. Meanwhile, the downregulation of ST6GAL1 was also observed in HCC-rat' liver tissues compared to the control group. Finally, the immunoassay results showed that the expression of ST6GAL1 was positively correlated with the immune infiltration level of dendritic cells, T helper cells, central memory T cells, and Th17 cells.
Conclusion: Decreased ST6GAL1 expression of tumor tissues was associated with poor prognosis of HCC, which could further to affect the infiltration of immune cells included T cells and dendritic cells. Our study indicated that ST6GAL1 could be a potential biomarker and therapeutic target to assess the prognosis and regulate immune infiltration level of HCC.



[OP-0573]

ROS mediated hepatic stellate cell activation during chemotherapy in liver cancer

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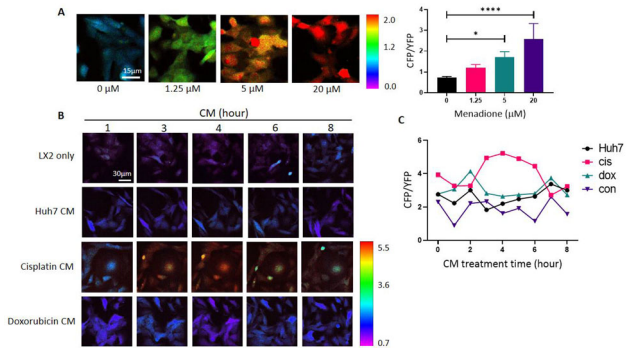
Objectives: The standard treatment of unresectable hepatocellular carcinoma (HCC) is transarterial chemoembolization (TACE) using chemotherapeutic drugs such as cisplatin and doxorubicin. However, Chemotherapy is considered a "double-edged sword" through renewing tumour microenvironments and activating hepatic stellate cells (HSCs) which can promote tumour growth and chemoresistance. Hence, a better understanding of the molecular mechanism mediated HSC activation in response to chemotherapy could reveal novel potential targets for the treatment of liver cancer.
Materials and Methods: The effect of chemotherapeutic drugs on HSC activation was examined in three in vitro models. Human HSC cell line LX2 cells were co-cultured with cisplatin-treated human HCC cell line Huh7 cells in a transwell system and 3D mixed-cell spheroids. LX2 cells and human primary HSCs were cultured in the conditioned medium (CM) collected from cisplatin/doxorubicin-treated or untreated Huh7 cells. The expression of activation markers was measured. The results were further validated in mouse orthotopic models. Finally, an HSP FRET biosensor was employed to detect reactive oxygen species (ROS) in LX2 cells cultured in Huh7-CM with or without treatment.
Results: HSCs can be activated by cisplatin-pretreated Huh7 cells via three in vitro models with a significant increase in the expression of activation markers. Cisplatin-induced HSC activation was further confirmed in vivo, evidenced by an obvious increase in the activation markers of tumour tissues. Cisplatin-pretreated cancer cells increased intracellular ROS of LX2 cells reflected by an increased ratio of CFP/YFP fluorescent intensity (Fig. 1). LX2 cells treated with H_2O_2 showed an elevated expression level of activation markers, indicating ROS generation can activate HSCs. In addition, activated HSCs further induced ROS elevation in cancer cells.
Conclusion: HSCs can be activated through a ROS-mediated pathway during chemotherapy in liver cancer. Understanding the HSC activation mechanism induced by chemotherapy could provide potential therapeutic targets as a complement to chemotherapy against liver cancer.



[PP-0579]

The inhibitory effect of ginsenoside Rh2-Rg5 complex on liver cancer in a preclinical study: A mechanism analysis based on next-generation sequencing

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Objectives: We had found that the anti-cancer effects of ginsenosides Rh2 and Rg5 were similar to that of sorafenib in a xenograft hepatoma animal model. We investigated whether Rh2-Rg5 complex effectively inhibits liver cancer while reducing cytotoxicity, and analyzed the mechanism of anticancer effect of Rh2-Rg5 complex.
Materials and Methods: The anticancer effects of Rh2, Rg5, and Rh2-Rg5 complex were evaluated and compared in vitro using an MTT assay with human hepatoma Hep3B cells. Hep3B cells were implanted on the flanks of BALB/C nude mice for in vivo experiments, and sorafenib, ginsenosides Rh2, Rg5, and Rh2-Rg5 complex were injected intraperitoneally twice a week for 4 weeks. Next-generation sequencing (NGS) of each tumor tissue was conducted to analyze gene expression differences in each treatment group.
Results: Of the three treatments in an in vitro experiment, ginsenoside Rh2 treatment showed the lowest cell viability. In the combination treatment of ginsenosides Rh2 and Rg5, the higher the concentration of Rg5, the higher the cell viability. Considering both cytotoxicity and anticancer effects, the most optimal ratio of ginsenoside Rh2 and Rg5 was 2:3 by volume. In animal experiments, increased necrotic area and higher levels of cleaved PARP protein expression were observed in sorafenib, Rh2, Rg5 and Rh2-Rg5 complex-treated groups compared to control group, of which Rh2-Rg5 complex-treated group showed the highest level of cleaved PARP protein expression. In NGS analysis, the final three genes were selected using adjusted P value (Benjamini-Hochberg) to adjust the false discovery rate of NGS and considering the known mechanisms of action and functions of each gene: Alpha kinase 2 (ALPK2) and Dehydrogenase/reductase 2 (DHRS2), known as tumor suppressor genes, and cytokine receptor like factor 1 (CRLF1), known as a oncogene.
Conclusion: Ginsenoside Rh2-Rg5 complex effectively inhibits liver cancer while reducing cytotoxicity, and ALPK2, DHRS2, and CRLF1 genes are involved in the anticancer mechanism.

[OP-0588]

Hepatocellular carcinoma: Epidemiological aspects, clinical features and personal experience

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Objectives: Hepatocellular carcinoma (HCC) is the most common primary malignant neoplasm of the liver. More than half a million new cases are diagnosed each year. In Kazakhstan, HCC has been ranked 10th in the structure of oncological diseases over the past 5 years. The aim of the research is to study the organizational and clinical features of providing care to patients with HCC at National Research Center of Surgery after A.N. Syzganov.
Materials and Methods: We study inpatient records of patients diagnosed with HCC at National Scientific Center of Surgery named after A.N. Syzganov from 2012 to 2020. It was processed in the statistical package IBM SPSS Statistics 20. To assess the severity of patients and staging, the CTP [23], MELD [24] and Barcelona and Milan criteria were used.
Results: The average age of the patients was 61.67 max = 84, min = 31. The average BMI of women is 25.45 (5.390), men—24.79 (3.453), (p = 0.321). Patients with high total bilirubin levels had a lower body mass index (Fig. 1). The ratio of total bilirubin to BMI is associated with the development of HCC, leading to liver failure and cell necrosis.
Conclusion: The study revealed a correlation between BMI and the level of bilirubin associated with the development of HCC and subsequent cell necrosis.

[OP-0622]

Frequency of infiltrating T cells and PD-L1 + cells as an indicator of multi-kinase inhibitor response in hepatocellular carcinoma

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Objectives: Sorafenib and lenvatinib are multikinase inhibitors approved for the unresectable hepatocellular carcinoma (HCC). Tumor microenvironment (TME) of HCC is composed of various cell types including T cells and tumor-associated macrophages (TAMs). In this study, we investigated the association between the number of infiltrating T cells or TAMs in TME and responses to sorafenib or lenvatinib in unresectable HCC.
Materials and Methods: Between December 2017 and November 2020, a total of twenty-one patients with unresectable HCC treated with sorafenib or lenvatinib were enrolled. Immunohistochemistry for CD3 (T cell marker), CD68 (macrophage marker) and PD-L1 was performed on specimens obtained from liver biopsy or surgery.
Results: Among the 21 patients enrolled, 8 patients were treated with sorafenib and 13 with lenvatinib. One patient (12.5%) with sorafenib and 7 patients (53.8%) with lenvatinib showed objective responses. For all enrolled patients, significantly higher numbers of T cells were infiltrated in TME of responders than in TME of non-responders (P = 0.002), although the number of infiltrating TAMs did not differ. When only considering the lenvatinib-treated patients (n = 13), similar tendency was observed in that more T cells were infiltrated in TME of lenvatinib responders (P = 0.043). PD-L1 was principally stained in peritumoral TAMs, and combined positivity score for PD-L1 was significantly higher in patients with objective responses (P = 0.047). At the time of survival assessment, 2 of 10 (20.0%) patients in high-T cell group (number of infiltrating T cells > median) died and 6 of 11 (54.5%) patients in the low-T cell group died, although log-rank test did not demonstrate the significant survival difference.
Conclusion: Tumor immunogenicity, as indicated by the frequency of infiltrating T cells and PD-L1$^+$ cells in TME, might be an indicator for objective response to multikinase inhibitor treatment.

[OP-0654]

CYGB promoter methylation as a biomarker for hepatocellular carcinoma

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Objectives: Cytoglobin (CYGB) acts as a tumor suppressor gene and DNA methylation in the CYGB promoter region has been reported in various types of cancers. This study aims to investigate whether CYGB promoter methylation contributes to CYGB inactivation in hepatocellular carcinoma (HCC).
Materials and Methods: Forty-two pairs of tumor and adjacent non-tumor tissues from liver cancer patients with chronic hepatitis C virus infection were evaluated for CYGB promoter methylation using Ion GeneStudio S5. Truncated mutation analysis of human CYGBpromoter region was performed. Restoration of CYGB expression was implemented in four HCC cell lines treated with 5-aza-2′- deoxycytidine (DAC).
Results: Next generation sequencing results clearly showed the methylation frequency in tumors is significantly higher than that in non-tumor tissues at all of 33 CpG sites (P = 1.02E-8) in promoter region. Reversely, CYGB mRNA expression in tumor is significantly lower than that in non-tumor tissues (–60%, $P < 0.05$). High methylation frequency and no CYGB expression at RNA and protein levels were found in HCC cells (HepG2, Huh7, SNU-387, HLE) and well-known myofibroblast LX-2 cells. In contrast, almost no methylation in human hepatic stellate cells (both primary and cell line) that correspond to positive CYGB expression. Luciferase assay data demonstrated that the CYGB promoter region spanning from –994 to –639 exhibited a significant decrease in luciferase activity. Interestingly, DAC treatment time- and dose-dependently restored CYGB expression at both mRNA and protein levels in SNU-387, HLE and Huh7, and at mRNA level in HepG2 cells while DAC did not induce CYGB expression in LX-2. Notably, after inducing CYGB expression in SNU-387, removal of DAC resulted in regressing of CYGB expression at both mRNA and protein levels.
Conclusion: CYGB methylation has significant discriminatory capacity at separating cancer from adjacent nonmalignant liver cancer tissue proposing the novel diagnosis marker. Demethylation of CYGB gene promoter may lead to cancer regression.

[PP-0717]

Is liver carcinogenesis after SVR due to intrahepatic metastasis (IM) or multicentric recurrence (MC)?; Analysis by gene profiling

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Objectives: Oral preparation of anti HCV drug completely changed the paradigm of Hepatology. We prospectively observed the recurrence of HCC after SVR. In this study, we performed genomic analysis of synchronous and metachronous hepatocellular carcinomas observed before and after DAA treatment, and aimed to clarify the carcinogenic mode by comparing the genetic profiles.
Materials and Methods: We enrolled 611 patients who achieved SVR after DAA between 2013 and 2020. These patients were prospectively observed for development of HCC. Genomic analysis was performed using a 72-gene panel of hepatocellular carcinoma-related genes spanning 285, 470 bases generated by In house. Oncogenic mutations were annotated by OncoKB. The mode of carcinogenesis was diagnosed by comparing the obtained gene profiles.
Results: The mean observation period for all 611 patients was 3.6 years, and HCC development was observed in 47 patients (8%) during follow-up. Genomic analysis was performed on 24 nodules of 10 patients, including 8 nodules in 3 patients with previous experience of HCC before DAA treatment (comparable before and after DAA treatment). As a result, 454 mutations were detected. Of these, 51 were oncogenic mutations, with the highest number of 20 in TP53. The genetic mode of the occurrence was IM only in one case and two nodules that developed before DAA treatment, but the remaining 9 cases and 22 nodules were genetically determined as MC.
Conclusion: Analysis of carcinogenesis patterns by gene profiles after SVR reveled the majority was multicentric in origin.

[OP-0734]

Ganji Formula inhibits lung metastasis of hepatocellular carcinoma through regulating LOXL2-mediated pre-metastatic niche formation

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Objectives: Recent studies have found that the tumor pre-metastatic niche (PMN) formation is an important mechanism of Hepatocellular carcinoma (HCC) metastasis. Ganji Formula (GJF), one Traditional Chinese medicine (TCM) formula can effectively inhibit lung metastasis in clinic. The present study aims to explore the mechanism of GJF in inhibiting lung metastasis based on regulating LOXL2/ the lung PMN formation.
Materials and Methods: To imitate tumor microenviorment of inflammation or hypoxia, HCC cells were induced by TGF-β for 48 h or incubated the inanaerobic box ($O_2\% < 0.1\%$) for 24 h respectively. At the same time, GJF were added to treat cells. The LOXL2 expression and related regulating molecules were examined. Subsequently, the effect of GJF on PMN were investigated. Human lung fibroblast (HELF) cells were induced by rhLOXL2, with the treatment of GJF drug-containing serum or control simultaneously for 24 h. Then the expression of fibronectin, MMP9 and CXCL12 were measured. Mice bone marrow derived cells (BMDCs) recruitment experiments induced by rhLOXL2 and the effect of GJF were

performed using Transwell method or FC analysis of isolated cells from lung tissues of mice induced by rhLOXL2 with/wihtout GJF treatment..

Results: HCC cells induced by TGF-β significantly unregulated LOXL2 and SMAD4 expression, while decreased by GJF. Similarly, hypoxia treatment increased LOXL2 expression and HIF-1α in HCC cells. GJF treatment can reverse their expression level. Furthermore, the results showed that rhLOXL2 enhanced the expression of CXCL12, MMP9 and fibronectin obviously in HELF cells, which was inhibited by GJF. Additionally, rhLOXL2 significantly accelerated the migration of BMDCs in vitro or in vivo, which was decreased by GJF treatment.

Conclusion: GJF could inhibit the increase of LOXL2 expression caused by HCC tumor microenvironment like inflammation and hypoxia. Moreover, it can down-regulate the LOXL2-induced gene expression related to PMN. These results suggest GJF may contribute to the mechanism of this formula in inhibiting lung metastasis of HCC.

[OP-0743]

Urinary 8-hydroxydeoxyguanosine in relation to XRCC1 rs25487 G/A (Arg399Gln) and OGG1 rs1052133 C/G (Ser326Cys) DNA repair genes polymorphisms in patients with chronic hepatitis C and related hepatoce

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Objectives: DNA repair represents a protective mechanism against cell injury and cancer. 8-hydroxy-deoxyguanosine (8-OHdG) is the main ROS-induced DNA mutation. The current study aimed to evaluate urinary 8-OHdG levels in patients with chronic hepatitis C virus (HCV) and its related hepatocellular (HCC) and correlate its level to XRCC1 rs25487 G/A and OGG1 rs1052133 C/G gene polymorphisms.

Materials and Methods: Urinary 8-OHdG assays were performed using HPLC technique, and XRCC1 rs25487 G/A and OGG1 rs1052133 C/G gene polymorphisms were analyzed by PCR using confronting two-pair primer method (PCR-CTPP) in 200 subjects allocated into 50 chronic HCV patients, 50 HCV-related HCC patients, and 100 controls.

Results: There were significantly increased urinary 8-OHdG levels in HCV-related HCC and chronic HCV patients when compared with the controls ($P < 0.05$ for all). Urinary 8-OHdG was associated with the tumor spread. Regarding, XRCC1 (Arg399Gln), AA (Gln/Gln) genotype and A-allele were more frequent in HCC and chronic HCV patients than in the controls ($P < 0.05$). ORs (95%CI) using the dominant and the recessive genetic models were; 2.1 (1.1–4.1), $P = 0.032$ and 1.9 (1–3.6), $P = 0.043$ respectively. For OGG1 (Ser326Cys), GG (Cys/Cys) genotype and G-allele were increased significantly in chronic HCV and HCC patients compared to the controls ($P < 0.05$). ORs (95%CI) under the dominant and the recessive genetic models were; 2.1 (1.1–4.1), $P = 0.032$ and 1.9 (1–3.8), $P = 0.049$ respectively. Additionally, XRCC1 (AA) and OGG1 (GG) genotypes had significantly increased urinary 8-OHdG levels among patients ($P < 0.05$).

Conclusion: XRCC1 (AA) and OGG1 (GG) could be considered as possible genotypic risk factors for HCV- related HCC development which were associated with significantly high urinary 8-hydroxy-deoxyguanosine levels, thus urinary 8-OHdG could be considered as non-invasive marker in follow-up chronic HCV progression into HCC.

[OP-0793]

Exogenous antioxidants, N-acetylcysteine and glutathione, enhance cancer initiation and growth in hepatocellular carcinoma

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Objectives: Controversy over the benefits of antioxidants supplements in cancers persists for long. Using hepatocellular carcinoma (HCC) as a model, we investigated the effects of exogenous antioxidants N-acetylcysteine (NAC) and glutathione (GSH) on tumor initiation and growth.

Materials and Methods: Multiple mouse models, including diethylnitrosamine (DEN)-induced and Trp53KO/C-MycOE-induced HCC models, mouse and human HCC cell xenograft models with subcutaneous or orthotopic injection were used. In vitro assays including ROS assay, colony formation, sphere formation, proliferation, migration and invasion, apoptosis, cell cycle assays were conducted. Western blot was performed for protein expression and RNA-sequencing to identify potential gene targets.

Results: In these multiple different mouse and cell line models, we observed that NAC and GSH promoted HCC tumor initiation and growth, accompanied with significant reduction of intracellular reactive oxygen species (ROS) levels. Moreover, NAC and GSH promoted cancer stemness, and abrogated the tumor-suppressive effects of Sorafenib both in vitro and in vivo. Exogenous supplementation of NAC or GSH reduced the expression of NRF2 and GCLC, suggesting the NRF2/GCLC-related antioxidant production pathway might be desensitized. Using transcriptomic analysis to identify potential gene targets, we found that TMBIM1 was significantly upregulated upon NAC and GSH treatment. Both TCGA and in-house RNA-sequence databases showed that TMBIM1 was over-expressed in HCC tumors. Stable knockdown of TMBIM1 increased the intracellular ROS; it also abolished the promoting effects of the antioxidants in HCC cells. On the other hand, BSO and SSA, inhibitors targeting NAC and GSH metabolism respectively, partially abrogated the pro-oncogenic effects induced by NAC and GSH in vitro and in vivo.

Conclusion: Our data implicate that exogenous antioxidants NAC and GSH, by reducing the intracellular ROS levels and inducing TMBIM expression, promoted HCC initiation and tumor growth, and counteracted the therapeutic effect of Sorafenib. Our study provides scientific insight regarding the use of exogenous antioxidant supplements in cancers.

[OP-0822]

Atorvastatin favorably modulates a clinical hepatocellular carcinoma risk gene signature in vitro and in vivo

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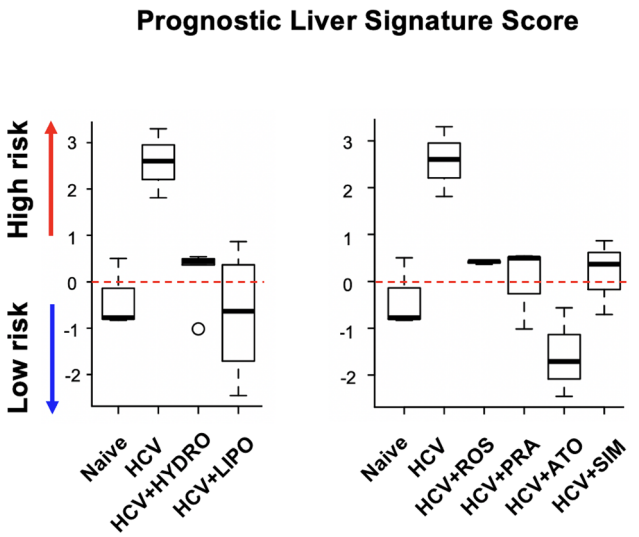
Objectives: Lipophilic but not hydrophilic statins have been shown to be associated with reduced risk for hepatocellular carcinoma (HCC) in patients with chronic viral hepatitis. We investigated differential actions of lipophilic and hydrophilic statins and their ability to modulate a clinical prognostic liver signature (PLS) predicting HCC risk in patients with liver disease.
Materials and Methods: Hepatitis C virus (HCV)-infected Huh7.5.1 cells, recently developed as a model to screen HCC chemopreventive agents, were treated with lipophilic statins (atorvastatin and simvastatin) and hydrophilic statins (rosuvastatin and pravastatin), and then analyzed by RNA sequencing and PLS.
Results: Lipophilic statins, particularly atorvastatin, more significantly suppressed the HCV-induced high-risk pattern of PLS and genes in YAP and AKT pathway implicated in fibrogenesis and carcinogenesis, compared to the hydrophilic statins. While atorvastatin inhibited YAP activation through the mevalonate pathway, the distinctive AKT inhibition of atorvastatin was mediated through stabilizing truncated retinoid X receptor alpha, which has been known to enhance AKT activation, representing a novel target for HCC chemoprevention. In addition, atorvastatin modulated the high-risk PLS in an in vitro model of non-alcoholic fatty liver disease (NAFLD) and in NAFLD patients with significant fibrosis.
Conclusion: Atorvastatin distinctively inhibits YAP and AKT activation, which are biologically implicated in HCC development, and attenuates a high-risk PLS in vitro model of HCV infection and NAFLD and in NALFD patients with fibrosis. These findings suggest that atorvastatin is the most potent statin to reduce HCC risk in patients with viral and metabolic liver diseases.



[OP-0886]

Proteomics analysis of HCC tumors treated with Sorafenib

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Objectives: Sorafenib is a multiple receptor tyrosine kinase inhibitor which is the standard systemic therapy for advanced hepatocellular carcinoma (HCC). However, the objective response rate is low only reaching 10% and since there are other new 1st line treatment options such as lenvatinib and immune checkpoint inhibitors, biomarkers that may predict patients who will respond well to sorafenib is required.
Materials and Methods: Tumor tissues of 28 HCC patients who had undergone liver resection prior to sorafenib treatment were enrolled. A total of 488 antibodies were used for reverse phase protein array (RPPA). Hierachical clustering was performed and association with overall survival (OS), progression free survival (PFS) and disease control rate (DCR) were analyzed.
Results: Among 28 patients, 71.4% of the patients had locoregional treatment prior to sorafenib and half of the patients switched to second-line chemotherapy due to HCC progression. The unsupervised clustering of protein expression in HCC tumors revealed two distinct groups where 9 patients (32.1%) were categorized to "good-response" group while 19 patients (67.9%) were categorized to "poor-response" group. The protein signature that divided patients into 2 distinct groups were named "Sorafenib response-related protein signature". The OS was tended to be higher in "good-response" group (log rank, p = 0.1) and similar results were observed for PFS (log rank, p = 0.06). DCR at 3 months were significantly higher in "good-response" group (44.4%) compared to 33% in "poor-response" group (p = 0.04). Druggable targets; STING, YAP and EGFR were significantly high in poor response group.
Conclusion: "Sorafenib response-related protein signature" had prognostic efficacy in identifying those who will respond to sorafenib. The cGAS-STING pathway is emerging as playing an important role in cancer immunotherapy while EGFR high HCCs were reported to

have synthetic lethality with lenvatinib. Our study presents a guide for combination therapy with STING or EGFR inhibitor for those who do not respond to sorafenib monotherapy.

[OP-0961]

Survival outcomes of hepatocellular carcinoma in non-alcoholic fatty liver disease (NAFLD) in comparison with other etiologies: A retrospective cohort study

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Objectives: There is an etiologic shift in hepatocellular carcinoma (HCC) from chronic viral hepatitis to non-alcoholic fatty liver disease (NAFLD). However, limited data exists on survival outcomes of NAFLD-related HCC in the Philippines and in Asia. This study determined clinical, demographic, and tumor profiles, and outcomes in patients with NAFLD-related HCC in comparison with non-NAFLD-related HCC.
Materials and Methods: This is an analytic single-center retrospective cohort study of adults diagnosed with HCC at the National Kidney and Transplant Institute from 2010 to 2020. Demographic data, tumor characteristics, and laboratory parameters at diagnosis were retrieved through review of medical records. Outcomes of interest were in-hospital mortality, overall survival, and predictive scores for survival.
Results: A total of 149 patients were included. Median follow-up was at 4.5 months. Majority had hepatitis B (n = 70, 47.0%) and NAFLD (n = 46, 30.9%). NAFLD-related HCC patients were older (67.4 + 10.2 years, $p < 0.01$), had diabetes (n = 27, 58.7%, $p < 0.01$), and had less alcohol consumption ($p < 0.01$). There were no differences in tumor size (9 cm + 5, p = 0.22), Child-Turcotte-Pugh (CTP) Class (mostly CTP A, n = 98, 65.8%, p = 0.45), Barcelona Clinic Liver Cancer (BCLC) staging (mostly BCLC B, n = 91, 61.1%, p = 0.17), Model for End-Stage Liver Disease (MELD) score (13 + 7.5, p = 0.83), and Albumin-bilirubin (Albi) scores (-2.1 + 0.7, p = 0.54) between NAFLD- and non-NAFLD-related HCC. Kaplan–Meier estimates did not show significant differences in cumulative survival across all timepoints (i.e. in-hospital, at 3 months, one year, and three years) between the two groups (log-rank test p = 0.96). Cox proportional hazard regression model did not demonstrate a significant difference in mortality among NAFLD-related HCC against HCC from other etiologies (p = 0.78).
Conclusion: Patients with NAFLD-related HCC were older, had diabetes, and had less significant alcohol history. There were no significant differences in tumor characteristics, predictive aggregate scores, and overall survival rates in patients with NAFLD-related HCC compared to HCC from other etiologies.

[OP-0979]

Bile acid-mediated induction of hepatic stellate cell activation enhances the invasion of hepatocellular carcinoma via Mcl-1 and COX-2

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Objectives: Activated hepatic stellate cells (HSCs) are the major subtype of stromal cells in the liver tumor microenvironment which can promote the growth and migration of hepatocellular carcinoma (HCC) cells. Indeed, senescent and cancer-associated fibroblasts express numerous inflammatory and tumor promoting factors that are collectively referred to as the senescence-associated secretory phenotype (SASP). In the present study, we investigated the mechanisms of bile acid-mediated induction of HSC activation via the expression of the SASP in HCC cells.
Materials and Methods: The immortalized human stellate cells (LX-2 cells) were used in this study. Invasion assay were done to evaluate the invasion of HCC cells (Huh-BAT, SNU-761, and Huh-SR) cocultured with HSCs. IL-6 and IL-8 mRNA was quantitated using real-time PCR. To investigate the mechanisms, western blot analyses were performed.
Results: Bile acid significantly increased the invasion of HCC cells when cocultured with HSCs as compared to monocultured HCC cells. Bile acid also increased protein expressions of the mesenchymal markers including α-SMA and vimentin in both HCC cells and HSCs. Moreover, bile acid increased the protein expressions of Mcl-1 and cyclooxygenase-2 (COX-2) in both HCC cells and HSCs. The inhibitors of either Mcl-1 induction by siRNA transfection or COX-2 activity by celecoxib decreased the bile acid-mediated HCC invasion. Mcl-1 and COX-2 induction was found to be due to transcriptional enhancement dependent on TGR-5 activation.
Conclusion: Bile acid-mediated induction of HSC activation enhances the invasion of HCC cells via the expression of the SASP. TGR-5 dependent overexpression of Mcl-1 and COX-2 may be the key factors which lead to HCC metastasis.

[PP-0982]

Loss of CD226 dictates tumor-specificity and severe dysfunction of TIGIT-expressing tumor-infiltrating T cells in hepatocellular carcinoma

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Objectives: TIGIT competes with its co-stimulatory counterpart CD226 which has the same ligand, CD155. In, particular, unexpectedly high expression of TIGIT in peripheral $CD8^+$ T cells even in healthy donors raise an important question regarding whether TIGIT expression alone can be an appropriate indicator of T-cell dysfunction. Therefore, in this study, we investigated the immunological context of TIGIT and CD226 in terms of T-cell exhaustion, tumor-specificity and proper targets for TIGIT blockade.
Materials and Methods: We obtained tumor tissues along with adjacent non-tumor tissues and blood samples from patients with hepatocellular carcinoma and prepared tissue single-cell suspension or peripheral blood mononuclear cells. Tumor-infiltrating lymphocytes (TILs) were analyzed by flow cytometry using tumor antigen- and virus antigen-specific MHC-I multimers.

Results: We found that expression of TIGIT was not significantly different between peripheral and tumor-infiltrating $CD8^+$ T cells, but CD226 expression was significantly reduced in tumor-infiltrating $CD8^+$ T cells. Dissected subsets of $CD8^+$ TILs in context of TIGIT and CD226 expression showed distinct exhaustion statuses and features of T-cell exhaustion of TIGIT-expressing $CD8^+$ TILs. Specifically, T-cell exhaustion was only observed when CD226 was lost. In addition, the loss of CD226 predominantly occurred in tumor antigen-specific $CD8^+$ TILs, but not in virus-specific bystander $CD8^+$ TILs.
Conclusion: In this study, we understand expression of TIGIT/CD226 axis as appropriate indicator of T-cell dysfunction and tumor specificity. We dictate exact meaning of CD226 loss on $TIGIT^+CD8^+$ TILs as specific subset for optimizing TIGIT-targeting therapies in terms of tumor specificity.

[PP-1075]

Cellular prion protein is closely associated with early recurrence and poor survival in patients with hepatocellular carcinoma

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Objectives: The cellular prion protein (PrP^c) is known to play a role in cancer proliferation and metastasis. However, PrP^c expression was not investigated in hepatocellular carcinoma (HCC).
Materials and Methods: In this study, we investigated whether overexpression of PrP^c influences (or affects) to the recurrence after surgical resection and the survival of HCC patients.
Results: A total of 110 HCC patients who underwent hepatic resection were included in the study. They were followed up for a median of 42 months (range 1–213 months) after hepatectomy. The PrP^c expression levels were determined by the proportion of immunopositive cells. The relationships between PrP^c expression and the HCC histologic features, the recurrence of HCC following surgical resection, and the survival of the patients were examined. Seventy-one cases (64.5%) of the HCCs demonstrated higher expression of PrP^c, although PrP^c expression of the surrounding liver tissues showed only 5 cases. The expression level of PrP^c was only correlated with diabetes mellitus ($P = 0.033$). There was no association between PrP^c expression and age, gender, hypertention, hepatitis B virus positivity, alcohol, Child–Pugh class, major portal vein invasion, the level of alpha fetoprotein, HCC size and number. The 1-year recurrence rates of patients with higher PrP expression was higher than those of lower PrP^c expression ($P = 0.04$). The cumulative survival rates of patients with higher PrP expression was significantly shorter than those of lower PrP^c expression ($P = 0.43$).
Conclusion: In conclusion, our data indicate that PrP^c expression is closely associated with early recurrence and poor survival of HCC patients following surgical resection.

[PP-1077]

Exploiting the sequence data of sodium/bile acid cotransporter encoding gene SLC10A1 involved in Hepatitis B virus infection leading to the pathogenesis of Hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) is most prevalent cancer. The mechanism of pathogenesis of HCC is complex and involve the accumulation of genomic, transcriptomic, and epigenomic alternation at molecular and cellular level. Majority of HCC occurs in cirrhosis associated with the Hepatitis B virus (HBV) infection. sodium/bile acid cotransporter (NTPC) is a cell surface receptor necessary for virus entry and is encoded by gene SLC10A1. NTPC-deficiency reported to provide protection against HBV infection. Objectives: Sequence analysis of SLC10A1gene involved in from various model species to evaluate their evolutionary conservation. In silico studies of SLC10A1 to gain insight to the domain organization and various important motifs present in sequences. Sequence analysis based on homology of genes for NTPC may lead to the effective drug designing.
Materials and Methods: In this study, Sequence and phylogenetic analysis has been performed by using NCBI database and MEGA 6.0 software. Sequence analysis of encoding gene SLC10A1 from various animal species. In silico studies of gene to analyse the domain organization and various important motifs present in sequences using MEME Suite-MEME version 4.11.2
Results: Multiple amino acid sequence alignment SLC10A1 with other animal orthologs by using ClustalW and Jalview software. Phylogenetic dendrogram for NTPC and other homologues was analyzed by using Neighbour-Joining method by MEGA5.22 software using 1000 bootstrap replicates. Distribution of conserved motifs in NTPC with other orthologs.
Conclusion: Sequence analysis based on homology of gene SLC10A1 may lead to the effective drug designing for treatment of HBV infection and associated HCC. Gene of unique protein isolated from diverse organisms are another promising genetic resource for the modification of molecular pathways.

[PP-1080]

Mechanisms and network pharmacological analysis of Yangyin Fuzheng Jiedu prescription in the treatment of hepatocellular carcinoma

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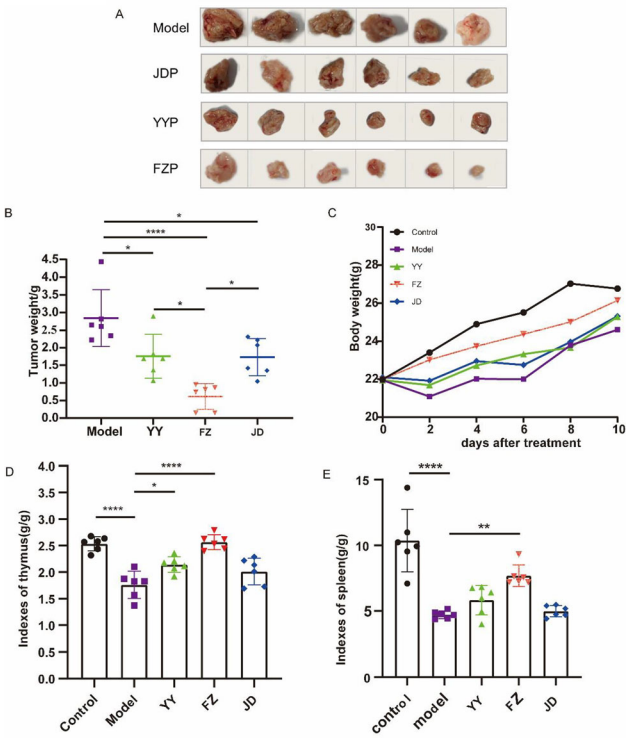
Objectives: Exploring the key drugs of Yangyin Fuzheng Jiedu Prescription(YFJP)to exert theraputic effects against HCC, and further investigate the potential mechanism of the key drugs on HCC by using network pharmacology.
Materials and Methods: Thirty H22 tumor-bearing mice were orally treated with the disassembled prescriptions of YFJP or saline solution for 14 days. The body weights and the appearances of tumors were recorded. The tumor inhibition rate and the immune organ indexes were calculated. The Histologic morphology of tumors were observed by HE staining. Flow cytometry was used to detect the proportion of lymphocytes, T cell subsets, and the expression of PD-1, Tim-3, and TIGIT on $CD8^+$T cells. The production of serum cytokines were detected by Milliplex map mouse highs sensitivity T Cell kit. The putative targets for HCC treatment were screened by target mapping, and putative components were screened by component-target network. Obtained the interactive targets of putative targets from the STRING database to construct the PPI network. GO and KEGG analysis were operated. The inner-network and the component-target-pathway network were constructed and analysed to screen the key targets. Results were verified by molecular docking.
Results: Among the disassembled prescriptions of YFJP, the Fuzheng Prescription(FZP) showed significant antitumor effects. FZP increased the immune organ index and the level of $CD3^+$T cells and $CD8^+$T cells in spleen and peripheral blood. FZP reduce the expression of PD-1, TIM3, and TIGIT. In addition, FZP can reduce the production of IL-4, IL-10, IL-6, and IL-1β. The key targets of FZP in the treatment of HCC were PIK3CA, TP53, MAPK1, MAPK3, and EGFR, the theraputic efftction was based on 26 HCC related signaling pathways. GO enrichment analysis indicated that FZP could inhibit the programmed cell death.
Conclusion: The key disassembled prescription of YFJP is FZP, which can alleviate T cell exhaustion and improve the immunosuppressive microenvironment.



[OP-1085]

TMEM2 promotes the progression of liver cancer

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Objectives: The purpose of this study was to investigate the effects and possible mechanisms relating to TMEM2 in liver cancer.
Materials and Methods: Immunohistochemistry staining, RT-qPCR, immunofluorescence, and western blotting were used to detect the expression of TMEM2 mRNA and protein in HCC cell lines (HepG2、Hep3B、HCCLM3、MHCC97H、MHCC97L), normal liver cell line (L02), and the liver cancer tissue samples, adjacent normal liver tissue samples. The TCGA database (the Cancer Genome Atlas, https://www.cancer.gov/tcga) was used to analyze the expression of TMEM2 in liver cancer and its clinical significance. The signaling pathways related to TMEM2 were screened by KEGG pathway analysis, RT-qPCR was used to detect the expression of the identified key genes to confirm the reliability of KEGG analysis. The effects of TMEM2 on the migrated abilities of liver cancer cells were assessed by wound-healing assay.
Results: We found that TMEM2 was upregulated in five kinds of liver cancer cell lines. There is a correlation between TMEM2 and the malignant degree of liver cancer cell lines. and the same time, the expression of TMEM2 in liver cancer tissues is higher than that in adjacent normal liver tissue. Bioinformatics analysis also found that TMEM2 is significantly overexpressed in multiple malignancies in the TCGA database, such as prostate adenocarcinoma, esophageal carcinoma, and hepatocellular carcinoma. Further analysis has shown that abnormally high expression of TMEM2 in liver cancer is closely related to tumor grade, metastasis status, cancer stage. and high TMEM2 expression is significantly correlated with reduced overall survival of patients with liver cancer. Genes related to the PI3K/AKT signaling pathway, such as SYK, FLT4, AKT3, and FLT1, are biological targets regulated by TMEM2, and this conclusion was verified by RT-qPCR. Wound healing assays revealed that knockdown of TMEM2 inhibits hepatocellular cell migration.
Conclusion: TMEM2 promotes the progression of liver cancer, and its mechanism may be related to the PI3K-AKT signaling pathway.

[OP-1148]

Prediction of hepatocellar carcinoma anti-PD-L1 treatment response by increasing tissue-resident lymphocytes in tumor

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Objectives: Many solid tumors, including HCC, are being studied and chosen for ICB(Immune checkpoint blockade)/IO(Immuno oncology) drugs. HCC, on the other hand, has a low therapeutic response rate, with less than 20% of patients responding to treatment. As a result, in order to identify an approproate therapy, a biomarker that can predict the therapeutic effect in advance muset be developde. Previously, it was reported that the more Tissue Resident memory T cells in other carcinomas, the better the anti-PD-1 treatment effect was. The purpose of this study is to analyze the correlation between anti-tumor effect and TRM % after anti-PD-L1 treatment by applying this to liver cancer.
Materials and Methods: Forming a Sygenic HCC model with Hep55.1c (Murine hepatoma cell line) in C57BL/6 wild-type male mouse and growing the tumor for 3–4 weeks, Isotype control and anti-PD-L1 mAb were administered twice a week (for 1–2 weeks). On the basis of changes in tumor volume, drug reactivity was evaluated. Flow cytometry analysis of CD3, CD103, CD69 and other immune cell phenotypes in mouse tumor and peritumor tissues was done in order to assess the immune cell phenotype by autopsy of the mouse after medication administration for a particular duration.
Results: The TRM percent among total tumor T cells in the anti-PD-L1 responder group was 31.8% greater than 4.05% in the non-responder goup in the subcutaneous HCC mouse model, which was statistically significant.
And the anti-PD-L1 response group was higher than that of the isotype control group (13.6%). ($p = 0.0145$). In the orthotopic HCC model, in peritumor tissue, the isotype, responder, and non-responder groups were 1.65%, 5.98%, and 3.99%, respectively, which were similar without statistical significance, but in Tumor, the responder (9.7%) and non-responder (5.9%) ($P = 0.0372$)) showed a difference in TRM%
Conclusion: Intratumoral tissue resident memory T cells may predict response to anti-PD-L1 immunotherapy in HCC.

[PP-1163]

Design, synthesis, molecular modeling of a new series of 1,2,3-triazole-cored sorafenib analogues and their highly selective cytotoxicity towards HepG2

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Objectives: To design and synthesys new Sorafenib analogues compounds via nucleophilic addition and copper-catalyzed azide-alkyne cycloaddition (CuAAC) in inhibition of hepatocellular carcinoma in in vitro model.
Materials and Methods: The synthetic analogues were treated with hepatocellular carcinoma HepG2, human lung carcinoma A549, Thai human cholangiocarcinoma HuCCA-1, T-cell acute lymphoblastic leukemia MOLT-3, and acute promyelocytic leukemia HL-60.
Results: The synthetic analogues exhibited superior cytotoxicity towards HepG2 over other cancer cell lines including A549, HuCCA-1, MOLT-3, and HL-60. Among the series, 2e and 2 m' exhibited the most potent IC_{50} values towards HepG2(IC_{50} = 5.02 and 5.57 μM), which were comparable to Sorafenib (IC_{50} = 5.97 μM), but less active than Doxorubicin(IC_{50} = 0.59 μM). Interestingly, cytotoxicity test against human embryonal lung fibroblast cell MRC-5 indicated that 2e and 2 m' were significantly less toxic than Sorafenib and Doxorubicin. Therefore, 2e and 2 m' possessed higher selectivity index than Sorafenib, and ca. 3.2 and 3.8-fold superior to that of Doxorubicin, respectively. The triazole linking a substituted benzene with electron withdrawing and bulky alkyl groups appeared to be a suitable structural feature for replacing the phenoxy and picolinamide portion of Sorafenib, since they could maintain good cytotoxicity towards HepG2 with much improved SI values. Molecular docking studies suggested that both 2e and 2 m' interacted with the active sites of B-Raf and VEGFR-2 at the same position of Sorafenib. Cell cycle analysis suggested that 2e and 2 m' likely share similar mechanism of action to Sorafenib. Induction of apoptosis was confirmed in the dose-dependent manner at 48 h on the HepG2 cell lines treated with 2e, 2 m' and Sorafenib. Furthermore, compounds 2e and 2 m' exhibited appropriate drug-likeness analyzed by SwissADME. With its anti-HepG2 activity over other cancer cell lines, selectivity index and druggability.
Conclusion: The triazole-cored analogues 2e and 2 m' were suggested to be promising candidates for development as targeted cancer agents and drugs used in combination therapy for treatment of HCC.

[L-PP-1223]

Two distinct stem cell-like subtypes of hepatocellular carcinoma with clinical significance and their therapeutic potentials

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Objectives: Stem cell-like characteristics have been regarded as a major contributor to poor prognosis of hepatocellular carcinoma (HCC). We aimed to define the stem cell-like characteristics of HCC and uncover their therapeutic implications.
Materials and Methods: Gene expression data from human fetal liver cells and primary HCC tumors (n = 1232) were integrated together to uncover hepatic stem cell subtypes and identify key regulators dictating clinical outcomes.
Results: The hepatic stem cell 1 (HS1) subtype has the strongest stem cell features and is characterized by poor survival; early recurrence; high genomic instability; activation of YAP1, BRD4, and stem cell factor SALL4; and low potential for response to immunotherapy. The hepatic stem cell 2 (HS2) subtype has moderate stem cell features and is characterized by moderate survival, slightly elevated mutation burden, and low potential for response to immunotherapy. We also identified potential serum markers that can stratify patients into the two hepatic stem cell subtypes. Gene network analysis and subsequent experiments demonstrated that the bromodomain and extraterminal domain (BET) family regulates YAP1 expression in the HS1 subtype and that treatment with JQ1, an inhibitor of the BET family, was sufficient to suppress the growth and invasion of HCC cells.
Conclusion: We identified two clinically and biologically distinct HS subtypes, potential biomarkers associated with these subtypes, and a new intervention associated with these subtypes. Our findings may offer the foundation for a biomarker-based clinical study to identify new therapeutic approaches, such as BET inhibitors, to refractory HCC.

[L-OP-1270]

A novel dimethylhydrazine induced pre-clinical liver tumor model

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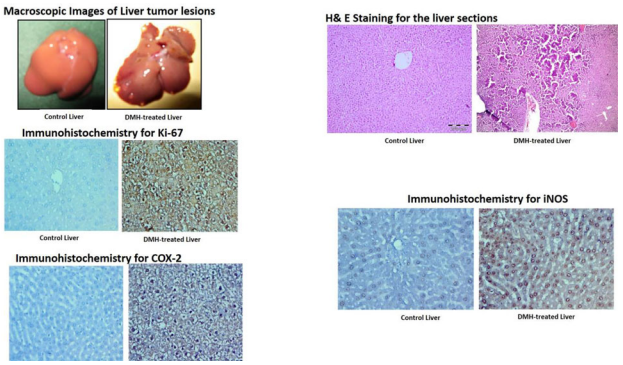
Objectives: Liver cancer is the major health concern globally related with high mortality. Currently used preclinical models of developing liver tumor using both diethylnitrosamine (DEN) as a initiator and 2-acetylaminofluorene (2AAF) as a promoter. But this model has certain limitations as no macroscopic tumor lesion were formed and mortality is high as sometime liver needs to be partially surgically excised to induce hyperproliferation. Therefore, we aim to develop more clinically relevant and simple pre-clinical chemically-induced liver tumor model in Wistar rats.
Materials and Methods: 1,2-dimethylhydrazine was injected intraperitoneally at the dose of 150 mg/kg body weight every week for 3 weeks and after the 19 weeks of latency period, all the rats were sacrificed after 22 weeks. The tumor incidence and multiplicity was investigated. Histology was performed using liver tumors. We have also performed immunohistochemistry for the biomarkers of cell proliferation (Ki-67) and inflammation (COX-2 and iNOS).
Results: The macroscopic tumor lesions were clearly visible on the livers of dimethylhydrazine treated rats. The tumor incidence was about 100% while number of tumors/tumor-bearing rat was 2.2. The histopathological alterations further confirmed that the hepatic lesions were hepato-carcinoma. Furthermore, we found that there was marked increased in immunopositive cells for Ki-67, COX-2 and iNOS as compared to control rats treated with vehicle control only.
Conclusion: This study concludes that dimethylhydrazine induced hepato-carcinoma in Wistar rat model are clinically relevant with very low mortality and have the potential to be use as pre-clinical liver tumor model to study drug testing. Our findings of immunohistochemistry further strengthen the reliability of liver tumor model as biomarkers of cell proliferation and inflammation found to be markedly enhanced in liver tumors.



[L-OP-1325]

Identification of the critical domain in extracellular vesicle-derived nidogen 1 (NID1) contributing to growth, motility and metastasis in hepatocellular carcinoma

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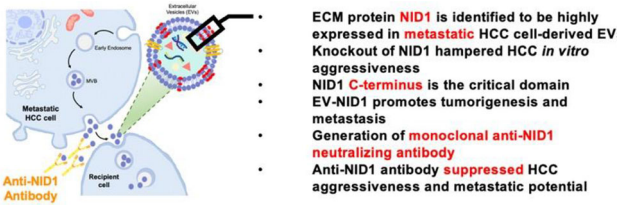
Objectives: Extracellular vesicles (EVs) facilitate favorable pre-metastatic niche and dynamic intercellular communication. Our previous study revealed that nidogen 1 (NID1), an essential sulphated glycoprotein of the basement membrane, was enriched in EVs derived from metastatic HCC cells (Advanced Science 2020). However, the underlying mechanism has not been uncovered. This study aims to (1) elucidate the oncogenic pathway of EV-NID1 in HCC and (2) assess its potential as a therapeutic target.
Materials and Methods: Stable clone of NID1 knockout (KO) was established in metastatic MHCC97L cell line. Different EV-targeting NID1 deletion mutants were then re-expressed in NID1-KO cells. EVs isolated from all control and stable clones were used to treat normal human hepatocyte and non-metastatic HCC cell lines for functional characterization. Custom-made anti-NID1 neutralizing antibody produced by hybridoma technology was evaluated for its therapeutic efficacy.
Results: The purity and integrity of EVs were validated for their EV markers, morphology and size range. Knockout of NID1 significantly hampered the oncogenic effect of EVs in colony formation, motility, and invasiveness of the recipient cells. Functional comparison of EVs isolated from stable clones of EV-targeting full-length and deletion mutants showed that loss of C-terminus domain demoted their oncogenic capacity. Overexpression of C-terminus alone was able to partially rescue EV-NID1 promoting ability. Administration of anti-NID1 antibody were able to neutralize against EVs derived from metastatic cells, NID1 overexpressing stable clone and late-stage patient. Treatment of anti-NID1 antibody significantly inhibited metastasis, growth of orthotopically implanted liver tumor, development of patient-derived xenograft and hepatocarcinogenesis induced by hydrodynamic tail vein injection. Combined treatment using anti-NID1 antibody and sorafenib showed enhanced therapeutic effect than sorafenib alone.
Conclusion: This study identified metastatic HCC cell-derived EV-NID1 as our target candidate, which the C-terminus domain was critical for EV-NID1's oncogenic effect. Custom-made monoclonal anti-NID1 antibody shows promising potential for alternative HCC treatment option.



[L-PP-1348]

Liquid crystalline nanoparticles (LCNPS) based delivery of an anticancer bioactive, methotrexate

Mani Bhargava[1], **Saurabh Bhargava**[2]

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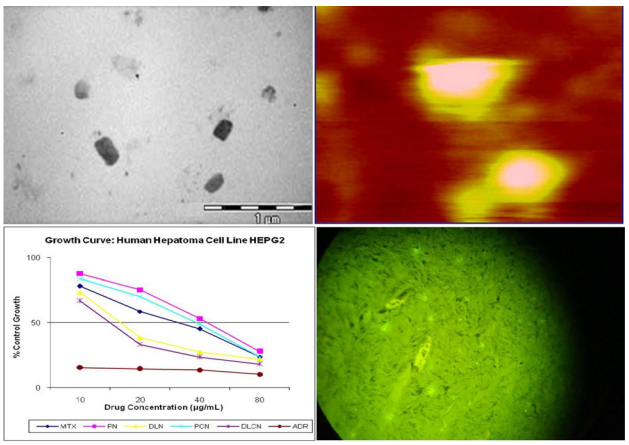
Objectives: Liver cancer is a disease of uncontrolled cell growth, which may invade adjacent tissue and cause infiltration beyond the liver. Most of the potent and effective anticancer drugs used in liver cancer therapy shows poor bioavailability at desired site as well as

toxic in nature. The aim of the study was to investigate mannose modified Liquid Crystalline Nanoparticle (LCNPs) carrier for efficient and site specific delivery of potent anticancer drug (Methotrexate) used in hepatic carcinoma therapy.
Materials and Methods: MTX loaded LCNPs were prepared by lipid cast film method and sonication method. The nanoparticles were characterized in-vitro for their shape, size, percent drug entrapment and stability by Optical Microscopy, Cross Polarized Light Microscpy (CPLM), Transmission Electron Microscopy (TEM), X-ray diffraction (XRD) and Atomic Force Microscopy (AFM).
Results: In-vitro stability studies reveal that LCNPs formulations are stable for 120 days at room temperature. Ex-vivo cell cytotoxicity was performed on Human hepatoma cell line. In-vivo studies included fluorescence microscopy and organ distribution studies which show the Mannose modified LCNPs exhibit better accumulation in liver as compared to unmodified system. The results of the present study indicate, this system is more stable as compared to other system.
Conclusion: Eventually it may be concluded that incorporation of MTX in mannose modified LCNPs increases the residing time of drug in the body by altering of pharmacokinetics and biodistribution pattern, and the drug primarily concentrates in the liver. This system showed excellent cytotoxicity towards cancer cells. From the present investigation it is evident that this system may be used for liver cancer and other liver disease.



Liver Cancer—Clinical

[OP-0021]

Comparative analysis of lenvatinib and hepatic arterial infusion chemotherapy in unresectable hepatocellular carcinoma: A multicenter, propensity score study

Jaejun Lee[1,3], Ji Won Han[1], Pil Soo Sung[1], Soon Kyu Lee[1], Hyun Yang[2], Heechul Nam[4], Sun Hong Yoo[5], Hae Lim Lee[6], Hee Yeon Kim[4], Sung Won Lee[6], Jung Hyun Kwon[5], Jeong Won Jang[3], Chang Wook Kim[4], Soon Woo Nam[5], Jung Suk Oh[7], Ho Jong Chun[7], Si Hyun Bae[2], Jong Young Choi[3], Seung Kew Yoon[3]

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Objectives: To compare the efficacy and safety between lenvatinib and hepatic artery infusion chemotherapy (HAIC) in patients with unresectable hepatocellular carcinoma (HCC).
Materials and Methods: This multicenter historical cohort study enrolled 244 patients with unresectable HCC who were treated with HAIC (n = 173) or lenvatinib (n = 71) between November 2012 and November 2020. Propensity score matching (PSM) was used to adjust for heterogeneity, and 52 patients were selected per group. The overall survival (OS), progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR) were compared between the two groups.
Results: The ORR was not significantly different between the two groups (26.0% vs. 23.1%, P = 0.736). There were no statistical differences in PFS and OS between the two groups after PSM (HAIC vs. lenvatinib, median PFS, 3.6 vs. 4.0 months, P = 0.706; median OS 10.8 vs. 7.9 months, P = 0.106). Multivariate Cox-regression analyses showed that alpha-fetoprotein $\leq$ 1000 ng/mL was only associated factor for the OS after PSM in all patients (hazard ratio = 0.421, P = 0.011). Subgroup analysis for patients with high tumor burden beyond the REFLECT eligibility criteria revealed that the HAIC group (n = 29) had a significantly longer OS than did the lenvatinib group (n = 30) (10.0 vs. 5.4 months, P = 0.004). More patients in the HAIC group achieved better liver function than those in the lenvatinib group at the time of best responses.
Conclusion: Lenvatinib is comparable to HAIC in terms of ORR and OS in unresectable HCC meeting REFLECT eligibility criteria.

[PP-0046]

Serum albumin levels association with aggressiveness of hepatocellular carcinoma

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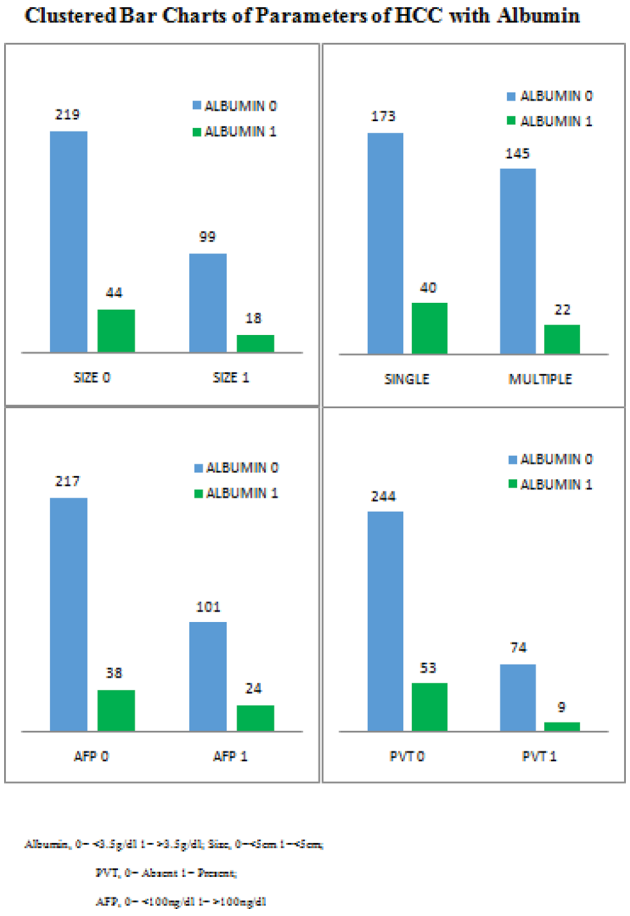
Objectives: Hepatocellular carcinoma (HCC) is the major cause of morbidity and mortality in patients with chronic liver disease. Studies have shown a correlation of low serum albumin levels with the aggressiveness of HCC and a direct effect of albumin on tumor cell suppression. The aim of the study is to determine the distribution of serum albumin and tumor parameters and to identify if any correlation exists between them.
Materials and Methods: This is a retrospective cross-sectional review with data collected at a single tertiary care center at Section of Gastroenterology, Department of Medicine, Aga Khan University Hospital Karachi, Pakistan. The association of serum albumin levels with all the parameters analyzed using chi-square test.
Results: Data from 380 patients in which majority of the patients were male, mean age of the patients is 58.8 years. Hypoalbuminemia makes approximately 83.7% of our cohort and mean serum albumin levels are of 2.79 g/dl. The distribution of the parameters is as such that mainly the tumors are smaller, solitary, with low AFP levels, portal vein thrombosis is seen in 21.8%. There is insignificant relationship at 5% significance level between serum albumin and AFP ($x^2 = 1.135$, df = 1, p = 0.287), PVT ($x^2 = 2.329$,df = 1, p = 0.127), size of tumor ($x^2 = 0.107$, df = 1, p = 0.743) and number ($x^2 = 2.154$, df = 1, p = 0.142).
Conclusion: We found no significant association between low serum albumin levels and other tumor parameters of HCC. It is crucial to consider other causes of hypoalbuminemia before using it as a

parameter of severity of the disease and to identify a severity marker in our population.



[OP-0076]

Impact of tumor size on outcome of hepatectomy for hepatocellular carcinoma: A nationwide propensity score adjusted analysis

Suk Kyun Hong[1], Kwang-Woong Lee[1], Sola Lee[1], Su Young Hong[1], Sanggyun Suh[1], Eui Soo Han[1], Youngrok Choi[1], Nam-Joon Yi[1], Kyung-Suk Suh[1]

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Objectives: Surgical outcomes of large hepatocellular carcinoma (HCC) have not yet been fully evaluated. The aim of this study was to compare the surgical outcomes after liver resection for HCC according to tumor using a large, nationwide cancer registry-based cohort and propensity score matching.
Materials and Methods: From 2008 to 2015, a total of 12,139 patients were diagnosed with liver cancer and registered in the Korean Primary Liver Cancer Registry (KPLCR). Of those, patients who underwent hepatectomy as primary treatment without distant metastasis were selected. We performed 1:1 propensity score matching between the small group (< 5 cm) vs. medium group (≥ 5 cm and < 10 cm) and medium group vs. large group (≥ 10 cm) each.
Results: Overall, 265 patients each in the small group and medium group were compared while 64 patients each in the medium group and the large group were compared. The proportion of microvascular invasion was higher in the medium group compared to the small group ($P < 0.001$) and higher in the large group compared to the medium group ($P = 0.023$). Overall survival rate and progression-free survival rate was lower in the medium group compared to the small group ($P < 0.001$ and $P < 0.001$). There was a tendency of poorer overall survival in the large group compared to the medium group ($P = 0.051$). Progression-free survival rate was significantly lower in the large group compared to the medium group ($P = 0.002$).
Conclusion: Although primary liver resection can be considered even in large HCC patients, greater caution with careful screening for recurrence is needed.

[OP-0102]

Effects of surgical resection versus radiofrequency ablation on clinical outcomes in very early stage hepatocellular carcinoma: A propensity score matching analysis

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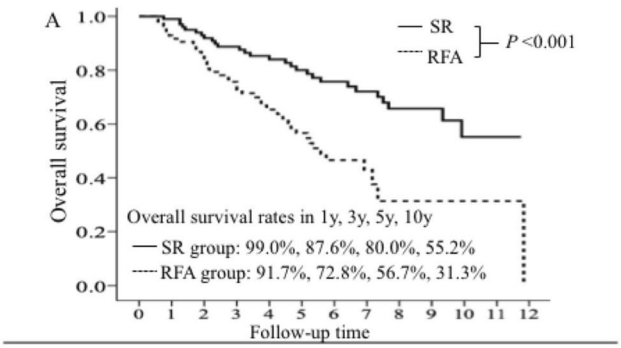
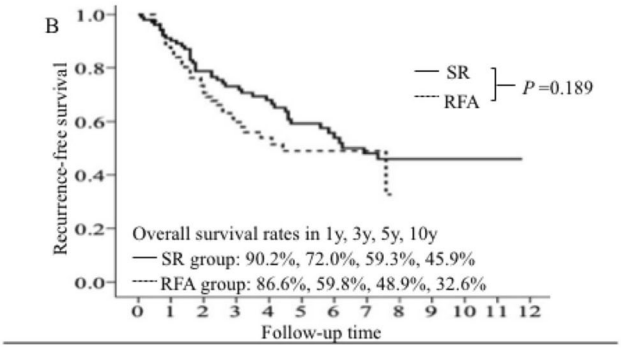
Objectives: The detection rate of Barcelona Clinic Liver Cancer (BCLC) very-early-stage hepatocellular carcinoma (HCC) is increasing. The differences in clinical outcomes between patients treated with Surgical resection (SR) and radiofrequency ablation (RFA) remain unclear. This study investigated the prognosis of SR and RFA for very-early?stage HCC patients with long?term follow?up.
Materials and Methods: This study collected overall survival (OS) and disease-free survival (DFS) of 188 very-early-stage HCC patients (≤ 2 cm single HCC).
Results: Of the 188 HCC patients, 103 received SR and 85 received RFA. The median follow?up time was 56 months. The SR group had significantly higher OS than the RFA group (10-year cumulative OS: 55.2% and 31.3% in the SR and RFA groups, respectively). After PSM, the OS in the SR group remained significantly higher than that in the RFA group (10-year cumulative OS: 54.7% and 42.2% in the SR and RFA groups, respectively). No significant difference was observed in DFS between the SR and RFA groups before and after PSM. Furthermore, in the multivariate Cox regression analysis, treatment type (hazard ratio (HR): 0.54, 95% confidence interval (CI): 0.31–0.95; $P = 0.032$) and total bilirubin (HR: 1.92; 95% CI: 1.09–3.41; $P = 0.025$) were highly associated with OS. In addition, age (HR: 2.14, 95% CI: 1.36–3.36; $P = 0.001$) and cirrhosis (HR: 1.79; 95% CI: 1.11–2.89; $P = 0.018$) were strongly associated with DFS.
Conclusion: For patients with very-early-stage HCC, SR was associated with significantly higher OS rates than RFA. However, no significant difference was observed in DFS between the SR and RFA groups.



Patients at risk	Year of follow-up												
	0	1	2	3	4	5	6	7	8	9	10	11	12
SR	103	99	88	77	66	58	45	36	28	16	9	5	0
RFA	85	77	67	53	41	31	15	8	2	1	0	0	0



Patients at risk	Year of follow-up												
	0	1	2	3	4	5	6	7	8	9	10	11	12
SR	103	89	73	60	48	38	29	23	18	8	5	3	0
RFA	85	68	49	33	22	17	9	4	0	0	0	0	0

[PP-0108]

Application of molecular barcode sequencing for detection of low-frequency variants in circulating tumor DNA in HCC

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Objectives: Liquid biopsy has emerged as a promising tool for detecting various malignancies, with minimal invasiveness and good accuracy. We sought to establish molecular barcode sequencing to circulating tumor DNA (ctDNA) in patients with hepatocellular carcinoma (HCC).
Materials and Methods: Patients with HCC or benign liver disease were enrolled between 2017 and 2018. Matched tissue and serum samples were obtained from patients. Plasma cell-free DNA was extracted and subjected to targeted sequencing with ultra-high coverage and molecular barcoding.
Results: The study included 102 patients with HCC, 7 with benign liver tumors, and 34 with chronic liver disease. No tier 1/2 or oncogenic mutations were detected in patients with benign liver disease. Among patients with HCC, 49 (48%) had tier 1/2 mutations in at least one gene, with detection rates being higher in advanced-stage (75%) compared with early-stages (26–33%) disease. TERT was the most frequently mutated gene (30%), followed by TP53 (16%), CTNNB1 (14%), ARID2 (5%), ARID1A (4%), NFE2L2 (4%), AXIN1 (3%), and KRAS (1%). Survival among patients with TP53 mutations was significantly poorer (p = 0.007) compared with survival among patients without such mutations, whereas CTNNB1 and TERT mutations did not affect survival. CtDNA testing combined with analyses of α-fetoprotein and PIVKA-II improved diagnostic detection of HCCs, even at an early stage.
Conclusion: We confirmed that ctDNA detection applied using molecular barcoding technology offers dynamic, personalized information on tumor biology suitable for guiding clinical diagnosis and management. It may also have potential use as a minimally invasive approach for prognostic stratification.

[PP-0121]

Safety and efficacy of liver-directed radiotherapy in combination with lenvatinib for hepatocelluar carcinoma with macroscopic tumor thrombosis

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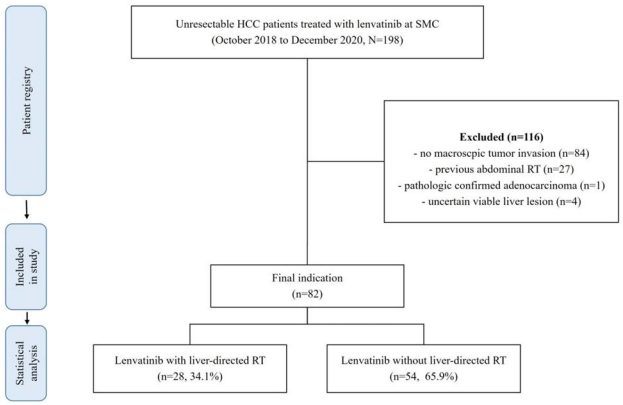
Objectives: This study aimed to compare the clinical outcomes in hepatocellular carcinoma (HCC) patients with macroscopic tumor thrombosis who were treated with lenvatinib with or without concomitant liver-directed radiotherapy (LRT).
Materials and Methods: From the institutional registry, we enrolled 82 patients diagnosed with HCC involving macroscopic tumor thrombosis, and treated with lenvatinib monotherapy (non-LRT group, n = 54, 65.9%) or lenvatinib in combination with LRT (LRT group, n = 28, 34.1%). The patients were classified as combination treatment group, if LRT was performed within 8 weeks of lenvatinib initiation. A detailed flow diagram of this study is provided in Supplementary Fig. 1.
Results: During the median follow-up period of 5.4 months (range 1.4 to 17.5), there was no significant difference between the two groups in terms of overall adverse events. Although there was no statistical difference between the two groups in terms of overall response rate (32.1% vs 20.4%, P = 0.15), a significantly higher treatment response was observed in the LRT group in terms of intrahepatic tumor response (67.9% vs 20.4%, P < 0.001). In the LRT group compared to the non-LRT group, there was no significant difference in terms of overall survival (60.4% in LRT group versus 36.9% in non-LRT group at 12-month, P = 0.22). Progression-free survival (64.3% in LRT group versus 34.8% in non-LRT group at 6-month, P < 0.05) and intrahepatic progression-free survival (69.9% in LRT group versus 41.0% in non-LRT group at 6-month, P = 0.007), however, were significantly superior in the LRT group.
Conclusion: The combination of lenvatinib and LRT is relatively safe and effective in HCC patients with macroscopic tumor thrombosis.



[PP-0128]

Significance of inflammatory markers in recurrence of early-stage hepatocellular carcinoma

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Objectives: Inflammatory response is known to play critical roles in various cancer developments. In hepatocellular carcinoma (HCC), there has been increase in interest to use inflammatory markers to predict patient outcomes. In this study, we evaluated the significance of inflammatory markers in recurrence of early-stage HCC after curative therapy.
Materials and Methods: This study was performed retrospectively using the prospectively collected registry data of newly diagnosed, previously untreated HCC between 2005 and 2017 at Samsung Medical Center. Inclusion criteria was patients with initial Barcelona Clinic Liver Cancer stage 0 or A, who underwent curative therapy. Recurrences were evaluated based on imaging studies during follow-up, and first intrahepatic recurrence after initial therapy was counted. Early and late recurrence was categorized based on time to recurrence, within 2 years from treatment and after. Inflammatory markers, along with patient and tumor factors, were analyzed to find factors correlated with early or late recurrence.
Results: Out of 9132 patients in registry data, 5554 patients were with BCLC stage 0 or A, and 4076 patients received curative therapy. Among them, 2142 (52.6%) patients experienced recurrence, with median 1.6 years from initial therapy (range, 0.1 – 13.4 years). Early recurrence was observed in 1247 (30.6%) patients and late recurrence was observed in 895 (22.0%) patients. Statistical analysis showed that initial platelet count and worsening of platelet-lymphocyte ratio (PLR) after treatment was correlated with early recurrence, and initial platelet count and initial PLR was correlated with late recurrence. Significance of inflammatory markers were consistent in multivariable analysis, independent from previously well-known patient and tumor factors.
Conclusion: Intrahepatic recurrence was observed in more than half of patients, even after curative treatment for early-stage HCC. Systemic inflammatory markers were expected to provide additional useful information in predicting intrahepatic recurrence.

[PP-0129]

Role of AFP and PIVKA-II as markers for monitoring response and recurrence after resection for HCC

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Objectives: Liver resection is the treatment of choice for most cases of early stage hepatocellular carcinoma (HCC). However, the recurrence rates of HCC remains high even after curative hepatectomy. The unresolved clinical issue is how to monitor HCC after curative surgical resection. In this study, we analyzed the association between changes in AFP and PIVKA-II with the recurrence of HCC after curative hepatectomy.
Materials and Methods: A total of seventy nine HCC patients who underwent curative hepatectomy were analyzed. The recurrence rates and postoperative survival rates were compared according to the tumor characteristics and preoperative and postoperative tumor marker values.
Results: During the median follow-up periods of 24.2 months (2.3–96.5 months), HCC recurrence developed in 32 of 79 patients (40.5%). The median time to the development of recurrence was 6 months. In the HCC recurrence group, the median AFP were 105, 7.45, 6.1, 16 and 5.25 ng/ml at pre-op, 1 month, 3 months, 6 months and 12 months after hepatectomy, respectively, compared with the non-recurrence group of 6.1, 4.4, 3.25, 2.9 and 3 ng/ml. The median PIVKA-II were 168, 19.5, 21, 27.5 and 27 mAU/ml in the recurrence group compared with the non-recurrence group of 26, 19, 16.5, 17, 15.5, respectively. In multivariate analysis for predictive markers of HCC recurrence, tumor size > 4 cm, preoperative AFP > 20 ng/ml, 1 month postoperative AFP > 20 ng/ml, and 1 month postoperative PIVKA-II > 40 mAU/ml were identified as significant factors ($p = 0.036$, $p = 0.047$, $p < 0.001$, and $p < 0.001$ respectively).
Conclusion: These results suggest that AFP or PIVKA-II values that exceed their normal range when measured at one month after hepatectomy may be predictive of HCC recurrence. The patients with these risk factors should be cautiously followed up at short-term intervals after curative hepatectomy.

[OP-0132]

Comprehensive immunological analysis of T cell cytokines as markers of hepatitis B virus reactivation in patients with hepatocellular carcinoma

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Objectives: The T cell mediated immunity has a crucial role in hepatitis B virus (HBV) reactivation but its underlying mechanism has not been clarified thus far. We aimed to evaluate the association between the various T cell cytokines, regulatory T cells (Treg) and HBV reactivation in patients with hepatocellular carcinoma (HCC).
Materials and Methods: A total of 252 consecutive patients who were diagnosed with HCC at Incheon St Mary's hospital between 2011 and 2012 were enrolled. Of these patients, 50 patients with HBV related HCC who did not receive antiviral therapy were analyzed. We have serially checked 13 serum T cell cytokines (IL-1β, -2, -4, -5, -6, -9, -10, -L-12p7, -13, -17A, -22, IFN-γ, TNF-α) and markers of Treg (CD4, CD25, FOXP3) at baseline, 3 and 7 days after the first cycle of TACE and before the second TACE. The association between each markers and time to HBV reactivation were investigated.
Results: Overall, 62% of the patients experienced an episode of HBV reactivation during the median follow-up period of 23.9 months. Reactivation-associated hepatitis developed in 14% of the patients and severe hepatitis in 10%. In univariate analysis, baseline TNF-α, HBV DNA and IL-6 before the second TACE were associated with HBV reactivation. Multivariate analysis showed that low baseline TNF-α (P = 0.037) and high IL-6 before the second TACE (P = 0.019) were the independent factors associated with HBV reactivation. Also, a 39.4–948.9 fold-increase in the IL-6 was observed in 4 out of 5 HBV reactivation cases that developed within 4.3 months, whereas no difference was observed except for one case in the non-reactivation group.
Conclusion: Our study demonstrated the dynamic change in T-cell mediated immunity that causes HBV reactivation during HCC therapy. Low baseline Th1 cytokine TNF-α is associated with HBV reactivation, and on-treatment IL-6 may be used as a surrogate marker of HBV reactivation.

[OP-0137]

Clinical features of recurrence after hepatic resection for early-stage hepatocellular carcinoma and long-term survival outcomes of patients with recurrence a multi-institutional analysis

Tian Yang[1], Lanqing Yao[1], Hai-Bo Qiu[1], Jia-Le Pu[2], Yong-Kang Diao[3], Chao Li[1], Ting-Hao Chen[4], Jian-Hong Zhong[5], Wei-Min Gu[6], Ya-Hao Zhou[7], Wan-Guang Zhang[8], Hong Wang[9], Yong-Yi Zeng[10], Han Wu[1], Ming-Da Wang[1], Xin-Fei Xu[1], Timothy M. Pawlik[11], Wan Yee Lau[12], Feng Shen[1]

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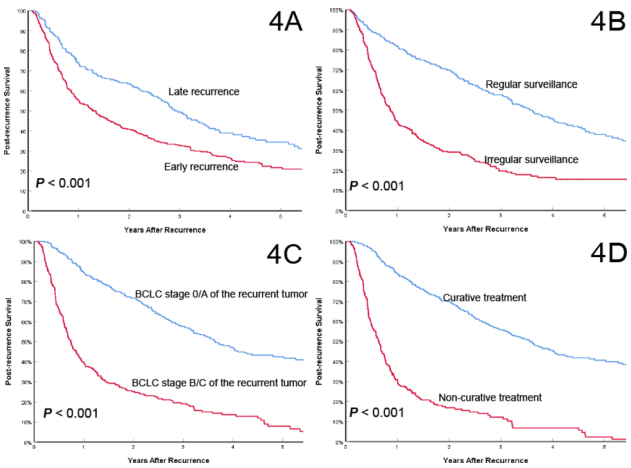
Objectives: A potentially curative hepatic resection is the optimal treatment for hepatocellular carcinoma (HCC), but most HCCs, even at an early stage, eventually recur after resection. To investigate clinical features of initial recurrence and long-term prognosis of patients after recurrence.
Materials and Methods: From a multicenter database, patients with early-stage HCC (Barcelona Clinic Liver Cancer [BCLC] stage 0/A) were retracted. Time to initial recurrence, patterns of recurrence, and treatment modalities for recurrent tumors were investigated. Univariable and multivariable analysis were used to identify independent risks associated with postoperative recurrence, as well as post-recurrence survival (PRS).
Results: Among 1,424 patients, 679 (47.7%) developed recurrence at a median follow-up of 52.9 months, including 412 (60.7%) early recurrence (≤ 2 years after surgery) and 271 (31.3%) late recurrence (> 2 years). Independent risks of postoperative recurrence included cirrhosis, preoperative alpha-fetoprotein level > 400ug/L, tumor size > 5 cm, multiple tumors, satellites, microvascular invasion, and intraoperative blood transfusion. The most common pattern for initial recurrence were intrahepatic only (87.3%), while the median PRS of patients with recurrence was 22.4 months. Multivariable analysis revealed that receiving irregular recurrence surveillance, beyond Milan criteria of the initial tumor, early recurrence, BCLC stage B/C of the recurrent tumor, and non-curative treatments were independently associated with poorer PRS.
Conclusion: Nearly half of patients with early-stage HCC experienced recurrence after resection. Understanding recurrence risks may help identify patients at high risk of recurrence who may benefit from future adjuvant therapies. Meaningful survival even after recurrence can still be achieved by postoperative regular surveillance and curative treatment.



[OP-0138]

Short-term and long-term outcomes of hepatectomy with and without concurrent splenectomy and esophagogastric devascularization among patients with hepatocellular carcinoma and clinical significantly P

Tian Yang[1,8], Zheng-Liang Chen[2], Lan-Qing Yao[1], Jia-Le Pu[3], Han Wu[1], Xin-Fei Xu[1], Ting-Hao Chen[4], Ya-Hao Zhou[5], Hong Wang[6], Zhi-Yu Chen[7], Li-Yang Sun[8], Yong-Kang Diao[8], Jian-Hong Zhong[9], Wan Yee Lau[1,10], Timothy M Pawlik[11], Dong-Sheng Huang[8,12], Feng Shen[1], Ying-Jian Liang[2]

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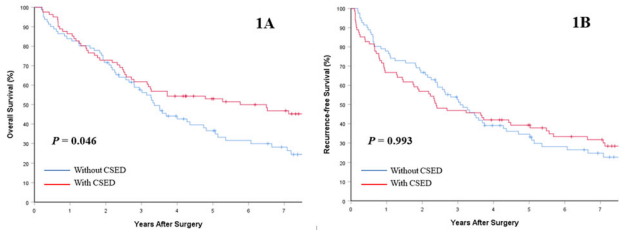
Objectives: Portal hypertension due to cirrhosis is common among patients with hepatocellular carcinoma (HCC). This study aimed to evaluate short-term and long-term outcomes of hepatectomy with or without concurrent splenectomy and esophagogastric devascularization (CSED) among patients with HCC and clinical significantly portal hypertension (CSPH).
Materials and Methods: A Chinese multicenter database of patients undergoing curative-intent hepatectomy for HCC identified those patients with CSPH (defined as having hypersplenism and intermediate/high-risk esophagogastric varices). Postoperative 30-day morbidity and mortality, and long-term overall survival (OS) and recurrence-free survival (RFS) were compared between patients undergoing hepatectomy with and without CSED before and after propensity score matching (PSM).
Results: Among the 358 enrolled patients, 86 patients underwent CSED. In the entire cohort, the postoperative 30-day morbidity and mortality rates were comparable between the CSED and non-CSED groups(43.0% vs. 42.3%, and 4.7% vs. 2.6%, both $P > 0.05$). Using PSM, 81 pairs of patients with and without CSED were created. In the PSM cohort, the 5-year OS rate of the CSED group were better than the non-CSED group(52.9% vs. 36.5%, $P = 0.046$), while their 5-year RFS rates were comparable (39.3% vs. 34.6%, $P = 0.993$). Meanwhile, the CSED group had a lower rate of postoperative variceal bleeding than the non-CSED group(7.4% vs. 21.7%, $P = 0.014$). After adjustment for other confounding factors on multivariable analysis, CSED was significantly associated with better OS(HR: 0.39, 95% CI: 0.26–0.60, $P < 0.001$).
Conclusion: Hepatectomy and CSED can safely be performed in selected patients with HCC and CSPH, which could improve long-term outcomes, including preventing variceal bleeding and prolonging postoperative survival.

FIGURE 1. Cumulative incidence of overall survival (1A) and recurrence-free survival (1B) curves comparisons between patients with and without concurrent splenectomy and esophagogastric devascularization (CSED) after hepatectomy for hepatocellular carcinoma in the propensity score matching (PSM) cohort.



[OP-0139]

Long-term oncologic prognosis after R0 liver resection for hepatocellular carcinoma: A propensity score matching study to compare the young (≤ 35 Years Old) with the elderly (≥ 70 Years Old)

Tian Yang[1], Jia-Le Pu[2], Zhong Chen[2], Lan-Qing Yao[1], Ji-Ye Feng[3], Yong-Kang Diao[4], Ming-Cheng Guan[5], Ju-Dong Li[6], Zheng-Liang Chen[7], Ya-Hao Zhou[8], Hong Wang[9], Wei-Min Gu[10], Jie Li[11], Chao Li[1], Ming-Da Wang[1], Hong Zhu[5], Ying-Jian Liang[7], Feng Shen[1], Timothy M. Pawlik[12], Wan Yee Lau[13]

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Objectives: While hepatocellular carcinoma (HCC) is the most common malignancy in the elderly worldwide, it is also common among younger individuals in areas with endemic hepatitis B virus infection. We sought to characterize differences in long-term oncological prognosis among young versus elderly patients after R0 liver resection for HCC.
Materials and Methods: Using a Chinese multicenter database, consecutive patients who underwent R0 liver resection for HCC between 2007 and 2019 were retrospectively analyzed. After excluding middle-aged (36 ~ 69 years old) patients, overall survival (OS), cancer-specific survival (CSS), and time-to-recurrence (TTR) were compared between young (≤ 35 years old) versus elderly (≥ 70 years old) patients using propensity score matching (PSM).
Results: Among 531 enrolled patients, 192 (36.2%) and 339 (63.8%) patients categorized as young versus elderly, respectively. PSM analysis created 140 pairs of matched patients. In the PSM cohort, 5-year OS was comparable among young versus elderly patients

(51.7%vs.52.3%, P = 0.533). Young patients did, however, have a higher 5-year TTR (62.1% vs. 51.6%, P = 0.011) and a worse 5-year CSS (54.0%vs.64.3%, P = 0.034) than elderly patients. On multivariable Cox-regression analyses, young patient age remained independently associated with an increased TTR (HR 1.62, P = 0.016) and decreased CSS (HR 1.69, P = 0.021) compared with elderly patients.

Conclusion: Following R0 liver resection for HCC, younger patients were at a higher risk of recurrence, yet elderly patients had a better CSS rate. While partial hepatectomy for HCC should be considered for both young and elderly patients if technically feasible, consideration should be given to enhanced surveillance for HCC among young patients following resection.

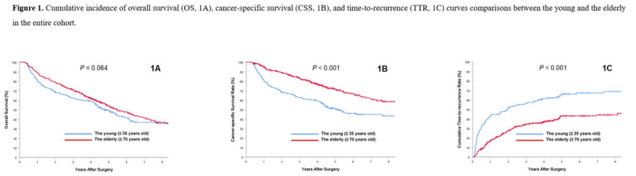

Figure 1. Cumulative incidence of overall survival (OS, 1A), cancer-specific survival (CSS, 1B), and time-to-recurrence (TTR, 1C) curves comparisons between the young and the elderly in the entire cohort.

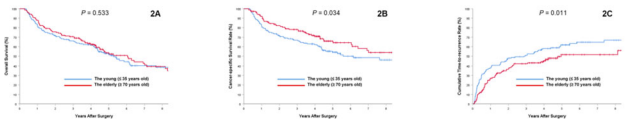

Figure 2. Cumulative incidence of overall survival (OS, 2A), cancer-specific survival (CSS, 2B), and time-to-recurrence (TTR, 2C) curves comparisons between the young and the elderly in the propensity score matching cohort.

[PP-0152]

Prognostic role of CA 19–9 in patients with hepatocellular carcinoma

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Objectives: Serum carbohydrate antigen 19–9 (CA 19–9) is a commonly used tumor marker for pancreatic and biliary cancer. However, it was recently suggested that CA 19–9 level could be elevated in hepatocellular carcinoma (HCC) patients with aggressive phenotype or stemness features. This study aimed to evaluate the significance and prognostic role of serum CA 19–9 in patients diagnosed with HCC.

Materials and Methods: This study enrolled 534 consecutive patients newly diagnosed with HCC and with serum CA 19–9 values at baseline between 2008 and 2017. Patients with combined hepatocellular-cholangiocarcinoma and other malignancies at baseline were excluded.

Results: During a median follow-up of 27.5 months (range 0.1–141.1), 178 patients (33.6%) survived and 180 (34.0%) expired. Baseline CA 19–9 level was within normal range in 410 patients (77.5%) and elevated (CA 19–9 > 37 U/mL) in 119 (22.5%). Patients with elevated CA 19–9 had a larger tumor size, a higher proportion of multiple tumors and portal vein tumor thrombosis than patients with normal CA 19–9 (all P values were < 0.05), and therefore presented with more advanced tumor characteristics. The cumulative overall survival (OS) in patients with elevated CA 19–9 was significantly lower than that in patients with normal CA 19–9 (P < 0.001). In the multivariate analysis, elevated CA 19–9 was an independent prognostic factor for OS (HR, 1.52; 95% CI, 1.06–2.16; P = 0.021). Subgroup analysis revealed that elevated CA 19–9 was associated with poor prognosis across all BCLC stages. The validity of CA 19–9 increased particularly in patients with CTP class A or AFP > 100 ng/ml.

Conclusion: Elevated CA 19–9 level is significantly associated with poor prognosis and advanced tumor characteristics in HCC patients. The CA 19–9 test is a simple adjuvant method that can be performed to predict the prognosis of HCC patients.

[OP-0164]

Liver resection for a solitary huge hepatocellular carcinoma (≥ 10 cm): A large-scale multicenter observational study

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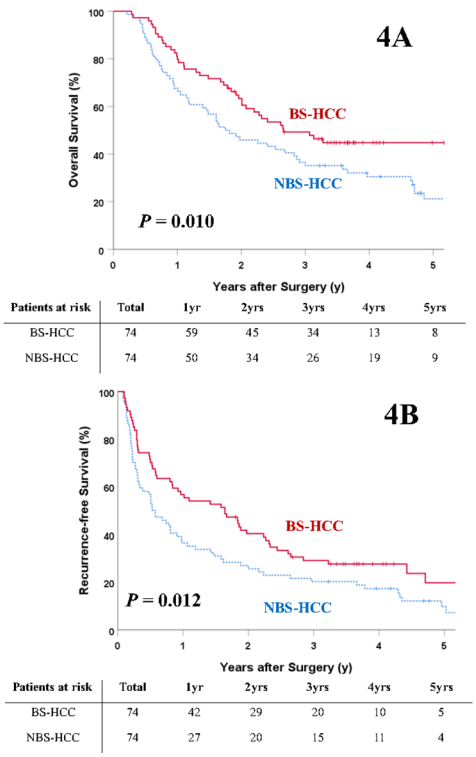
Objectives: Solitary hepatocellular carcinoma (HCC) without macrovascular invasion and distant metastasis, regardless of tumor size, is currently classified as early-stage disease by the latest Barcelona Clinic Liver Cancer (BCLC) staging system. While the preferred treatment is surgical resection, the association of tumor shape with long-term survival outcomes after liver resection for a solitary huge HCC of ≥ 10 cm has not been defined.

Materials and Methods: Patients who underwent curative liver resection for a solitary huge HCC were identified from a multicenter database. Preoperative imaging findings were used to define spherical- or ellipsoidal-shaped lesions with smooth edges as balloon-

shaped HCCs (BS-HCCs); out-of-shape lesions or lesions of any shape with matt edges were defined as non-balloon-shaped HCCs (NBS-HCCs). The two groups of patients with BS-HCCs and NBS-HCCs were matched in a 1:1 ratio using propensity score matching (PSM). Clinicopathologic characteristics, long-term overall survival (OS) and recurrence-free survival (RFS) were assessed.
Results: Among patients with a solitary huge HCC, 74 pairs of patients with BS-HCC and NBS-HCC were matched. Tumor pathological features including proportions of microvascular invasion, satellite nodules, and incomplete tumor encapsulation in the BS-HCC group were lower than the NBS-HCC group. At a median follow-up of 50.7 months, median OS and RFS of all patients with a solitary huge HCC after PSM were 27.8 and 10.1 months, respectively. The BS-HCC group had better median OS and RFS than the NBS-HCC group (31.9 vs. 21.0 months, P = 0.01; and 19.7vs.6.4 months, P = 0.015). Multivariate analyses identified BS-HCC as independently associated with better OS (HR 0.637, P = 0.026) and RFS (HR 0.657, P = 0.025).
Conclusion: For a solitary huge HCC, preoperative imaging tumor shape was associated with prognosis following resection. In particular, patients with BS-HCCs had better long-term survival following liver resection versus patients with large NBS-HCCs.

Figure 4. Comparison curves of overall survival (OS, **4A**) and recurrence-free survival (RFS, **4B**) after liver resection for a solitary huge HCC between patients with balloon-shaped hepatocellular carcinoma (BS-HCC) and non-balloon-shaped hepatocellular carcinoma (NBS-HCC).



Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
BS-HCC	74	59	45	34	13	8
NBS-HCC	74	50	34	26	19	9

Patients at risk	Total	1yr	2yrs	3yrs	4yrs	5yrs
BS-HCC	74	42	29	20	10	5
NBS-HCC	74	27	20	15	11	4

[PP-0165]

Whole blood viscosity is associated with extrahepatic metastases and survival in patients with hepatocellular carcinoma

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Objectives: Whole blood viscosity (WBV) is increased in cancer patients and associated with the advanced stage with systemic metastases. However, relevance of WBV in hepatocellular carcinoma (HCC) remains unclear.
Materials and Methods: This pilot study included a discovery cohort of 148 treatment-naïve HCC patients with preserved liver function, and a validation cohort of 33 treatment-experienced HCC patients with nivolumab. Systolic and diastolic WBV was measured using an automated scanning capillary tube viscometer at diagnosis or before the nivolumab treatment.
Results: Extrahepatic metastases were observed in 15 treatment-naïve patients (11.3%) at diagnosis. Portal vein tumor thrombosis (PVTT), tumor size, number of tumors, and systolic/diastolic WBV were factors associated with extrahepatic metastases. Systolic WBV and diastolic WBV were significantly increased in patients with metastases compared with patients without metastases. Multivariate logistic regression showed that high diastolic WBV > 16 cP was an independent factor associated with metastases. Notably, patients who developed extrahepatic metastases during the observation period among patients without metastases at diagnosis had higher diastolic WBV initially. Patients with high diastolic WBV had poor survival, and multivariate Cox regression analyses showed high diastolic WBV was an independent risk factor for poor survival with the Child–Pugh B7 and PVTT. High diastolic WBV also predicted poor survival in patients with low alpha-fetoprotein (AFP) and proteins induced by vitamin K antagonist-II (PIVKA-II) levels. In 33 nivolumab-treated patients, high diastolic WBV before the treatment was also tended to be associated with overall and progression-free survival.
Conclusion: Our study is the first in which high WBV is associated with the distant metastases and survival in patients with HCC, but future prospective, large cohort studies are necessary to validate the results.

[PP-0172]

Korean validation and comparison of prognostic scores for transarterial chemoembolization: ART, ABCR, HAP, and modified HAP

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Objectives: Transarterial chemoembolization(TACE) is one of the treatment options for unresectable hepatocellular carcinoma(HCC). There are four prognostic scores for TACE: ART, ABCR, HAP, and modified HAP(mHAP). However, there is a lack of validation of these scores, especially in Korea. The aim of this study is to validate and compare these scores.
Materials and Methods: From October 2008 to February 2014, a total of 1211 patients with HCC were treated with TACE in Seoul Saint Mary's Hospital. Among them, 800 patients underwent at least two sessions of TACE within 90 days. 549 patients were excluded according to exclusion and inclusion criteria. Finally, a total of 251

patients were analyzed. The validation in ART, ABCR, HAP, and mHAP scores was performed and these scores were compared using the AUROC curve.
Results: Mean age was 59.2, median follow up period was 24.2 months and median cycles of TACE was four. From these scores, OS of each group was calculated: ART(63.7, 37.7 months in 0–1.5, $\geq$ 2, P = 0.142), ABCR(57.6, 18.1, 7.9 months in $\leq$ 0, 1–3, $\geq$ 4, P < 0.001), HAP(60.2, 52.2, 20.8, 10.8 months in 0, 1, 2, > 2, P < 0.001), mHAP(58.7, 48.7, 16.6, 7.9 in 0, 1, 2, > 2, P < 0.001). and the AUROC of survival was calculated(0.508, 0.709, 0.662, 0.657 in 1 year and 0.498, 0.679, 0.654, 0.650 in 2 years, in ART, ABCR, HAP, mHAP, respectively).
Conclusion: In this study, ABCR, HAP, and mHAP were well applicable for the prediction of the prognosis of TACE. However, ART was not applicable. According to the comparison of these scores, ABCR was the best predictable prognostic score for TACE.

[OP-0182]

Efficacy of treatment to subclassification of intermediate-stage hepatocellular carcinoma patients using KINKI criteria

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Objectives: To determine the efficacy of treatment to substage B hepatocellular carcinoma (HCC) patient on Kinki criteria.
Materials and Methods: This was a prospective study on 71 naive HCC patients. Patients would be treated with one of the following methods: transarterial chemoembolization (DEB-TACE), Radio Frequency Ablation (RFA), or liver resection. The treatment response and laboratory outcomes were assessed within the first month after therapy according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) on a CT scan.
Results: The mean age of the patients was 60.6 $\pm$ 12.6, 87,3 male. Child A was 93.0%. Patients with stage B2 accounted for the largest proportion of 64.8%, stage B1 was 31,0%. AFP (> 200 ng/ml) was 45,1%. Number of tumor $\leq$ 3: 91,6%, size of tumor > 6 cm: 66.2%. Moderately differentiated HCC had the highest rate of 22.5%. Patient stage B1 mainly chosen the method of resection 57.1% and RFA 66.7%. TACE was mainly selected for patients with stage B2 with 72.1%. After treatment, the AFP response rate of the three treatment methods was 62.2%. Resection had the highest complete response rate with 85.7%, TACE had a complete response rate of 26.2%. Patients stage B1 had the highest complete response rate with 54.5%.
Conclusion: The subclassification of the intermediate stage helps to provide more treatment options for patients with HCC, the initial results show that treatment with multiple choices has a better response rate than treatment with TACE alone for HCC stage B.

[PP-0184]

Consecutive increment of serum AFP level is a useful surrogate marker in predicting HCC in liver cirrhosis patients

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Objectives: The role of alpha-feto protein(AFP) in the diagnosis of hepatocellular carcinoma(HCC) is getting smaller due to the advances of imaging modalities. However, consecutive increment of AFP level in liver cirrhosis patients is presumed to be associated with the higher risk of developing HCC in clinical settings. Such a notion instigated us to analyze serial AFP levels of HCC patients in a retrospective manner.
Materials and Methods: From January 2002 to December 2016, 2259 patients were diagnosed with HCC in Seoul St. Mary's hospital. Among them 236 cirrhotic patients were found to have a serial record of AFP measurements for over one year. We assessed AFP levels at the time the diagnosis of HCC was made and compared them with that of patients at 3,6 and 12 months prior to the diagnosis.
Results: Baseline characteristics were as follows; mean age 58.89 years(32–87), median tumor size 2.1 cm(0.7–26.3), median AFP level 20.35 ng/mL(0.75–32,134). Median AFP level of 12 months, 6 months and 3 months before the diagnosis of HCC was 6.26 ng/mL(0.6–513), 8.73 ng/mL(0.66–1287.86), 12.95 ng/mL(0.91–1461), respectively. We divided patients by two groups; one was AFP > 20 ng/mL at the time of diagnosis of HCC (n = 119), and the other one was not (n = 115). Repeated-measure ANOVA was used to analyze the significance of increase in consecutive AFP levels in HCC surveillance. In elevated AFP group, Consecutive increment of AFP level was statistically significant in time dependent manner(P $\leq$ 0.000) with linear relationship(P $\leq$ 0.000). There was no significant change of consecutive AFP level In non-elevated AFP group.
Conclusion: Early detection of HCC with relatively smaller sizes was possible due to the close observation of increase in serial AFP levels. We suggest increase in serial AFP level as a strong surrogate marker in the prediction of HCC and that those with consecutive increments of AFP levels for more than 2 times should be candidates for active surveillances for HCC.

[PP-0195]

The imbalance of NKG2A+/NKG2D+ ratio is involved in NK cell immunosuppression and disease progression in patients with hepatitis B virusrelated hepatocellular carcinoma

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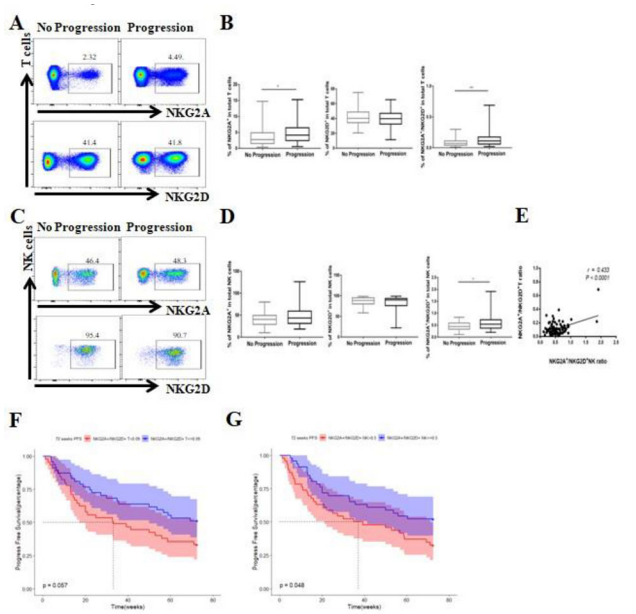
Objectives: Immunosuppression in tumor microenvironment affects disease progression. NKG2 family proteins include inhibitory receptors and activators, and can be used as attractive targets for immunotherapy using immune checkpoint inhibition (ICI). NKG2A is involved in NK cell exhaustion as a co-inhibitory molecule, while

NKG2D is involved in tumor progression and recurrence as an activated receptor. Therefore, we further explore the expression level prognostic value of NKG2A and NKG2D in hepatitis B virus-related hepatocellular carcinoma (HBV-HCC).
Materials and Methods: We analyzed the expression and related functions of NKG2A, NKG2D and $NKG2A^+/NKG2D^+$ ratio in peripheral blood of patients with HBV-HCC and analyzed tumor progression.
Results: In the HBV-HCC patients with tumor progression, the $NKG2A^+/NKG2D^+$ ratio is higher in NK cells and T cells. The K-M survival curve showed that there was a significant difference between the $NKG2A^+/NKG2D^+$ ratio of NK cells and the tumor progression of HBV-HCC (P = 0.048). It was further found that the imbalance of $NKG2A^+/NKG2D^+$ ratio on NK cells was related to the inhibition of NK cell function.
Conclusion: The $NKG2A^+/NKG2D^+$ ratio imbalance of NK cells is involved in NK cell immunosuppression, and the increase of the $NKG2A^+/NKG2D^+$ ratio is related to the tumor progression of HBV-HCC.



[OP-0199]

Comparison between bone scintigraphy and computed tomography for the detection of bone metastases in hepatocellular carcinoma

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Objectives: To compare the diagnostic accuracy of bone scintigraphy (BS) and computed tomography (CT) in detecting skeletal metastases for hepatocellular carcinoma (HCC) patients with suspicious bone metastasis.
Materials and Methods: A prospective study was carried out in 57 HCC patients. The accuracies of BS and CT were determined by comparing with a final diagnosis with criteria obvious progression of the lesion revealed from the follow-up examinations and treatment.
Results: This study included 48 males and 9 females, the mean age was 60.5 ± 12.9. Reasons for bone scintigraphy: Tumor extent surveillance: 54.4%, bone pain: 29.8%, limb weakness: 14%, palpable chest wall mass: 1.8%. There was a significant difference in bone metastatic detection between BS (45.6%) and CT (29.8%), p = 0.001. There were 23 metastatic regions on CT, tended to identify more positive lesions in the spine: 14/23, pelvis: 5/23; 45 regions in BS, tended to show more positive lesions in the spine: 19/45, ribs: 12/45. According to the follow-up result and palliative treatment by SBRT, for detecting metastatic bone lesions by CT: Sensitivity = 72.2%, Specificity = 89.7%, Positive Predictive Value = 76.5%, Negative Predictive Value = 87.5%, Accuracy = 84.2%; by BS: Sensitivity = 100%, Specificity = 79.5%, Positive Predictive Value = 69.2%, Negative Predictive Value = 100%, Accuracy = 86.0%.
Conclusion: BS has significantly better accuracy than CT in detecting metastatic HCC bone lesions, but to determine bone metastases, careful history taking, meticulous physical examination, and performing many bone scan methods are very important.

[OP-0201]

Efficacy and safety of stereotactic body radiation therapy combined with transcatheter arterial chemoembolization for intermediate hepatocellular carcinoma

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Objectives: This study was undertaken to evaluate the efficiency of stereotactic body radiation therapy (SBRT) combined with transcatheter arterial chemoembolization (TACE) for intermediate hepatocellular carcinoma (HCC).
Materials and Methods: This prospective study was conducted on 42 intermediate HCC patients. The patients received Drug-eluting bead TACE one time subsequent they underwent SBRT. The dose of SBRT was 27.5–48 Gy prescribed in 3–5 fractions. Hematologic toxicity was scored using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Tumor response was evaluated using modified Response Evaluation Criteria in Solid Tumors (mRECIST). Patient survival was assessed using the Kaplan–Meier method.
Results: Among 42 patients (male 83.3%), mean age 60.86 ± 13.25. Patients who had ECOG score = 0 were 97.6%, Child–Pugh A was 95.2%. The solitary tumor rate was 69%, median tumor size was 6.6 cm (range, 3.0–11.4 cm). Tumor response in patients followed for three months after SBRT included a complete response to treatment in 42.5%, partial response in 15.0%, stable disease in 22.5%, and progressive disease in 20.0%. The mean overall survival (OS) was 27.68 ± 1.68 months. The 1-, 2- and 3-year OS was 89.8, 79.6, and 72.3%. The 1-, 2- and 3-year progression-free survival (PFS) was 71.4, 63.9, and 40.3%. None of the patients developed toxicity and radiation-induced liver damage more than Grade 2.
Conclusion: Combination therapy of SBRT and TACE is a safe and effective modality for the treatment of intermediate HCC, and could be potentially a suitable option.

[PP-0205]

Prognostic significance of cachexia index in patients with advanced hepatocellular carcinoma treated with lenvatinib therapy

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Objectives: Cancer cachexia affects quality of life, response to chemotherapy, and survival in many advanced cancer patients. The aim of this study was to evaluate the prognostic value of pretreatment cachexia index (CXI) in patients with advanced hepatocellular carcinoma (HCC) treated with lenvatinib.
Materials and Methods: Methods Patients with advanced HCC treated with lenvatinib therapy between October 2018 and October 2020 were retrospectively studied. The CXI was calculated as (L3 skeletal muscle index) × (serum albumin)/(neutrophil-to-lymphocyte ratio). The association with treatment response and early adverse events within the first two months of lenvatinib therapy was investigated. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan–Meier method with log-rank test. Multivariable Cox regression was used to identify the predictors of survival.
Results: A total of 116 patients (median age: 60, male: 84.5%) with calculated CXI. They divided into two groups: high CXI ($\geq$ 53, n = 82) and low CXI ($<$ 53, n = 34). Patients with low CXI had a significantly lower disease control rate (61.8% vs. 89.0%, p = 0.001) and a shorter median OS (8.0 [95% CI 6.2–9.8] vs. 12.3 [95% CI 10.1–14.4] months, p = 0.002) than those with high CXI. In multivariable analysis, low CXI was independently associated with shorter OS (HR: 2.59, 95% CI: 1.48–4.54, p = 0.001) and PFS (HR: 1.87, 95% CI: 1.13–3.08, p = 0.01). Of note, during the first two months of lenvatinib therapy, anorexia (41.2% vs. 22.0%, p = 0.04) developed more frequently among patients with low CXI than those with high CXI.
Conclusion: The CXI may be a clinically useful index for predicting poor treatment response and prognosis in patients with advanced HCC undergoing lenvatinib treatment.

[OP-0213]

Comparison of treatment outcomes for single small hepatocellular carcinoma in patients with impaired liver function

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Objectives: This study aimed to compare clinical outcomes between radiofrequency ablation (RFA) and transarterial chemoembolization (TACE) in patients with solitary small hepatocellular carcinoma (HCC) and impaired liver function.
Materials and Methods: From January 2005 to December 2018, a hospital-based retrospective cohort of 200 patients with solitary small ($\leq$ 3 cm) HCC and Child–Pugh class B liver function who were initially treated with RFA (n = 131) or TACE (n = 69) were analyzed. The primary outcome was overall survival. Secondary outcomes were HCC progression-free survival and decompensation-free survival. HCC progression was defined as HCC progression beyond the Milan criteria. Decompensation was defined by variceal bleeding, spontaneous bacterial peritonitis, or hepatic encephalopathy.
Results: During a median 5.6 years of follow-up, mortality was observed in 140 patients. Overall survival was better for patients treated with RFA than TACE (61.5% vs. 43.2% at 5 years, P $<$ 0.001) and was independent factor for overall survival (hazard ration (HR) 1.36, 95% confidence interval (CI) 1.14–1.61). HCC progression free-survival for patients treated with RFA than TACE (78.4% vs. 56.9% at 5 years, P = 0.003), while decompensation-free survival was similar in both groups (58.0% vs. 51.8% at 5 years, P = 0.44). For early mortality (within 2 years from diagnosis), history of previous decompensation was the only independent factor while initial treatment modality (RFA vs. TACE) was not. For later mortality (after 2 years from diagnosis), initial treatment modality (RFA vs. TACE) was independent factor.
Conclusion: For patients with single small tumor and impaired liver function, RFA provided better outcome than TACE, explained by better progression-free survival with similar decompensation-free survival. These findings suggest RFA can be preferred option over TACE in these patients.

[OP-0215]

The survival strength of younger patients in BCLC stage 0-B of hepatocellular carcinoma: Basing on competing risk model

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Objectives: It is unclear whether patients at different stages of hepatocellular carcinoma(HCC) actually have a survival advantage. The aim of this study was to investigate whether age differences in different Barcelona Clinic Liver Cancer (BCLC) classification system contribute to the long-term survival outcome of HCC patients.
Materials and Methods: A total of 1602 patients with HCC admitted to Beijing Ditan Hospital were included in this study. They were divided into a younger group (age group $\leq$ 45y) and an older group (age group $>$ 45y) according to age. Factors determining overall survival (OS) and progression-free survival (PFS) were analyzed by univariate and multivariate analyses using the Kaplan–Meier method and the Cox proportional hazard regression model. We calculated the cumulative incidence function (CIF) using Fine-Gray model. The effect of mortality with age was also estimated using Restricted cubic spline(RCS).
Results: After matching, OS and PFS were significantly better in younger than in older patients with BCLC stage 0-B (p = 0.015 and p = 0.017, respectively). In BCLC stage 0-B, all-cause mortality increased with age and increased rapidly around the age of 40 years. (non-linear P $<$ 0.05). In BCLC stages 0-B, HCC-related and nonHCC-related death, were significantly different between younger and older individuals (p = 0.0019).
Conclusion: In stage BCLC 0-B, age affects the long-term prognosis of patients.

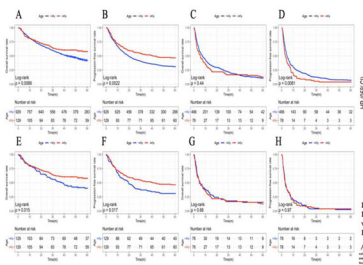

Fig.1. The Kaplan-Meier survival curves of Overall survival (OS) and Progression-free survival (PFS) in different BCLC stage HCC patients before and after PSM. (A,B) The OS (A) and PFS (B) in BCLC stage 0-B before PSM. (C,D) The OS (C) and PFS (D) in BCLC stage C-D before PSM. (E,F) The OS (E) and PFS (F) in BCLC stage 0-B after PSM. (G,H) The OS (H) and PFS (H) in BCLC stage C-D after PSM. HCC, hepatocellular carcinoma; BCLC, Barcelona Clinic Liver Cancer; PSM, Propensity Score Matching.

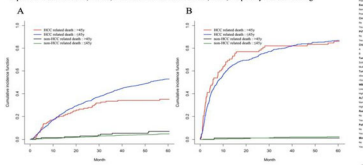

Fig. 3. In BCLC 0-B group (A) and BCLC C-D group (B), overall survival by cause of death was observed in age>45y and age≤45y. The curves were estimated based on a Fine-Gray model. HCC, hepatocellular carcinoma.

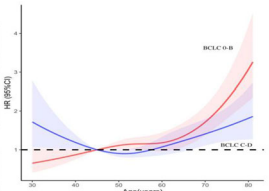

Fig. 2. Age-varying effects on all-cause mortality in BCLC 0-B group and BCLC C-D group. Using the 95% confidence interval as a reference, different hazard ratios were plotted over 40 years. HR, hazard ratios; CI, confidence interval; BCLC, Barcelona Clinic Liver Cancer.

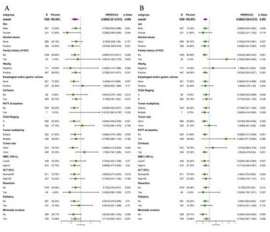

Fig.4. Forest map comparing mortality risk in Overall survival (A) and Progression-free survival (B) between BCLC 0-B group HCC patients in age >45y and age≤45y groups. Numbers in parentheses are 95% CIs. HR, hazard ratio; PVTT, portal vein tumor thrombus; WBC, white blood cell; ALT, alanine aminotransferase.

[OP-0216]

Nomogram for macrovascular invasion after transarterial chemoembolization with unresectable hepatocellular carcinoma

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Objectives: The aim of our Nomogram is to select those patients who have an advantage for TACE treatment.
Materials and Methods: In total, 1,135 patients with HCC admitted to the Beijing Ditan Hospital of Capital Medical University were enrolled in this study. We used a 7: 3 random splits between a training set(n = 796) and a validation set(n = 339). The Nomogram was established by multiple logistic regression and evaluated by the C-indices. We generated calibration plots, decision analysis curve and a clinical impact curve to assess the clinical usefulness of the Nomogram. MVI incidence curves were constructed using the Kaplan–Meier method and compared by the log-rank test.
Results: Multivariate logistic regression analysis identified six risk factors independently associated with MVI: BCLC staging B vs 0-A (2.350 [1.222–4.531]; P = 0.010) and staging C vs 0-A (3.652 [1.212–11.184]; P = 0.022), Treatment -TACE (2.693 [1.824–3.987]; P < 0.001), Tumor size ≥ 3 cm (2.239 [1.452–3.459]; P < 0.001), GGT ≥ 60 (1.685 [1.100–2.579]; P = 0.016), AFP ≥ 400 (2.681 [1.692–4.248]; P < 0.001) and CRP ≥ 5 (3.560 [2.361–5.388]; P < 0.001). The C-indices was 0.817 (95% CI, 0.778- 0.856) and 0.829 (95% CI, 0.79- 0.868) in the training and validation sets, respectively. The calibration curves showed good agreement between the predicted risk by the nomogram.
Conclusion: Our study developed and validated a Nomogram for the occurrence of MVI after TACE in patients with unresectable HCC, which can effectively distinguish the occurrence of MVI and provide a reliable basis for clinical decision making.

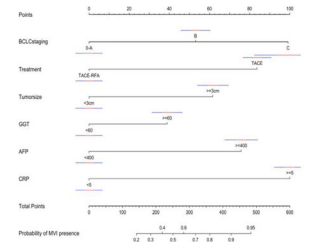

Fig. 1. Nomogram for predicting the presence of MVI preoperatively in patients with hepatocellular carcinoma. When using the nomogram, find the position of each variable on the axis and the corresponding point vertically. Then, add the points of all variables, and determine the prediction probability of MVI on the bottom axis. The red and blue line are the confidence interval. MVI, Macroscopic vascular invasion; OR, odds ratio; CI, confidence interval; BCLC, Barcelona Clinic for Liver Cancer; TACE, transcatheter arterial chemoembolization; RFA, radiofrequency ablation; GGT, γ-glutamyl transferase; AFP, α-fetoprotein; CRP, C reactive protein.

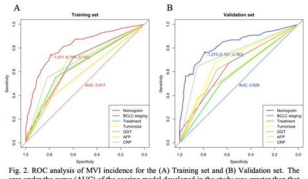

Fig. 2. ROC analysis of MVI incidence for the (A) Training set and (B) Validation set. The area under the curve (AUC) of the scoring model developed in the study was greater than that of a single indicator. ROC, receiver operating characteristic; AUC, area under the curve.

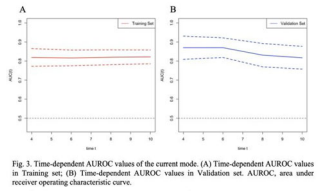

Fig. 3. Time-dependent AUROC values of the current mode. (A) Time-dependent AUROC values in Training set; (B) Time-dependent AUROC values in Validation set. AUROC, area under receiver operating characteristic curve.

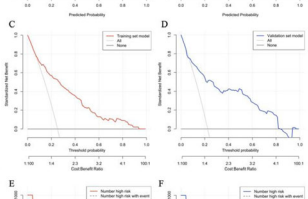

Fig. 4. Evaluate the prediction effect of nomogram in the Training (A,C,E) and Validation (B,D,F) set. (A,B) Calibration plot, (C,D) decision curve and (E,F) clinical impact curve of the nomogram for critical probability in the HCC patients, in which the predicted critical probability was compared well with the actual probability and had superior standardized net benefit.

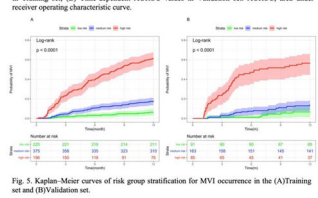

Fig. 5. Kaplan–Meier curves of risk group stratification for MVI occurrence in the (A)Training set and (B)Validation set.

[PP-0219]

Peripheral blood monocyte ratio is not related to tumor factor, and predicts late recurrence in curatively resected hepatocellular carcinoma

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Objectives: The prognostic significance of systemic inflammatory markers such as neutrophils-to-lymphocytes (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) have been regarded as prognostic indexes in hepatocellular carcinoma (HCC). Likewise, absolute monocyte count (AMC) have been also suggested as a poor prognostic factor in few studies. We postulated that the percentage of monocytes out of total leukocytes (monocyte%) will more precisely reflect the integrated immune activity toward monocyte activation than AMC which could be influenced by patient's liver function with the complex mechanism of cirrhosis and hypersplenism. We investigated the prognostic effect of SIMs, focusing monocyte%, in HCC patients.
Materials and Methods: 283 patients for training set and 1004 patients for validation set who underwent curative resection for primary HCC at Samsung Medical Center, Seoul, Korea, were enrolled. Pre- and post-operative SIMs of these patients and relevant clinicopathologic parameters were obtained. Association between SIMs and clinicopathologc parameters and prognostic significance of SIMs were evaluated.
Results: NLR, LMR, and PLR were associated with various aggressive tumor factor such as stage, intrahepatic metastasis and so

on, and the abnormal value of each variables was returned to normal range after removing tumor by surgery. In contrast, monocyte% didn't only manifest no association with adverse tumor factors, but also it wasn't reverted to normal range by surgical removal. Interestingly, monocyte% was associated with HCV infection and smoking history. The prognostic effect of AMC was marginal without statistical significance. In a multivariate analysis incorporating of all SIMs, only monocyte% was clarified as an independent prognostic factor for recurrence free survival (RFS) and late RFS.
Conclusion: Monocyte% could be related host factor, not tumor factor, and be used as a prognostic factor for survival status of HCC patients with curative resection, particularly late RFS.

[PP-0220]

TRPV6 expression as a prognostic factor for hepatocellular carcinoma treated with curative resection

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Objectives: Transient receptor potential vanilloid 6 (TRPV6) is a Ca^{2+} selective endothelial entry channel and its overexpression or downregulation have been reported in a variety of cancer types. Recently, a selective TRPV6 inhibitor was recently developed and ongoing clinical trial. However, TRPV6 expression in hepatocellular carcinoma (HCC) has not been reported yet.
Materials and Methods: We evaluated TRPV6 expression by immunohistochemistry in 219 cases of HCC, and analyzed its association with clinicopathologic parameters and prognostic significance. TRPV6 expression was compared between HCC and non-tumor liver, and the prognostic effect of TRPV6 expression was validated using public datasets (GSE36376, GSE14520 and GSE149614).
Results: Low TRPV6 expression was found in 37.4%, and it was significantly associated with well-known adverse prognostic factors such as large tumor size, high Edmonson grade, microvascular invasion, major portal vein invasion, tumor necrosis, intrahepatic metastasis, advanced AJCC T or BCLC stage, and high serum AFP. Patients with low TRPV6 expression showed shorter recurrence free survival and disease specific survival. Adverse prognostic effect of low TRPV6 expression was validated in an independent cohort from public dataset. TRPV6 expression was much lower in HCC than in non-tumor liver tissue, not only at the whole tissue level but also at the individual cell level.
Conclusion: TRPV6 expression is down-regulated in HCC, and might be used as a prognostic biomarker in surgically resected HCC.

[OP-0222]

Clinical outcome and sub-classification of patients with advanced stage hepatocellular carcinoma: A real world observational study of 1329 cases

Myung Ji Goh[1], Jong-In Chang[1], Dong Hyun Sinn[1], Moon Seok Choi[1], Wonseok Kang[1], Geum-Youn Gwak[1], Yong-Han Paik[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1]

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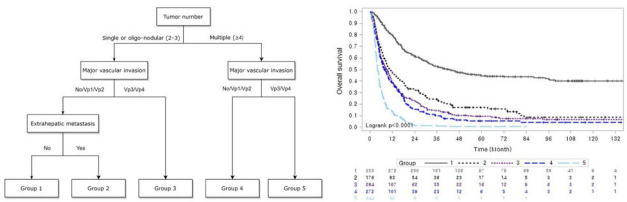
Objectives: Advanced stage hepatocellular carcinoma (HCC) comprises a heterogeneous population and are treated with various treatment modality. Sub-classification is needed to minimize heterogeneity, however, best way to classify advanced stage HCC remains further clarification.
Materials and Methods: Between 2008–2016, a total of 1,329 BCLC stage C patients [age: 56.1 ± 10.8, males: 1,115 (83.9%), hepatitis B virus = 1,036 (78.0%)] with preserved liver function (Child–Pugh A) and good performance status (ECOG stage ≤ 1) were analyzed.
Results: During a median 9.5 months of follow-up, mortality was observed in 1.075 patients. Decision tree analysis classified patients into five subgroups, based on tumor number (≤ 3 vs. ≥ 4), extent of portal vein invasion (PVI) (none or ≤ Vp2 vs. ≥ Vp3) and presence of extrahepatic metastasis (EHM). Group 1 was characterized by 1–3 tumor number, no or minor PVI, and without EHM. Group 2 was characterized by 1–3 tumor number, no or minor PVI, and with EHM. Group 3 was characterized by 1–3 tumor number with major PVI regardless of EMH. Group 4 was characterized by multiple (≥ 4) tumors with minor PVI regardless of EMH. Group 5 was characterized by multiple (≥ 4) tumors with major PVI regardless of EMH. and without EHM. The median survival was significantly different according to 5 subgroups (42.3 months, 10.9 months, 9.2 months, 7.9 months, 4.1 months for group 1, group 2, group 3, group 4 and group 5 respectively, $P < 0.001$). The most commonly applied treatment was TACE (53.8%) followed by systemic chemotherapy (18.6%) with survival rate of 51.8%, 14.3% at 12 months. Treatment patterns were very heterogeneous within subgroups. Generally, locoregional treatment showed better overall survival compared to systemic treatment in all subgroups.
Conclusion: Advanced stage HCC was consisted of heterogeneous population. Tumor number, extent of PVI, and EHM were factors that determined and classified patient outcomes of advanced stage HCC patients that can be used to minimize heterogeneity.



[OP-0242]

A prognostic nomogram for progression-free survival of patients with primary liver cancer after transarterial chemoembolization

Dong Xi[1], Mengying Xu[1], Meiwen Han[1], Qianting Guan[1], Ming Wang[1], Ke Ma[1], Weipeng Qi[1], Qin Ning[1]

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Corresponding author: Qin Ning, Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

Objectives: To identify relevant risk factors and construct a predictive model of nomogram for hepatocellular carcinoma (HCC) patients receiving tansarterial chemoembolization (TACE).
Materials and Methods: A total of 346 patients with primary liver cancer who underwent TACE as initial treatment were retrospectively included, of which 208 patients were allocated to derivation cohort randomly. 12-month Progression free survival (PFS) was used as

follow-up time endpoint according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Univariate analysis by Kaplan–Meier and multivariate analysis by COX regression model screened out indicators associated with short-term prognosis, and R language was further used to construct a nomogram. Then the remaining 138 patients were allocated to validation cohort. and the nomogram was compared with the classical BCLC staging system.
Results: After univariate and multivariate analyses of the derivation cohort, some independent predictors affecting the PFS in patients with liver cancer undergoing TACE included: 1. baseline indicators: age (P = 0.013), ALBI grade (grade 2 vs grade 1, P = 0.029, grade 3 vs grade 1, P = 0.000), and portal vein tumor thrombus (P = 0.000); 2. indicators of 1 month follow-up after initial TACE treatment: NLR (P = 0.032), the change of AFP (P < 0.05), and the change of DCP (P = 0.000). 3. the numbers of TACE in 6 months after initial TACE (P = 0.007). These predictors were used to construct a prognostic nomogram for PFS. In the derivation cohort, calibration curve of the nomogram showed high consistency between the predicted and the actual PFS probability with C-index = 0.712, which outperformed BCLC staging system (C-index = 0.688, P = 0.004). This result was confirmed in the validation cohort, whose C-index was 0.734 and better than BCLC staging system (C-index = 0.663, P = 0.012).
Conclusion: Our study showed the prognostic nomogram had good predictive efficacy and could be used as a complementary assessment to predict the survival and prognosis of patients with liver cancer treated with TACE.

[OP-0252]

Prothrombin induced by vitamin K absence-II versus α-fetoprotein in detection of both resectable HCC and early recurrence after curative liver resection: A large-scale cohort study from China

Tian Yang[1,2], Ming-Da Wang[1,2], Lei Liang[2], Li-Yang Sun[2], Lan-Qing Yao[1], Chao Li[1], Han Wu[1], Xin-Fei Xu[1], Dong-Sheng Huang[2]

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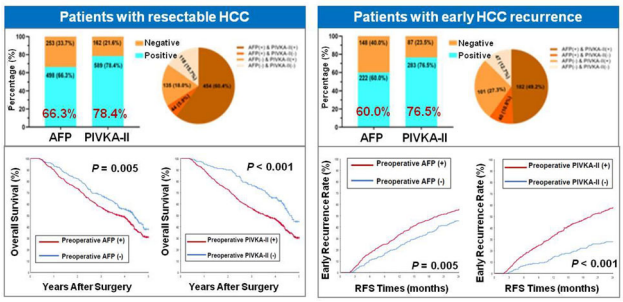
Objectives: Alpha-fetoprotein (AFP) and prothrombin induced by vitamin K absence-II (PIVKA-II) are two commonly used biomarkers for detection and prognostic prediction of hepatocellular carcinoma (HCC). This study sought to evaluate and compare the use of these values to detect HCC, as well as predict postoperative early recurrence (within 2 years after HCC resection).
Materials and Methods: Data on patients who underwent curative resection for HCC between 2014 and 2020 was prospectively collected and reviewed. Serum AFP and PIVKA-II levels within one week before surgery or at the time of detection of early recurrence were assessed; the AFP ≥ 20 ng/ml and PIVKA-II ≥ 40 mAU/ml were examined relative to recurrence using univariate and multivariate Cox-regression analyses.
Results: Among 751 patients who underwent curative HCC resection, 589 (78.4%) patients had a preoperative PIVKA-II ≥ 40 mAU/ml versus 498 (66.3%) patients had an AFP ≥ 20 ng/ml (P < 0.001). With a median follow-up of 41.6 months, 370 (50.1%) patients had an early HCC recurrence; among patients with an early recurrence, the proportion of patients with PIVKA-II ≥ 40 mAU/ml versus AFP ≥ 20 ng/ml (76.5% vs. 60.0%, P = 0.002) was higher. On multivariate analysis, preoperative PIVKA-II ≥ 40 mAU/ml, yet not preoperative AFP ≥ 20 ng/ml was an independent risk factor to predict early recurrence after HCC resection.
Conclusion: AFP and PIVKA-II are useful biomarkers to detect resectable HCC and predict early recurrence after HCC resection, with the latter showing higher positive rates. Preoperative PIVKA-II ≥ 40 mAU/ml was independently associated with early recurrence following curative HCC resection.



[PP-0272]

Serum sorbitol dehydrogenase as a novel prognostic factor for hepatocellular carcinoma after surgical resection

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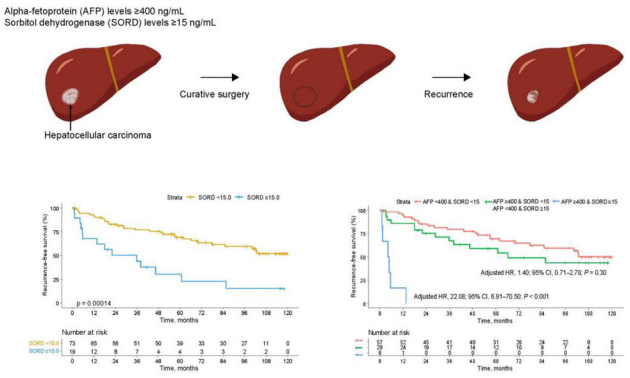
Objectives: The majority of patients with hepatocellular carcinoma (HCC) undergoing curative resection experience tumor recurrence. The purpose of this study was to examine the association between preoperative serum sorbitol dehydrogenase (SORD), a liver-derived enzyme that reflects liver damage, and recurrence of HCC after curative resection.
Materials and Methods: We randomly selected 92 patients who underwent curative resection for HCC between 2011 and 2012 from a prospective registry at a single tertiary care center in Korea. Baseline serum SORD levels were measured based on the serum samples attained preoperatively and stored for special uses in the future, such as research. The primary outcome was recurrence-free survival (RFS), which was compared based on serum SORD levels. Cox proportional hazard models were used to investigate prognostic factors for RFS.
Results: During a median follow-up duration of 57.1 months, 43 patients experienced HCC recurrence. Patients with recurrence have higher values of SORD levels than those without recurrence (10.0 ng/mL vs. 7.1 ng/mL; P = 0.04). Patients with serum SORD ≥ 15 ng/mL (HR, 3.46; 95% CI, 1.76–6.81; P < 0.001) had worse RFS compared with patients with serum SORD < 15 ng/mL. Serum alpha-fetoprotein (AFP) and SORD levels were two independent prognostic factors for RFS. When patients were stratified by baseline serum SORD and AFP levels, patients with serum AFP levels ≥ 400 ng/mL and serum SORD levels ≥ 15 ng/mL had a distinctly poor prognosis with the lowest RFS rates (HR, 22.08; 95% CI, 6.91–70.50; P < 0.001).

Conclusion: Baseline serum SORD is an effective prognostic factor for HCC after resection. It may help guide patient selection for surgery, especially when combined with serum AFP levels.



[OP-0277]

Comparison of overall survival between surgical resection and radiofrequency ablation for hepatitis B-related hepatocellular carcinoma

Moon Haeng Hur[1], Jeong-Hoon Lee[1], Ju Yeon Kim[1], Ji Hoon Hong[1], Min Kyung Park[1], Hee Jin Cho[1], Na Ryung Choi[1], Jihye Kim[1], Minseok Albert Kim[1], Joon Yeul Nam[1], Yun Bin Lee[1], Eun Ju Cho[1], Su Jong Yu[1], Yoon Jun Kim[1], Dong Ho Lee[2], Jeong Min Lee[2], Suk Kyun Hong[3], Nam-Joon Yi[3], Kwang-Woong Lee[3], Kyung-Suk Suh[3], Jung-Hwan Yoon[1]

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Objectives: It remains controversial whether surgical resection provides superior overall survival (OS) for hepatocellular carcinoma (HCC) compared to radiofrequency ablation (RFA). This study aimed to compare OS after RFA with that after resection for HCC.
Materials and Methods: This retrospective study included patients who underwent RFA or surgical resection as initial treatment for hepatitis B virus (HBV)-related HCC at a very early or early stage. A total of 761 patients (RFA, n = 194; resection, n = 567) from a tertiary center and 1,277 patients (RFA, n = 352; resection, n = 925) from Korean Primary Liver Cancer Registry were included in the hospital and nationwide cohorts, respectively. Primary and secondary endpoints were OS and recurrence-free survival (RFS), respectively. Additional analysis was performed when the history of antiviral treatment was confirmed. The rate of complication was compared between the two treatment groups in the hospital cohort. Baseline characteristics were balanced using inverse probability of treatment weighting (IPTW).
Results: In the hospital cohort, during 81.0 (interquartile range, 62.3–107.1) months of follow-up, there was no difference in OS (adjusted hazard ratio [aHR] = 0.870, 95% confidence interval [CI] = 0.400–1.897, P = 0.73) and RFA was associated with shorter RFS (aHR = 1.562, 95% CI = 1.099–2.219, P = 0.01) after employing IPTW. Antiviral treatment was independently associated with longer OS (aHR = 0.444, 95% CI = 0.251–0.786, P = 0.01) as well as RFS (aHR = 0.544, 95% CI = 0.391–0.757, P < 0.01) in the hospital cohort. In the nationwide cohort, there was no difference in OS (aHR = 0.981, 95% CI = 0.661–1.456, P = 0.92) between the two treatment groups when adjusted for antiviral treatment. The overall incidence of complication was higher in the resection group (26.3%) than in the RFA group (13.9%) (P < 0.01).
Conclusion: RFA may provide comparable OS to resection in the treatment of very early or early HCC with lower rates of complication, although RFS is marginally shorter than in the resection group after adjusting for antiviral treatment.

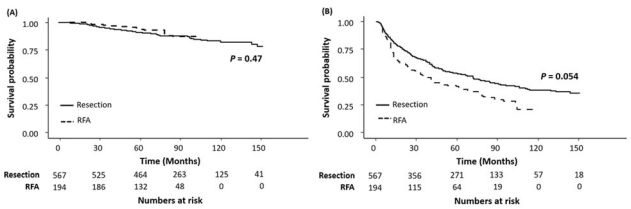

Figure. Kaplan-Meier estimates of (A) OS and (B) RFS in the hospital cohort after IPTW.

[PP-0282]

A Korean Nationwide outcome study of patients with hepatocellular carcinoma and Child–Pugh Class B liver function by tumor stage

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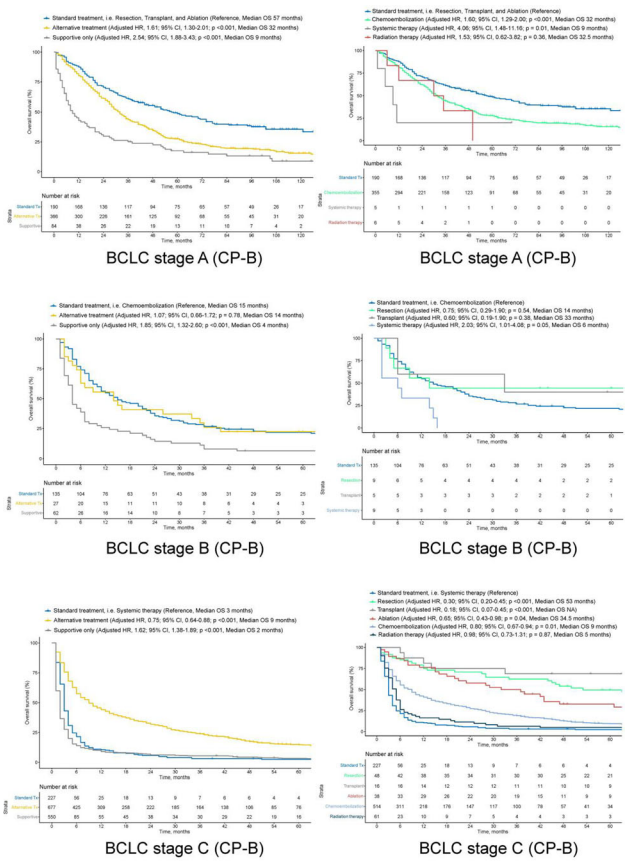
Objectives: There are no established practice guidelines for treating hepatocellular carcinoma (HCC) in patients with Child–Pugh class B (CP-B) liver function. We aimed to evaluate whether it is justifiable to choose a therapeutic option according to the BCLC tumor stage-based algorithm in treating such patients.
Materials and Methods: Among 13,838 HCC patients registered at the Korean Central Cancer Registry from 2008 through 2016, 7758 CP-A and 2318 CP-B patients were included in this study. Patients were treated according to algorithm-based standard or alternative methods, or with the best supportive care by the BCLC stage determined after excluding liver function. The main analysis is to compare overall survival (OS) across therapy per stage in CP-B patients. Hazard ratios (HRs) for OS and their 95% confidence interval (CI) were calculated using a Cox proportional hazard model.
Results: Overall, CP-A patients had longer median OS than CP-B patients, regardless of the BCLC tumor stage (all Ps < 0.05). In the BCLC-A group, receiving therapies other than standard options such as liver resection, transplant, and local ablation was independently associated with worse OS (adjusted HR, 1.61; 95% CI, 1.30–2.01; P < 0.05). Therapeutic modality did not significantly affect OS in the BCLC-B group with an adjusted HR of 1.07 (95% CI, 0.66–1.72; P = 0.78). In contrast, OS was superior in BCLC-C patients treated with alternative options to those with systemic chemotherapy, in which liver transplant lowered most a risk of overall death (adjusted HRs [95% CIs], 0.18 [0.07–0.45], followed by resection (0.30 [0.02–0.45]), ablation (0.65 [0.43–0.98], and chemoembolization (0.80 [0.67–0.94]) (all Ps < 0.05).
Conclusion: Our referential findings suggest that it is likely better to consider algorithmically standard therapies for HCCs at a BCLC A or B tumor stage, and surgical or interventional approaches rather than systemic therapy, if indicated, for those at stage C as the first-line treatment in patients with moderately preserved liver function.



[OP-0283]

Early extrahepatic recurrence after hepatectomy for hepatocellular carcinoma significantly reduces survival: A 15-year observational study

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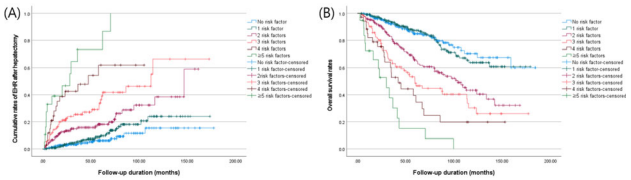
Objectives: Extrahepatic recurrence (EHR) after curative hepatectomy for hepatocellular carcinoma (HCC) is closely associated with a poor prognosis. We investigated the features and mortality regarding early EHR and identified the predictive factors and its association with survival.

Materials and Methods: This retrospective study included 779 treatment-naive patients who underwent curative hepatectomy for HCC at two tertiary academic hospitals from January 2004 to December 2019. Multivariate analysis via Cox-regression was performed to identify the variables associated with EHR. Early EHR was defined as EHR development within 2 years after curative hepatectomy.

Results: Early EHR was diagnosed in 74 patients (9.4%) over a median follow-up period of 14.3 years, most commonly in the lungs (36.5%) followed by lymph nodes (32.4%), bone (20.3%), peritoneum (13.5%), and adrenal gland (13.5%). The median time to EHR was 0.73 year in early EHR group and 4.87 years in non-early EHR group. The median survival duration of early EHR group, non-early EHR group, and non-EHR group was 3.05, 6.62 and 11.53 years, respectively ($p < 0.001$) and early EHR was significantly associated with survival duration (Exp(B) = 7.897, $p < 0.001$). On multivariate analysis, serum albumin < 4.0 g/dL, serum alkaline phosphatase > 100U/L, surgical margin involvement, venous and/or lymphatic involvement, satellite nodule, tumor necrosis at pathology, sum of tumor size ≥ 7, and macrovascular invasion at diagnosis were predictive of early EHR. As the numbers of the risk factors increased, the probability of early EHR and the overall mortality rate inclined exponentially. (Probability of early EHR; 0/1/2/3/4/5 $\geq$ risk factors, 4.1/5.0/13.2/21.1/42.5/44.6%, respectively, median survival duration; 0/1/2/3/4/5 $\geq$ risk factors, 12.1, 11.5, 8.4, 7.0, 5.0, 2.7 years, respectively, Fig. 1).

Conclusion: Early EHR significantly deteriorates the prognosis of HCC patients and our risk factors clarifies the clinical course of EHR and could improve the follow-up strategy to improve outcomes in high risk patients.



[OP-0288]

Various uses of ramucirumab in real world practice for patients with advanced hepatocellular carcinoma

Naoya Kanogawa[1], Sadahisa Ogasawara[1,2], Susumu Maruta[3], Yotaro Iino[4], Masamichi Obu[4], Ei Itobayashi[3], Ryosaku Azemoto[4], Sae Yumita[1], Takamasa Ishino[1], Keita Ogawa[1], Terunao Iwanaga[1], Hidemi Unozawa[1], Miyuki Nakagawa[1], Kisako Fujiwara[1], Takafumi Sakuma[1], Naoto Fujita[1], Ryuta Kojima[1], Hiroaki Kanzaki[1], Keisuke Koroki[1], Kazufumi Kobayashi[1], Soichiro Kiyono[1], Masato Nakamura[1], Takayuki Kondo[1], Tomoko Saito[1], Ryo Nakagawa[1], Shingo Nakamoto[1], Ryosuke Muroyama[1], Tetsuhiro Chiba[1], Naoya Kato[1]

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Objectives: Ramucirumab was shown to be effective as second-line treatment after sorafenib in advanced hepatocellular carcinoma (HCC) patients with AFP $\leq$ 400 ng/mL in the global phase 3 trial. Although the strict evidence is for second line treatment after

sorafenib, ramucirumab has been used in patients who have been pretreated with a variety of systemic therapies in clinical practice since it approved. In this study, we retrospectively examined the treatment outcomes of ramucirumab in patients that administrated after diverse treatments.
Materials and Methods: We corrected data on patients who received ramucirumab in patients with advanced HCC at three institutions in Japan. Radiological assessments were determined according to RECIST version 1.1 and the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 was used for the assessment of adverse events.
Results: Between June 2019 and August 2020, 21 patients inducted with ramucirumab were included in this study The median AFP was 1965 ng/mL and AFP value of all patients were higher than 400 ng/mL (range: 409–93,036 ng/mL). None of patients received ramucirumab as second line treatment after sorafenib. Second-, third-, and forth lines treatments were 6 patients (57%), 10 patients (48%), and 5 patients (24%), respectively. All patients who administrated ramucirumab as second line were pre-treated with lenvatinib. Of 15 patients who started ramucirumab after third or later lines, 11 patients had a history of treatment with both sorafenib and regorafenib. Median progression-free survival (PFS) and treatment duration of ramucirumab in this cohort were 2.3 months and 2,2 months, respectively. We confirmed that there were no notable adverse events and no significant changes of ALBI score during ramucirumab treatment.
Conclusion: Even though ramucirumab has been used for other lines than second line treatment immediately after sorafenib, its safety and efficacy seemed to be not significantly different from that of the clinical trial.

[OP-0310]

Impact of PLT as a prognostic factor in HBV-related Hepatocellular Carcinoma: The survival strength of the patients in BCLC stage 0-B

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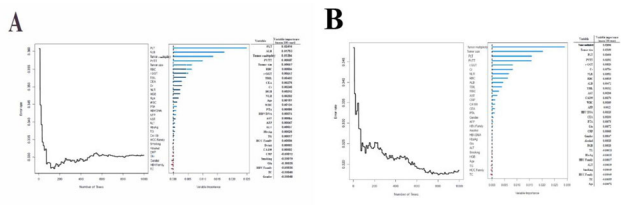
Objectives: Thrombocytopenia has been acknowledged to be a crucial risk factor for cirrhosis formation and hepatocarcinogenesis in chronic liver diseases. However, to date, the association between platelet count (PLT) and the prognosis of hepatocellular carcinoma (HCC) remains inconsistent and controversial. The aim of the present study was to determine whether PLT could be used as a useful predictor of survival in patients with HCC.
Materials and Methods: Retrospective analysis of 1250 patients with HBV-related Hepatocellular carcinoma diagnosed in Beijing Ditan Hospital from January 2008 to December 2014. Barcelona Clinic Liver Cancer (BCLC) stages were divided into BCLC stage 0-B and BCLC stage C-D. Factors determining overall survival (OS) and progression-free survival (PFS) were analyzed using Cox single-factor and multifactor analysis. The primary cohort and validation cohort were also applied to the BCLC stage 0-B patients using a randomized 7:3 ratio, and randomized forest was applied to model and screen the optimal factors.
Results: The cohort consisted of 850 patients with BCLC stage 0-B and 400 patients with BCLC stage C-D HBV-related Hepatocellular carcinoma. In BCLC stage 0-B patients, PLT < 100 was an independent risk factor for OS (HR = 0.467; 95% CI = 0.361–0.605; $p < 0.01$) and PFS (HR = 0.570; 95% CI = 0.390–0.832; $p = 0.04$); in BCLC stage C-D patients, PLT < 100 was not significantly different for OS and PFS. The random forest was applied for modeling in BCLC stage 0-B, and it was found that PLT < 100 was one of the optimal subsets for both OS and PFS, with good model prediction (OS: AUC primary cohort 0.828, AUC validation cohort 0.728; PFS: AUC primary cohort 0.818, AUC validation cohort 0.770).
Conclusion: PLT < 100 is an independent risk factor for predicting OS or PFS in patients with BCLC stage 0-B HBV-related Hepatocellular carcinoma.



[PP-0311]

Comparison of the outcomes between sorafenib and lenvatinib as the first-line systemic treatment for HBV-associated hepatocellular carcinoma: A propensity score matching analysis

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Objectives: In a randomized controlled trial, lenvatinib was non-inferior to sorafenib in overall survival (OS) of patients with unresectable hepatocellular carcinoma (uHCC). This study was aimed to compare the effects between sorafenib and lenvatinib as the first-line systemic therapy for uHCC with real-world data.
Materials and Methods: This retrospective single-center study involved 132 patients with HBV-related uHCC. Propensity score matching (PSM) was utilized to balance the baseline characteristics including age, sex, serum level of alpha-fetoprotein, Child–Pugh class, tumor size and tumor stage. Primary endpoint was overall survival (OS) and secondary endpoints included progression-free survival (PFS), time to progression (TTP), and tumor response.
Results: The final analysis included 44 patients who had treated with lenvatinib and 88 with sorafenib after PSM. OS (7.0 vs. 9.2 months, $p = 0.070$) and PFS (4.6 vs. 2.4 months, $p = 0.134$) were comparable between lenvatinib and sorafenib. In multivariable analysis, lenvatinib or sorafenib was not an independent predictor of OS (adjusted hazard ratio = 1.46, 95% confidence interval = 0.97–2.22, P = 0.070) after adjustment for baseline alpha-fetoprotein level, aspartate transaminase level, prothrombin time, performance status, and

previous and following treatments for HCC. However, the lenvatinib group showed significantly prolonged TTP (5.2 vs. 2.5 months, p = 0.018), higher objective response rate (18.2% vs. 4.5%, p = 0.020), and disease control rate (77.3% vs. 47.7%, p = 0.001) than the sorafenib group.
Conclusion: Our study demonstrates that lenvatinib showed comparable OS and PFS, but longer TTP and better tumor response compared to sorafenib in patients with HBV-related uHCC.

[OP-0312]

Primary non-response affects the prognosis of hepatitis B virus-related hepatocellular carcinoma after antiviral therapy

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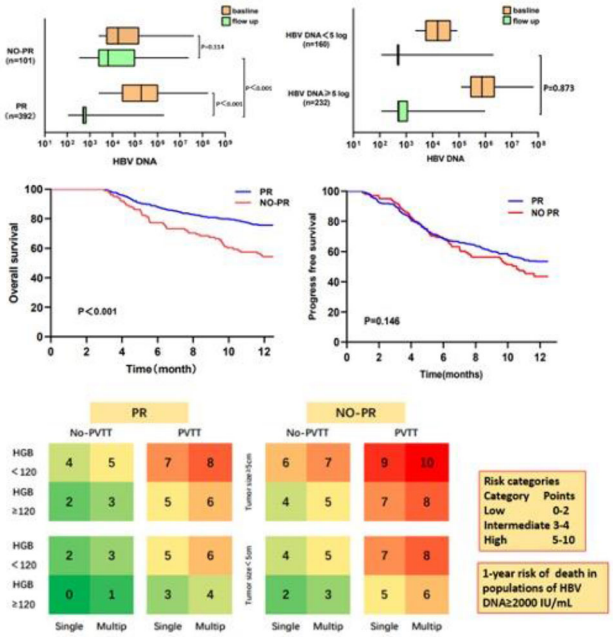
Objectives: The effect of different response on clinical outcomes after antiviral therapy remains unclear. This study aims to assess the effect of primary non-response on survival or prognosis of hepatocellular carcinoma patients with high-level hepatitis B virus(HBV) DNA.
Materials and Methods: A total of 493 patients with HBV-HCC admitted to the Beijing Ditan Hospital of Capital Medical University were enrolled in this study. Patients were divided into primary response group and primary non-response group. This bar graphs were used to compare the changes in virus levels between different groups. Risk factors, serum viral load, and other clinical variables were analyzed.
Results: The cohort consisted of 392 patients in primary response group and 101 in primary non-response group. The median survival time of PR group and no PR group was 39.6 months and 15 months. The average level of HBV DNA in primary response was higher than non-response group after 3 months of antiviral treatment. Then we divided the PR patients into higher level group(HBV DNA $\geq$ 5log) and relatively lower level group(HBV DNA $<$ 5log) based on baseline virus levels. As a result, there were no statistical differences between the two subgroups. The Kaplan–Meier curve showed that primary non-response had a lower overall survival in different categories of HBV DNA and hepatitis B e antigen. Primary non-response had lower overall survival and progress free survival in patients with alanine aminotransferase(ALT) $<$ 50 IU/L and cirrhosis. A multivariate Cox regression analysis indicated that primary non-response was an independent risk factor for 1-year survival(HR = 1.883, 95%CI 1.289–2.751, P = 0.001). All patients were divided into high(61.7%)-, medium(30.5%)-, and low(14.1%)-risk groups according to the score chart.
Conclusion: The level of viral decline at 3 months can predict the overall survival, and primary non-response probably shorten the median survival time among patients of HCC with high HBV DNA levels.



[OP-0313]

A novel nomogram for predicting overall survival in patients with liver cancer-related anemia

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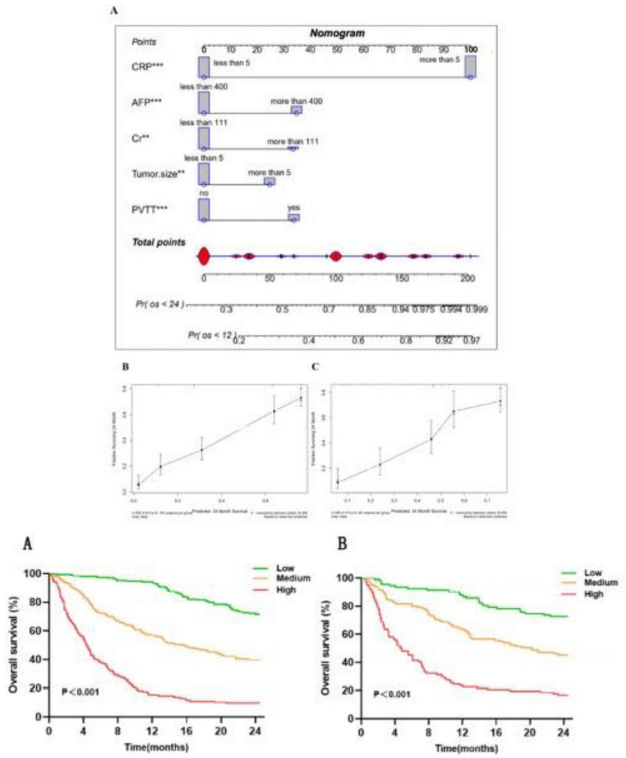
Objectives: The study aims to develop a model for predicting overall survival of liver cancer-related anemia, providing a reference for the adjustment of clinical treatment methods.
Materials and Methods: A total of 860 patients with hepatocellular carcinoma(HCC) related anemia were included in the current study and randomly divided into training and validation cohort. Cox multivariate regression analysis was used to construct a nomogram. The performance of nomogram was evaluated with the concordance index (C-index), calibration curves, area under the curve (AUC), and score risk charts. The survival curve is used to assess the overall survival of subgroups.
Results: The median survival time was 26.2 months in whole study population. Cox multivariate regression analysis showed tumor size, PVTT at baseline, Cr, AFP level, CRP were independent risk factors associated with 2-years OS. Then the nomogram for 2-year overall survival was constructed. Calibration curves showed good agreement between actual observation and nomogram prediction. The c-index was 0.761 (95%CI 0.739–0.783)in training cohort, and 0.736(95%CI 0.701–0.771) in validation cohort. The AUROC in two cohorts were 0.805 (95% CI 0.760–0.837) and 0.775 (95% CI 0.724–0.820), respectively. The c-index and AUROC of the nomograms were substantially higher than those of the six conventional HCC models. All patients were divided into high-, medium-, and low-risk groups, according to the nomogram score. Survival curves are well distinguished among subgroups of patients.

Conclusion: The conveniently nomogram shows good accuracy in predicting two-year mortality risk of patients with HCC-related anemia.



[PP-0334]

Comparison of survival outcomes in patients treated with nivolumab and regorafenib as second-line systemic therapy after sorafenib failure in patients with advanced hepatocellular carcinoma

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Objectives: Nivolumab and regorafenib are used as second-line therapies for patients with advanced hepatocellular carcinoma (HCC) after sorafenib failure. We aimed to compare the effectiveness of nivolumab to regorafenib.
Materials and Methods: Patients were retrospectively reviewed who were treated with second-line nivolumab (n = 27) or regorafenib (n = 66) between 2017 and 2021 after sorafenib failure for advanced HCC. Overall survival (OS) were calculated by Kaplan–Meier method from the drug administration. Inverse probability of treatment weighting (IPTW) using the propensity score was conducted to reduce selection bias.
Results: Between nivolumab and regorafenib groups, no differences in extrahepatic metastases (75.0% vs. 67.2%), portal invasion (39.3% vs. 35.8%), and median time interval from sorafenib administration to starting second-line therapy (median: 3.4 vs. 4.2 months) were revealed (all $P > 0.05$). Nivolumab was preferred in young (median age: 59.0 vs. 62.0) and patients with higher prevalence of Child–Pugh B and C (60.7% vs. 17.9%) than did those in regorafenib group (all $P < 0.05$); however, the differences were diminished after IPTW analysis. Median OS was 2.9 (95% confidence interval [CI]: 2.2–5.1) and 4.9 (95% CI: 4.1–6.6) months in nivolumab and regorafenib group, respectively (P = 0.050). However, after IPTW, nivolumab group showed similar OS with regorafenib group (median: 3.3 [95%CI: 2.7–8.9] vs. 4.7 [95%CI 3.1–5.8] months, P = 0.728). Multivariate Cox regression analyses revealed the weak association of nivolumab (vs. regorafenib) use with OS, both in raw (adjusted hazard ratio [aHR] = 0.796, 95% confidence interval: 0.418–1.516; P = 0.487) and IPTW (aHR = 0.982, 95% CI: 0.498–1.939; P = 0.959).
Conclusion: Survival outcomes in patients treated with nivolumab and regorafenib after sorafenib failure did not differ significantly in this retrospective study.

[OP-0336]

Efficacy of surgery and external radiotherapy for hepatocellular carcinoma with portal vein thrombosis: A meta-analysis

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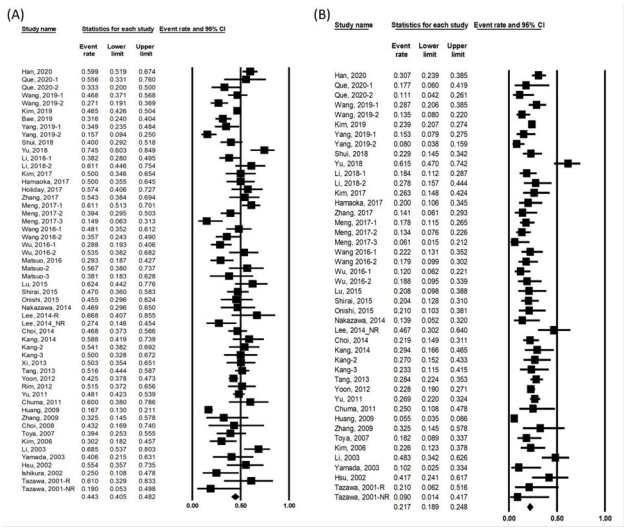
Objectives: External beam radiation therapy (EBRT) and surgery have recently been performed for hepatocellular carcinoma (HCC) with portal vein thrombosis (PVT). This meta-analysis aimed to evaluate the efficacy and feasibility of this approach.
Materials and Methods: PubMed, Medline, Embase, and the Cochrane library were systematically searched until January 2021. Overall survival (OS) and grade ≥ 3 toxicities were clinical endpoints.
Results: In total, 62 studies involving 9,562 HCC patients with PVT (4,159 patients in the EBRT and 5,403 patients in the surgery arms) were included. The pooled rates of Child–Pugh class A were 75.0% and 96.8% ($p < 0.001$), and those of PVT were 41.2% and 15.5% in EBRT and surgery arms ($p < 0.001$), respectively. The pooled 1- and 2-year OS rates were 44.3% (95% CI: 40.5–48.2) and 21.7% (95% CI: 18.9–24.8) in EBRT arm, respectively. In surgery arm, the corresponding rates were 65.1% (95% CI: 58.0–71.7) and 42.5% (95% CI: 34.4–51.0); both rates were higher in surgery arm than in EBRT arm (all $p < 0.001$). Such differences in 1- and 2-year OS rates were not significant comparing subgroup of EBRT studies with main PVT rate of $< 30\%$ and surgery arm (all $p > 0.05$). In studies on surgery with EBRT, the 1- and 2-year OS rates were 77.1% (95% CI: 69.6–83.2) and 45.4% (95% CI: 19.8–73.7), respectively; the 1-year OS rate was significantly higher than that in surgery arm (p = 0.007); however, this difference was not observed for the 2-year OS rate (p = 0.849). Pooled rates of grade ≥ 3 toxicities ranged from 1.8% to 4.3% in EBRT arm, and 3.8% to 4.0% in surgery arm, respectively.
Conclusion: Both modalities were efficient and feasible in HCC patients with PVT. Surgery could yield a favorable survival outcome, whereas EBRT could be considered for a wide range of patients. The combination of surgery and EBRT showed encouraging results.



[PP-0343]

Kinetics of the neutrophil–lymphocyte ratio during PD-1 inhibition predict prognosis in advanced hepatocellular carcinoma

Won-Mook Choi[1], Jonggi Choi[1], Danbi Lee[1], Ju Hyun Shim[1], Young-Suk Lim[1], Han Chu Lee[1], Changhoon Yoo[2], Min-Hee Ryu[2], Baek-Yeol Ryoo[2], Kang Mo Kim[1]

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Objectives: Programmed death-1 (PD-1) inhibitors such as nivolumab have improved survival outcomes and produced durable responses in advanced hepatocellular carcinoma (HCC). However, predictive biomarkers to identify suitable patients for these treatments are still lacking. Here, we evaluated the relationship between the baseline and kinetics of the neutrophil–lymphocyte ratio (NLR) and clinical outcomes in nivolumab-treated HCC patients.
Materials and Methods: All consecutive HCC patients treated with nivolumab between July 2017 and June 2020 were screened for the eligibility. The NLRs were calculated before and at 2, 4, and 6 weeks after treatment. Survival outcomes were compared based on the baseline and kinetics of NLR. We additionally analyzed the association between the baseline and dynamic changes in the NLR with hyperprogression (HPD).
Results: Among the 194 included cases, most patients were male (82.0%) and had a Child–Pugh class A disease (70.6%). Patients with a baseline NLR $\geq$ 3 (hazard ratio [HR] 2.46; 95% CI 1.63–3.71) had a poorer overall survival compared to patients with baseline NLR $<$ 3. During the treatment, the NLR increased rapidly in the patients developing HPD and only a ΔNLR at 4 weeks was predictive of HPD. Indeed, the risk of HPD increased by 20% for every 20% increase in the ΔNLR at 4 weeks, and a ΔNLR $>$ 75% at this timepoint had an 86.1% accuracy for predicting HPD. Accordingly, an NLR increase at 4 weeks (HR 1.79; 95% CI 1.19–2.68) was associated with an increased risk of death, especially among patients with a baseline NLR $\geq$ 3.
Conclusion: The baseline and on-treatment kinetics for the NLR are effective prognostic indicators in nivolumab-treated patients with HCC. This may help to guide patient selection and on-treatment strategies for immunotherapies in advanced HCC.

[PP-0352]

Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients

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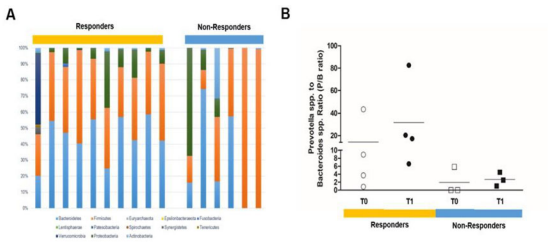
Objectives: Immunotherapy has revolutionized the clinical outcomes of intractable cancer patients. Little is known about the intestinal nonpathogenic bacterial composition of hepatocellular carcinoma (HCC) patients treated by immunotherapy.
Materials and Methods: From September 2019 to March 2020, we prospectively collected fecal samples and examined the gut microbiome of 8 advanced HCC patients treated with nivolumab as a second- or third-line systemic treatment. Fecal samples were collected before the start of immunotherapy. Fecal samples of patients with progression during treatment were collected at the time of progression, and fecal samples of patients who showed good response to nivolumab were collected after 5–7 mo as follow-up. Metagenomic data from 16S ribosomal RNA sequencing were analyzed using CLC Genomics Workbench. Microbiome data were analyzed according to therapeutic response.
Results: All 8 patients were male, of which 6 had underlying chronic hepatitis B. A higher Shannon index was found in the responders than in the non-responders after nivolumab therapy ($P = 0.036$). The unweighted beta diversity analysis also showed that the overall bacterial community structure and phylogenetic diversity were clearly distinguished according to therapeutic response. There was no significant difference in the diversity or composition of the patient gut microbiome according to the immunotherapy used. Several taxa specific to therapeutic response were designated as follows: Dialister pneumosintes, Escherichia coli, Lactobacillus reteri, Streptococcus mutans, Enterococcus faecium, Streptococcus gordonii, Veillonella atypica, Granulicatella sp., and Trchuris trichiura for the non-responders; Citrobacter freundii, Azospirillum sp. and Enterococcus durans for the responders. Of note, a skewed Firmicutes/Bacteroidetes ratio and a low Prevotella/Bacteroides ratio can serve as predictive markers of non-response, whereas the presence of Akkermansia species predicts a good response.
Conclusion: The current presumptive study suggests a potential role for the gut microbiome as a prognostic marker for the response to nivolumab in treatment of HCC patients.



Potential prognostic markers associated with gut microbiota of nivolumab therapy in HCC patients. (A) At the Phylum level, the deviated Firmicutes/Bacteriodetes ratio (<0.5 or >1.5) was more frequently found in the non-responders (non-responders vs. responders, 66.7% vs. 10.0%, $p = 0.018$). **(B)** At the genus level, the ratio of *Prevotella* species to *Bacteroidetes* species (P/B ratio) as a prognostic marker of nivolumab therapy in HCC patients. When we compared the ratio of Prevotella species to Bacteroidetes species (P/B ratio) between the responders and the non-responders, the responders showed significantly higher ratio of Prevotella species to Bacteroidetes species (P/B ratio) than the non-responders (mean P/B ratio, responders vs. non-responders, 22.99 vs. 2.312, p=0.024).

[PP-0382]

Compliance of the screening for hepatocellular carcinoma in patients with chronic hepatitis B or C

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Objectives: This study aimed to investigate the compliance of the screening for hepatocellular carcinoma (HCC) in patients with chronic viral hepatitis.
Materials and Methods: A cross-sectional study was conducted based on nationally representative samples from the Korean National Health and Nutrition Examination Survey 2007–2012. Of 50,405 participants, a total of 1,275 patients with chronic hepatitis B or chronic hepatitis C were included in the final analysis. We investigated compliance of HCC screening using ultranonography and serum alpha-protein. Univariable and multivariable logistic regression analyses were performed to evaluate the screening compliance associated risk factors such as age, sex, marital status, residential area, self-rated health status, education level, income status, private insurance for health care, alcohol and smoking.
Results: The mean age of 1,275 patients was 49.4 years and male was 51% (n = 618). The compliance of HCC screening was observed in 508 patients (40%): within 6 months before the survey, 12% (n = 155); 6–12 months, 11% (n = 134); > 12 months, 17% (n = 219). The multivariable analysis showed that compliance of HCC screening was significantly associated with age: 40–60 years (odds ratio [OR] 3.06 with 95% confidence interval [CI]: 2.26–4.15, $p < 0.001$), age: > 60 years (OR 2.92 with 95% CI: 1.93–4.42 $p < 0.001$), self-rated health status: moderate (OR 1.42 with 95% CI: 1.07–1.89, p = 0.016), self-rated health status: poor (OR 152 with 95% CI: 1.08–2.13, p = 0.015), education: university or higher (OR 1.37 with 95% CI: 1.04–1.81, p = 0.025), income: > 50 percentile (OR 1.95 with 95% CI: 1.49–2.56, $p < 0.001$) and private insurance for health care (OR 1.40 with 95% CI: 1.02–1.91, p = 0.038).
Conclusion: Compliance of HCC screening was favorable in patients with older age, poor health status, higher education level, high income and private insurance for health care in Korea. These findings may be helpful to increase HCC screening and surveillance rate in patients with chronic viral hepatitis.

[PP-0386]

The overall survival of hepatocellular carcinoma after resection according to the cause of liver disease

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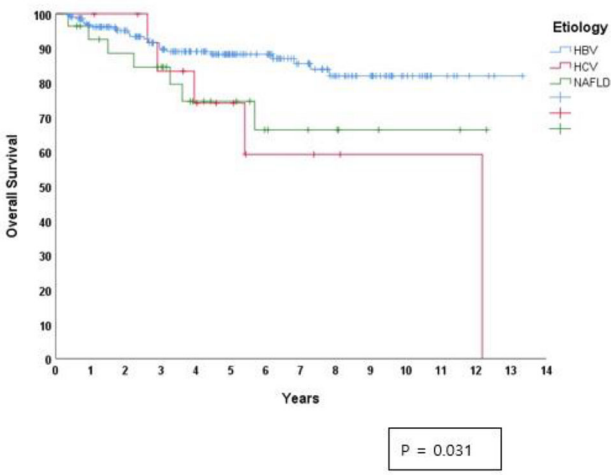
Objectives: Some studies have shown a poor prognosis for hepatocellular carcinoma (HCC) patients whose etiology is viral. This study is to evaluate the outcomes of patients diagnosed to resectable HCC, according to the etiology of the disease due to the difference in prognosis between viral and non-alcoholic fatty liver disease (NAFLD).
Materials and Methods: A total of 264 patients were performed a review of medical records of patients undergoing hepatectomy between 2005 and 2019 for the treatment of HCC. They were divided into groups according to the cause of liver disease, followed by overall and disease-free survival analysis for comparison.
Results: The cause of HCC consisted of 222 hepatitis B virus (HBV) (69.4%), 14 HCV (4.4%), and 28 NASH (7.9%). There was no statistically significant difference in the sex, tumor stage (BCLC and AJCC 7th) of the groups of patients divided according to the etiology of HCC. However, the mean age is higher in NAFLD (NAFLD 72 years, vs. HBV 62 years, HCV 68 years, $p < 0.001$), The presence of liver cirrhosis is lower in NAFLD (NAFLD 14.3%, vs. HBV 51.8%, HCV 50%, p = 0.001). Overall survival (OS) at five years of the patients with HBV, HCV and NAFLD were 88.2%, 74.1%, and 74.6%, respectively (p = 0.031). Disease-free survival at five years of patients with HBV, HCV and NAFLD were 72.5%, 69.3%, and 77.9%, respectively (p = 0.370). In multivariate analysis, age, and baseline AFP were significant prognostic factors of OS (hazard ratio [HR] for age; 0.938, confidential interval; 0.886–0.994, p = 0.03, HR for AFP; 1.000; 1.000–1.000, p = 0.001).
Conclusion: Baseline age and AFP levels showed significant prognostic differences among the groups of HCC patients of the various etiologies. NAFLD induced HCC had shown slightly lower OS at five years than viral induced HCC.

Figure: Kaplan-Meier plots of overall survival



[PP-0391]

Comparison of dexamethasone and celecoxib for prophylaxis for transarterial chemoembolization

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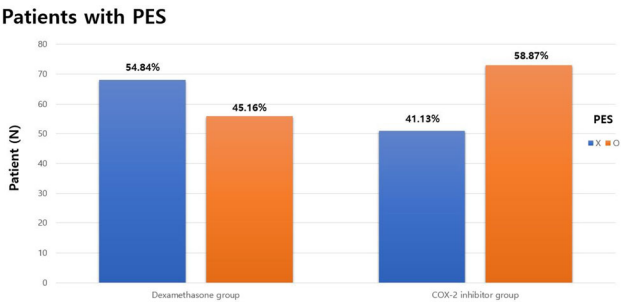
Objectives: Transarterial Chemoembolization(TACE) is one of the most frequently used treatment method for hepatocellular carcinoma(HCC). The prevalence of Post-embolization syndrome(PES) has been reported till 90%, but its significance has been ignored. Recently, studies using steroids and non-steroidal anti-inflammatory drugs been published to prevent PES. However, its stability and practical application are not yet known. In this study, we compared the effect of COX-2 inhibitor and high-dose dexamethasone on the prevention of PES and its safety.
Materials and Methods: This prospective, randomized trial was conducted in a single center from May 2019 to December 2020. A total of 248 patients with HCC were enrolled. After randomization, 124 patients were assigned each group equally. The dexamethasone group received intravenous dexamethasone 15 mg on the first day, and 5 mg on the second, and third day. In the COX-2 inhibitor group, celecoxib 200 mg was administered at 12-h intervals for 3 days.
Results: The incidences of PES were 58.9% in the COX-2 inhibitor group and 45.2% in the dexamethasone group (P = 0.042). Severe adverse events occurred in 3 patients of dexamethasone group which included ischemic liver injury, liver abscess,and biloma. One patient in COX-2 inhibitor group was treated with liver abscess. Mean age was 68.3 year-old in both groups with 77.4% and 82.3% of male ratio in COX-2 inhibitor group and dexamethasone group. 92.7% of patients in COX-2 inhibitor group and 87.9% of patients in dexamethasone group were Child–Pugh class A. 92.7% of patients in COX-2 inhibitor group and 94.3% of patients in dexamethasone group were Barcelona Clinic Liver Cancer stage A & B. Clinical staging of HCC between two groups showed no statistical difference including modified UICC stage.
Conclusion: This study demonstrates that the prophylactic administration of high-dose dexamethasone before TACE is better to prevent PES than COX-2 inhibitor without significant complication.



[PP-0392]

End stage of primary hepatocellular carcinoma with combined treatment bases on immuno-check point inhibitor one case of report

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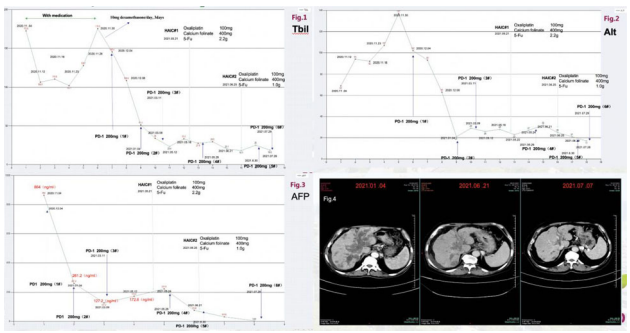
Objectives: A 82-year-old male patient was hospitalized due to "Jaundice with intermittent low fever for 1 month". The MRI showed: 1. Multiple intrahepatic lesions compressing the hilar bile duct, the intrahepatic bile duct was dilatated and formation of portal vein thrombosis. 2. Liver cirrhosis and splenomegaly; AFP: 864 ng/ml, CA19-9:33.85U/ml, HBsAg (+), TBIL: 172.6umol/L, ALB: 30.7 g/L, AST: 255u/L。Admission diagnosis: 1. Primary hepatocellular carcinoma (stage IV) 2. Hepatitis B cirrhosis 3. Obstructive jaundice 4. Splenomegaly 5. Cholecystitis. CTP score: C-10; PS: 3 points.
Materials and Methods: Conservative supportive treatment was given on November 4. 2020. With medication, the bilirubin decreased to 102.1umol/l. and then increased to 175.5umol/l due to cholangiolitis. Low dose of hormone treatment was given (Fig. 1). The patient was given carrelizumab 200 mg on December 4. 2020. Bilirubin decreased from 145.4umol/l to 108.6umol/l after 4 days (Fig. 1), and ALT decreased from 102u/L to 63u/L. (Fig. 2) One month later, AFP decreased from 864 ng/ml to 261.1 ng/ml. (Fig. 3) imaging showed remission of liver mass and tumor thrombus in portal vein (Fig. 4).
Results: After two cycles of carrelizumab, the patient's tumor achieved partial response in imaging and tumor markers. Figure 3 and Fig. 4. With liver function was restored, two circle of transarterial infusion chemotherapy were performed on May 21. 2021 and June 25, 2021. (Fig. 1.2). AFP decreased from 222.9 ng/ml to 3.82 ng/ml. (Fig. 3) The patient was followed up for more than 12 months, and the tumor reached partial response.
Conclusion: 1. Could the indications of immunotherapy be expanded for the treatment of patients with end-stage primary hepatocellular carcinoma complicated with poor physical strength score?2. The time to take effect of immunotherapy in this patient was only 4 days. Therefore, if the patient whose life expectancy is less than 2 months, Shall we actively try immunotherapy.



[PP-0402]

Surgery versus radiofrequency ablation in patients with Child-Pugh class-A/single small (≤ 3 cm) hepatocellular carcinoma

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Objectives: We compared the post-treatment overall survival (OS) and recurrence-free survival (RFS) between patients with Child-Turcotte-Pugh (CTP) class-A and a single small (≤ 3 cm) hepatocellular carcinoma (HCC) treated by surgical resection (SR) and radiofrequency ablation (RFA).
Materials and Methods: We retrospectively analyzed 391 patients with CTP class-A who underwent SR (n = 232) or RFA (n = 159) as first-line therapy for a single small (≤ 3 cm) HCC. Survival was compared according to tumor size (≤ 2 cm/2-3 cm) and the presence of cirrhosis. Inverse probability of treatment weighting (IPW) method was used to estimate the average causal effect of treatment.
Results: The median follow-up period was 64.8 months (range 0.1–162.6 months). After IPW, the estimated OS was similar in the SR and RFA groups (p = 0.215), and even in patients with HCC of ≤ 2 cm (p = 0.816) and without cirrhosis (p = 0.195). The estimated RFS was better in the SR group than the RFA groups (p = 0.005), also in patients without cirrhosis (p < 0.001), but not in those with HCC of ≤ 2 cm (p = 0.234). The weighted Cox proportional hazards model with IPW provided adjusted hazard ratios (95% confidence interval) for OS and RFS after RFA versus SR were 0.698 (0.396–1.232) (p = 0.215) and 1.698 (1.777–2.448) (p = 0.005), respectively.
Conclusion: SR was similar for OS compared to RFA, but a better for RFS in patients with CTP class-A and a single small (≤ 3 cm) HCC. The RFS was determined by the presence or absence of cirrhosis. Hence, SR rather than RFA should be considered in patients without cirrhosis to prolong RFS although there is no OS difference.

[OP-0422]

Multidisciplinary predictive models for recurrence and survival after Radiofrequency ablation for Hepatocellular carcinoma

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Objectives: To develop predictive models and to build nomograms using clinical, laboratory, and imaging findings for individualized estimation of early (≤ 2 years) tumor recurrence (ETR) and recurrence-free survival (RFS) after percutaneous radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC).
Materials and Methods: Patients who underwent RFA for single HCC (≤ 3 cm) between 2012 January and March 2014 (n = 152) were reviewed. Multivariable analysis using a stepwise variable selection method was performed to build a predictive model to estimate the probability of ETR and RFS, respectively. A nomogram using the results of the multivariable analysis was constructed for each outcome.
Results: The patient's age, albumin-bilirubin (ALBI) grade, model to predict the tumor recurrence after liver transplantation (MoRAL) score, non-rim arterial enhancement, enhancing capsule, signal intensity on hepatobiliary phase (HBP) on gadoxetic enhanced MRI, and positive for a model to predict high risk for microvascular invasion (MVI) were variables selected for the predictive model for ETR. The predictive model for RFS included AST/platelet ratio index (APRI), Child Pugh grade, and tumor location in relation to the hepatic capsule in addition to the variables for the model for ETR.
Conclusion: Predictive models were made for ETR and RFS after RFA for HCC, respectively. Nomograms were built which would serve as a useful tool for an individualized estimate of the outcomes.

[OP-0427]

Percutaneous radiofrequency ablation of solitary hepatic metastasis from colorectal cancer: Risk factors of local tumor progression-free survival and overall survival

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Objectives: The aim of this study was to evaluate local tumor progression-free survival (LTPFS) and overall survival (OS) after percutaneous radiofrequency ablation (RFA) for single metastatic colorectal cancer (CRC) < 3 cm and to assess risk factors associated with poor LTPFS and OS after percutaneous RFA.
Materials and Methods: This study screened 219 patients who underwent percutaneous RFA for metastatic CRC between January 2013 and November 2020, from whom 92 patients with a single hepatic metastasis from CRC measuring < 3 cm were included. LTPFS and OS were generated using the Kaplan–Meier method, and differences between curves were compared with the log-rank test. Risk factors of LTPFS or OS were assessed by Cox proportional hazards regression models.
Results: Technique efficacy was achieved in a single (n = 91) or second (n = 1) RFA session. During the follow-up (median, 20.0 months), cumulative LTPFS rates at 1, 3, and 5 years were 92.4%, 83.4%, and 76.5%, respectively. During the follow-up (median, 27.8 months), corresponding OS rates were 97.5%, 81.3%, and 74.8%, respectively. Multivariable Cox regression analyses showed that the group with both tumor-puncturing RFA and primary tumor staging of T4 (hazard ratio, 3.3; 95% CI: 1.1, 10.2; P = 0.037) was associated with poor LTPFS. No factors were identified to be significantly associated with poor OS based on univariable analysis.
Conclusion: Both LTPFS and OS were promising after percutaneous RFA of single metastatic CRC. The group with both tumor-puncturing RFA and T4 staging was associated with the poor LTPFS. No risk factor was identified for poor OS.

[PP-0438]

Survival impact of sustained virological response in hepatocellular carcinoma after curative treatment

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Objectives: Direct acting antivirals (DAA) has dramatically improved the sustained virological response (SVR) rate of hepatitis C virus (HCV). However, its survival impact in HCC patients has a few evidence. The aim of this study was to evaluate the survival impact of HCV-SVR in early-stage HCC after curative treatment.
Materials and Methods: Among 2340 HCC patients treated at our institution from January 2003 to March 2020, we retrospectively collected data of patients with HCV and early-stage HCC who received surgical resection or local ablation as initial treatment. Primary outcome was overall survival (OS), and secondary outcomes were recurrence free survival (RFS) and stage progression free survival (SPFS). We compared outcomes between three periods based on the time of diagnosis; 2003–2010: period 1, 2011–2013: period 2, and 2014–2020: period 3. Furthermore, we compared outcomes between three groups according to the date of SVR achievement: non-SVR, SVR before and after initial treatment.
Results: Of 513 patients who included in this study, 253, 107, and 153 were classified as period 1, 2, and 3. SVR rates of period 1, 2, and 3 were 14, 42, and 76%. 5-year OS, RFS, and SPFS rates of period 1, 2, and 3 were 59/73/79% ($p < 0.01$), 20/21/32% ($p = 0.13$), and 43/54/68% ($p < 0.01$), respectively. Non-SVR was 316, SVR before initial treatment was 96, and SVR after initial treatment was 101. 5-year OS, RFS, and SPFS rates by the three groups were 52/89/97% ($p < 0.01$), 12/42/40% ($p < 0.01$), and 34/77/84% ($p < 0.01$), respectively. No significant difference was observed in outcomes between the SVR before and after initial treatment.
Conclusion: Patients who achieved SVR increased over time, and the overall survival was significantly prolonged. Regardless of timing of SVR achievement, SVR contributed to prolonged OS, RFS and SPFS. HCV elimination should be considered for patients after curative treatment of HCC.

[PP-0446]

Imaging features of hepatobiliary MRI and the risk of hepatocellular carcinoma development

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Objectives: This study aimed to determine whether HCC risk and time to HCC development differ according to hepatobiliary MRI findings among people at risk for hepatocellular carcinoma (HCC).
Materials and Methods: A total of 199 patients aged 40 years or older with liver cirrhosis or chronic liver disease who underwent gadoxetic acid-enhanced hepatobiliary MRI between 2011 and 2015 were analyzed. An independent radiologist retrospectively reviewed MRI findings, blinded to clinical information, and categorized them into three groups: normal, high-risk features, and high-risk nodules. High-risk features were defined as multiple regenerative nodules and confluent fibrosis. High-risk nodules were defined as LR-3 or LR-4 nodules based on the Liver Reporting and Data System version 2018. The primary outcome was the development of HCC within three years of MRI.
Results: HCC was diagnosed in 22 patients (11.1%). There was no HCC development within three years for those with normal findings (n = 84). The cumulative incidence rate of HCC was 0%, 2.3%, and 13.5% at one, two, and three years for those with high-risk features (n = 64), and was 19.1%, 31.8%, and 37.3% at one, two, and three years for those with high-risk nodules (n = 51). The median time from baseline MRI to HCC diagnosis was 27.6 months (range: 23.5–33.4 months) for high-risk feature group, and 9.2 months (range: 3.1–30.9 months) for high-risk nodule group.
Conclusion: HCC risk and time to HCC development differ according to baseline hepatobiliary MRI findings, indicating that hepatobiliary MRI findings can be used as biomarkers to differentiate HCC risk.

[OP-0467]

Intracranial hemorrhage due to brain metastasis of hepatocellular carcinoma

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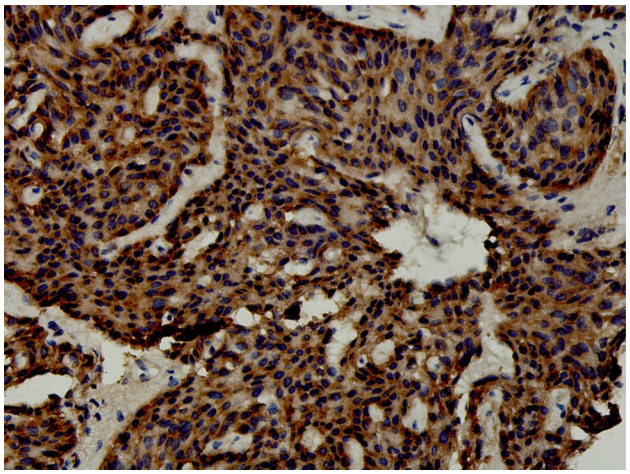
Objectives: Hepatocellular carcinoma (HCC) is the sixth most prevalent cancer in the world and brain metastases (BM) are extremely rare occurring in 1% of HCC patients.
Materials and Methods: A 62-yo man presented with severe headache, gradual onset loss of consciousness, sudden onset of limb weakness, and difficulty swallowing since morning before admission to emergency department. His past medical history revealed hepatitis B related HCC since December 2016 and undergone liver resection in January 2017. Patient undergone jejunal resection due to HCC metastasis in October 2019. Physical examination found altered consciousness, focal neurological deficit, and positive pathological reflexes. Laboratory revealed anemia and AFP 2.2 ng/mL. Head CT scan showed multiple intracerebral hemorrhage (ICH) on left cerebellar, left occipital, and right occipital with perifocal edema and midline shift to the left. The patient underwent brain surgery. Histopathologic and immunohistochemical result showed positive AFP and Glypican 3 indicating HCC metastasis. This patient's symptoms resolved after surgery.
Results: HCC is a highly invasive tumor that metastasizes to distant sites by hematogenous and lymphogenous spread. Because of improved diagnostic methods and prolonged survival, extrahepatic metastases are now seen more frequently. Frequent sites are lung, regional lymph node, bone, and adrenal gland. However, BM are rare. A multidisciplinary approach is required for optimum therapy. Surgery should be considered for BM patients with a single or few (< 3) lesions, especially if the systemic disease is under control and the BMs are symptomatic. Surgical resection remains an effective treatment option for eligible patients with BM. Surgical can improve life-threatening status, decrease focal neurological deficit, and symptom-producing mass effect. However, the survival of BM patients is poor with a median survival time of 2 months.

Conclusion: HCC patients with BM have a poor prognosis with a median survival time of 2 months.



[PP-0472]

Association with BMI and risk of HCC according to liver disorder status

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Objectives: BMI is known to be associated with higher risk of HCC in the general population. However, the association between BMI and risk of HCC in patients with various liver disease is not well understood.
Materials and Methods: We used Korean National Health Insurance Service(NHIS) database and analysed 15,016,551 adults(aged 18–99 years) underwent health examinations between 2003 and 2006. Participants were classified into 6 groups according to liver diseases; cirrhosis(LC), hepatitis(HBVHCV), other liver disease(O-LD), unidentified liver disease with ALT $\geq$ 40 or AST $\geq$ 40(ALT40), no known liver diseases with 20 $\leq$ ALT $<$ 40 or 20 $\leq$ AST $<$ 40 IU/ml(ALT2040), and ALT $<$ 20 and AST $<$ 20(ALT20).
Results: During mean 13.7 years follow-up. HCC occurred in 71,570 individuals. In total population, BMI had non-linear association with HCC. In BMI above 25 kg/m^2, BMI was positively associated with HCC risk regardless of liver disorder. HR per 5 kg/m^2 increase in BMI above 25 kg/m^2 was 1.48(95% CI 1.44–1.52) in total, 1.11(95% CI 1.00–1.23) in LC, 1.12(95% CI 1.44–1.52) in HBVHCV, 1.32(95% CI 1.22–1.44) in O-LD, 1.07(95% CI 1.03–1.12) in ALT40, 1.47 (95% CI 1.38–1.57) in ALT2040, 1.67(95% CI 1.32–2.09) in ALT20. In subgroup analysis for high-risk HCC group, the HR of HCC(95% CI) for 5 kg/m^2 increase in BMI was 1.21 in HBV-LC(1.01–1.46), 1.13 in other LC(1.08–1.19) and 1.15 in HBV without LC(1.04–1.27), 1.14 in HCV without LC(0.92 –1.40) and 1.05 in HCV-LC(0.64–1.74). Associations between BMI and HCC risk in HBV(HR; 1.46 vs 1.05), HCV(HR; 1.30 vs 0.92) and LC(HR; 1.28 vs 1.02) patients were stronger in female than in male.
Conclusion: Our study showed that BMI was positively associated with HCC risk regardless of liver disorder in BMI above 25 kg/m^2. As the severity of liver disease weakened, the association between increased BMI and HCC became stronger. In patients with hepatitis and LC, the harmful effects of higher BMI on HCC risk was stronger in women than in men.

[OP-0487]

Outcome of initial progression during nivolumab treatment for hepatocellular carcinoma: Should we use iRECIST?

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Objectives: Immune response evaluation criteria in solid tumors (iRECIST) is recommended during immune checkpoint inhibitors (ICIs) treatment, due to the possibility of pseudoprogression. We aimed to evaluate the clinical value of iRECIST in hepatocellular carcinoma (HCC) patients treated with ICIs.
Materials and Methods: This retrospective study involved 158 consecutive patients who underwent nivolumab treatment for HCC after sorafenib failure at three tertiary hospitals in Korea. We calculated the proportion of patients who were confirmed to have progressive disease (iCPD) at the second response evaluation after continual nivolumab therapy, out of those who showed unconfirmed progressive disease (iUPD) at the initial evaluation.
Results: At the initial evaluation performed median of 46 days (range = 14–94 days) after the start of nivolumab therapy, 94 patients presented with iUPD, among which 22 continued nivolumab. At the second evaluation performed at median interval of 50 days (range = 20–119 days), 21 of the 22 patients (95.5%) had iCPD and the other patient showed a stable tumor burden compared to the initial evaluation; no pseudoprogression was observed.
Conclusion: Considering low possibility of pseudoprogression, iRECIST may not be required for HCC patients undergoing ICI treatment.

[PP-0489]

Efficacy and safety of stereotactic body radiation therapy for hepatocellular carcinoma in elderly patients

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Objectives: The purpose of this study was to investigate the efficacy and safety of stereotactic body radiation therapy (SBRT) for elderly (≥ 75 years) patients with hepatocellular carcinoma (HCC).
Materials and Methods: Between January 2012 and December 2018, 83 patients with HCC who underwent SBRT were reviewed. A total dose of 36 – 60 Gy (median, 45) was delivered with the fraction size of 12 – 15 Gy (median, 15) over 3 – 4 consecutive days. Radiologic response was assessed according to the modified Response Evaluation Criteria in Solid Tumors (RECIST). Adverse events were graded according to the Common Terminology Criteria for Adverse Events version 5.0.
Results: Patients were 75 to 90 years of age, and 49 (59.0%) were male. Most (93.6%) patients had an Eastern Cooperative Oncology Group performance status of 0 or 1. Seventy-four (89.2%) patients had Child–Pugh class A hepatic function before SBRT. The median tumor size was 1.6 cm (range, 0.7 – 3.5) using the modified RECIST measurement. Three patients (3.6%) were treatment-naïve, and all other patients had received various courses of locoregional therapies before receiving SBRT. The objective response for each lesion at 3 months after SBRT was 77.6% and finally, 92.1% of lesions achieved complete response. The median follow-up period of all patients was 36.5 months (range, 7.3 – 99.3) The 3- and 5-year overall survival rates were 57.1% and 40.7%, respectively. The 3- and 5-year local tumor control rates were 97.7% and 90.1%, respectively. Grade ≥ 3 acute toxicities were observed in 3 (3.6%) patients; one patient (1.1%) experienced elevation in the Child–Pugh score to ≥ 2 after SBRT. There was no grade ≥ 3 late toxicity.
Conclusion: SBRT showed an excellent local tumor control with acceptable toxicities for elderly patients with HCC. SBRT can be a good treatment option in elderly patients with HCCs that are not suitable for curative treatments.

[PP-0533]

Clinical characteristics and risk factors of extrahepatic recurrence after hepatectomy of hepatocellular carcinoma without intrahepatic hepatocellular carcinoma: Multi-institutional 15-year observation

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Objectives: Extrahepatic recurrence (EHR) is a well-known poor prognostic factor regarding hepatocellular carcinoma (HCC). Although EHR after hepatectomy of HCC may occur in high risk group of patients, little is known about EHR when there are no intrahepatic HCC. We investigated the clinical features and risk factors regarding EHR without remnant intrahepatic HCC at the time of EHR diagnosis.
Materials and Methods: This retrospective study included 1,069 treatment-naive patients who underwent curative hepatectomy for HCC at four tertiary academic hospitals from January 2004 to December 2019. Multivariate analysis via Cox-regression was performed to identify the variables associated with EHR.
Results: One hundred and sixty five patients developed EHR after hepatectomy of EHR during median follow-up duration of 4.01 years. Among patients with EHR, 58 patients (35.2%) had no viable intrahepatic HCC at EHR diagnosis. There was no significant difference in time to initial HCC recurrence and EHR development between patients group with intrahepatic HCC and without intrahepatic HCC at EHR diagnosis; 18.16 vs. 19.79 months, and 37.14 vs. 28.43 months (p = 0.337), respectively. Compared to patients with intrahepatic HCC at EHR, patients without intrahepatic HCC at EHR showed higher portion of worst Edmondson Steiner grade ≥ 3 (74.8 vs. 89.7, p = 0.022), mUICC stage (≥ III) at 1st recurrence (45.8 vs. 74.1, p < 0.001) and with lower mUICC T stage (≥ III) at 1st recurrence (34.6 vs. 13.8, p = 0.004). On multivariate analysis, presence of metastatic lymph nodes at pathologic examination, tumor necrosis, micro-/macro-vascular invasion, and HCC stage beyond Milan criteria was closely associated with EHR without intrahepatic HCC.
Conclusion: EHR without remnant viable HCC may occur in considerable number of patients after hepatectomy for HCC. Close monitoring for EHR is warranted in high risk group of patients despite of no HCC in liver.

Table 1. Univariate and multivariate analyses of factors associated with no intrahepatic HCC at EHR.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Worst Edmonson-Steiner grade ≥ 3	3.291 (1.413-7.661)	0.006		
Pseudoglandular type	1.878 (1.122-3.145)	0.017		
pmUICC stage ≥ 3	2.515 (1.471-4.302)	0.001		
Metastatic lymph node[1]	15.246 (3.644-63.785)	<0.001	**12.923 (2.926-57.079)**	**0.001**
Venous/Lymphatic involvement	2.839 (1.610-5.007)	<0.001		
Tumor necrosis	3.656 (1.965-6.802)	<0.001	**2.767 (1.501-5.102)**	**0.001**
Absence of fatty change	2.043 (1.057-3.950)	0.034		
Tumor size > 9cm	4.662 (2.286-9.508)	<0.001		
Micro-/Macro-vascular invasion	3.360 (1.852-6.096)	<0.001	**1.928 (1.079-3.444)**	**0.027**
Beyond Milan criteria	3.337 (1.989-5.598)	<0.001	**2.110 (1.200-3.708)**	**0.009**
Serum AFP >700 IU/mL	2.731 (1.548-4.819)	0.001		

EHR, extrahepatic recurrence; HR, hazards ratio; CI, confidence interval; mUICC, modified Union for International Cancer Control; BCLC, Barcelona classification of liver cancer

1, confirmed at pathologic examination.

[OP-0545]

Prognostic value of the EZ (easy)-ALBI in patients with intermediate stage hepatocellular carcinoma (HCC) undergoing trans-arterial chemoembolization (TACE): A single tertiary referral center study

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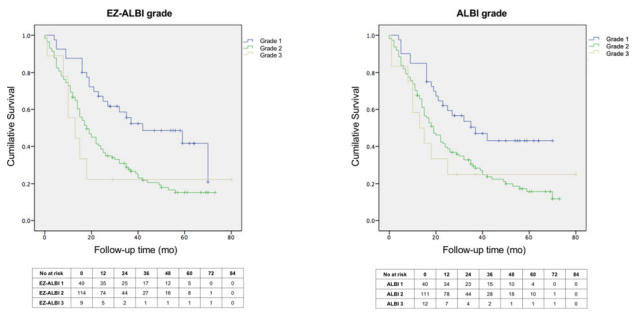
Objectives: Liver function and tumor burden can be variable in intermediate stage hepatocellular carcinoma (HCC), resulting in different clinical outcomes among patients treated with trans-arterial

chemoembolization (TACE). EZ (easy)-ALBI, a simplified ALBI score, was recently purposed. Our study aimed to validate EZ-ALBI score among patients with intermediate HCC undergoing TACE in tertiary center.

Materials and Methods: All HCC patients treated with TACE at King Chulalongkorn Memorial Hospital between January 2015 and December 2019 were enrolled. Intermediate stage HCC was defined by either multinodular lesions or unresectable single HCC with size > 5 cm. Liver function tests were retrospectively collected before and 1–3 months after TACE. EZ-ALBI and ALBI score were calculated and stratified into 3 grades. Overall survival (OS) was assessed by Kaplan–Meier curve and Cox proportional hazard.

Results: Among TACE cohort of 672 cases, 166 patients with intermediate stage HCC were enrolled. Majority of patients had hepatitis B infection (39.8%) and cirrhosis (94%); Child A (80.7%) and B (13.3%). The median follow-up time was 53 months (IQR 37–62). The median OS of all cohort was 22 months. A good correlation between EZ-ALBI and ALBI score was observed (correlation coefficient 0.987, $p < 0.001$). Patients with baseline EZ-ALBI grade 1/2/3 were 40(24.5%)/ 114(70%)/ 9(5.5%).The median OS according to baseline EZ-ALBI grade 1/2/3 were 41/18/13 months ($p = 0.002$) (Fig. 1) After TACE, 42 patients (29.6%) showed worsening EZ-ALBI grade. In multivariate analysis, baseline EZ-ALBI grade 2, 3 and AFP > 20 ng/ml were significantly associated with OS [hazard ratio (HR) 2.196 ($p = 0.007$)/ 3.262 ($p = 0.016$) and 1.768 ($p = 0.018$)]while dynamic changes of EZ-ALBI grade seemed not to be related with OS.

Conclusion: EZ-ALBI score showed strong correlation with conventional ALBI. Baseline EZ-ALBI demonstrated good prognostic ability to predict OS in patients with intermediate HCC receiving TACE. Dynamic change of the score after TACE was not associated with survival.



[PP-0571]

Impact of alpha-fetoprotein levels on survival in patients with unresectable hepatocellular carcinoma that progressed on sorafenib treatment

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Objectives: Regorafenib has demonstrated its survival benefit for unresectable hepatocellular carcinoma (uHCC) patients in a phase III clinical trial. We aimed to assess the efficacy and tolerability of regorafenib and the predictors of treatment outcomes in Taiwanese patients.

Materials and Methods: We analyzed the survival, best overall response, predictors of treatment outcomes, and safety for uHCC patients who had tumor progression on sorafenib therapy and received regorafenib as salvage therapy between March 2018 and November 2020.

Results: Eighty-six patients with uHCC were enrolled (median age, 66.5 years; 76.7% male). The median regorafenib treatment duration was 4.0 months (95% confidence intervals [CI], 3.6–4.6). The most frequently reported adverse events were hand-foot skin reaction (44.2%), diarrhea (36.0%), and fatigue (29.1%). No unpredictable toxicity was observed during treatment. The median overall survival (OS) with regorafenib was 12.4 months (95% CI, 7.8–17.0), and the median progression-free survival (PFS) was 4.2 months (95% CI, 3.7–4.7). Of 82 patients with regorafenib responses assessable, 4 patients (4.9%) achieved a partial response, and 33 (40.2%) had stable disease, leading to a disease control rate (DCR) of 45.1% (n = 37). Patients possessing baseline AFP < 400 ng/mL exhibited a markedly longer median OS, median PFS, and higher DCR compared with their counterparts (15.7 vs. 8.1 months, 4.6 vs. 3.7 months, 60.9% vs. 27.5%, respectively). Despite possessing high baseline AFP levels, patients with early AFP response (> 10% reduction at 4 weeks or > 20% reduction at 8 weeks after regorafenib administration) exhibited comparable treatment outcomes to those with baseline AFP < 400 ng/mL.

Conclusion: The results of this real-world study verified the tolerability and efficacy of regorafenib treatment for uHCC patients who failed prior sorafenib therapy, especially for those with lower baseline AFP levels or with early AFP response.

[OP-0585]

Stereotactic body radiation therapy for pulmonary oligometastasis from hepatocellular carcinoma

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Objectives: Stereotactic body radiation therapy (SBRT) has been used for many localized primary or metastatic tumors throughout the whole body. The purpose of this study was to investigate the efficacy and safety of SBRT for pulmonary oligometastasis from hepatocellular carcinoma (HCC).

Materials and Methods: Between January 2008 and December 2018, the patients with pulmonary metachronous oligometastasis from HCC who underwent SBRT as a first-line treatment were reviewed retrospectively. The inclusion criteria were as follows: patients aged 20 years or older with controlled and/or stable intrahepatic tumor

burden after various liver-directed locoregional therapies; one to five pulmonary metastatic lesions; no extrahepatic metastasis other than the lungs; a Child–Pugh class A or B hepatic function; an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 – 2; and no previous history of liver transplantation.
Results: A total of 60 patients (82 metastatic lung lesions) were included in this study. Fifty (83.3%) patients were male with a median age of 60 years (range, 33–77). The median tumor size of pulmonary metastatic nodule was 1.1 cm (range, 0.5 – 3.5). A total dose of 48 – 60 Gy was delivered with the fraction size of 10 – 20 Gy. The median follow-up period of all patients was 28.1 months. The 2- and 5-year overall survival rates were 58.3% and 27.8%, respectively. The 5-year freedom from local progression was 91.6%. The 2- and 5-year freedom from overt systemic progression were 47.1% and 33.1%, respectively. Multivariate analysis revealed that ECOG performances status, the number of prior liver-directed treatments, intrahepatic disease status, and alpha-fetoprotein level were significantly associated with overall survival rates. No grade ≥ 3 late toxicity was observed.
Conclusion: SBRT showed excellent results as an ablative treatment for pulmonary oligometastasis from HCC while showing minimal toxicities. SBRT can be a good first-line treatment option in patients with pulmonary oligometastasis from HCC.

[OP-0591]

Exploring the tumor microenvironment transition in hepatocellular carcinoma

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Objectives: The combination of atezolizumab and bevacizumab has become a standard treatment for advanced hepatocellular carcinoma (HCC). Although exploring tumor microenvironment has essential clinical implications, most of the studies on tumor microenvironment in HCC are based on the analysis of archive samples at the time of diagnosis as HCC. Considering a lengthy clinical course, tumor microenvironment at the time of diagnosis may differ from that at the time of systemic therapy indication. The present study aimed to assess the changes in the tumor microenvironment during the evolution to advanced HCC using archival samples and samples obtained prior to systemic therapy from the same patients.
Materials and Methods: The tumor microenvironment was compared in 20 cases by immunohistochemical analyses of CD8 and PD-L1 expression. Of the 20 cases, gene expression analysis was performed by the PanCancer IO360^{TM} Panel in 13 cases.
Results: Approximately 40% of the archived samples were obtained at the early stage. Comparison of the tumor microenvironment between the two time points showed that 35% of the patients changed to CD8-positive lymphocyte high infiltration, 20% to positive PD-L1 expression. The result of comparing gene profile was different between the archival samples and those prior to systemic therapy in 69% of the patients on the expression heat map. Immune subtype changed to inflamed over time in 23% of the patients.
Conclusion: The tumor microenvironment might not be constant, but may change during the evolution to advanced HCC.

[PP-0595]

Tenofovir alafenamide used for HBV reactivation in patients of HBV-related hepatocellular carcinoma–preliminary results

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Objectives: Entecavir (ETV) is the most commonly used antiviral medicine in China. Most HBV-related Hepatocellular carcinoma (HCC) patients who received ETV antiviral treatment maintain serum HBV DNA undetectable. However, some of them will develop HBV reactivation. Salvage antiviral treatment of HBV reactivation and the treatment efficacy requires further study.
Materials and Methods: We screened HBV-related HCC inpatients admitted in our hospital from March to July 2021, and those who developed HBV reactivation were included. Inclusion criteria: 1. ETV was used for at least 6 months, and HBV-DNA was undetectable before the admission, 2. HBV reactivation was detected (defined as ≥ 1 log increase of HBV-DNA). The patients were randomly assigned into two groups: switching to TAF or adding on TAF. The patients were followed up for 3 months.
Results: A total of 665 patients with HBV-related HCC were screened, and 48 cases were found HBV reactivation (7.2%). 31 patients were excluded because of lost-follow-up. 17 patients were enrolled in the cohort (14 males and 3 females, mean age 57.4 ± 7.7 years) and randomly assigned into TAF group (group A, $n = 9$) and ETV plus TAF group (group B, $n = 8$). There was no significant difference in HBV-DNA level, ALT level and Child–Pugh classification between the two groups ($p = 0.149$, 0.469, 0.670, respectively). After 3 months, 5 patients in group A and 3 patients in group B achieved HBV-DNA undetectable. ALT level decreased in both groups, and serum creatinine value and Child–Pugh score remained stable. One patient in each group developed obstructive jaundice caused by tumor progression during follow-up. No death event occurred.
Conclusion: TAF is an alternative, either used alone or in combination with ETV, for HCC patients with HBV reactivation treated

with ETV. Larger sample size and longer term of follow-up are required in further study to demonstrate differences and effectiveness of the salvage treatments.

Table Clinical characteristics, biological and viral responses of the patients

	Total (n = 17)	Group A (n = 9)	Group B (n = 8)	p
age, y(Mean ± SD)	57.4 ± 7.7	57.4 ± 9.2	57.2 ± 6.1	0.96
BCLC stage, n(%)				0.762
Early (A)	5(29.4)	2(22.2)	3(37.5)	
Intermediate (B)	2(11.8)	1(11.1)	1(12.5)	
Advanced (C)	10(58.8)	6(66.7)	4(50.0)	
HBVDNA△, IU/mL[Median (IQR)]	197 (149, 2910)	249 (197, 3200)	159 (127, 873)	0.149
HBVDNA▲, IU/mL[Median (IQR)]	33 (20, 142)	20 (20, 620)	69 (20, 120)	0.879
HBV DNA<20IU/mL▲, n (%)	8 (47.1)	5 (55.6)	3 (37.5)	0.637
HCC progress▲, n (%)	7 (41.2)	4 (44.4)	3 (37.5)	0.579
Child score△, n (%)				0.67
A	11 (64.7)	7 (77.8)	4 (50)	
B	6 (35.3)	2 (22.2)	4 (50)	
Child score▲, n (%)				0.153
A	10 (58.8)	7 (77.8)	3 (37.5)	
B	7 (41.2)	2 (22.2)	5 (62.5)	
ALT△, U/L[Median (IQR)]	24.0 (22.0, 39.0)	24.0 (14.0, 27.0)	27.0 (22.8, 60.5)	0.469
ALT▲, U/L[Median (IQR)]	22.0 (19.0, 29.0)	20.0 (19.0, 26.0)	26.5 (20.2, 30.0)	0.531
CRE△, umol/L(Mean ± SD)	62.0 ± 12.6	62.7 ± 10.6	61.2 ± 15.3	0.826
CRE▲, umol/L(Mean ± SD)	64.3 ± 12.8	63.0 ± 10.2	65.8 ± 15.8	0.672

Notes: △time point of HBV reactivation, ▲time point of 3 months after switch or add-on TAF; HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; CRE, creatinine.

[PP-0599]

Epidemiological and clinical manifestation of hepatocellular carcinoma in patients Mongolia and Russia

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Objectives: The current study is aimed at determining differences of epidemiological and clinical profiles associated with HCC in patients belonging to ethnic groups of Asians from Mongolia and Caucasians from Asian region of Russia.
Materials and Methods: The studies were carried out in the cross-border regions of Mongolia and Asian part of Russia (Irkutsk region). 300 patients with hepatocellular carcinoma (HCC) of the Caucasian and Mongolian races were enrolled in the study. The level of alpha-fetoprotein (AFP) in the serum was determined by the chemiluminescence technique.
Results: The long-term dynamics of the HCC incidence shows more unfavourable trends in the territory of Mongolia compared to Irkutsk region. In both groups, male patients over 60 years of age predominated. Patients from Mongolia often have a history of jaundice and alcohol abuse. Out of the etiological factors, HCC is more often associated with the hepatitis B virus in Mongolia than in the Asian part of Russia. At the same time, in Caucasians, HCC develops primarily on the background of liver cirrhosis. In patients with HCC, AFP level higher than 20 ng/ml were significantly more frequent in the ethnic group of Caucasoids than in Mongoloids.
Conclusion: Mongolia in terms of the incidence of HCC belongs to the hyperendemic regions of the world. In this country, among the risk factors for the development of the disease, hepatitis B virus plays a major role, which significantly differs from the Asian part of Russia. For the purpose of early diagnosis of HCC, it is necessary to search for new molecular markers or their combinations due to the insufficient diagnostic efficiency of AFP determination.

[OP-0608]

Systemic prognostic score based on artificial neural network in hepatocellular carcinoma: A long term follow-up analysis

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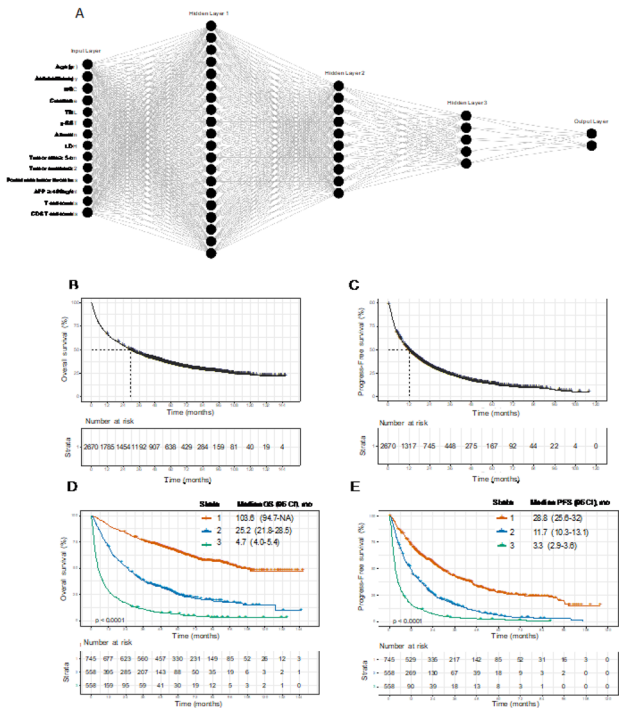
Objectives: T cell immunity plays a critical role in the anti-tumor effect, and immunosuppression promotes the occurrence and progress of hepatocellular carcinoma (HCC). This study was to investigate the effect of T cell number on the long-term prognosis of HCC patients, and to construct an artificial neural network models (ANNs) to evaluate its prognostic value.
Materials and Methods: We enrolled 2670 HCC patients in Beijing Ditan Hospital, Capital Medical University, and randomly divided them into two groups. Cox univariate analysis and multivariate analysis were used to screen the independent risk factors affecting the survival of HCC patients. These factors are used to build ANNs model with Python programming language.
Results: The median overall survival (OS) was 29.3 months (95% CI: 27.3–31.9). The 1-year, 3-year and 5-year cumulative OS were 66.9%, 45.7% and 34.9% respectively. The ANNs model including T cell count and CD8 T cell counts for long-term survival was constructed. The area under the ROC curve (AUC) of 1-year, 3-year and 5-year OS predicted by ANNs were 0.838, 0.833 and 0.843, respectively; which were higher when compared with BCLC, TNM, Okuda, CUPI, CLIP, JIS and ALBI models ($P < 0.0001$). According to the scores of ANNs model, all patients were divided into high-, middle-, and low-risk groups. Compared with low-risk patients, the hazard ratios (HRs) of 5-year OS of high-risk group were 8.11 (95% CI: 7.0–9.4; 95% CI: 7.0–9.4), 6.13 (95%CI 4.28–8.79; $P < 0.0001$) in training set and validation set, respectively.
Conclusion: High levels of circulating T cells and $CD8^+$ T cells in peripheral blood may benefit the long-term survival of HCC patients. ANNs model has good individual prediction performance, which can be contribute to assess the prognosis of HCC patients and lay the foundation for the implementation of precision treatment in the future.



[OP-0610]

Effects of CRP and triglycerides on short-term and long-term prognosis of primary liver cancer

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Objectives: We aim to analyze and compare clinical markers and outcomes among primary liver cancer patients, and to identify risk factors among commonly used clinical markers that affect short-term and long-term prognosis for clinical guidance.
Materials and Methods: A total of 3180 newly diagnosed primary liver cancer patients from the Beijing Ditan Hospital Capital Medical University from June 2008 to June 2017 that fulfilled the enrollment criteria were enrolled in the study. We followed-up with the patients and assessed their outcomes. Demographic characteristics and relevant clinical markers of the patients were collected. SPSS 20.0 software was used for descriptive analysis of age, gender, and laboratory markers of patients. COX regression analysis was used to screen for independent risk factors of mortality in patients.
Results: 1. COX regression analysis revealed that among the common independent risk factors that affect the 1-year survival, 1-year recurrence, and 5-year survival for primary liver cancer patients, C-reactive protein (CRP) had the highest hazard ratio (HR). The HR and 95% confidence interval (CI) of CRP are 6.704 (5.275 8.520), 2.562 (2.060 3.186), and 2.593 (2.263, 2.972) for 1-yr survival, 1-yr recurrence and 5-yr survival, respectively. In addition, CRP is also a predictor for prognosis in different subgroups of primary liver cancer patients. 2. Triglyceride (TG) concentrations greater than 1.71 mmol/L (TG > 1.71 mmol/L) are a common independent protective factor for 1-year survival, 1-year recurrence, and 5-year survival for primary liver cancer patients.
Conclusion: 1. CRP was a risk factor for short-term and long-term prognosis in primary liver cancer and affects patient subgroups differently. 2. TG level > 1.71 mmol/L was a favorable factor for short-term and long-term prognosis in primary liver cancer.

Table 1. COX regression analysis of 1-year mortality in PLC patients

Variables	Univariate analysis			Multivariate analysis		
	HR	95%CI	*P values*	HR	95%CI	*P values*
Gender	1.234	1.015-1.462	0.014			
Age	0.869	0.745-1.014	0.074			
History of smoking	1.234	1.078-1.413	0.002			
History of alcohol use	1.365	1.192-1.563	<0.0001			
Diabetes	0.873	0.736-1.035	0.119			
Hypertension	0.812	0.691-0.953	0.011			
Hepatitis B	1.013	0.854-1.202	0.879			
Hepatitis C	0.682	0.524-0.887	0.004			
Alcoholic liver disease	1.466	1.201-1.79	<0.0001			
Child-Pugh class	2.049	1.877-2.236	<0.0001			
BCLC staging	2.011	1.896-2.134	<0.0001	1.274	1.165-1.393	<0.0001
multiple tumors	2.304	2.003-2.649	<0.0001	1.367	1.168-1.598	<0.0001
Tumor size≥5cm	1.948	1.817-2.088	<0.0001	1.236	1.146-1.334	<0.0001
Treatment method	0.309	0.272-0.351	<0.000	0.550	0.476-0.636	<0.0001
Cirrhosis	0.613	0.455-0.825	0.001			
WBC>4 (*10⁹/L)	1.549	1.343-1.786	<0.0001			
N/L>2.74	2.486	2.166-2.853	<0.0001	1.264	1.08-1.48	0.004
HGB≥120 (g/L)	0.613	0.536-0.702	<0.0001			
PLT≥100 (*10⁹/L)	1.266	1.107-1.449	<0.0001			
CRP>5 (mg/L)	15.656	12.76-19.21	<0.0001	6.704	5.275-8.52	<0.0001
Cr>97 (μmol/L)	2.037	1.663-2.495	<0.0001			
AST>40 (U/L)	3.272	2.805-3.816	<0.0001			
TBIL>18.8 (μmol/L)	2.292	1.989-2.641	<0.0001	1.214	1.017-1.45	0.032
ALB≥35 (g/L)	0.422	0.367-0.486	<0.0001			
A/G≥1	0.425	0.371-0.487	<0.0001			
LDH>250 (U/L)	2.699	2.29-3.181	<0.0001	1.258	1.04-1.52	0.017
r-GGT>60 (U/L)	4.052	3.473-4.728	<0.0001	1.717	1.432-2.059	<0.0001
TG>1.71 (mmol/L)	0.204	0.148-0.282	<0.0001	0.336	0.236-0.478	<0.0001
PTA≥70 (%)	0.554	0.484-0.634	<0.0001			
AFP (>350 ng/ml)	3.387	2.956-3.881	<0.0001	1.778	1.515-2.087	<0.0001

[OP-0612]

Analysis of the efficacy and superiority of TCM treatment for HBV-related HCC and comorbid CRA

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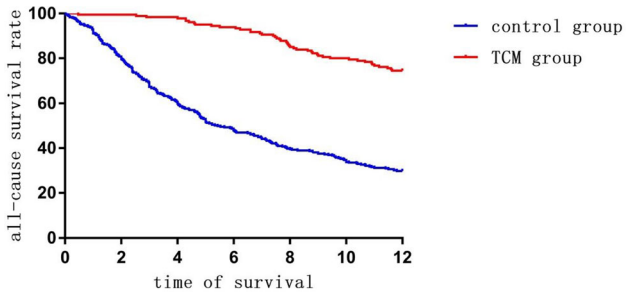
Objectives: To analyze the independent risk factors that influence the prognosis of patients with comorbid hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) and cancer-related anemia (CRA); to further explore the effect of traditional Chinese medicine (TCM) on the prognosis of patients; and to analyze the optimal patient population that will benefit from TCM to guide clinical treatment.
Materials and Methods: A sample set of 532 patients who were first diagnosed with comorbid HBV-related HCC and CRA from June 2008 to June 2017 in the Beijing Ditan Hospital was analyzed: 181 patients were treated with TCM, and 351 patients were not treated. Patient survival was followed up, and demographic characteristics and relevant clinical indicators were collected. SPSS 20.0 software

was used to perform the analysis; protective factors for patient survival were screened by COX regression analysis, and survival analysis of patients from different groups was performed.
Results: Statistical analysis showed that the Barcelona clinic liver cancer (BCLC) stage, platelet (PLT) count, alpha-fetoprotein (AFP) level, the use of TCM, and hepatitis B virus DNA (HBVDNA) levels are all independent risk factors for the 1-year survival rate of patients with comorbid HBV-related HCC and CRA. The use of TCM conferred a protective effect on patients' prognosis, and prognosis was better for patients receiving long-term medication. The efficacy of TCM is better in patients with low CRP and AFP levels.
Conclusion: TCM exerted protective effects in patients with HBV-related HCC and comorbid CRA, and survival was positively correlated with the duration of medication. The effect of TCM was stronger in patients with low CRP and AFP levels.



[OP-0613]

Exploring the effect and mechanism of Yiqi Liangxue detoxification formula on precancerous lesions in the liver by the canonical Wnt pathway

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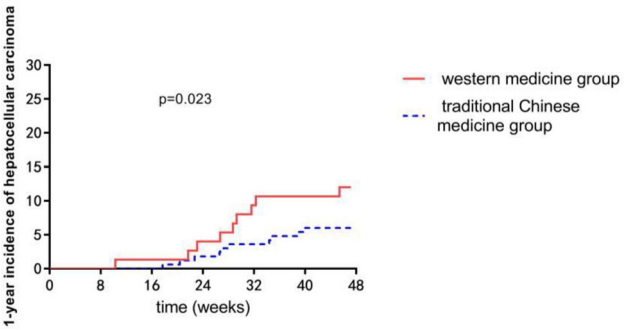
Objectives: To determine the therapeutic efficacy of Yiqi Liangxue detoxification formula in clinical patients with precancerous liver lesions and to explore and validate its possible effector mechanism.
Materials and Methods: First, data from 241 patients with cirrhosis and abnormal alpha-fetoprotein (AFP) at Beijing Ditan Hospital from 2015 to 2020 were collected and divided into the traditional Chinese medicine group (Yiqi Liangxue detoxification formula group) and Western medicine group according to the treatment modality. The 1-year incidence of hepatocellular carcinoma was also assessed and immunohistochemical assays were performed using samples from 17 hepatocellular carcinoma patients to: compare the expression of Wnt1 and β-catenin in hepatocellular carcinoma and paracancerous tissues; and to evaluate the role of the canonical Wnt pathway in the development of hepatocellular carcinoma to ultimately explore the possible effector mechanism of Yiqi Liangxue detoxification formula. Finally, a rat precancerous lesion model was established and Yiqi Liangxue detoxification Formula was administered to the model group. The differences in Wnt1 and β-catenin expression levels among the blank control group, model group, and intervention group were determined to verify the effector mechanism of Yiqi Liangxue detoxification Formula.
Results: The 1-year incidence of hepatocellular carcinoma in the traditional Chinese medicine group was lower than that in the Western medicine group, and the canonical Wnt pathway was aberrantly overexpressed in human hepatocellular carcinoma tissues. In rat liver tissues, the aberrantly overexpressed canonical Wnt pathway was significantly downregulated after treatment with the Yiqi Liangxue detoxification formula.
Conclusion: The Yiqi Liangxue detoxification formula can reduce the 1-year incidence of hepatocellular carcinoma in patients with clinical precancerous liver lesions. Further, the effector mechanism of this formula is related to the downregulation of the canonical Wnt pathway.



[OP-0627]

Superiority of laparoscopic radiofrequency ablation over percutaneous radiofrequency ablation for recurrence and overall survival in hepatocellular carcinoma

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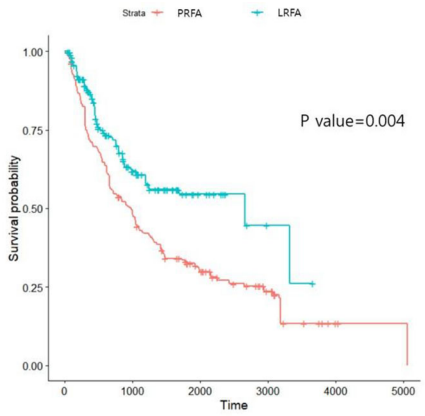
Objectives: Laparoscopic radiofrequency ablation (LRFA) has several advantages over percutaneous radiofrequency ablation (PRFA) for the treatment of patients with hepatocellular carcinoma (HCC), in terms of access to lesions or detection of tiny tumors. However, there are few studies that compared the therapeutic outcomes between HCC patients underwent LRFA and PRFA. We conducted this study to compare the recurrence and survival outcomes of two RFA methods in patients with HCC.
Materials and Methods: Of patients who underwent RFA at Chungnam National University Hospital between April 2005 and August 2020, 307 patients who underwent LRFA (n = 151) or PRFA

(n = 156) as a treatment method for de novo HCC were analyzed in terms of recurrence and survival outcomes.
Results: There were no significant differences in major baseline characteristics between two groups. However, the proportion of cirrhotic patients was higher in the LRFA group (p = 0.002), and the LRFA group had more tumor and far advanced TNM stage compared with the PRFA group (both, $p < 0.001$). Moreover, mean tumor size was significantly larger in the LRFA group (mean; 1.73 cm) than the PRFA groups (mean; 1.59 cm) (p = 0.038). In a multivariable analysis, serum albumin level (HR; 0.47, $p < 0.001$), tumors more than three (HR; 3.43, p = 0.011), and RFA method (LRFA/PRFA HR; 0.57, p = 0.002) were identified as being significant predictors of recurrence-free survival. Moreover, for overall survival of HCC patients, serum albumin level (HR; 0.22, $p < 0.001$), days of hospital stay during RFA (HR; 1.03, p = 0.016), and RFA method (HR; 0.38, p = 0.012) were independent predictors. In IPTW-adjusted analysis, the LRFA group showed significantly longer recurrence-free survival (p = 0.004) and overall survival (p = 0.005).
Conclusion: Our study revealed that LRFA was associated with longer recurrence-free survival and favorable overall survival compared with PRFA in patients with HCC. Therefore, LRFA should be considered the primary therapy in patients with HCC eligible for RFA, especially tumors more than three.



Survival curves comparing the cumulative recurrence-free survival rates between patients who underwent laparoscopic radiofrequency ablation and those who underwent percutaneous radiofrequency ablation for de novo hepatocellular carcinoma (p=0.004)

[PP-0629]

Major signaling pathways in 195 HCC samples including multiple occurence

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Objectives: Genetic analysis has revealed abnormalities in intracellular signaling pathways in hepatocellular carcinoma (HCC), and signaling pathway-oriented therapies are getting important. We performed targeted sequencing to identify gene alterations and dysregulated pathways in HCC. and we searched for drug-matched alterations.
Materials and Methods: 90 patients, 163 nodules and 195 samples were collected. DNA was extracted from tumor FFPE (Formalin-fixed paraffin embedded) tissues by laser capture microdissection (LCM). Next generation sequencing was performed using the HCC Comprehensive Panel (72SMGs: 59,016 aa), which contains genes involved in the Wnt/βcatenin pathway, TP53/cell cycle pathway, PIK3CA/RAS pathway, Chromatin Remodeling pathway, and Oxidative Stress pathway, which are major pathways in hepatocarcinogenesis. Oncogenisity and drug-matched alternation were confirmed using the OncoKB database (https://www.oncokb.org/).
Results: Oncogenic variants were found in 36 nodes (28%) of the Wnt/βcatenin pathway, 54 nodules (42%) of the TP53/cell cycle pathway, 9 nodules (7%) of the PIK3CA/RAS pathway, 24 nodules (19%) of the Chromatin Remodeling pathway, and 5 nodules (4%) of the Oxidative Stress pathway. Drug-matched variants were found in 8 genes in 21 patients (23%) and 26 nodes in 28 samples. 11 patients with multiple HCC did not share the drug matched alternation, as each tumor had a different genetic profile.
Conclusion: The TP53/cell cycle pathway and Wnt/βcatenin pathway were the major pathways in HCC. Drug-matched variants are different for each tumor in multiple HCC cases, and genetic analysis for each tumor is necessary for precision therapy.

[OP-0630]

A competing risk nomogram predicting hepatocellular carcinoma on antivirals for hepatitis B-caused cirrhosis

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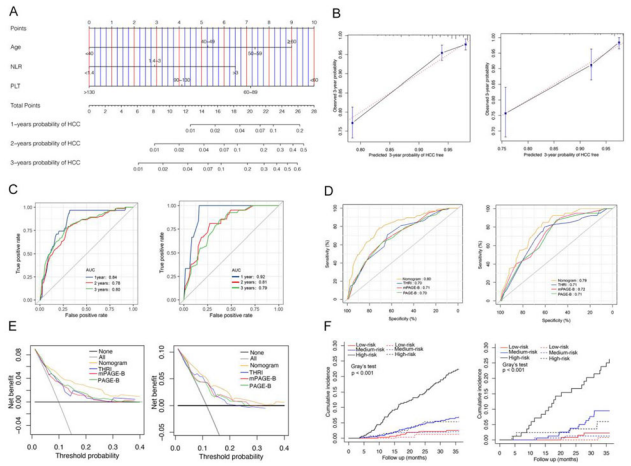
Objectives: The risk of hepatocellular carcinoma (HCC) varies among cirrhotic patients. We aimed to develop and validate a nomogram to estimate HCC risk in Chinese patients with hepatitis B-caused cirrhosis (HBC).
Materials and Methods: A total of 1291 patients with HBC receiving entecavir or tenofovir at Beijing Ditan Hospital between January 2013 and July 2017 were recruited. The cumulative incidence function was used with Gray's test to assess the 3-year probabilities of HCC and mortality. The Fine and Gray's proportional subdistribution hazard approach was utilized to perform multivariable competing risk analyses and a nomogram was developed. The discrimination and clinical usefulness of the nomogram were assessed by time-dependent area under the receiver operating characteristic (AUC) curve and decision curve. The model was validated in an external cohort of 374 patients.
Results: The 3-year cumulative incidence rates of HCC and mortality were 9.6% and 2.7% in the derivation cohort and 10.7% and 2.1% in the validation cohort. The competing risk nomogram included three risk factors (age, platelets, and neutrophil–lymphocyte ratio

[NLR]). The calibration plots indicated the nomogram had good agreement between the predicted and the observed probability. The time-dependent AUCs for HCC in the derivation cohort were 0.84, 0.78, and 0.80 at the 1-, 2-, and 3-year, respectively. This nomogram demonstrated significantly better performance than other models in the derivation and validation cohorts (all $p < 0.05$). The decision curve illustrated that the nomogram had high standardized net benefit. Patients with a score less than 9.5 or 17.8 points or greater were exposed to low or high risk of HCC, respectively.

Conclusion: The competing risk nomogram is a reliable score for predicting HCC risk in patients with HBC on antivirals.



[OP-0637]

Second-line therapy for advanced hepatocellular carcinoma with regorafenib or cabozantinib. Multicenter French clinical experience of real-life after matching

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Objectives: Primary: to evaluate the progression-free survival (PFS) of patients treated in second-line with REG or CBZ; Secondary: disease control rate (DCR), overall survival (OS), and safety; to identify the variables associated with disease progression during the first 6 months.

Materials and Methods: Retrospective multicenter comparative study (01/2017–03/2021) with matching (BCLC, Child–Pugh (CP), Vascular invasion (MVI), Metastasis, AFP) by propensity score method. PFS, OS by Kaplan–Meier method. Multivariate analysis (MA) of progression risk factors over time.

Results: 58 patients 68 (62–74) years with HCC, BCLC B/C (86%, MVI 51%), CP-A/B (24%) received REG for 3.4 (1.4–10.5) months as second-line therapy. 28 patients 68 (60–73) years, BCLC B/C (75%, MVI 46%), CP-A/B (25%) received CBZ for 3.7 (1.8–4.9) months, after a first-line with sorafenib (3 (2–4) (CBZ) vs. 4 (2.9–11.8) months (REG), p = 0.0226). 20% of patients received a third-line therapy. After matching, there were 28 patients in each group. PFS was not significantly different (p = 0.3289), nor was the DCR after a median follow-up period of 7.4 (2.6–15.0) (REG) vs 5.2 (4.1–9.4) months (CBZ), p = 0.6836. The mortality rate was higher in the REG group (p = 0.02), as CBZ initiation was more recent. CP-A patient's OS was 8.3 (5.2–24.8) vs. 4.9 (1.6–11.7) months (CP-B) (p = 0.0468). There was no difference in grade 3/4 toxicities, dose reductions, interruptions. MA of risk factors for progression over time identified CRP > 10 mg/L, Neutrophil/Lymphocyte ratio (NLR) > 3, AST > 45 IU as predictive factors. From this analysis, a 2-month progression risk calculation is proposed.

Conclusion: This multicenter indirect comparative study found no significant difference in PFS between regorafenib and cabozantinib as second-line therapy for advanced HCC. Most patients did not have a controlled disease at the end of follow-up. Raised inflammatory markers (CRP, NLR) and AST are associated with non-control on TKIs over time. We propose a simple online score assessing the risk of progression based on these variables.

HCC-RECA Score : Second-Line Systemic Treatment with TKI
(<0.15: Very Low Risk ; 0.15-0.40: Low risk: 0.40-0.60: Moderate Risk; >0.60: High Risk)

https://jscalc.io/calc/3nzmguiJK5QIn8eQ#%7B%221%22:null,%222%22:null,%223%22:null%7D

[PP-0650]

Impact of myosteatosis and visceral adiposity on mortality in patients with hepatocellular carcinoma treated with sorafenib

Min Kyu Kang[1], Yu Rim Lee[2], Jae Young Jang[2], Jeung Eun Song[3], Young Oh Kweon[2], Won Young Tak[2], Se Young Jang[2], Changhyeong Lee[3], Byung Seok Kim[3], Jae Seok Hwang[4], Woo Jin Chung[4], Byoung Kuk Jang[4], Jeong Ill Suh[5], Jung Gil Park[1], Soo Young Park[2]

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Objectives: Recently, low skeletal muscle mass is significant predictor of mortality in patients with hepatocellular carcinoma (HCC). However, the role of myosteatosis and visceral adiposity in patients with HCC is not well understood. This study aimed to evaluate the association between body composition and mortality in patients with HCC treated with sorafenib.

Materials and Methods: From 2008 to 2019, this multicenter, retrospective study included patients with advanced HCC who treated with sorafenib. Body composition parameters including adipose, skeletal muscle tissue, and myosteatosis were measured using the cross-sectional CT images at the level of L3 vertebra. Visceral adipose tissue index (VATI) and skeletal muscle index (SMI) are defined as the body composition area (cm^2) by height squared (m^2). Myosteatosis is defined as mean muscle attenuations values using Hounsfield units (HU).

Results: Of the total 245 patients, 168 (68.6%) died. The non-survival group had higher VATI levels (32.6 vs. 45.7 cm^2/m^2, p = 0.005) and lower HU levels (53.3 vs. 51.0 HU; p = 0.023) than the survival group. By multivariate Cox regression analysis, age (hazard ratio (HR), 0.98, 95% confidence interval (CI), 0.97–1.00; p = 0.018), history of previous treatment (HR, 0.55; 95% CI, 0.40–0.76; $p < 0.001$), albumin (HR, 0.59; 95% CI, 0.42–0.80; $p < 0.001$),

presence of visceral adiposity (HR, 2.25; 95% CI, 1.49–3.42; p = 0.001), and presence of myosteatosis (HR, 2.21; 95% CI, 1.53–3.19; p < 0.001) were independently associated with mortality in patients with HCC treated with sorafenib.
Conclusion: Visceral adiposity and myosteatosis may be associated with mortality in patients with HCC treated with sorafenib.

Table 1. Factors associated with overall survival by multivariate Cox analysis in HCC patients treated with sorafenib

Variable	Univariate	Multivariate analysis	
	P value*	*P* value*	Hazard ratio (95% CI)
Age, years	0.148	0.018	0.982 (0.967-0.997)
Male, yes/no	0.955		
BMI, kg/m^2	0.588		
Diabetes, yes/no	0.654		
Hypertension, yes/no	0.905		
Largest tumor diameter, mm	<0.001		
Vessel invasion, yes/no	<0.001		
Extrahepatic metastasis, yes/no	0.698		
Previous treatment history, yes/no	<0.001	<0.001	0.552 (0.400-0.761)
AST, IU/L	<0.001	0.004	1.003 (1.001-1.005)
ALT, IU/L	0.453		
Total bilirubin, mg/dL	0.001		
Albumin, g/dL	0.003	<0.001	0.583 (0.424-0.801)
Total bilirubin, mg/dL	0.831		
Platelet count, 10^9/L	0.224		
Prothrombin time, INR	0.866		
AFP, ng/mL	<0.001	<0.001	1.002 (1.001-1.005)
Creatinine, mg/dL	0.804		
Sarcopenia, yes/no	0.245		
VATI, high/low	0.006	<0.001	2.253 (1.485-3.416)
SATI, high/low	0.146		
Myosteatosis, yes/no	0.008	<0.001	2.210 (1.533-3.185)

*Calculated by Cox proportional hazards regression test

BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AFP, alpha fetoprotein; VATI, visceral adipose tissue index; SATI, subcutaneous adipose tissue index.

[PP-0686]

The clinical usefulness of PIVKA-II as biomarker for prognosis in patients with localized hepatocellular carcinoma receiving stereotactic body radiotherapy

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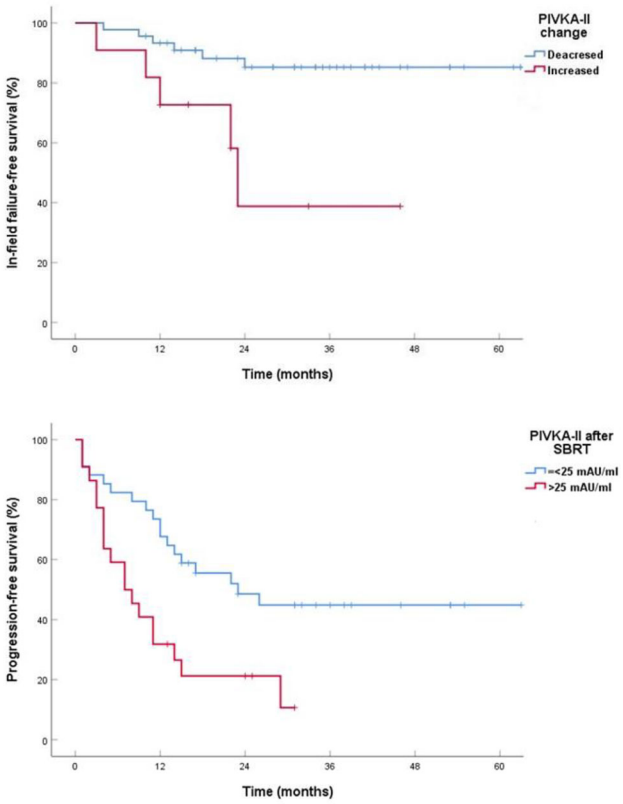
Objectives: This study aimed to determine the correlation between protein induced by vitamin K absence or antagonist-II (PIVKA-II) and stereotactic body radiotherapy (SBRT) in patients with hepatocellular carcinoma (HCC).
Materials and Methods: Patients with an Eastern Cooperative Oncology Group performance score of ≤ 2, preserved liver function of Child–Pugh score (CPS) 5 to 7, and no prior history of radiotherapy were included. Exclusion criteria were as follows: presence of an extrahepatic metastatic lesion, a history of other malignancies, no regular imaging follow-up after SBRT, and other locoregional therapy within 6 months after SBRT without any sign of disease progression. Sixty-one patients received SBRT between 2015 and 2020 with a median dose of 48 Gy (range, 39–60 Gy) with a median of 4 fractions. Changes in tumor markers before and after SBRT were analyzed.
Results: The median follow-up period was 31 months (range, 12–64 months). The estimated 2-year in-field failure-free survival, progression-free survival (PFS), and overall survival rates were 82.0%, 39.3%, and 96.7%, respectively. In univariate analysis, patients with decreased PIVKA-II levels through SBRT had significantly fewer in-field failures (p = 0.005). Patients with PIVKA-II levels of ≤ 25 mAU/ml after SBRT had significantly longer PFS (p = 0.004). In multivariate analysis, a decreased change in PIVKA-II level after SBRT was significantly associated with IFFS (p = 0.011), and a PIVKA-II level of ≤ 25 mAU/ml after SBRT was significantly associated with a good PFS (p = 0.006).
Conclusion: Patients with a decreased change or a lower level of PIVKA-II after SBRT showed good tumor control and survival. PIVKA-II could be a useful surrogate marker for response or survival outcomes in patients with localized HCC receiving SBRT.



[PP-0694]

A comparative study for repeated transarterial chemoembolization therapy with palliative therapy following incomplete lipiodolized tumor during transarterial chemoembolization therapy for hepatocellular carcinoma

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Objectives: It has been remained uncertain whether repeated transarterial chemoembolization (TACE) therapy for the patients with incomplete lipiodolization after TACE on hepatocellular carcinoma is associated with improved overall survival of the patients. The aim of study is to investigate of the comparative clinical overall survival analysis for the repeated TACE with the palliative therapy on incomplete lipiodolized HCC tumor.
Materials and Methods: Incomplete lipiodolization of the tumor was defined as the presence of an arterial enhancing lesion, as assessed by

dynamic CT or MRI 1 to 3 months for the first time after treatment. The patient enrolled when incomplete lipiodolization was confirmed on imaging study.
Results: Baseline characteristics were analyzed between two groups that the patients received TACE alone (n = 45) or TACE with other treatment modalities (n = 16) and the patients received palliative care alone (n = 32) or palliative care with systemic chemotherapy (n = 3). As a result, there were no significant differences except minor differences in age. Especially, there is no significant difference of overall survival for incomplete lipiodolized HCC between repeated TACE therapy group (1175.1 days, 95% C.I.:971.1 ∼ 1379.2) and palliative therapy group (1021.5 days, 95% C.I.:797.2 ∼ 1245.7) on Kaplan–Meier analysis (p = 0.217). The 2- and 4-year survival rates of patients received palliative therapy were 71.8% and 47.9% compared to 74.8% and 42.5% in patients received repeated TACE. Furthermore, on subgroup analysis between the repeated TACE alone (n = 45) group and best supportive care alone group (n = 32), there was no significant difference for all of the baseline characteristics. A further important consideration is that there is no significant difference of overall survival between the patients received repeated TACE alone (1086.6 days, 95% C.I.:870.7 ∼ 1032.6) and the patients received palliative care alone (1071.8 days, 95% C.I.:836.9 ∼ 1306.7) on Kaplan–Meier Estimates (p = 0.576).
Conclusion: In our study, on treatment of incomplete lipiodolized HCC, repeated TACE therapy does not contribute to overall survival compared with palliative care.

[OP-0706]

Perspectives in Japanese cancer registry regarding the prognosis of hepatocellular carcinoma after the confirmation of overall survival and death; Fixed point observation over 15 years

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Objectives: The purpose of this study was to examine whether the prognosis of liver cancer has improved since the introduction of Sorafenib, in order to discuss the new treatment of advanced liver cancer in the era of combined immunotherapy.
Materials and Methods: Of the 16,181 cases of all cancers registered during the 9-year period from 2007 to 2015, 516 cases of liver cancer were included in the analysis. All cases were classified by UICC (Union for International Cancer Control) stage according to tumor factors at the time of carcinogenesis. 214 cases of UICC Stage I, 126 cases of Stage II, 110 cases of Stage III, and 66 cases of Stage IV were registered. The cancer registration period was divided into three periods: Period I, 2007–2009 (167 cases); Period II, 2010–2012 (209 cases); and Period III, 2013–2015 (140 cases), and the overall survival of each stage was compared.
Results: The Median Survival Time (MST) for UICC Stage I (IA + IB) was 75.6 months for Period I, 45.6 months for Period II, and 57.6 months for Period III. The MST for Stage II was 42.0 months for Period I, 22.8 months for Period II, and 27.6 months for Period III. The MST of Stage IV was 2.4 months in Period I, 1.8 months in Period II, and 4.8 months in Period III. Although the number of patients varied, the prognosis for Stage IV was grim even with the advent of molecular targeted drugs.
Conclusion: Since the introduction of Sorafenib, several drugs has been shown to improve the overall survivals in phase 3 trials. However, the prognosis of hepatocellular carcinoma did not improve when observed from this perspective of cancer registry. Now, we have entered the era of combined immunotherapy, further discussion is needed on how to improve the prognosis of hepatocellular carcinoma in the future.

[PP-0716]

Laparoscopic surgery is the third, but could be most frequently employed as a treatment for HCC in sustained virological responder (SVR)

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Objectives: Oral preparation of anti HCV drug completely changed the paradigm of Hepatology. In this communication, we addressed the issue whether any drastic change be needed for surgical and loco-regional treatment of HCC in SVR era.
Materials and Methods: We enrolled 611 patients who achieved SVR after DAA (Direct Acting Antiviral) between 2013 and 2020. The patient was prospectively observed for develop of HCC. In this communication we assessed the utility of 3 major interventions; open & laparoscopic (LAP) surgeries, and radiofrequency ablation (RFA) in real world settings.
Results: HCC developed in 48 of 611 (7.8%) patients. The treatment options included 7, 15, and 16 of open, LAP, and RFA, respectively. The other 10 patients received various treatments. The 1-, 3-, and 5-year recurrence-free survival rates were 60%, 30%, and 30% for open, 93%, 93%, and 93%for LAP, and 63%, 47%, and 28% for RFA, respectively, significantly better in the LAP group ($p < 0.05$). The overall survival rates at 1, 3 and 5 years were 100%, 80% and 80% for open and 93%, 93% and 93% for LAP, and 93%, 83%, and 80% for RFA, respectively. As with time after antiviral treatment, liver fibrosis resolved and liver function improved which was advantageous for any treatments.
Conclusion: Recently, pivotal prospective study of randomized control study (open surgery vs. RFA completed in Japan. In real world setting, especially in SVR era, laparoscopic surgery be "new" and could be the most preferred.

[PP-0718]

Early outcomes of atezolizumab plus bevacizumab therapy in lenvatinib-refractory patients; A GTO Group multicenter study

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Objectives: Atezolizumab (ATZ) plus bevacizumab (BEV)therapy was approved in Japan for the treatment of advanced hepatocellular carcinoma. We evaluated the safety and efficacy of ATZ plus BEV therapy as second-line therapy in patients with PD on lenvatinib.
Materials and Methods: Of the 26 patients who received ATZ + BEV therapy between September 2020 and January 2021, 20 patients who received ATZ + BEV after lenvatinib PD were included in this analysis. The primary endpoint was the response rate by m-RESIST on the first imaging study. Secondary endpoints were disease control rate and adverse events. Dosing criteria and adverse event managements for ATZ + BEV treatment had followed the guidelines for proper use. Adverse events were evaluated according to CTCAE ver. 5.0.
Results: The median age was 71 years, and 18 patients (90%) were male. There were 19 cases (95%) of more than Up-to-7. Five patients (25%) had portal vein tumor invasion, and eight patients (40%) had distant metastasis. The median observation period was 3 months. Of the 17 patients with evaluable images, 4 patients had a response, with a response rate of 24%. Disease control was achieved in 15 of 17 patients (88%). Some adverse events were observed in 18 of 20 patients (90%). CTCAE Grade 1–2 adverse events accounted for the majority (78%). One patient had grade 5 liver damage.
Conclusion: As a second-line treatment option after lenvatinib therapy, ATZ + BEV therapy appears to be a disease controllable therapy. However, care must be taken to avoid liver damage.

[PP-0759]

Early changes in the circulating monocyte population on anti-PD-1 blockade predict clinical outcomes in advanced hepatocellular carcinoma

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Objectives: We aimed to discover peripheral blood biomarkers that predict clinical response of advanced hepatocellular carcinoma (HCC) to anti-PD-1 therapy.
Materials and Methods: Total 45 sorafenib-experienced patients with advanced HCC who underwent nivolumab were enrolled. No evidence of progression until 6 months after therapy was defined as durable clinical benefit (DCB) and otherwise non-durable clinical benefit (NDB). Peripheral blood samples, obtained at baseline (D0), day 7 (D7), day 14, and day 28 or later, were analyzed by flow cytometry. RNA-sequencing was performed using sorted classical monocytes from 4 DCB patients and 4 NDB patients.
Results: The relative frequency of classical ($CD14^+CD16^-$) monocytes among $CD45^+$ cells significantly increased at D7 with a greater increase in patients with DCB. Among differentially expressed genes identified by RNA-sequencing of sorted classical monocytes, Cd274, encoding PD-L1, was upregulated on classical monocytes from patients with NDB compared to those from patients with DCB at D7, which was confirmed by flow cytometry at the protein level. PD-L1 expression on classical monocytes was associated with increased plasma levels of IL-6 and IL-10. We defined a 'monocyte index' as upregulation of PD-L1 expression relative to increase in the classical monocyte frequency at D7. The monocyte index was significantly higher in patients with NDB than patients with DCB. In multivariate analysis, the monocyte index was an independent prognostic factor for progression-free survival and overall survival.
Conclusion: Early changes in the circulating classical monocyte population could predict clinical outcomes of patients with advanced HCC undergoing anti-PD-1 therapy.

[PP-0762]

Low-dose liver dynamic CT for the detection and characterization of HCC and image quality in patients with chronic liver disease or liver cirrhosis

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Objectives: We aimed to prospectively evaluate the image quality and diagnostic performance of liver dynamic CT according to radiation dose using a dual-source CT scan.
Materials and Methods: Sixty-seven consecutive patients underwent liver dynamic CT using a dual-source scanner to obtain three radiation dose CT scans (100%, standard-dose CT[SDCT]; 66.7%, low-dose CT[LDCT]; 33.3%, ultralow-dose CT[ULDCT]). The diagnostic performance of three radiation dose CT scans for detection and characterization of the hepatic focal lesion ($\geq$ 5 mm) were analyzed by two independent readers. The image quality of three different dose scans was also evaluated quantitatively and qualitatively.
Results: Diagnostic performance of each dose of liver dynamic CT was as follows: mean effective dose for LDCT and ULDCT was respectively 8.91 $\pm$ 2.19 mSv and 3.82 $\pm$ 0.94 mSv, a 70% and a 30% reduction. Per-lesion performance data (sensitivity/specificity/PPV/NPV/accuracy) were 0.91/1.00/1.00/0.97/0.98 for SDCT, compared with LDCT 0.72/1.00/1.00/0.91/0.93; ULDCT 0.59/1.00/1.00/0.87/0.89. As a result, SDCT scan showed no significant difference ($p = 0.0625$), compared with LDCT scan, while ULDCT scan showed significant difference as compared with SDCT scan ($p = 0.0020$). Qualitative image quality and signal to noise ratio (SNR) were significantly different among different radiation doses (SDCT/LDCT/ULDCT, 4.36 $\pm$ 0.60/3.86 $\pm$ 0.53/2.88 $\pm$ 0.55 and 15.66 $\pm$ 2.53/13.87 $\pm$ 2.33/12.45 $\pm$ 2.78; $p < 0.001$).
Conclusion: Diagnostic performance of liver dynamic LDCT (30% reduced dose) was acceptable, although its image quality was

qualitatively and quantitatively low. Reduced the radiation dose by 30% would be allowed for suspicious HCC patients in follow-up.

[PP-0778]

Acute obstructive cholangitis with lipiodol laden tumor after transarterial chemoembolization

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Objectives: Transarterial chemoembolization (TACE) is an effective treatment modality for patients with advanced hepatocellular carcinoma (HCC). Treatment complications associated with TACE include postembolization syndrome (fever, abdominal pain, nausea, vomiting) and transient impairment of liver and kidney functions. Ischemic hepatitis may also occur in patients with partial portal vein thrombosis or if TACE has not been performed selectively. Amongst these complications of TACE, acute obstructive cholangitis due to migration of a tumor fragment after TACE is rare. Here, we report a patient with acute obstructive cholangitis complicated by migration of a lipiodol laden tumor cast after treating HCC with TACE.
Materials and Methods: A 71-year-old man, who had been followed for alcoholic liver cirrhosis for 10 years, was admitted to our hospital for evaluation of a liver mass detected during HCC surveillance. TACE was performed and the patient was discharged without any immediate complications. About 2 weeks after TACE, the patient presented with abdominal pain and fever. Abdominal CT showed the formation of a liver abscess and percutaneous drainage was performed. After about 2 weeks of drainage, abominal CT was performed again. There was migration of the lipiodol laden material to the common bile duct.
Results: ERCP showed an elongated filling defect in the lower part of the CBD. After a sphincterotomy, a dark green colored, friable material was removed from the CBD. After removal of the necrotic tissue, the patient was free of symoptoms and the serum bilirubin levels returned to normal.
Conclusion: In summary, physicians caring for patients treated with TACE should be aware of acute obstructive cholangitis complicated by tumor migration. In such cases, ERCP may be an effective and safe treatment modality for removal of the lipiodol laden tumors.

[OP-0794]

Value of precontrast and portal venous phases in differentiating AP shunts from small atypical HCCs

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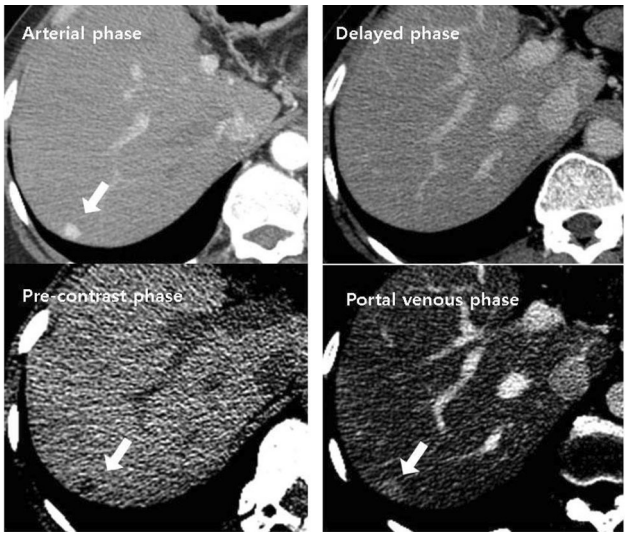
Objectives: To evaluate the value of precontrast phase (PP) and portal venous phase (PVP) for differentiation of small hypervascular hepatocellular carcinoma (HCC) without delayed washout from arterioportal (AP) shunt at high-risk patient of HCC.

Materials and Methods: 122 lesions (73 AP shunts and 49 HCCs) detected on quadriphasic CT in 101 patients with chronic liver disease were enrolled. All lesions showed arterial enhancement and isodensity on delayed phase (DP) with equal or less than 2 cm, and exclusion of typical features of AP shunts. Morphologic features of each lesion (size, location, shape, margin) on biphasic CT (arterial phase and DP), AFP values and coexistent HCC were evaluated. The qualitative and quantitative analysis for lesion attenuation on quadriphasic CT were performed. Diagnostic performances for prediction of AP shunts over HCC were compared among the biphasic CT, triphasic CT (adding PP or PVP), and quadriphasic CT.
Results: The presence of concomitant HCC ($p = 0.00$, Odds ratio [OR] = 0.1089), visual hypodensity on PP ($p = 0.0004$, [OR] = 17.7168) and visual hyperdensity on PVP ($p = 0.0003$, [OR] = 0.0507) were independent predictors for differentiating AP shunts from HCC in multivariate analysis. The additional review of both PP and PVP revealed significantly increased diagnostic performance for both observers and yielded the highest diagnostic performance.
Conclusion: Hypodensity on PP and hyperdensity on PVP are significant predictive features in diagnosis of atypical small hypervascular HCC over AP shunts in high-risk patients with HCC. Careful evaluation of the PP and PVP may reduce underdiagnosis and lead to earlier diagnosis of atypical small HCCs.



[PP-0803]

Ramucirumab for patients with advanced hepatocellular carcinoma (HCC) and elevated α-fetoprotein (AFP) following a non-sorafenib-based first-line therapy: Final results from an expansion cohort of REA

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Objectives: This global open-label expansion cohort of REACH-2 was initiated to study ramucirumab in patients with advanced HCC and baseline AFP $\geq$ 400 ng/mL following a non-sorafenib-based systemic therapy, representing one of the first sequencing studies in HCC.
Materials and Methods: This single-arm study investigated ramucirumab in patients with advanced HCC (BCLC stage C/B), Child–Pugh A, ECOG PS 0/1 and baseline AFP $\geq$ 400 ng/mL who received 1–2 prior systemic regimens for advanced HCC, excluding prior sorafenib/chemotherapy. Enrolled patients received ramucirumab 8 mg/kg IV once every 14 days. Primary endpoint: safety. Secondary endpoints included overall survival (OS), progression-free survival (PFS), objective response rate and time-to-progression (TTP). Final analysis occurred after all enrolled patients completed $\geq$ 3 treatment cycles/discontinued treatment.
Results: 47 patients were treated at 21 investigative sites in USA(n = 12)/Taiwan(n = 10)/mainland China(n = 8)/Hong Kong(n = 8)/Germany(n = 8)/Switzerland(n = 1). At baseline, these patients with 2nd-3rd + line advanced HCC had ECOG PS 1(51%), with vascular invasion or extrahepatic spread(85%), viral hepatitis B(55%), BCLC stage C(92%) and median AFP = 3236 ng/mL(IQR = 1332,18,210). Prior systemic regimens included lenvatinib(n = 20), checkpoint inhibitor (CPI) monotherapy(n = 11), CPI + antiangiogenic(n = 15) and CPI + CPI(n = 4). Grade $\geq$ 3 TEAEs were reported in 27(57%) patients and were deemed to be treatment-related in 11(23%) patients. Grade $\geq$ 3 AEs occurring in $\geq$ 5% patients were hypertension (n = 5[11%])/proteinuria (n = 3[6%])/hyponatremia(6%)/AST increased(6%). Two deaths occurred due to treatment-related AEs on therapy/within 30 days of treatment discontinuation (myocardial infarction and upper GI hemorrhage). Median OS = 8.7 months (95%CI = 4.6–12.2), median PFS = 1.7 months (95%CI = 1.5–4.1), median TTP = 2.8 months (95%CI = 1.5–4.2). Number of patients achieving an objective response was 5(10.6%, 95%CI = 1.8–19.5), with median duration of response = 8.3 months(95%CI = 2.4-NR).
Conclusion: This expansion cohort of REACH-2 represents a non-sorafenib sequencing study in patients with advanced HCC. The safety/efficacy profile of ramucirumab following a non-sorafenib-based systemic therapy was consistent with that observed in patients who received prior sorafenib in Ph3 REACH-2.

[OP-0814]

Laparoscopic versus open repeat liver resection for recurrent hepatocellular carcinoma in hepatectomy patients: Inverse probability of treatment weighting

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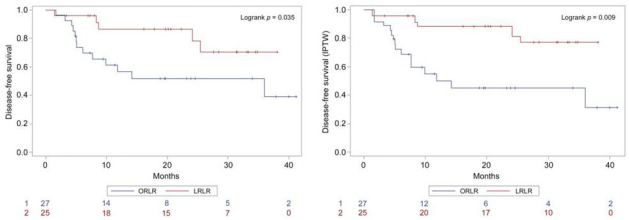
Objectives: Repeat liver resection (RLR) is a good treatment option for recurrent hepatocellular carcinoma (HCC). However, laparoscopic repeat liver resection (LRLR) is more technically demanding than open repeat liver resection (ORLR). The purpose of our study is to compare the surgical outcomes of ORLR and LRLR and to carefully present LRLR guidelines for HCC.
Materials and Methods: We performed RLR at a single institution from January 2017 to November 2019. We divided the patients into an ORLR group and an LRLR group. Inverse probability of treatment weighting was applied in this study to compare the ORLR group and the LRLR group.
Results: There was no difference between the two groups in patient characteristics, preoperative blood tests and pathological characteristics except tumor size ($p = 0.021$) and tumor grade ($p < 0.001$). The LRLR group had less blood loss (100 mL vs. 200 mL, $p = 0.011$) and shorter hospital stay (6 days vs. 8 days, $p = 0.002$). Disease-free survival was also significantly higher in the LRLR group than in the ORLR group ($p = 0.009$).
Conclusion: If regular radiologic examination is performed, most of the recurrent tumors could be detected less than 3 cm. LRLR yielded better short-term outcomes than ORLR. LRLR might be feasible and useful for recurrent HCC located contralateral to the previous tumor at a size of less than 3 cm.



[PP-0818]

Clinical impact of preoperative 18F-FDG-PET/CT on hepatocellular carcinoma patients treated with curative resection

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Objectives: Positron emission tomography/computed tomography with fluorine-18fluorodeoxyglucose (18F-FDG-PET/CT) has proven to be a valuable tool in pre- and post-treatment work-up of several solid tumors. However, there has been a matter of debate whether the potential use of 18F-FDG-PET/CT is informative in hepatocellular carcinoma (HCC). This study aims to investigate clinical significance of preoperative 18F-FDG-PET/CT in HCC patients who have received curative resection.

Materials and Methods: A total of 60 HCC patients who underwent ^{18}F-FDG-PET/CT before surgical resection were selected for retrospective review of medical records. The HCCs' metabolic activity displayed on ^{18}F-FDG-PET/CT was incorporated into clinical characteristics and outcomes.
Results: Thirty-six HCCs revealed a hypermetabolic activity on ^{18}F-FDG-PET/CT: 24(66.7%) moderately differentiated (MD) and 12(33.3%) poorly differentiated (PD), while twenty-four HCCs showed a isometabolic activity/low FDG uptake on PET/CT: 4(16.6%) well differentiated, 19(79.2%) MD, and 1(4.2%) PD. Standardized uptake value (SUV) of PD HCCs on PET/CT was significantly higher than that of MD HCCs (5.2 ± 2.4 vs. 3.8 ± 1.2, $p = 0.045$). The serum PIVKAII level and tumor size in HCC patients showing a hypermetabolic activity were significantly larger than those in isometabolic HCC patients (log PIVKAII 2.9 ± 1.0 vs. 1.6 ± 0.7, $p < 0.001$; tumor diameter 6.6 ± 4.5 vs. 2.9 ± 2.0 cm, $p < 0.001$). The SUV was positively correlated with tumor size ($r = 0.340$, $p = 0.043$) and serum alpha-fetoprotein level ($r = 0.556$, $p < 0.001$). HCC recurrence and disease-free survival were not correlated with SUV on PET/CT.
Conclusion: Preoperative ^{18}F-FDG-PET/CT seems to be clinicopathologically informative in aspects of tumor size, differentiation, tumor markers, but not tumor recurrence and disease-free survival in HCC patients treated with curative resection.

[PP-0819]

Clinical exploration of postembolization syndrome following transcatheter arterial chemoembolization for hepatocellular carcinoma

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Objectives: Transcatheter arterial chemoembolization (TACE) is the most commonly used therapeutic approach for hepatocellular carcinoma (HCC) globally. Postembolization syndrome (PES), which defined as fever without associated infection, pain in the upper abdomen, and nausea/vomiting after TACE, is common in clinical practice, However, few studies have reported about such events. We analyzed the incidence and risk factors of PES after TACE.
Materials and Methods: This study was a single-center retrospective analysis of a prospectively maintained medical reports. Between March 2013 and June 2018, total 559 TACE episodes of 214 HCC patients were explored for incidence and preprocedural risk factors of PES.
Results: The incidence of PES was 32.9% (abdominal pain 16.8%, fever 9.3%, nausea 3.0% and vomiting 3.8%). Patients who developed PES had more advanced stage (stage I vs. II vs. III, 18.6% vs. 29.4% vs. 57.8% respectively, $p < 0.001$) and larger size of tumor compared to those without PES (3.4 ± 2.7 cm vs. 2.1 ± 1.5 cm, respectively, $p < 0.05$). The dose of lipiodol used was increased with tumor size (6.23 ± 3.81 mL vs. 4.10 ± 2.75 mL, respectively, $p < 0.05$). Younger patients correlated to a higher incidence of PES as well (63.04 ± 9.35 vs. 65.96 ± 9.70, respectively, $p < 0.05$). There was no statistical significance in the incidence of PES in Child–Pugh classification, ECOG performance status, the number of tumor, past therapeutic modality, and biochemical liver tests. Multivariate analysis by logistic regression analysis demonstrated that age was the most independent predictive factor of PES (odds ratio: 0.961, 95% CI: 0.934–0.990, $p < 0.05$).
Conclusion: Postembolizaiton syndrome is common in HCC patients treated with TACE. Recognition of the TACE-related risk factors is important for timely proper management of PES. In near future, the prospective study for the prophylaxis of PES is required.

[PP-0824]

Unusual presentation of hepatocellular carcinoma—cannonball pulmonary metastasis

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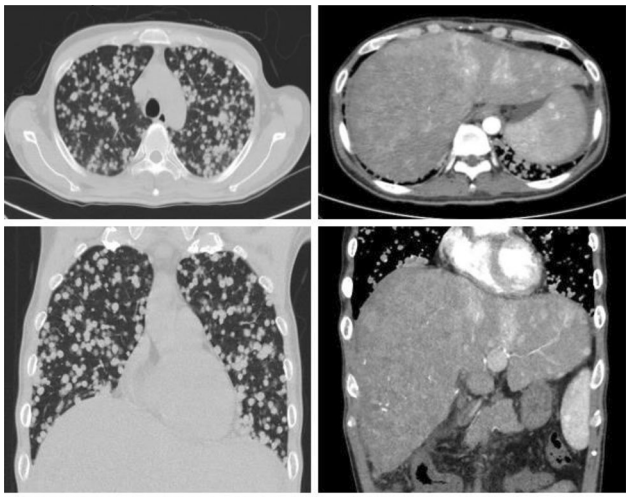
Objectives: Cannonball metastasis refers to well-circumscribed, spherical nodules scattered over both lungs, usually occur due to hematogenous spread of tumor, classically seen in germ cell tumor, renal cell carcinoma, choriocarcinoma, endometrial cancer but it is a rare and an unusual phenomenon in hepatocellular carcinoma.
Materials and Methods: Case description:
Results: We report a case of hepatocellular carcinoma with unusual presentation of pulmonary cannonball lesions. A 41-year-old Chinese man who attended to ED on 8.10.2021 with one month duration of abdominal discomfort and progressive dyspnea. He has past history of chronic hepatitis B infection since the age of 16 years but he did not receive any treatment. He denied fever and no history of TB contact. His oxygen saturation was 89% on room air. On examination, he was dyspneic, tachypneic, few crepitations in both lungs, hepatomegaly was noted. Covid PCR test was negative. Imaging tests revealed cannonball lesions were seen in both CXR and CECT chest (Figure-1) and infiltrative type of hepatocellular carcinoma both lobes of liver with portal vein thrombosis detected in CECT Liver (Figure-1). Blood tests showed elevated bilirubin (3.5 g/dl), AST 122, ALT 30, hypoalbuminemia (3.2), AFP 8421, HBeAg negative, antiHBeAb negative, qHBsAg 2793 IU/ml. His Child Pugh stage B (score 9), MELDNa 12 and BCLC stage C. Therefore, we diagnosed him to have advanced hepatocellular carcinoma with cannonball pulmonary metastasis with underlying chronic hepatitis B infection, for which we started Tenofovir (TDF) 300 mg OD and Lenvatinib 4 mg OD. Unfortunately, he expired on 17.10.2021.
Conclusion: Hepatocellular carcinoma is one of the commonest cancers in the world with chronic hepatitis B and C infection. Extrahepatic spread to lung is common and about one third of these patients developed pulmonary metastasis. However, cannonball pulmonary metastasis is rare and is an unusual presentation in hepatocellular carcinoma. Moreover, prognosis of these patients is poor and survival is usually only days.



CECT (thorax) – innumerable small rounded nodules in both lungs

CECT (Liver) – ischemic-necrosis infiltrated liver mass involved both right and left lobe with portal veins invasion

[OP-0831]

Lower overall survival in hepatocellular carcinoma in populations with low socio-economic profiles

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Objectives: The national overall survival (OS) for Hepatocellular carcinoma (HCC) in Australia is 62% at 1 year and 21% at 5 years. Western Health is a tertiary hospital servicing a large proportion of culturally and linguistically diverse groups and people of lower socioe-conomic status. We aimed to study the outcomes in HCC in this cohort.
Materials and Methods: This retrospective study analysed patients diagnosed with HCC from 2005–2020. Univariate analysis and multivariate Cox regression were used to identify patient and tumour characteristics associated with survival.
Results: We identified 235 patients with HCC, of which 80% were male, mean age at diagnosis 64.5 years and 64.7% aged under 70 at diagnosis. Most patients had cirrhosis (80%) and were immigrants (68%). Only 32% of eligible patients with Chronic Hepatitis B (CHB) were adherent to HCC screening, 66.5% of HCC's were diagnosed at an early Barcelona Clinic Liver Cancer (BCLC) stage (0, or A). Median OS was 264 days, 45.1% at 1 year and 16.4% at 5 years. On multivariable analysis, BCLC class B, C or D and an older age at diagnosis remained significant for reduced OS ($p < 0.001$ and $p = 0.006$ respectively). Those born in Asia had longer OS than those born in Australia (895 vs 433 days, $p = 0.027$). There were 84 CHB patients; 75 on treatment at diagnosis (Entecavir; 74, Tenofovir;1), and 9 on no treatment. Those on active CHB treatment had a longer OS compared to no treatment (1744 vs 77, $p = 0.0015$).
Conclusion: Despite a majority of early diagnoses, the 1 and 5-year survival of 45.1% and 16.4% represented in this cohort are lower than national rates. 68% were immigrants, reflecting a demographic with a proportionally high immigrant population compared to the national average of 30%. Further studies are required to elucidate the demographic factors predictive of HCC survival and adherence to screening in the Victorian population.

Variable						
Overall cohort (n = 235)	Univariate Analysis			Multivariate Analysis		
	Hazard ratio	95% CI	p	Hazard ratio	95% CI	p
Stage of disease at diagnosis (0/A)	0.21	0.14 - 0.3	0.0001			
BCLC B, C or D at diagnosis				5.5	3.2 - 9.3	<0.001
Sex (male)	0.75	0.52 - 1.07	0.11			
Australian born	1.14	0.82 - 1.58	0.43	1.7	0.96 - 3.2	0.068
Australian born (compared to Asian born)	1.57	1.05 - 2.33	0.027			
Age at diagnosis >70 yrs.	1.7	1.26 - 2.31	0.00053	2.1	1.23 - 3.5	0.006
HBV	0.65	0.45 - 0.94	0.02	1.1	0.61 - 2.1	0.685
HCV	1.07	0.78 - 1.47	0.68			
Cirrhosis	1.02	0.67 - 1.51	0.93			

[PP-0832]

Diagnostic and prognostic roles of serum sulfatase-2 in HBV-related hepatocellular carcinoma

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Objectives: Up-regulated expression of sulfatase-2 (SULF-2), an extracellular enzyme promoting tumor proliferation, has been reported in tissues of patients with hepatocellular carcinoma (HCC). This study was aimed at assessing the diagnostic and prognostic roles of serum SULF-2 in patients with HBV-related HCC.
Materials and Methods: Three groups including 146 patients with HCC, 119 patients with non-malignant chronic HBV infection and 50 healthy subjects were recruited. Serum SULF-2 and alpha-fetoprotein (AFP) levels were measured by enzyme-linked immunosorbent assay (ELISA) method.
Results: The HCC group was significantly older with higher proportion of male compared with the non-HCC group and healthy controls ($P < 0.001$). Patients with HCC had higher levels of serum SULF-2 than those without HCC and controls (27.3 ± 10.3 vs. 18.5 ± 5.2 vs. 15.8 ± 4.3 ng/ml, $P < 0.001$). The area under the curve (AUROC) for differentiating HCC from the other groups were 0.79 (95%CI; 0.73–0.84, $P < 0.001$) for SULF-2 and 0.90 (95%CI; 0.86–0.94, $P < 0.001$) for AFP. In the HCC group, serum SULF-2 levels positively correlated with AFP levels ($r = 0.461$, $P = 0.001$), Child–Pugh classification ($r = 0.206$, $P = 0.016$), tumor size ($r = 0.277$, $P = 0.001$) and tumor stage (BCLC stage) ($r = 0.274$, $P = 0.001$). High SULF-2 level (above median value as a cut-off point of 20 ng/ml) was significantly correlated with poor overall survival and was independently associated with the prognosis of HCC.

Conclusion: Serum SULF-2 was significantly correlated with progressive HCC, which might suggest that this marker play crucial roles in promoting tumor progression. Additionally, our findings have revealed that serum SULF-2 could be a new biomarker for HBV-related HCC.

[PP-0833]

Predictive role of pretreatment circulating miR-221 in patients with hepatocellular carcinoma undergoing transarterial chemoembolization

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Objectives: Aberrant expression of circulating microRNAs (miRNAs) has been shown to play an essential role in diagnosis and prognosis of several cancers, including hepatocellular carcinoma (HCC). In this study, we investigated the predictive role of selected miRNAs in patients with hepatitis B virus (HBV)-related HCC, who underwent transarterial chemoembolization (TACE).
Materials and Methods: Stored serum samples prior to 1st TACE were used to assess serum miR-122, miR-221 and miR-224 expression by Taqman probe using quantitative real time PCR assay.
Results: A total of 100 patients with HCC (84% male, mean age 60 years) treated with TACE were included. During the median follow up of 18.5 months (range 3–60 months), 42 (42.0%) patients experienced TACE refractoriness. Based on multivariate analysis, high miR-224 expression ($\geq$ 4.0 $\log_{10}$ copies) and the BCLC staging were significantly associated with TACE refractoriness and poor overall survival. In contrast, serum miR-122 and miR-224 were not identified as independent predictors for treatment outcome and overall survival.
Conclusion: These data indicated that pretreatment serum miR-221 level could serve as a potential biomarker for TACE therapy. Incorporation of this novel to the conventional staging systems might provide a better prediction of treatment outcome and prognosis of patients with HCC.

[PP-0834]

Differential phosphoproteomics in liver tissues of various types of liver cancers

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Objectives: Information on posttranslational modification (PTM), particularly protein phosphorylation, is essential for a better understanding of hepatocarcinogenesis. This study was aimed at identifying tissue phosphoprotein signatures among various liver cancers, including hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC) and liver metastasis of colorectal cancer (CRC).
Materials and Methods: Paired cancerous and adjacent non-cancerous liver tissues of 12 patients with HCC, 12 patients with ICC and 10 patients with CRC were collected from surgical resection. Quantitative phosphopeptides were enriched and analyzed by LTQ-Orbitrap-XL mass spectrometer. Assessment of protein–protein interactions were predicted using STRING database.
Results: Compared with adjacent non-cancerous tissues, a total of 34, 25 and 14 phosphoproteins were significantly increased in cancerous tissues of HCC, ICC and CRC, respectively. In HCC, the most common up-regulated phosphoproteins were related to several biological processes and cellular components, as well as enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways involved in immunological response. In CRC, the present phosphoproteins were associated with biological process and cellular components. In contrast, phosphoproteins in ICC exhibited no significant functional enrichment.
Conclusion: Our study reported the phospho-proteome dataset that might be involved in district hepatocarcinogenesis. These novel phosphoprotein biomarkers could potentially be useful to differentiate primary and secondary liver cancers.

[OP-0835]

Selective internal radiation therapy for hepatocellular carcinoma in Australia A 15-year multicentre cohort study

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Objectives: The optimal therapeutic role for Selective internal radiation therapy (SIRT) for hepatocellular carcinoma (HCC) is debated and in Australia it is not publicly funded. There are limited data on indications for use, efficacy and safety within Australia.
Materials and Methods: We performed a multicentre retrospective cohort study of patients undergoing SIRT for HCC in Sydney Australia between 2005–2019. The primary outcome was overall survival (OS). Secondary outcomes were progression free survival (PFS), adverse events, and inter-institutional variation.
Results: 156 patients underwent SIRT across ten institutions (mean age 67 years, 81% male). SIRT use progressively increased from 2005 (n = 2) peaking in 2017 (n = 42) before declining (2019: n = 21). Common aetiologies of HCC were hepatitis C (36%), NAFLD (28%), alcohol excess (27%) and hepatitis B (21%). BCLC stages at treatment were: A (13%), B (33%), C (52%) D (2%). Fourth-four (28%) patients had tumour thrombus. SIRT was the initial HCC

therapy in 49% of patients. SIRT characteristics were: median dose (1.53 GBq) lung shunt (5.7%) and extent of treatment (segmental = 8%, lobar = 59%, whole liver = 33%). After a median follow-up of 13.9 months, there were 117 deaths (105 liver-related). Median OS was 15 months (95%CI: 11–19) and varied by BCLC stage: 46, 22, 9 and 7 months for A-D respectively ($p < 0.001$). Independent predictors of mortality on multivariable analysis were extent of liver involvement, BCLC stage, baseline ascites, AFP and MELD score. Median PFS was 6.0 months. SIRT-related complications occurred in 17%: radiation induced liver disease (RILD)(11%), pneumonitis (3%, n = 6), gastrointestinal ulceration and cholecystitis (1% each). Baseline ascites predicted RILD. Following SIRT, 20% of patients had prolonged response or were downstaged to curative therapy.

Conclusion: We present the largest Australian SIRT cohort for HCC. Outcomes were comparable to other real-world cohorts and therapy appeared safe. Patients with early-stage disease had the most benefit with some downstaged to curative therapy.

Table 1 – Baseline factors predictive of mortality on regression analysis

	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	aHR	95% CI	P
Extent of liver involvement			<0.001			0.001
25-50% vs <25%	1.4	0.9-2.1	0.089	1.6	0.99-2.5	0.054
51-75% vs <25%	5.1	2.7-9.9	<0.001	4.6	2.2-9.7	<0.001
Ascites (yes vs no)	2.3	1.3-4.1	0.003	3.0	1.4-6.1	0.003
BCLC stage ‡			<0.001			<0.001
B vs A	2.3	1.1-4.8	0.026	2.2	1.0-4.7	0.048
C/D vs A	4.3	2.1-8.8	<0.001	4.1	2.0-8.4	<0.001
Baseline AFP (per ng/mL increase)	1.00	1.0-1.0	<0.001	1.0	1.0-1.0	0.002
Baseline MELD score (per point increase)	1.1	1.01-1.2	0.016	1.1	1.01-1.2	0.002
Tumour thrombus (yes vs no)	2.4	1.6-3.6	<0.001			
CTP score (per 1 point increase)	1.3	1.1-1.5	0.003			
Bilobar disease (yes vs no)	1.7	1.2-2.5	0.003			
Size of tumour (per cm increase)	1.1	1.0-1.1	0.004			
Institution where SIRT performed†			0.004			
Hospital A vs B	2.2	1.2-4.3	0.015			
Hospital A vs H	24.4	2.9-202.6	0.003			
Hospital A vs J	2.3	1.1-4.8	0.028			
Baseline albumin (per umol/L increase)	0.96	0.9-0.99	0.010			
Whole liver vs selective SIRT	1.6	1.1-2.4	0.011			
SIRT dose (per Gbq increase)	1.2	1.0-1.5	0.052			
Female vs male gender	1.5	0.98-2.4	0.074			

‡BCLC C and D patients combined for purpose of analysis as only three BCLC D patients;
† hospital 1 set as reference institution, other hospital comparisons to hospital 1 not significant and not presented here

Abbreviations: BCLC – Barcelona clinic liver cancer, AFP – alpha fetoprotein, MELD – Model for end stage liver disease, CTP – Child Turcotte Pugh, Gbq – gigabecquerel

[PP-0847]

Gadoxetic acid-enhanced MRI features for predicting treatment outcomes of early hepatocellular carcinoma (< 3 cm) after transarterial chemoembolization

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Objectives: Magnetic resonance imaging (MRI) is the most useful imaging tool for small hepatocellular carcinoma (HCC) evaluation. Patients undergoing transarterial chemoembolization (TACE) might have predictive imaging prognostic factors. This study aimed to find predictive gadoxetic acid (GA)-enhanced MRI features that affect tumor response and outcomes in patients with early HCC who underwent conventional TACE.

Materials and Methods: Among patients who underwent conventional TACE as a first-line treatment for Barcelona clinic liver cancer stage 0 or A (< 3 cm), 135 patients who underwent GA-enhanced MRI before treatment were included in this retrospective study. The patients' pretreatment clinical characteristics and MRI features were evaluated. Post-treatment tumor response, progression-free survival (PFS), and overall survival (OS) were also investigated.

Results: The median follow-up period was 47 (range: 7–133) months, with 90 (67%) patients showing complete remission (CR) at the 1-month follow-up after TACE. Tumor number (odds ratio [OR] 0.602, 95% confidence interval [CI]: 0.375–0.967), central location (OR: 0.349, 95% CI: 0.145–0.837) were inversely associated with CR achievement. Median PFS and OS time were 22 (range: 1–133) and 67 (range: 7–133) months, respectively. The MRI features affecting poor survival outcomes were tumor number (PFS: hazard ratio [HR] = 1.444, 95% CI = 1.124–1.854; OS: HR = 1.459, 95% CI = 1.018–2.090), central location (PFS: HR = 1.664, 95% CI = 1.038–2.667; OS: HR = 1.890, 95% CI = 1.021–3.497), and marginal irregularity (PFS: HR = 3.099, 95% CI = 1.953–4.979; OS: HR = 1.985, 95% CI = 1.084–3.634).

Conclusion: Multiplicity, central location, and marginal irregularity of HCC on GA-enhanced MRI were significant factors associated with poor prognosis of patients with early HCC after conventional TACE.

[OP-0862]

Circulating tumor suppressor microRNAs Let-7 profiling in CHC patients with HCC risk after anti-viral treatment

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Objectives: Hepatocellular carcinoma (HCC) is the leading cause of cancer-related mortality worldwide and the majority of cases are diagnosed with advanced disease. Patients with an FIB-4 score < 3.25 also showing an annual HCC risk of 0.24% after SVR, highlights the unmet need for continuous surveillance. Stable and cost-effective biomarkers, such as circulating microRNAs, need to be established. This study aimed to clarify whether the Let-7 family in serum can predict CHC with HCC risk.

Materials and Methods: We retrospectively analyzed the sera Let-7 family from 236 patients with CHC (including development of HCC in 54 patients with CHC) using real-time quantitative PCR (qPCR) and univariate and multivariate regression models.

Results: The results of qPCR showed differences in Let-7 family serum levels between patients with CHC with and without HCC at post-antiviral treatment (interferon and ribavirin for 6 months). We also found that the Let-7 family (except for Let-7c) exhibited significant negative correlations with fibrosis score ($r = -0.13$ to -0.33, $p = 0.0149$ to < 0.0001) stratified by FIB-4 index (< 3.25). We further conducted multivariate analysis with Let-7 family, age, sex, HCV log RNA, HCV type, SVR, and LC (FIB-4 > 3.25) as covariables. The only independent factors for HCC were Let-7a and Let-7i sensitivity (0.8286 and 0.9143, respectively) with

area under the curve (AUC) 0.825, odds ratio (OR) 0.41, 95% confidence interval (CI) 0.19–0.87, p = 0.0211 and AUC 0.831, OR 0.32, 95% CI 0.14–0.73, p = 0.0070, respectively.
Conclusion: Circulating tumor suppressor microRNAs Let7a and Let7i can be used in early surveillance for CHC with HCC risk.

[PP-0920]

Screening program for early stage of liver cancer in Ulaanbaatar: Single center study

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Objectives: Screening and diagnosis in early stage of liver cancer in high-risk population group.
Materials and Methods: These patients are controlled in screening in early stage of liver cancer in Happy Veritas Clinic and Diagnostic Center. The total number of patients included for screening was 10,682 patients such as abdominal ultrasound and to identify serum alfa fetoprotein (AFP) every 3 months. 181 patients were included in the study, who had complete set of data, and are regularly controlled for screening in early stage of liver cancer. Medical history, results of blood test, liver function tests, AFP, liver fibrosis stage (TE) and abdominal ultrasound examination results were collected for each patient.
Results: 181 patients with an average age of 54 ± 11 (range: 23—89 years old) were included in the study. In the result, causes of liver fibrosis were HCV 59.1% (107), HBV 24.9% (45), HBV/HDV 13.3% (24), HCV/HBV 2% (3), HCV/HBV/HDV 0.6% (1) and without hepatitis viruses 0.6% (1). According to the study, F2 stage was 64.6% (117), F3 stage 27.1% (49) and F4 stage 8.3% (15). We studied the changes in laboratory tests and depending on the patient's fibrosis stage. Increasing fibrosis stage or liver cirrhosis has decreased platelets, albumin and total protein level ($p \leq 0.001$). However, we observed ALT level, which increased in F3 stage and decreased fibrosis stage F4. Liver cancer nodule is detected in 4 patients from 181 participants during the follow-up.Those 4 patients had fibrosis stage F4 in Fibroscan analysis and average level of AFP was 86.
Conclusion: We conclude that patients in F4 stage in Fibroscan analysis have higher risk of developing liver cancer. Therefore, health care providers need regularly screening and testing in early stage of liver cancer in high-risk population.

[OP-0923]

Long-term outcomes of proton beam therapy for the oldest-old patients with hepatocellular carcinoma

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Objectives: The incidence rate of hepatocellular carcinoma (HCC) in oldest-old (85 years or older) is rising along with the progression of aging society. However, the optimal management of this population has to be elucidated due to the paucity of published studies. Usefulness of proton beam therapy (PBT) for the treatment of HCC has been shown with good local control and tolerable adverse events. However, published outcomes for elderly patients with HCC were short-term with small sample size. We aimed to investigate long-term outcomes and toxicity of PBT for oldest-old patients with HCC.
Materials and Methods: 201 elderly patients treated with PBT for HCC between November 2001 and November 2014 were retrospectively investigated. 98 patients (48.8%) were young-old (age: 75–80), 74 (36.8%) were old-old (80–85), and 29 (14.4%) were oldest-old ($\geq$ 85). Overall survival (OS) and progression-free survival (PFS) rates were estimated by Kaplan–Meier method and log-rank test was used for comparisons. Local recurrence (LR) was computed by competing risk analysis with death as a competing event. Prognostic analysis was conducted using Cox proportional hazard model. Toxicities were graded according to the Common Terminology Criteria for Adverse Events version 4.0.
Results: The median age of all patients was 80 (range, 75–92). The median size of a tumor was 3.9 (range, 1.0–15.5) cm. The majority of patients had solitary tumor (n = 145, 72.1%), hepatitis C virus as an underlying cause (n = 123, 61.2%), and no previous treatment history (n = 106, 52.7%). OS rates at 1, 3, and 5 years were 89.7%, 54.1%, and 32.1%. PFS were 63.1%, 28.5%, and 16.0% and LR were 4.7%, 9.6%, and 11.4%, respectively. No significant difference was observed in OS rates between three subgroups (P = 0.4). No grade 3 or worse toxicity was observed.
Conclusion: Our results indicate that PBT is effective and tolerable for oldest-old patients with HCC.

[PP-0925]

Serum exosomal miRNA-720 as a diagnostic marker for hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) remains with a poor prognosis, largely due to late detection. Highly accurate biomarkers are urgently needed to detect early-stage HCC. Exosomal microRNAs (miRs) recently emerged as a biomarker for various cancers. Our study aims to explore the diagnostic performance of serum exosomal miR-720 for HCC.
Materials and Methods: Exosomal miRNA was measured by quantitative real-time PCR. A correlation analysis was done between exosomal miR-720 and tumor or clinico-demographic data of patients with HCC. The receiver operating characteristic (ROC) curve was applied to assess the diagnostic capacity of serum exosomal miR-720 for HCC, in comparison with AFP (a-fetoprotein) and prothrombin-induced by vitamin K absence or antagonist-II (PIVKA-II).
Results: miR-720 was chosen as a potential HCC marker through miR microarray, due to significantly differential expression between tumor and non-tumor samples. Serum exosomal miR-720 was significantly upregulated in patients with HCC (n = 114) and other liver disease (control, n = 30), with the higher area under the ROC curve (AUC = 0.931) than the other markers. Particularly, serum exosomal miR-720 showed superior performance in diagnosing small HCC (< 5 cm; AUC = 0.930) to AFP (AUC = 0.802) or PIVKA-II (AUC = 0.718). Exosomal miR-720 levels marginally correlated with tumor size and number. The proportion of high-level miR-720 increased with intrahepatic tumor stage progression. Unlike AFP or PIVKA-II showing significant correlation with aminotransferase levels, exosomal miR-720 exhibited no correlation with aminotransferase levels.
Conclusion: Serum miR-720 is an excellent biomarker for diagnosis of HCC, with better performance than AFP or PIVKA-II. Its diagnostic utility is maintained even for small HCC and not affected by aminotransferase levels.

[PP-0927]

A case of subcutaneous fat necrosis after transaterial chemoembolization for hepatocelluar carcinoma

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Objectives: Transcatheter aterical chemoembolization (TACE) is a therapeutic option for unresectable hepatocelluar carcinoma (HCC). Subumbilical skin rash is rare complication of TACE caused by patent hepatic falciform artery. We report a case supraumbilical skin rash and nodule developed after TACE for HCC.
Materials and Methods: A 73-year-old female admitted epigastric area pain and supraumbilical palpable nodule with skin color change. She was diagnosed with HCC four years ago. She was performed total 8th TACE for HCC treatment. Last TACE was taken 2 weeks ago. There was no history of alcohol or drug use. Mental status was alert. Initial vital sign shows blood pressure 141/84 mmHg, heart rate 93/min, body temperature 37.0C. Review of system was supraumbilical pain, fever and chill. Physical examination was supraumbilcal area direct tenderness and no rebound tenderness, small palpable nodule. Complete blood count showed WBC 7,900/mm^3(Segform 62.1%), Hb 10.1 g/dL and platelet 385,000/mm^3. Biochemical tests showed serum AST 31 IU/L, ALT 28 IU/L, albumin 2.4 g/dL, total bilirubin 7.2 mg/dL. C reactive protein was 7.73. PT(INR) was 1.34. Chest PA shows no active lung lesion. Abdominal CT scan shows thickening of the supraumbilical skin associated with increase-density subcutaneous fat.
Results: She was treated antibiotics treatment for two weeks. She was improved subumbilical pain, fever, chill and palpable nodule.
Conclusion: Subcutaenous fat necrosis is very rare complication after TACE for HCC. We are reported subcutaneous fat necrosis after TACE for HCC.

[OP-0949]

Radiomics-based differentiation of hepatocellular carcinoma from dysplastic nodule on abbreviated non-contrast magnetic resonance imaging

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Objectives: It was recognized that there were limitations with ultrasound surveillance for hepatocellular carcinoma (HCC) in patients with liver cirrhosis, and recent studies have suggested the possibility of the application of abbreviated non-contrast magnetic resonance imaging (MRI) as a potential alternative surveillance tool for HCC. However, it is still difficult to differentiate a HCC from dysplastic nodule (DN). Recently, radiomics-based machine learning has emerged as a powerful methodology to determine the characteristics of tumors. This study aimed to investigate the diagnostic performance of abbreviated non-contrast MRI-based radiomics signatures for differentiation of HCCs from DNs.
Materials and Methods: This study enrolled a total of 189 patients with histologically confirmed HCCs (n = 148) or DNs (n = 41) between February 2009 and May 2021 at Gachon University Gil Medical Center. Abbreviated non-contrast MR images of hepatic nodules included in-phase and out-of-phase T1-weighted imaging, T2-weighted imaging (T2WI), and diffusion-weighted imaging (DWI) sequences. The outline of each nodule was hand-drawn, and radiomics features were extracted. We used four machine learning-based algorithms including Logistic Regression (LR), Support Vector Machine (SVM), Random Forests (RF) and Extreme Gradient Boosting (XGB) to differentiate the hepatic nodules. Each sub dataset was tested with fivefold cross-validation.
Results: Radiomics features on in-phase, out-of-phase, T2WI and DWI sequences were analyzed, and four top-ranked features were selected to construct the radiomics model. The average area under the curve (AUC) of cross validation to differentiate between HCC and DN was 0.798 (sensitivity 71%; specificity 75%) with LR, 0.790 (sensitivity 67%; specificity 81%) with SVM, 0.781 (sensitivity 70%; specificity 76%) with RF and 0.758 (sensitivity 74%; specificity 61%) with XGB.
Conclusion: We developed the radiomics signatures as an adjunct tool to distinguish HCCs from DNs on abbreviated non-contrast MRI. Further multi-center validation studies are warranted.

[OP-0987]

Racial-ethnic disparities in curative treatment for early-stage intrahepatic cholangiocarcinoma in the United States

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Objectives: Incidence rates of intrahepatic cholangiocarcinoma (iCCA) increase in western countries. Significant racial-ethnic disparities exist for hepatocellular carcinoma treatment, but this has not been investigated in early-stage iCCA.
Materials and Methods: We used National Cancer Database, which represents more than 70% of newly diagnosed cancer in the United States. Patients diagnosed with iCCA between 2004 and 2018 were analyzed. Early-stage iCCA was defined as single cancer less than 3 cm in size without lymph node or extrahepatic involvement. Multivariable logistic regression was used to investigate the association between race-ethnicity and curative treatment receipt among early-stage iCCA patients after adjusting for age, socioeconomic factors, medical comorbidities, regions, and facility types.
Results: The proportion of early-stage iCCA was 4.5% in 2004 and 7.3% in 2018, with the odds of diagnosing early-stage iCCA increasing by 3.1% per year (95% confidence interval [CI]: 1.5–4.9%). Among 1093 patients with early-stage iCCA, 55% were male and the majority (77%) were Whites. Regarding treatments, 464 (42%) received resection, 113 (10%) received ablation, 62 (6%) received liver transplant, and 454 (42%) received other noncurative treatments including supportive care. Hispanics (adjusted odds ratio [aOR]: 0.58, 95% CI: 0.34–0.98) and Blacks (aOR: 0.47, 95% CI: 0.29–0.76) were less likely to receive curative therapies than Whites. Old age (aOR: 0.66 per 10 years, 95% CI: 0.57–0.75), South (aOR: 0.61, 95% CI: 0.42–0.89) or West (aOR: 0.51, 95% CI: 0.33–0.79) vs. Northeast region was inversely associated with receiving curative therapies while patients receiving care at academic vs. comprehensive community cancer center were more likely to undergo curative treatments (aOR: 1.60, 95% CI: 1.13–2.26).
Conclusion: Early-stage iCCA patients have been increasing over the past two decades. Among patients with early-stage iCCA, Hispanics and Blacks were less likely to receive curative treatments. A comprehensive approach will be needed to eliminate disparities in access to curative treatment among racial-ethnic minorities.

[OP-0993]

Applicability on prognostic biomarker for hepatocellular carcinoma with combinational score using TXNIP and hepatic fibrosis markers

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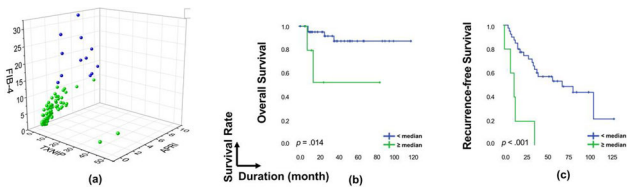
Objectives: Novel noninvasive prognostic markers are urgently needed to improve the prognosis of hepatocellular carcinoma (HCC), especially of chronic viral hepatitis B (HBV)-related HCC. Already, thioredoxin interacting protein (TXNIP) was widely known to act as appears in many cancers. Here, we apply on prognosis biomarker for HCC using TXNIP and several hepatic fibrosis markers.
Materials and Methods: We analyzed in a cohort of 86 patients with HCC with or without HBV. The concentrations of TXNIP levels were measured with a sandwich enzyme-linked immunosorbent assay (ELISA) using Human TXNIP ELISA Kit (Novus biologicals, Colorado, USA) according to the manufacturer's instructions.
Results: We showed that combinational prognostic scores of non-alcoholic fatty liver disease fibrosis score (NFS) x TXNIP and BARD x TXNIP were significantly higher in patients with HCC associated with HBV than HCC patients with non-HBV. Indeed, HCC patients with non-HBV had statistically shorter recurrence free survival (RFS) than those with HCC patients with HBV in higher combinational score of BARD x TXNIP (Median recurrence survival time, 24.6 ± 7.2 vs. 56.4 ± 8.7, $p = 0.013$). Moreover, the high combinational scores of AST to platelet ratio index (APRI) x TXNIP and Fibrosis-4 (FIB-4) x TXNIP were shown significantly shorter overall survival (OS) and RFS than low combinational scores in HCC patients. Interestingly, we performed the clustering and principal component analysis on samples using TXNIP, FIB-4, and APRI factors from patients with HCC for prognosis prediction of survival outcomes. Kaplan–Meier survival analysis demonstrated that patients with higher combinational score ($\geq$ median) was a 10.4 ± 4.2 shorter mean RFS than those with lower combinational score ($<$ median).
Conclusion: Our results suggest that the combinational scores of BARD x TXNIP reflect the potential of HBV-related HCC. Furthermore, combinational scores of APRI x TXNIP and FIB-4 $\times$ TXNIP could be a useful prognosis biomarker for HCC patients.



[PP-0995]

A case of fibrolamellar hepatocellular carcinoma successfully treated with surgical resection

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Objectives: The fibrolamellar hepatocellular carcinoma (HCC) accounts for 1% of all primary liver cancers. Unlike typical HCC, fibrolamellar HCC occurs in young patients without underlying liver disease. We report a case of fibrolamellar HCC which was successfully treated with surgical resection.
Materials and Methods: A case report and literature review.
Results: A 19-year-old female without underlying chronic liver disease visited the outpatient clinic because of abnormal liver enzyme levels from two years ago. The laboratory examination showed elevated liver enzyme tests (AST 66 IU/L, ALT 106 IU/L, alkaline phosphatase 602 U/L). The abdominal ultrasonography showed 13 cm sized lobulated mass in the right liver. The levels of AFP and CA 19–9 levels were within normal range. The magnetic resonance imaging (MRI) showed lobulated liver mass with central scar and prominent arterial enhancement and low signal intensity on delayed and hepatobiliary phase. The biopsy result showed large, polygonal cells with abundant eosinophilic cytoplasm and fibrous stroma arranged in parallel lamellae around tumor cells. Tumor was diagnosed as fibrolamellar HCC. The right hemihepatectomy was performed and she was followed up for 3 years without recurrence.
Conclusion: We report a case of fibrolamellar HCC which was successfully treated with surgical resection.

[PP-0996]

Combined tyrosine kinase inhibitor and immunotherapy therapy as the 1st-line treatment for patients with advanced hepatocellular carcinoma: A real-world single-center experience

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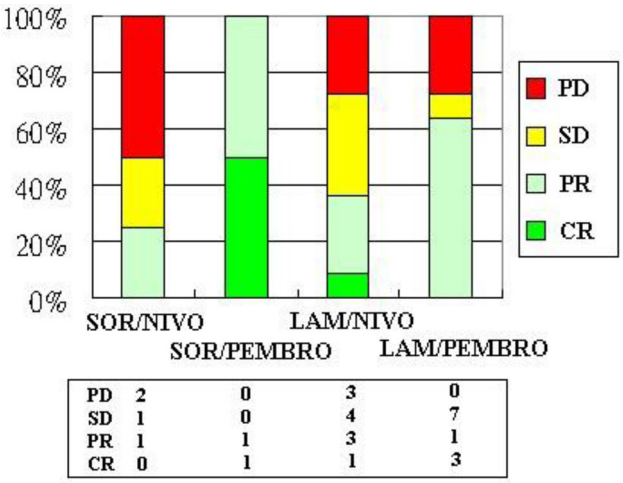
Objectives: Tyrosine kinase inhibitor (TKI), including sorafenib (SOR) or lenvatinib (LEN), and immunotherapy (IO), such as nivolumab (NIVO) or pembrolumab (PEMBRO), are currently accepted the standard treatment for advanced hepatocellular carcinoma (HCC). The aim of the study was to determine the primary outcomes of HCC patients received combined TKI and IO therapy.
Materials and Methods: Data on patients who were receiving combination therapy as the 1st-line treatment for advanced HCC at Taichung Veterans General Hospital from April 2019 to July 2021 were collected. The inclusion criteria included Child–Pugh stage A or B, tolerable to TKI and IO, and survival longer than two months. The general data and outcomes were analyzed.
Results: Among a total of 27 patients, 4, 2, 11, 10 cases received sorafenib SOR/NIVO, SOR/PEMBRO, LEN/NIVO and LEN/PEMBRO respectively. The ORR was 51.8% (14/27) and DCR was 74.1% (20/27). The most common adverse effect was fatigue (33.3%), following by diarrhea (25.9%), hand-foot syndrome reaction (18.5%) and hypertension (11.1%). Further logistic analysis disclosed no predisposing factors were identified to achieve objective response with combination therapy. PEMBRO-based combination therapy had a higher ratio of objective response, but the difference was insignificant (HR 6.01, 95% CI 0.81–44.84, p = 0.085).
Conclusion: Combination therapy with TKI and IO provide acceptable therapeutic outcomes to patients with advance HCC.



[PP-0998]

Prognostic factor analysis of HCC patients who were treated with Sorafenib

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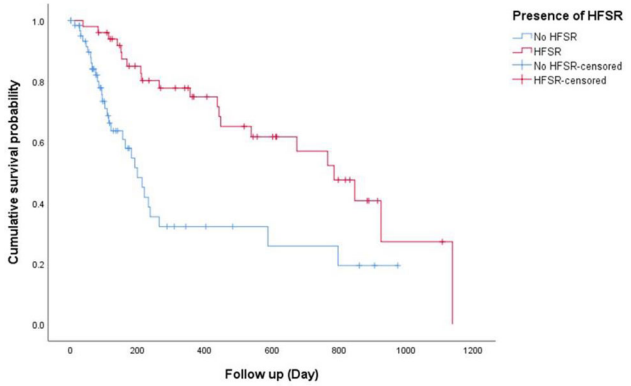
Objectives: Sorafenib is a standard first-line systemic therapy of advanced hepatocellular carcinoma (HCC). However there are few prospective studies that have examined prognostic factors of sorafenib response. In this prospective study, we analyze prognostic factors of HCC patients who were treated with sorafenib.
Materials and Methods: Between May 2016 and May 2018, 288 advanced HCC patients treated with sorafenib were enrolled at 13 hospitals. We analyzed possible prognostic factors of sorafenib response (overall survival and progression free survival) by Univariate and Multivariate analyses using Cox proportional hazards regression model.
Results: Among the 288 patients, chronic hepatitis B (68.4%) was main etiologic factor in development of HCC. Most of the patients (85.4%) were in the advanced Barcelona Clinic Liver Cancer Stage. Hand-foot skin reactions (HFSR) were observed in 142 patients (49.2%). The univariate analysis identified presence of ascites, serum albumin level and creatinine level, presence of HFSR as potential prognostic factors for overall survival (OS). In multivariate analysis for OS, presence of HFSR (HR 0.144; 95% CI: 0.063–0.330, p 0.002), albumin level (HR ratio 0.283; 95% CI: 0.148–0.544, $p < 0.001$), creatinine level (HR 1.395; 95% CI 1.133–1.717, p 0.002) were significant factors of OS. Prognostic factors for PFS were analyzed in the same method. In univariate and multivariate analysis, presence of HFSR (HR 0.212; 95% CI: 0.091–0.495, $p < 0.001$), serum albumin level (HR 0.30, 95% CI: 0.158–0.568, $p < 0.001$) were show significant correlation with PFS.

Conclusion: Developing HFSR from sorafenib therapy and high serum albumin level were associated with improved OS and PFS. Developing HFSR have been suggested as possible predictor of good sorafenib response. Our findings support this suggestion.



[PP-1008]

Rare case of sternal metastasis in unresectable hepatocellular carcinoma treated with lenvatinib

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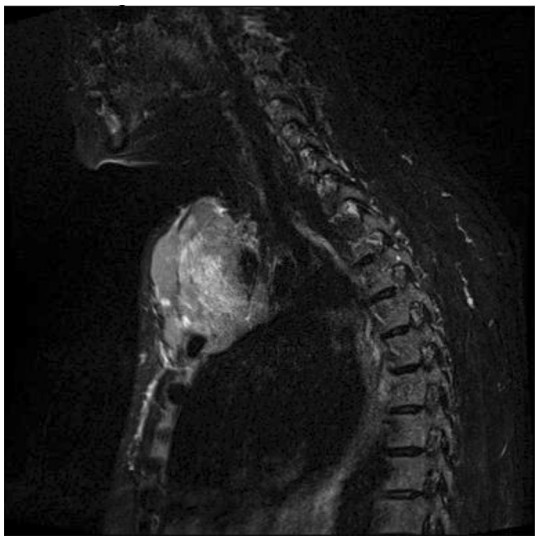
Objectives: Liver cancer ranked seventh as the most common cancer and second as the most common cause of cancer deaths in the world according to GLOBOCAN 2020. Most cases present with right upper abdominal pain. Various studies have reported extrahepatic metastasis in up to 30–50% of cases of HCC, with lungs as the most common site, followed by lymph nodes and bones. However bone metastasis especially in sternum is uncommon. Here, we report a patient with hepatocellular carcinoma who presented with a mass on the chest wall.We reported a 37 year old male HCC patient who presented with soft tissue and bone metastases which initially suspected to have a soft tissue sarcoma.
Materials and Methods: The patient presented with painless mass on chest wall. MRI of the sternum with contrast revealed a large destructive expansive necrotic mass with 11 cm × 6,6 cm × 8,4 cm in size extending to the muscle and subcutaneous tissue over the sternum. Cytologic evaluation of the mass and liver confirmed the diagnosis of hepatocellular carcinoma. The patient was then started with Lenvatinib.
Results: Metastasis to the bone has been found in less than 10% of HCC cases. Bony involvement include vertebrae, pelvis, and very rarely sternum. Treatment options for patients in HCC-BCLC C include systemic chemotherapy. Targeted systemic chemotherapy with Lenvatinib has shown convincing results in the recent REFLECT trial with significant improvement in survival compare to Sorafenib.
Conclusion: Metastatic HCC should be considered as differential diagnosis of rapidly growing metastatic lesions in unusual locations.



[OP-1011]

Safety of percutaneous echo-guided implantation of fiducial markers for respiratory synchronization in stereotactic radiotherapy

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Objectives: Stereotactic body radiotherapy is considered to be effective as a local therapy for hepatocellular carcinoma. However, in many cases, fiducial markers need to be implanted in the body for respiratory synchronization during radiation therapy. The purpose of this study was to evaluate the safety of percutaneous echo-guided marker implantation.
Materials and Methods: We collected demographic data on marker implantation procedures performed at our hospital from March 2012 to December 2020. We investigated the occurrence of complications related to the implantation procedure.
Results: During the above period, 129 patients underwent marker implantation. The age of the patients was 72 (range 40–90). All patients underwent percutaneous implantation of markers under echo guidance. The location of implantation was intrahepatic in 114 cases and extrahepatic lesions in 15 cases. Complications associated with marker implantation included marker dropout in 4 cases and marker stray into the right atrium in 1 case. All of them required reimplantation of the markers, but there were no physical problems for the patients. No complications such as bleeding were observed.
Conclusion: Percutaneous echo-guided implantation of fiducial markers for respiratory synchronization in stereotactic radiotherapy is a safe and essential technique for accurate stereotactic radiotherapy.

[OP-1019]

Thigh muscle thickness can assess sarcopenia in hepatocellular carcinoma

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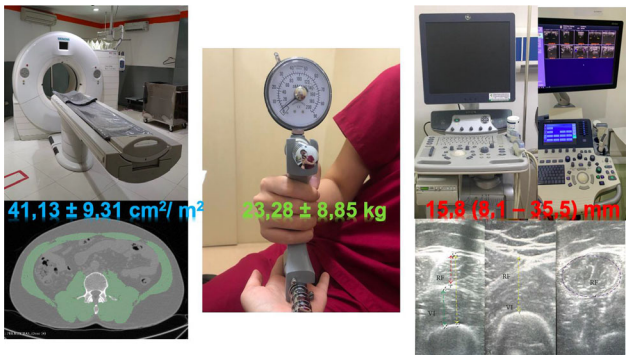
Objectives: This study aimed to compare the thigh muscle thickness (TMT) measured by ultrasound and sarcopenia assessment by lumbar 3 skeletal muscle index (L3SMI), and to investigate the validity and cutoff value of the ultrasonography.
Materials and Methods: We analyzed a total of 85 participants (63 male and 22 female participants, median age, 52 years) visited Hepatology Clinic Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, from January until October 2021. TMT was measured using ultrasound at mid-thigh in the supine position. Skeletal muscle index was measured using CT-scan. Cutoff value of TMT was determined through the receiver operating characteristic analysis. We defined sarcopenia with the diagnostic algorithm of Japan Society of Hepatology.
Results: TMT was significantly reduced in subject with sarcopenia than in those without sarcopenia in both genders. Muscle measurements obtained using the CT-scan methods (L3SMI) and ultrasound methods (TMT) showed a significant correlation, with a correlation coefficient of 0,467 ($p < 0,001$). Area under curve was 0,846 in the male population with cutoff value, sensitivity, and specificity of TMT in diagnosis of muscle loss were 16 mm, 70%, and 77%, respectively.
Conclusion: In conclusion, the ultrasonography for thigh muscle might be a simple diagnostic method for sarcopenia in HCC.



[PP-1020]

A rare case of metastatic bone disease in hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death and the most common primary liver tumor. HCC is an aggressive tumor, especially in tumors greater than 5 cm, known for its propensity to directly invade the portal and hepatic veins. Extrahepatic spread of HCC in metastatic bone disease, frequently multiple and most seen in vertebra, bone lesion comprises only 6–39% of all extrahepatic metastases.
Materials and Methods: We present a rare case of a 58-year-old female with metastatic bone disease in proximal humerus sinistra as extrahepatic spread of HCC.
Results: Patient was diagnosed with HCC and had been given trans arterial chemoembolization (TACE) treatment three times, the last in 2020, came with complaints of pain in the left arm for 2 months that was getting bigger. Left shoulder X-ray results showed a bulging mass in the surgical neck up to the proximal third of the diaphysis of the left humerus, which could be a metastatic process. Cytological biopsy of the mass of humerus sinistra was performed with histopathological features suggesting metastases from HCC. Alpha-fetoprotein (AFP) was high, more than 1000 ng/mL.
Conclusion: This case illustrates of metastatic bone disease in HCC, as uncommon finding extrahepatic spread of HCC, so we must really make sure whether this is a synchronous tumor or coming from the same origin, to determine the best therapy for the patient. But unfortunately, Eastern Cooperative Oncology Group (ECOG) Performance status of this patient was 2, as Barcelona Clinic Liver Cancer (BCLC) system guidelines, we decide to give best supportive care to this patient.

[OP-1024]

Impact of adherence to guidelines on the prognosis of BCLC stage B hepatocellular carcinoma

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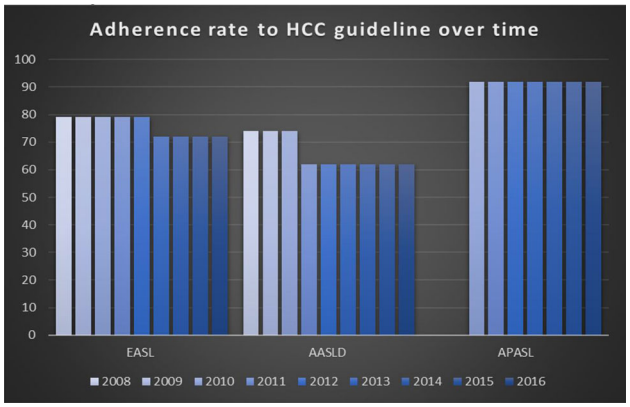
Objectives: We analyzed the impact of adherence to guidelines for the management of hepatocellular carcinoma (HCC) on survival in patients with BCLC stage B HCC.
Materials and Methods: A total of 13,818 subjects with BCLC stage B HCC who were registered in the Central Cancer Registration Program in Korea were followed from 2008 until 2016. Asian–Pacific, European and American Association for the Study of Liver Diseases (respectively, APASL, EASL and AASLD) guidelines was used as criteria for management of HCC. We divided the subjects based on guideline revision year; APASL 2010–16; EASL 2008–12, 2013–16; AASLD 2008–10, 2011–16. The subjects was divided into three groups; the adherence group to guideline (reference group), upward treatment group with curative therapy and downward treatment group with non-curative group. We analyzed overall survival (OS), risk factors for death.
Results: The guideline adherence rate decreased (EASL: 78% to 69%, AASLD: 74% to 62%) over time. The risk of death from HCC in upward treatment group was significantly lower than adherence group except in APASL 2010–16. Median OS (mOS) was significantly higher than adherence group except in AASLD 2011–16; EASL 2008–12, hazard ratio (HR) 0.487 ($p < 0.001$), mOS 69 months; EASL 2013–16, HR 0.542 ($p = 0.0168$), mOS 38 months; AASLD 2008–10, HR 0.368 ($p < 0.001$), mOS 78 months; AASLD 2011–16, HR 0.618 ($p = 0.0015$), mOS 42 months; APASL 2010–16, HR 0.621 ($p = 0.1887$), mOS 39 months. Other risk factors for death from HCC were old age (> 70 years old), high tumor burden (size > 10 cm, number > 3), poor liver function (MELD score > 9 or CPS score > 6) and low serum albumin level (albumin < 3.5 g/dL).

Conclusion: In Korea, the guideline non-adherence rate of up to 38% in patinets with BCLC B HCC. Upward treatment including liver resection, liver transplantation or RFA can improve OS in selected BCLC B HCC patients.



[PP-1031]

Immediate results of surgical treatment of hepatocellular cancer

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Objectives: to evaluate the immediate results of surgical treatment of HCC.
Materials and Methods: From 2012 to 2020 the results of treatment of 25 patients with hepatic GCC were analyzed.14 of them were men (56.0%), 11 (44.0%)-women.The average age of patients was 61 ± 9 years. In 9 patients, the formation was localized in the left lobe, in 13 in the right lobe and 3 patients with bilobar lesion of the liver.
Results: The following types of liver resection were performed: PGE-13, LGEH-9, LLE-1, exploratory laparotomy-2. Blood loss averaged 798 ± 256 ml. Minimum 200 ml. According to the international classification of TNM, patients were distributed as follows: T2N0M0 (stage I)—19, T3N0M0 (stage II)—6, T4N1M0 (stage IV)—1 patients, There were the following types of complications in the postoperative period: hepatic failure of 6 patients, received conservative therapy; in 2 patients, the formation of a nidus of fluid in the abdominal cavity, followed by drainage under local anesthesia, received conservative treatment. One patient had a biliary fistula, which closed on the 14th day after surgery. Postoperative mortality was not observed.
Conclusion: The presence of cirrhosis (CP) and hepatitis in patients with GCC of the liver impair the immediate and long-term results of treatment, but is not a contraindication to surgical treatment. Surgical treatment of HCC requires an accurate preoperative assessment of the functional reserve of the liver.

[OP-1042]

Less intensive HCC surveillance for low PAGE-B or modified PAGE-B scores, is it practical?

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Objectives: PAGE-B and modified PAGE-B scores had been shown to have good predictive performance of HCC risk among chronic hepatitis B (CHB) patients receiving NAs. We conducted a retrospective study of HCC patients diagnosed at our clinic during regular surveillance and analysed how many HCC cases would have been missed if we adopt a less intensive surveillance for the low risk group.
Materials and Methods: Our centers routinely received referrals of CHB patients for initiation antiviral treatments. All these patients had HCC surveillance with ultrasound and AFP determinations every 6 months irrespective of the PAGE-B and modified PAGE-B scores. More frequent surveillance would be performed if deemed necessary by the physicians. We calculated the PAGE-B and modified PAGE-B scores of HCC subjects at 3 years before the diagnosis of HCC to determine how many of them had a low-risk score at that time.
Results: 595 CHB patients were followed up at our center from 01/112013 to 30/09/2021 and 77 HCC patients were diagnosed during this period. Among the HCC patients, 13 had either a low-risk PAGE-B (?9, n = 9) or modified PAGE-B score (≤ 8, n = 11), 8/13 (61%) had BCLC stage A HCC at the time of diagnosis. Four subjects had an immediate PAGE-B score of 12, but a low risk modified PAGE-B score of 4–7. On the other hand, one subject had a PAGE-B score of 6, and a modified PAGE-B score of 7. Mean age of these subjects was 36, range 17–54. Four subjects (30%) were female. Using the PAGE-B score or modified PAGE-B score alone, 11.6% (9/77) and 14.3% (11/77) of HCC subjects could have been missed if they had less intensive HCC surveillance.
Conclusion: The PAGE-B score or modified PAGE-B score could have missed 10% of HCC subjects if a less intensive surveillance program is adopted for CHB subjects with low- risk score.

[OP-1043]

Risk factors associated with post hepatectomy liver failure in patients with hepatocellular carcinoma

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Objectives: Post-hepatectomy liver failure (PHLF) is characterized by an increased international normalized ratio (INR) and hyperbilirubinemia on or after postoperative day 5. PHLF is a serious complication of liver surgery that occurs in about 10% of patients undergoing major liver surgery. It is the main source of morbidity and mortality. We therefore explored the risk factors for PHLF in patients with hepatocellular carcinoma (HCC) undergoing liver resection.

Materials and Methods: This is a retrospective case–control pilot study. We recruited HCC patients who underwent hepatectomy at Fifth Medical Center of Chinese PLA General Hospital from October 2020 to May 2021. Patients were divided into two groups according whether there was development of PHLF. Pre-operative clinical factors were analysed for association with PHLF development.
Results: 62 HCC patients eligible for hepatic resection were analysed, 32 developed PHLF (51.6%). The mean age was 53.02 ± 1.11 years old, 49 (79%) male, 56(90.32%) were hepatitis B infected. Eight patients had portal vein thrombosis, seven and one in the groups with or without PHLF respectively. Presence of portal vein thrombosis ($p = 0.03$), elevated preoperative gamma-glutamyl transpeptidase (GGT > 100 U/L, $p = 0.001$) and aspartate aminotransferase (AST > 40 U/L, upper limit of normal in our laboratory, $p = 0.04$) were associated with development of PHLF. Six subjects with portal vein thrombosis plus either elevated GGT or AST or both developed PHLF. Tumor size, Child scores and segmentectomy versus hepatectomy were not associated with development of PHLF.
Conclusion: Presence of portal vein thrombosis plus elevated GGT or AST may identify a group of patients at high risk of PHLF development. The findings need to be validated with a larger cohort.

[OP-1053]

Impact of initial treatment modality and interval of treatment on survival outcomes of hepatocellular carcinoma

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Objectives: Since repeated treatments damage not only tumor cells but also normal hepatocytes. Therefore, selection of a treatment with a long interval between the first and second treatments may reduce the deterioration of hepatic functions, and also affect survival rates. Thus, this study aims to investigate whether the interval between first and second treatment and choices of first treatment methods affect the survival rates of HCC patients.
Materials and Methods: Among the 10,742 patients with HCC extracted randomly from 2008–2015 national cohort of the Korean Central Cancer Registry, we selected 3,832 patients who had undergone the second treatment. Firstly, BCLC stages were further categorized according to Child-Turcotte-Pugh (CTP) groups, and the interval between the first and second treatments was examined according to the first treatment method. Next, the factors independently affecting the survival rates were evaluated through the Cox proportional hazards regression analysis.
Results: In the BCLC stage 0 and CTP A patient group, there was no significant difference between 19.1 months in the surgical treatment group and 18.3 months in the locoregional therapy group. Interestingly, in HCC patients with BCLC stage A and CTP A, the overall survival was superior to 17.4 months in the group receiving locoreginal treatment compared to the surgical treatment group having a treatment period of 14.7 months. In addition, the BCLC stage C and CTP A patients showed longer treatment interval in the locoregional treatment group, which had a treatment interval of 13 months, compared to the surgical treatment group, which had a treatment interval of 10.5 months. In survival anaylsis, the interval between the first and second treatments is was significant risk factor for overall survival [HR: 0.983 (95% C.I. 0.977–0.989), $P < 0.001$].
Conclusion: Therefore, in selecting treatment modality for HCC, choosing a treatment method that can lengthen the treatment interval could improve the survival of HCC patients.

[OP-1072]

Temporal trends of percutaneous radiofrequency ablation for treatment-nave hepatocellular carcinoma in Milan criteria: 20 years of single-center experience

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Objectives: Radiofrequency ablation (RFA) is widely used for treating hepatocellular carcinoma (HCC) because of its safety, shorter hospital stay, and the conservation of liver function. We aimed to examine temporal trends of long-term results of RFA for treatment-naïve HCC within Milan criteria and analyzed factors affecting treatment outcomes.
Materials and Methods: We retrospectively analyzed 1,099 HCC cases within Milan criteria treated by percutaneous RFA from January 2000 to December 2019 in a single center. Overall survival (OS) and recurrence–free survival (RFS) and factors affecting survivals and local tumor progression (LTP) were analyzed. The trend test was performed to analyze the trend changes in subjects and treatment outcomes.
Results: OS and RFS rates of patients treated in 2010–2019 were higher than those of patients of 2000–2009. Viral hepatitis related HCC has decreased, otherwise, alcohol or NAFLD related HCC has increased. Tumor size and AFP has decreased. Older age, Child–Pugh class B, presence of cirrhosis, and non–viral etiology, and large tumor size were independent prognostic factors for predicting poor OS. Older age, Child–Pugh class B, presence of cirrhosis, non–viral etiology, more than two tumors, large tumor size, and high AFP were independent prognostic factors for predicting poor RFS. Only large tumor size was a factor for predicting LTP. Tumor location, such as subcapsular, subphrenic, or perivascular, was not a significant factor for survival or local tumor progression.
Conclusion: Twenty–year outcomes of RFA showed excellent results in treating early–stage HCC within the Milan criteria. Both characteristics of subjects and treatment outcomes of RFA have changed according to time.

[PP-1090]

The benefit of diabetes-specific oral nutrition support on blood glucose control in a patient with hepatocellular carcinoma and recurrent hypoglycemia: A case report

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Objectives: Patients with advanced hepatocellular carcinoma (HCC) occasionally develop a paraneoplastic syndrome that manifests as hypoglycemia due to the tumor's high metabolic requirements. Hypoglycemia may be caused by both islet and non-islet origin. This may lead to severe complications such as hypoglycemic seizures and associated with a poor prognosis. The objective of this report is to determine whether Diabetes–Specific Oral Nutrition Support (ONS) that contains low glycemic index carbohydrate and fiber could improve blood glucose control in an HCC patient with recurrent hypoglycemia.
Materials and Methods: This is a case report about a 39-year-old-woman with HCC consulted to the clinical nutrition department due to recurrent hypoglycemia despite receiving oral corticosteroid and 40% dextrose via continuous infusion. Her hypoglycemic episodes usually occurred in the early morning. The patient was then given a modified diet consisting of diabetes-specific ONS with a glycemic index of 31 which was consumed before bedtime.
Results: Within 3 days of diet intervention, blood glucose levels were stable ranging from 102 to 154 mg/dL, and the dextrose infusion was tapered down. There were no episodes of hypoglycemic during the intervention. The patient was then discharged home.
Conclusion: Diabetes-specific ONS maintained blood glucose levels and prevent further hypoglycemic episodes in a patient with HCC and recurrent hypoglycemia. The benefit of diabetes-specific ONS in stabilizing blood glucose may be contributed to a low glycemic index, in which the carbohydrates are slowly digested and absorbed.

[OP-1091]

Elasticity characterisation of malignant and benign liver lesions by two-dimensional shear wave elastography

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Objectives: Detection and characterization of focal liver lesions (FLLs) poses a frequent challenge in clinical practice. 2D-Shear Wave elastography (2D-SWE) is a recent technique which uses acoustic radiation force to induce mechanical vibrations and assess tissue elasticity. Our objective in this study was to measure the elasticity characteristics of focal liver lesions by 2D shear wave elastography and to determine if it can be used to differentiate benign from malignant lesions.
Materials and Methods: A cross sectional study done over 2 years in a tertiary hospital. All patients with FLL underwent 2D-SWE and elasticity quantification. Contrast enhanced CT or MRI findings reported by experienced radiologists was used as the reference method for the diagnosis of FLLs.
Results: 216 patients with FLL were evaluated by the 2D-SWE. 130 patients had malignant FLLs of which 90 had Hepatocellular Carcinoma (HCC), 20 had Intrahepatic Cholangiocarcinoma (IHCC) and 20 had metastatic lesions. Of the 86 benign FLL, there were 36 Hemangiomas, 12 FNH, 24 simple cysts, 4 complex cysts, and 10 abscesses. Mean liver stiffness of various lesions by 2D-SWE was 65.7(IHCC), 60.5(HCC), 45.4(Metastases), 7.6(Hemangioma), 16.9(FNH), 9.14(abscess), 8.62(simple cyst) and 2.95(complex cyst). ROC analysis revealed that a SWE cut off of 40 kPa could distinguish between benign and malignant lesions with sensitivity of 100% and specificity of 80%(AUROC of 0.871). The lesion to background liver parenchyma stiffness ratio in cirrhotic patients was 4.81 for IHCC, 3.16 for metastasis and 1.93 For HCC. Therefore in cirrhotic patients, a lesion to liver stiffness ratio < 2 along with SWE of lesion more than 40kpa favors HCC. However in non-cirrhotic livers, there was no statistically significant difference between stiffness ratio of various malignant focal lesions.
Conclusion: 2D-SWE could be a useful non-invasive method for the differentiation of benign and malignant focal lesions of the liver.

[OP-1103]

Clinical impact of screening for HCC in CLD patients: A south Indian teritiary centre persepective

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Objectives: Hepatocellular carcinoma is one of the SOL in liver when diagnosed earlier have very good prognosis. The late diagnosis of HCC leads to high mortality and makes the disease one of the deadliest complication of cirrhosis. We aim through this study to determine incidence, risk factors and Barcelona Clinic Liver Cancer Staging (BCLC) status of the HCC diagnosed during screening at a tertiary care hospital in south india.
Materials and Methods: We undertook an retrospective study at department of hepatology, rajiv Gandhi hospital, india during the period of January 2016 to October 2021. patients of 40 $\geq$ years with diagnosis of cirrhosis, all patient with diagnosis of hbv, hcv were eligible for this study. Symptomatic patients,previous history of hcc was excluded in the study. Screening of patients included ultra sound abdomen with alfa feto protein. Diagnosis was confirmed with triple phase ct abdomen. BCLC criterion was used to stage the disease.
Results: A total of 18,670 patients were inducted in the study.112 patients had SOL Liver.79(0.9%) had diagnosed hcc. Majority of the patients were male 58 (73.5%)0.49 (61.8%) patients had HBV,16(20.1) patients had HCV and 14(18.1%) had other causes.53(68%) had cirrhosis.33(42%)had BCLC A,34(43%) had BCLC B,8(10%) had BCLC C and 4% had BCLC D. median Over all survival was 28.6 months. Patients who underwent screening presented with a better survival ($p < 0.001$).
Conclusion: Our study signifies the importance of screening for HCC and impact on the staging of the HCC. Our study demonstrates earlier screening may open the door of curative treatment for the patients rather than the palliative cure if the diagnosis become late. More stringent screening measure should be implemented in the follow up of the cirrhosis and hepatitis patients.

[OP-1106]

Prognostic nutritional index as a predictor of overall survival in cirrhotic patients with hepatocellular carcinoma

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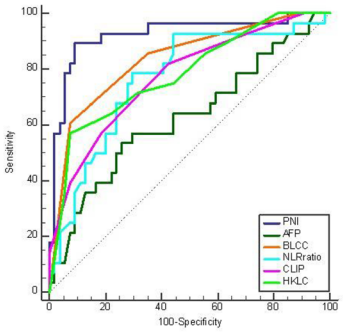
Objectives: There is increasing evidence that the presence of an ongoing systemic inflammatory response is a stage-independent predictor of poor outcome in patients with cancer. We tried to see whether an inflammation-based prognostic score, the prognostic nutritional index (PNI), is associated with overall survival (OS) in cirrhotic patients with hepatocellular carcinoma (HCC).
Materials and Methods: All cirrhotic patients with HCC from September 2019 to March 2021(n = 82) were included and followed up for 6 months. De-novo HCC and other malignancies were excluded. Demographic and clinical data were collected. PNI was calculated as 10 × serum albumin [g/dL]) + (0.005 × lymphocytes/μL). Univariate and multivariate analysis were performed to identify clinicopathological variables associated with OS.
Results: 82 cirrhotic patients with HCC were included and followed up for 6 months. 85% were males and 15% were females. Mortality was 34% at 6 months. Univariate analysis showed that PNI ($p < 0.001$), BCLC score($p < 0.001$), Portal vein thrombus(p-0.038), Hepatic Encephalopathy ($p < 0.001$) and CHILD status ($p < 0.001$) predicted OS. Multivariate analysis showed that PNI was an independent predictor of OS. Receiver Operator Curve (ROC) analysis showed an optimum cut-off value of PNI of 34.8 (sensitivity-89.29, specificity-90.74, Positive predictive value 83.3, Negative Predictive Value- 94.2) (see figure). Multivariate comparison of the prognostic power of PNI and BCLC was done using Cox regression model which showed PNI had a hazard ratio of 17.96 vs 2.1 for BCLC.
Conclusion: The presence of a systemic inflammatory response, as measured by the PNI < / = 34.8 is an independent predictor of poor OS in patients with HCC. The prognostic power of PNI was better than BCLC.

Figure: Comparison of ROC curves of parameters to predict overall survival



	AUC	SE	95% CI
PNI	0.923	0.0363	0.842 to 0.970
AFP	0.627	0.0682	0.513 to 0.731
BCLC	0.836	0.0456	0.737 to 0.908
NLRratio	0.766	0.0567	0.660 to 0.853
CLIP	0.773	0.054	0.667 to 0.858
HKLC	0.781	0.055	0.676 to 0.865

[PP-1115]

Long-term outcomes and evaluation of HCC recurrence after HCV eradication by DAA treatment

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Objectives: Hepatitis C virus (HCV) infection is a risk factor for liver cirrhosis and hepatocellular carcinoma (HCC). In recent years, direct-acting antiviral (DAA) agents have been developed for HCV infection, and current DAA treatment has dramatically improved the cure rate to over 95%. There are limited reports evaluating the long-term outcomes of patients with HCC recurrence after DAA treatment. We conducted a multicenter, longitudinal, 41-month study to retrospectively evaluate the incidence, characteristics, and predictors of HCC recurrence (HCC-R) in a large cohort of HCV patients treated with DAAs.
Materials and Methods: We conducted a multicenter, longitudinal, 41-month study to retrospectively evaluate the incidence, characteristics, and predictors of HCC recurrence (HCC-R) in a large cohort of HCV patients treated with DAAs. The median observation time was 41 ± 13.9 months after DAA treatment.
Results: The recurrence rates of HCC were 23.2%, 32.5%, 46.3%, and 59.4% at 6, 12, 24, and 36 months, respectively. Multivariate analysis showed that palliative treatment before DAAs (HR = 3.755; 95% CI 1.722–7.716; P = 0.0014) and alpha-fetoprotein at sustained virological response12 (HR = 1.043; 95% CI 1.009–1.073; P = 0.0133) were associated with independent factors for HCC recurrence (HCC-R). The 12, 24, and 36 month overall survival rates were 97.6%, 94.0%, and 89.8%, respectively. The 12?, 24?, and 36?month survival rates of the no?recurrence and recurrence groups were 97.7%, 97.7%, and 94.1% and 97.6%, 92.3%, and 87.9%, respectively (P = 0.3404). The size of the main tumor lesion and the serological data were significantly improved at the time of HCC-R after DAA treatment.
Conclusion: This study showed an improved prognosis regardless of recurrence rate, which suggests that DAA treatment in HCV patients should be considered.

[PP-1118]

Usefulness of colorized fusion using CEUS for RFA

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Objectives: Evaluated of usefulness of new technology using colorized fusion with CEUS for RFA.
Materials and Methods: Before RFA, we extracted DICOM data using the 3D volume analyzer system SYNAPSE VINCENT called Synapse 3D internationally and integrated these DICOM data onto US platform. Using this method, we can make colorized fusion images and this new technology can also use contrast enhanced US mode.
Results: 17 patients with eleven HCC and six liver metastasis nodules were enrolled in this study. All cases were able to get the complete response using colorized fusion technology after RFA. This new technology is very useful to understand the segmentation in the liver more easily and visually than usual gray scale US, especially for beginner operators.

Conclusion: This new technology is useful for education and support of CEUS and RFA.

[PP-1120]

Extrahepatic recurrence of hepatocellular carcinoma after radiofrequency ablation or surgery: A 15-year observational study using propensity score matched analysis

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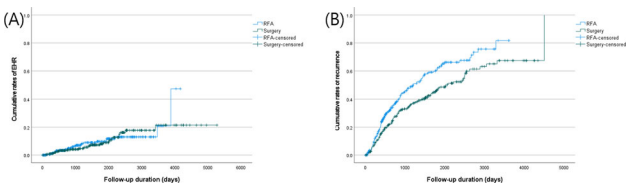
Objectives: Surgery and radiofrequency ablation (RFA) remains the mainstay of treatment of early stage hepatocellular carcinoma. Although extrahepatic metastasis (EHM) of HCC associated with poor outcomes develops in patients after surgery or RFA, the clinical features and risk factors of EHM of HCC remain unclear. We compared and elucidated the characteristics and risk factors of EHM after surgery of RFA for HCC.
Materials and Methods: From January 2008 to December 2019, we retrospectively enrolled 661 patients who underwent RFA and 1069 patients who underwent surgery as first-line treatment for HCC at four tertiary academic hospitals. Using propensity score matching analysis, surgery group patients were 1-on-1 matched to the RFA group using the nearest available pair matching method. Univariate analyses were performed using the chi-squared test, and univariate and multivariate analyses were performed via logistic regression, as appropriate.
Results: After propensity score matching analysis, two hundred and ninety-one patients were finally enrolled from each group. There was no difference regarding tumor size and portion of multiple tumors in RFA and surgery group, 2.51 ± 1.20 vs. 2.54 ± 1.11 (cm), and 10.6% vs. 12.4%, respectively. EHR was diagnosed in 25 patients (8.6%) in RFA group and 28 patients (9.6%) in surgery group (HR 0.93 (0.51–1.60, 95% CI), p = 0.803) during a median follow-up period of 1,498 days. The 10-year cumulative rate of EHR were 20.9% in RFA group and 21.5% in surgery group (p = 0.803). However, RFA group showed higher recurrence rate of HCC than surgery group (51.9% vs. 45.0%, HR 0.67 (0.53–0.85), p = 0.001). The 10-year cumulative rate of recurrence of HCC were 81.7% in RFA group and 67.4% in surgery group (p < 0.001).
Conclusion: RFA and surgery group showed no difference in EHR in long- term follow-up duration, however RFA group showed higher rates of recurrence rates compared to surgery group.



[OP-1130]

Usefulness of serum angiogenic molecules as predictive biomarkers of the early disease progression in atezolizumab plus bevacizumab combination therapy for hepatocellular carcinoma

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Objectives: Atezolizumab (Atezo) plus bevecizumab (Bev) therapy is the first combined immunotherapy that has been shown to be effective for unresectable hepatocellular carcinoma (HCC). However, in some cases, patients switch to other molecular targeted therapies due to early progressive disease (PD), and the development of predictive biomarkers is needed for the response of Aezo + Bev therapy.
Materials and Methods: Forty-one patients with unresectable HCC treated with Atezo + Bev combination therapy at our hospital from September 2020 to October 2021 were included in this study. The changes of angiogenic molecules including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF) and angiopoietin (Ang) in serum samples during the clinical course were analyzed by enzyme-linked immuno-sorbent assay. Therapeutic effects were evaluated by modified RECIST.
Results: Twenty-six patients were found to have the disease control (DC: complete response, 3 patients; partial response, 8 patients; stable disease, 15 patients) and 15 patients have the PD. There were no significant differences in median VEGF, PDGF, FGF, and Ang levels at baseline between the DC and PD groups. Within a day after treatment, VEGF levels decreased to below detection sensitivity in the two groups (median levels at baseline, 234.7 vs 317.2 ng/ml, p = 0.074; and median levels the day after treatment, 0.0 vs 0.0 ng/ml, p = 0.778, in the DC and PD groups, respectively). Although the ratio of VEGF levels a week after treatment relative to baseline was not significantly different in the both groups, the ratio of those 3 weeks after treatment was significantly higher in the PD group than that in the DC group (ratio at a week, 0.49 vs 0.54, p = 0.187; and ratio at 3 weeks, 0.98 vs 1.38, p < 0.01, in the DC and PD groups, respectively).
Conclusion: Serum VEGF might be a predictive biomarker for detection of early PD in Atezo + Bev therapy.

[PP-1147]

Multidisciplinary management with immune checkpoint inhibitor for treatment of advanced HCC

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Objectives: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related death and its incidence continuously rises

worldwide. Because the previous study showed remarkable advancement in HCC treatment with atezolizumab plus bevacizumab versus sorafenib, now, it became the first-line treatment for the advanced stage of HCC from Barcelona Clinic Liver Cancer (BCLC) staging system. Since our two patients had the advanced stage of HCC with good liver function and performance status, we performed multidisciplinary treatment including atezolizumab plus bevacizumab.
Materials and Methods: N-A.
Results: The first case had 11 cm-sized HCC on the left hemisphere related to chronic hepatitis B infection with main and left portal vein tumor. Modified UICC stage IVa and advanced stage from BCLC staging system. He showed partial response (PR) after the 8th cycle of atezolizumab plus bevacizumab treatment followed by hepatic arterial infusion chemotherapy (HAIC) based on cisplatin and 5-fluorouracil with 2-week of radiotherapy on the abdomen. The second case had 24 cm-sized huge HCC on the right hemisphere which was related to alcohol intake with multiple lung metastases. Modified UICC stage IVb and advanced stage from BCLC staging system. We started treatment with trans-arterial chemoembolization (TACE) and HAIC but multiple lung metastases were progressed so changed the therapeutic plan with atezolizumab plus bevacizumab. Because his tumor showed progressive lung metastasis after the 13th cycle of atezolizumab plus bevacizumab treatment, his therapeutic plan was changed to lenvatinib, then PR was observed for 5 months.
Conclusion: Because HCC is a highly chemotherapy-resistant tumor and most HCC has underlying liver cirrhosis from multiple origins—such as viral infection, alcohol intake, non-alcoholic steatohepatitis-related, autoimmune-related, et cetera (etc.), it is difficult to make standardized therapeutic plan, especially advanced stage. Further studies are needed to prove the effectiveness of multidisciplinary treatment including radiotherapy, TACE, HAIC, etc. with atezolizumab plus bevacizumab than a single treatment.

[PP-1155]

Surveillance of hepatocelluar carcinoma in Korea after National reimbursement

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Objectives: Biannual hepatocellular carcinoma (HCC) surveillance of ultrasound (US) and alpha-fetoprotein (AFP) is recommended for chronic viral hepatitis and liver cirrhosis. In Korea, US was reimbursed in April 2018. After reimbursement, nationwide situation of the HCC surveillance program could be analyzed. We aimed to check if the HCC surveillance program was progressed as scheduled, and whether biannual surveillance can detect early HCC compared to insufficient surveillance.
Materials and Methods: The National Health Insurance database was reviewed, and patients diagnosed with chronic viral hepatitis and liver cirrhosis from 2018 to 2019 were extracted. Surveillance schedule and development of HCC was analyzed. Early HCC was defined by treatment methods.
Results: A total of 731,691 patients were included: chronic viral hepatitis 562,962 (76.9%), liver cirrhosis (23.1%). In chronic viral hepatitis patients, biannual surveillance was performed in 333,223 (59.2%), insufficient surveillance in 164,653 (29.2%), excess surveillance in 65,086 (11.6%). In liver cirrhosis patients, biannual surveillance was performed in 91,990 (54.5%), insufficient surveillance in 46,966 (27.8%), excess surveillance in 29,773 (17.6%). Higher proportion of early HCC patients was detected in the biannual surveillance group compared to the insufficient surveillance group.
Conclusion: In Korea, HCC surveillance program was performed in 71% patients as scheduled, and regular surveillance detected more early HCC patients.

[L-PP-1211]

Clinical outcomes and genomic evolution of FGFR2 fusions/rearrangements in intrahepatic cholangiocarcinoma

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Objectives: Fibroblast growth factor receptor 2 (FGFR2) alterations are found 14–20% patients with intrahepatic cholangiocarcinoma. FGFR inhibitors, pemigatinib and infigratinib received approval for advanced cholangiocarcinoma with FGFR2 fusions/rearrangements in second-line setting. There are limited data about evolution of mutational profiles post-progression from FGFR2 inhibition.
Materials and Methods: Clinical outcomes and mutational data - were collected via an institutional tissue DNA sequencing panel and cell-free DNA (cfDNA). A total of 102 patients treated at MD Anderson Cancer Center from 2013–2021 with intrahepatic cholangiocarcinoma harboring FGFR2 fusions (91 patients) and rearrangements (11) were analyzed.
Results: Female 55 (54%), male 47 (46%); 99 patients had stage IV, 3 with stage IIIB at initiation of FGFR inhibition; median age, 59. Out of 91 with FGFR2 fusions, 52 different fusion partners were BICC1, AHCYL1, TACC2, and NOL4 in 24, 5, 4, and 3. 42 with FGFR2 fusions and 9 with FGFR2 rearrangements received FGFR inhibitors: these include infigratinib (13), pemigatinib (17), futibatinib (14), derazantinib (5), and zoligratinib (2). Out of 51, 14 (28%) received FGFR inhibition in front-line setting, 15 (29%) and 22 (43%) received one prior, two/more (2—6). Median progression-free survival in 51 patients was 8.8 months (95% CI, 7.2—10.3), and median overall survival was 24.7 months (95% CI, 15.9—33.2). 18 patients with FGFR2 fusions had mutational profiles before and post-progression on FGFR2 inhibition: 15 (83%) showed no more FGFR2 fusions; 3 showed the same fusions after progression. New FGFR alterations post-progression included FGFR1_K139I, FGFR2_N549K (2), FGFR2_N549H, FGFR2_V564F, FGFR2-SYNPO2. New gene mutations that did not exist before FGFR inhibition but developed post-progression included PIK3CA (2), APC (2), BRAF V600E/A694T, NRAS, BAP1, GNAS, TP53, and others.
Conclusion: Genomic evolution post-progression on FGFR inhibition involves acquired resistance in multiple pathways. Targeting co-alterations post-progression with drug combination may overcome these resistance mechanisms and potentiate efficacy of FGFR inhibition.

[L-PP-1212]

Clinical outcomes analysis of TP53-mutated advanced and metastatic biliary tract cancers

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Objectives: Cholangiocarcinoma (CCA) is lethal malignancy with short survival. Median progression-free survival (mPFS) is 8.0 months with gemcitabine-cisplatin (GC) in front-line setting. TP53-mutation is known to be associated with poor prognosis in other cancers, but its impact on survival in CCA has not been detailed.
Materials and Methods: Mutational profiles were obtained via institutional DNA sequencing panels. Out of 149 patients with TP53-mutations in CCA, 90 had metastatic CCA in 2015–2021. These were not candidates for surgery, radiation, or liver-directed therapy.
Results: Intrahepatic, hilar, distal CCA and gallbladder cancer were confirmed in 66, 11, 10, and 3. Median age, 63; male:female ratio, 1:1. Poorly, moderately, and well-differentiated adenocarcinomas, in 62, 20, and 1 (not available in 7). The most common TP53-mutations were R175H (n = 5) and R248Q (n = 4). Common co-mutations included KRAS (n = 15), ARID1A (n = 15), FGFR2 fusion (n = 14), IDH1 (n = 13), BAP1 (n = 10), CDKN2A (n = 9), HER2-amplification (n = 8). Microsatellite unstable tumors were in 3. Median tumor mutational burden, 2.5/Mb. Patients received front-line GC (n = 54), GC-nab-paclitaxel (GAP, n = 14), FOLFIRINOX (n = 3), and GC with targeted or trial-therapy (n = 11). mPFS with front-line therapy was 5.0 m (n = 90); 4.7 m with GC and 5.1 m with GAP. Patients who had co-mutated IDH1 or FGFR2 had longer mPFS (9.5 and 6.9 m) than those who did not (n = 63, 3.7 m, $p < 0.05$) from front-line chemotherapy. mPFS after second-line FOLFOX (n = 17) and FOLFIRI (n = 10) was 2.1 and 1.9 m, and mPFS after third-line FOLFOX/FOLFIRI was 1.8 m (n = 8). Median overall survival (OS) in co-mutated FGFR2, IDH1, or neither was 34.5, 22.0, and 13.1 m ($p < 0.05$). TP53-mutated CCA with mutations other than FGFR2/IDH1 did not show significant difference in PFS or OS.
Conclusion: Patients with TP53-mutations have shorter PFS than those without TP53-mutation in front/further-line settings. Presence of co-mutated FGFR2/IDH1 is associated with improved PFS with chemotherapy (not FGFR/IDH1 inhibitors) and longer OS. Other co-mutations do not have survival benefit.

[L-PP-1222]

Resection of liver metastases from colorectal cancer. Indications and results

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Objectives: This study was undertaken to determine the indications for and value of liver resection for metastases from colorectal cancer.
Materials and Methods: From 1978 through 1991, 66 patients were operated on for liver metastases from colorectal cancer. All patients had had a curative resection of their colorectal cancer. Forty resections of the liver were major anatomic resections.
Results: Five patients died in the postoperative period. All resections were intended to be curative, but in 16 of the patients the resection became noncurative. None of these patients lived more than two years after liver resection. Fifty patients with a curative resection had a three-year survival rate of 36 percent, postoperative death included. Recurrence in the liver was observed in 30 patients (60 percent) from 3 to 33 (median, 11) months after the liver resection. Four patients had repeated resections performed. Two of them are alive without recurrences 34 and 60 months after the first liver resection, respectively. The difference in survival between curative and noncurative liver resection was highly significant (P = 0.01).
Conclusion: Sex, age, Dukes stage of primary colorectal cancer, synchronous or metachronous appearance of metastases, or number of metastases could not predict long-term prognosis. The only factors of predictive value were tumor size less than 4 cm in diameter, a free resection margin, and no extrahepatic tumor. If it is possible to do a curative resection, there should be few contraindications against liver surgery as it is the only treatment that can demonstrate long-term survival for approximately one-third of the patients, and it is the only possibility of a cure.

[L-OP-1224]

Circulating tumor cells (CTCs); A prognostic biomarker in patients with hepatocellular carcinoma (HCC)

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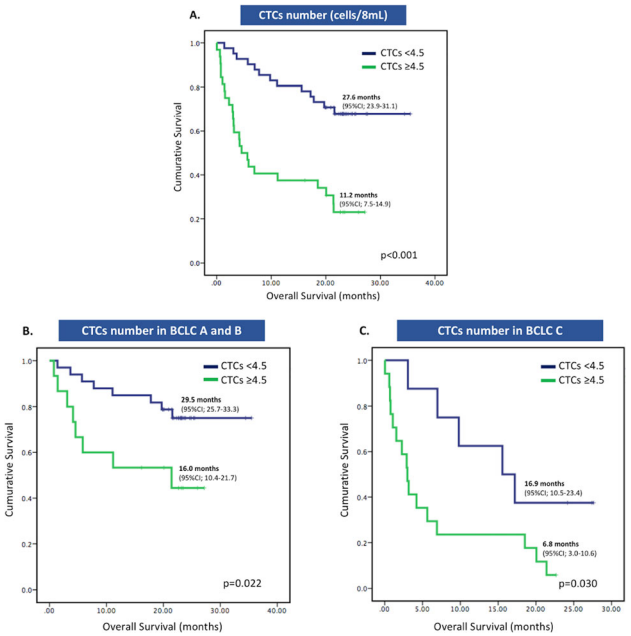
Objectives: Circulating tumor cells (CTCs) have been shown as a surrogate for tumor progression and metastasis. CTCs may determine treatment options, treatment response, and patient prognosis. We aimed to assess the association between CTCs and the survival of hepatocellular carcinoma (HCC) patients.
Materials and Methods: A single-center, prospective cohort study was conducted between April 2019 and November 2021. Peripheral blood of 8-mL was collected to measure the number of CTCs, defined as cells positive for epithelial cell adhesion molecule (EpCAM) and mucin 1 (MUC1) on fluorescent microscopy. Survival and associated with survival were analyzed.
Results: Seventy-three HCC patients were included with 56 (77%) males, mean age 60 + 12 years. There were 26 (35.5%), 22 (30.1%) and 25 (34.2%) patients with Barcelona Clinic Liver Cancer (BCLC) stage A, B and C, respectively. The median survival time was 20.1 months (range: 0.03–35.5). During 3-year follow up period, 37 (50.7%) patients had died. The number of CTCs had significant inverse correlation with the survival (r = -0.288, p = 0.014), with more number of CTCs in the deceased group than the survived group (37.8 + 116.5 vs. 4.3 + 7.8 cells/8-mL, p = 0.001). With a cutoff of 4.5 cells/8-mL, patients with CTCs < 4.5 had significantly longer survival than those with CTCs > 4.5 (27.6 vs. 11.2 months, $p < 0.001$) (Fig. 1A). This finding remained consistent when classified by BCLC stages (29.5 vs. 16.0 months and 16.9 vs. 6.8 months,

for BCLC A/B and C; p = 0.02 and 0.03, respectively (Fig. 1B-1C). By multivariate analysis, BCLC B and C, MELD score > 15 and CTCs > 4.5 cells/8 mL were independently associated with survival, with adjusted HRs (95%CI) of 5.0 (1.5–17.3), 8.3 (2.4–28.8), 5.5 (2.1–14.5), and 2.2 (1.0–4.7; p = 0.009, 0.001, 0.001, and 0.041, respectively.
Conclusion: This study demonstrates the potential of peripheral CTCs as a prognostic biomarker for HCC. A large prospective cohort study is warranted to validate these findings.



[L-PP-1235]

Cause of death from liver metastases in colorectal cancer

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Objectives: Surgically directed therapy for liver metastases from colorectal cancer (CRC) has received substantial attention in the literature as a major focus of treatment for metastatic CRC. It is presumed, but not proven, that liver metastases are a major threat to life. This study examined the course of a cohort of consecutive patients who died with CRC to determine the role played by the presence of liver metastases.
Materials and Methods: This is single-institution retrospective observational study involved all patients who died of CRC. Records were examined and imaging studies reviewed to determine the extent of liver and extrahepatic metastases in these patients. Overall survival in patients with and without liver metastases and those in whom liver metastases were thought to contribute to death was determined.
Results: After patient exclusions, the study population totaled 121 patients. There were 75 patients (62%) with liver metastases at death. In 40 of 75 (53%) patients, the liver metastases contributed to the patients' death. In 46 of 121 patients (38%), metastatic disease did not include liver metastases. Overall survival in patients with and without liver metastases (median survival 12 vs. 8.5 months, p = 0.089) and in those whose liver metastases did or did not contribute to death (median survival 11.5 vs. 14 months, p = 0.361) was not significant.
Conclusion: The presence of liver metastases seemed to contribute to death in approximately half of the study patients, although there did not appear to be a survival disadvantage in these patients.

[L-PP-1244]

Postoperative prediction of and strategy for metastatic recurrent hepatocellular carcinoma according

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Objectives: The hepatitis activity index (HAI) score describes the histologic status of accompanying chronic hepatitis and was established by pathologists. The aim of this study was twofold: 1) to investigate the correlation between intrahepatic metastatic recurrence (IM) and the HAI score of the noncancerous region of the liver and 2) to estimate the usefulness of postoperative preventive chemotherapy in patients with hepatocellular carcinoma.
Materials and Methods: The study included 158 consecutive patients who underwent curative resection for HCC and had been observed for > 1 year. Based on the HAI scores of the noncancerous region the patients were classified into 3 groups: those with mild hepatitis (n = 33) (i.e., with HAI scores of 0–5), those with moderate hepatitis (n = 77) (with HAI scores of 6–9), and those with severe hepatitis (n = 48) (those with HAI scores of > or = 10). In addition, a prospective randomized trial of postoperative adjuvant chemotherapy was performed for 21 patients with moderate hepatitis.
Results: The patients in the moderate hepatitis group were found to be at higher risk for IM recurrence within 2 years after HCC resection compared with those patients in the mild (P = 0.05) and severe (P < 0.01) hepatitis groups. Multivariate analysis showed that intraoperative bleeding volume, the number of nodules, portal vein involvement, and moderate hepatitis were independent predictive factors for IM recurrence free survival. Ten patients with moderate hepatitis had received postoperative intrahepatic arterial chemotherapy (2–3 courses with a maximum dose of 80 mg of cisplatin and 10 mg of mitomycin C at 1-month intervals) for the last 3 years.
Conclusion: The patients with moderate hepatitis (HAI score of 6–9) had the highest rate of IM recurrence among the three HAI groups. Postoperative hepatic arterial chemotherapy may be useful in improving the rate of disease free survival after surgery among these patients.

[L-PP-1245]

Portal vein embolisation for extended hepatectomy: Single-centre experience

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Objectives: Portal vein embolisation (PVE) induces contra-lateral liver hypertrophy to facilitate an extended hepatectomy. This paper aims to analyse our data on PVE and extended hepatectomy. Outcome measures included success of PVE, feasibility of resections, operative morbidity and survival.
Materials and Methods: A retrospective analysis of data collected prospectively on 33 patients (2004–2008) was performed. Survival curves were estimated by the Kaplan–Meier (Breslow) method. Significance was defined as $p < 0.05$.
Results: A total of 31 patients had successful PVE. There were 24 patients who underwent surgery. Significant hypertrophy of residual liver was noted from 230.15 (pre-embolisation) to 428.50 ml (post-embolisation) (median, $p < 0.0001$). A total of 16 patients had hepatectomy (14: R0; 2: R1) with a single mortality (6.25%) and 56.25% morbidity, and a median length of stay of 17 days. Median overall survival was 14 (95% CI 7.8–20.2) months. Patients who underwent resection had a median disease-specific survival of 33 (95% CI 4–62) months compared with 8.6 (95% CI 0–19.9) months for patients without resection ($p = 0.14$). For patients with primary hepato-biliary tumours, the median disease-specific survival was 7.9 (95% CI 4.5–11.3) months compared with a median survival of 19.7 (95% CI 0–42.2) months for patients with metastases ($p = 0.07$).
Conclusion: PVE is safe, facilitates R0 resection and offers the best chance of cure, especially for liver metastases.

[L-OP-1248]

The impact of high body mass index on hepatocellular carcinoma in persons with no liver diseases: Prospective cohort study in over 14million Korean adults

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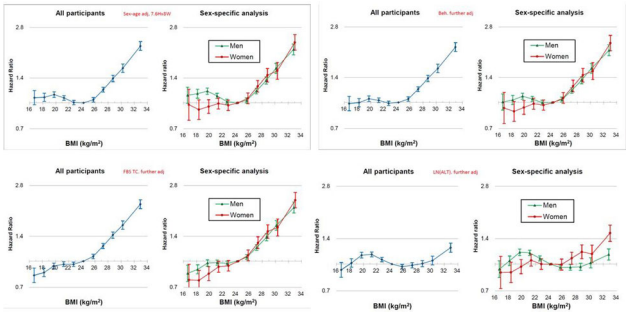
Objectives: The impact of overweight, defined by body mass index (BMI), on hepatocellular carcinoma (HCC) has been unclear. The impact of obesity per se was less apparent in Asian populations. We investigated the association between BMI and HCC in Korean general populations.
Materials and Methods: In total, 14,265,822 Korean adults who underwent routine health examinations during 2003–2006 were followed up for HCC until December 2018 via linkage to the national hospital discharge records. Multivariable-adjusted hazard ratios (HRs) associated with BMI were calculated using Cox models.
Results: During mean 13.7 years of follow-up, 47,308 individuals developed HCC. Multivariable-adjusted HRs of HCC associated with BMI of 23.0–24.9 (reference), 25.0–27.4, 27.5–29.9, and $\geq$ 30 kg/m^2 were 1.0, 1.09, 1.38 and 1.89, respectively. In the BMI range $<$ 25 kg/m^2, linear associations between BMI and HCC was not apparent. Assuming linear associations in the range $\geq$ 25 kg/m^2, HR per each 5 kg/m^2 increase in BMI was 1.60 for all participants, 1.60 for men, and 1.59 for women. the corresponding HRs were 1.56, 1.61, and 1.60 for individuals aged $<$ 45, 45–64, and $\geq$ 65 years old, respectively. Further adjustment for the mediators of the effect of BMI, especially, alanine aminotrasferase (ALT) levels, substantially reduced HRs associated with high BMIs, especially in men and younger adults.
Conclusion: BMI had a non-linear association with HCC risk: in the BMI range of $\geq$ 25 kg/m^2, a higher BMI increased the risk of HCC, regardless of sex and age, but not in the range $<$ 25 kg/m^2. The impact of high BMI on HCC development may be substantially mediated through high ALT levels especially in men and younger adults, but less in women and older adults.



[L-OP-1266]

Acute critical illness and liver cancer risk: Implications from a nationwide population based study in Asia

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Objectives: The objective of this study was to identify the risk of incident cancer among patients with acute critical illness.
Materials and Methods: The study applied the big database from the National Health Research Institutes in Taiwan. The risk of incident cancer over a 12-year period in patients with 4 types of newly diagnosed acute critical illness (septicemia/septic shock, acute myocardial infarction, hemorrhagic stroke and ischemic stroke) was investigated using Cox proportional hazards regression model with further controlling for the competing risk of death.
Results: This study included 42,675 patients in the acute critical illness cohort and 42,675 patients in the age- and sex-matched comparison cohort. Correlation between the incidence of cancer and critical illness was found after adjusting for age, sex, comorbidities and further controlling for death [adjusted subhazard ratio (aSHR) = 1.73, 95% confidence interval (CI) = 1.63–1.84]. Five common incident cancers associated with acute critical illness were hematologic malignancy (aSHR = 4.00, 95% CI = 3.11–5.14), cancers of liver (aSHR = 2.25, 95% CI = 1.93–2.63), uterus (aSHR = 1.86, 95% CI = 1.32–2.61), head and neck (aSHR = 1.79, 95% CI = 1.39–2.30) and esophagus (aSHR = 1.62, 95% CI = 1.09–2.42). Among these cancers, septicemia/septic shock was found to confer a higher risk of incident cancer compared to other subtypes of acute critical illness.
Conclusion: This research is the first to tackle this clinically relevant issue regarding the types of acute critical illness most associated with cancer development with a very large sample size and robust methods. After adjustment for the potential confounding factors and consideration of the competing risk of death, the association between having an acute critical illness and incident cancer was noted.

[L-PP-1321]

Utilisation of PIVKA-II in the surveillance and monitoring of hepatocellular carcinoma in the Asia–Pacific region

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Objectives: Though PIVKA-II (protein-induced vitamin K absence II) has shown some utility in surveillance, treatment monitoring, and predicting recurrence in HCC, it is still not recommended as a routine biomarker test.
Materials and Methods: Seventeen experts in hepatology, surgical and medical oncology, and laboratory medicine from across Asia–Pacific gathered to discuss the clinical usefulness and value of PIVKA-II in HCC surveillance and treatment monitoring within the region. Six predetermine statements were voted on (agree/disagree) based on evidence review, and the clinical experiences and opinions of the experts. In total, four rounds of voting were conducted. The statements for each round were refined based on the experts' comments. The resultant outcomes for the statements were "strongly agree" (> 80% agreement), "agree with condition" (50–80% agreement), and "inconclusive" (< 50% agreement).
Results: The level of consensus for each of the final six statements were, (1) PIVKA-II is best used in combination with AFP in the detection of HCC, including small sized tumours ($\leq$ 3 cm), compared to either biomarker alone (88.2%), (2) PIVKA-II is valuable in the detection of HCC in AFP-negative HCC patients (100%), (3) Pre-operative PIVKA-II measurement predicts the microvascular invasion risk, which may be useful in the assessment of tumour prognosis (94.1%), (4) PIVKA-II measurements, before and after curative treatment, (resection and radiofrequency ablation) are useful for monitoring treatment outcomes and recurrence (100%), (5) PIVKA-II measurements before and after intra-arterial treatment (transarterial chemoembolisation and transarterial radioembolisation) are clinically useful to indicate response (94.1%), and (6) Pre-liver transplant PIVKA-II levels are associated with the risk of post-operative HCC recurrence, potentially facilitating the patient selection (88.2%).
Conclusion: Implementation of PIVKA-II in the region will have some challenges such as requiring standardisation of cut-off values, evidence of its cost-effectiveness and improving awareness among healthcare providers.

[L-OP-1330]

Extracellular vesicle-derived von Willebrand factor (vWF) activates VEGF-A and FGF2 pathway to promote tumorigenesis in hepatocellular carcinoma

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Objectives: Hepatocellular carcinoma (HCC) is a hypervascular tumor by which angiogenesis facilitates tumor growth and dissemination. Here, we aim to delineate the functions of crosstalk between cancer and endothelial cells mediated by HCC-derived extracellular vesicles (EVs) and to evaluate the clinical significance of EV components in HCC.
Materials and Methods: Proteomic profiling of circulating EVs of control individuals and HCC patients was performed to identify functional proteins in patients' EVs. The identified target was examined for its expression in HCC patients and functionally characterized by in vitro assays and animal models.
Results: Von Willebrand factor (vWF) in circulating EVs was found to be increased progressively along HCC development. Using ELISA, elevation of EV-vWF was validated in a cohort of early and late stage patients and metastatic cell lines compared to corresponding controls. Late stage patient-derived circulating EVs augmented metastasis, angiogenesis and pulmonary leakiness in mice. The promoting effects of patient's EVs was significantly dampened by anti-vWF antibody. To corroborate the role of EV-vWF, vWF was expressed in non-metastatic cells using CRISPR/Cas9 synergistic activation mediator (SAM). Consistently, EVs with increased vWF-SAM expression exerted enhanced promoting effect compared to control EVs. Mechanistically, EV-vWF activated the release of VEGF-A and FGF2 by endothelial cells, resulting in promoted angiogenesis and tumour-endothelial attachment. A positive feedback response mediated by FGF2 released by endothelial cells enhanced the cancerous properties of HCC cells. Knockdown of FGF2 receptor in HCC cells compromised the enhancing effect of FGF2. Lastly, the administration of VEGF-A and FGF2 antibodies significantly inhibited metastasis induced by EV of vWF-SAM cells.
Conclusion: This study unveils a mutual stimulation between HCC and endothelial cells mediated by EVs of cancer cells and endothelial angiogenic factors, facilitating cancer metastasis. It also provides insights into the exploitation of blocking cancer-endothelial communication as a therapeutic strategy for HCC.

[L-OP-1333]

Do ω-3 polyunsaturated fatty acids benefit patients undergoing liver operation? A systematic review and meta-analysis of randomized control trials

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Objectives: As a component of parenteral nutrition emulsion, ω-3 polyunsaturated fatty acids are widely adopted in postoperative patients. This meta-analysis of randomized controlled trials (RCT) aims to evaluate the effect of ω-3 polyunsaturated fatty acids on patients undergoing liver surgery.
Materials and Methods: The papers of this meta-analysis were collected from these databases: PubMed, the Cochrane Central Register of Controlled Trials, Springer link, Web of Science, China National Knowledge Infrastructure, and VIP Database. and this meta-analysis was conducted mainly using RevMan 5.3.5 software.
Results: 8 randomized control trials including 748 patients (I: 374; C: 374) were finally enrolled in the meta-analysis. The ω-3 polyunsaturated fatty acids significantly decrease the levels of AST (MD -42.72 [-71.91, -13.52]; $p = 0.004$), ALT (MD -38.90 [-65.44, -12.37]; $p = 0.004$), WBC (MD -0.93 [-1.60, -0.26]; $p = 0.007$), and IL-6 (MD -11.37 [-14.62, -8.13]; $p < 0.00001$) in patients who undergo the liver operation, and increase the albumin levels (MD 0.42 [0.26, 0.57]; $p < 0.00001$). They also reduces the infection complication (OR 0.44 [0.28, 0.68]; $p = 0.0003$) and duration of hospital stay (MD -2.17 [-3.04, -1.3]; $p < 0.00001$). However, there are no significant differences in the levels of Tbil, TNF-α, IL-2, IgA, IgG, IgM and CD3, biliary leakage, and mortality.
Conclusion: According to the results of this meta-analysis, the ω-3 polyunsaturated fatty acids can benefit patients undergoing liver operation by promoting liver function, decreasing related inflammation makers, and improving certain clinical indexes. But the RCT studies of the application of ω-3 polyunsaturated fatty acids on patients undergoing liver surgery remain few. Further evidence of the benefit of ω-3 polyunsaturated fatty acids for these patients is needed in the future.

[L-OP-1336]

Long-term effectiveness of population-wide multifaceted interventions for hepatocellular carcinoma in Taiwan

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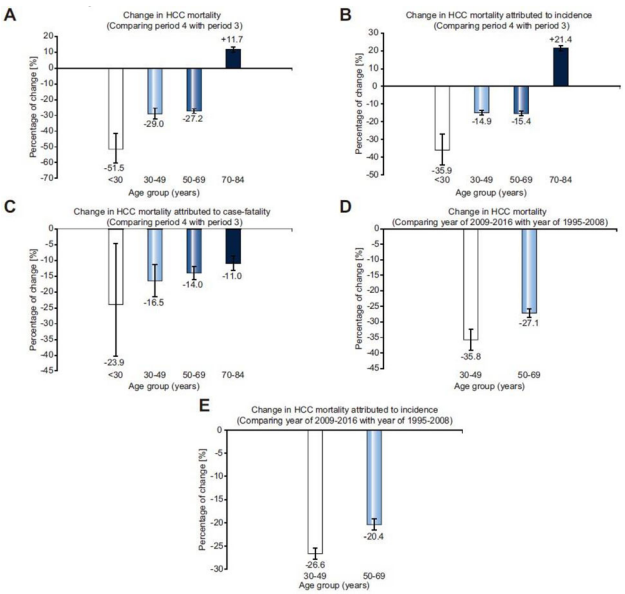
Objectives: Taiwan has launched a series of population-wide interventions on hepatocellular carcinoma (HCC) related to hepatitis B and C virus infection since 1984. It therefore provides a natural opportunity to evaluate whether the reduction of HCC incidence, to a greater extent, and the improvement of case-fatality, to a lesser extent, or vice versa make contribution to the resultant mortality reduction given each intervention program.
Materials and Methods: Population-based registry data on HCC mortality and incidence of individuals aged 0 to 84 years between 1979 and 2016 were collected before (period 1) and after intervention with three periods, universal hepatitis B vaccination from 1984 (period 2), universal health care from 1995 (period 3), and viral hepatitis therapy from 2003 (period 4). A Bayesian Poisson regression model for decomposing mortality rate was developed to estimate respective contributions to the reduction of incidence and case-fatality rate by various age groups.
Results: The mortality trends of children, young- and middle-aged groups substantially declined but there was only a slight decrease in the elderly group. The declining trends of mortality were in part explained by incidence reduction and in part by a remarkable decline in case-fatality rate attributed to universal health care. Hepatitis B vaccination led to 35.9% (26.8% to 44.4%) reduction of incidence for aged 30 years or below, whereas antiviral therapy made contribution to the reduction of 14.9% (11.8% to 17.9%) and 15.4% (14.1% to 16.6%) for aged 30–49 years and 50–69 years, respectively.
Conclusion: Vaccination and anti-viral therapy were effective in reducing HCC incidence and mortality for the young and middle-aged groups when the case-fatality was improved due to universal health care for all age groups.



[L-OP-1338]

Comparison of sorafenib and lenvatinib for the management of pulmonary metastasis of hepatocellular carcinoma

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Objectives: Lenvatinib has been approved as a first-line therapy for unresectable hepatocellular carcinoma (HCC), with comparable efficacy of previously approved sorafenib. However, it is not established whether lenvatinib has similar efficacy in controlling extrahepatic metastasis. The objective of this study was to compare the effect of

lenvatinib and sorafenib for the treatment of pulmonary metastastasis in patients with HCC.
Materials and Methods: We enrolled 365 patients treated with sorafenib or lenvatinib as the first?line therapy for hepatocellular carcinoma with pulmonary metastasis for at least 8 weeks. The progression-free survival (PFS) was assessed by Kaplan–Meier analysis and predictors of survival were analyzed by Cox proportional hazard model.
Results: The median PFS was similar between lenvatinib and sorafenib (5 vs. 4 months; P = 0.718) Serum albumin level was a significant predictor for PFS(hazard ratio[HR] = 0.785, 95% CI = 0.635-0.969), whereas choice of targeted agent was not significant (HR 0.935; 95% CI = 0.732 – 1.194).
Conclusion: Our findings suggests that the clinical outcomes in HCC patients with pulmonary metastasis were similar between patients who received sorafenib or Lenvatinib treatment.

[ABST-0544]

Microwave ablation for the treatment of larger than 5 cms hepatocellular carcinoma, the guatemalan experience

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Background: Thermal ablative therapies continue to demonstrate to be safe and effective for the treatment of patients with non resectable hepatocellular carcinoma. Microwave ablative therapy which is a relatively new technique has the advantage in providing faster ablation of larger tumors due to it´s capability to perform a high-powered (80–100 W) procedure in contrast to RFA therapies. This study aimed to evaluate MWA treatment of large HCCs (5-7 cm) and to assess it´s effect on local tumor progression, prognostic outcome and patient's survival.
Methods: Sixty four patients with HCC tumors larger than 5 cm were managed by our group from November 2012 to January 2022. For the procedure we used microwave ablation machine HS AMICA, operating at frequency of 2450 MHz and a power up to 100 Watts, using Multiple needle insertions in one or two sessions according to the size of the lesion. Patients were assessed for efficacy and safety. Complete ablation rate, local tumor progression and overall survival analysis were evaluated.
Results: Complete ablation was achieved in 65% of the cases, the other 35% needen a second treatment or a different ablation technique. No major complications or deaths were related to the procedure no matter conventional open surgery or percutaneous ablation was performed but the hospital stay was shorter in the percutaneous group.
Conclusions: Microwave ablation by percutaneous approach is safe and effective in the treatment of large HCC tumor. The survival and local tumor control were acceptable.

Other Hepatobiliary Neoplasia

[PP-0347]

A case of Kasabach-Merritt syndrome: Huge hepatic hemangioma with hematologic abnormality

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Objectives: Kasabach-Merritt syndrome is rare but known as life-threatening complication of hemangioma, characterized by consumptive coagulopathy with large vascular tumors. Almost all cases occur within first year of life, however, it is extremeley rare in adults. Here we report the case of unresectable giant hepatic hemangioma in adult with mild consumptive coagulopathy.
Materials and Methods: A 76-year-old male visited OPD due to vague abdominal discomfort for years with palpable mass on his abdomen. He had medical history of hypertension, chronic kidney disease, benign prostate hyperplasia. He denied alcohol drinking but was 58 pack-year of current smoker.
Results: CT scan showed the 25 cm sized huge exophytic liver mass replacing Lt. lobe which was extended to upper pelvis (Fig. 1-A, B). Physical exam showed palpable hard mass with mild tenderness on epigastrium. On laboratory findings, Hb level was 7.1 g/dL, WBC 3,900/mm^3, and platelet count 101,000/mm^3. Liver function test was normal. However, PT was 11.2 s, aPTT was 29.8 s, and fibrinogen level was 222 mg/dL. D-dimer was elevated (31.3 ug/ml FEU) and FDP was higher than 80 ug/dl. PBS showed pancytopenia with anisocytosis, poikilocytosis (ovalocyte, teardrop cell). AFP level was normal (3.6 ng/ml), but CA-19–9 and PIVKA-II were elevated (40.8 U/ml, 187.06 mAU/ml, respectively). PET-CT scan showed 25 cm sized huge isometabolic liver mass without extrahepatic uptake (Fig. 2). The Hemangioma SPECT also showed huge mass like lesion with increased RBC accumulation in Lt. hepatic lobe (Fig. 3). On endoscopic exam, there was no anemia focus on upper GI tract.
Conclusion: To rule out the hepatic malignancy such as angiosarcoma, we performed the US-guided liver biopsy which revealed the mass as cavernous hemangioma without evidence of malignancy (CD31 immunohistochemistry positive) (Fig. 4-A, B). During the hospitalization period, he only wanted the symptomatic management and refused any type of further treatment except pRBC transfusion. On hospital day 10, he was self discharged.

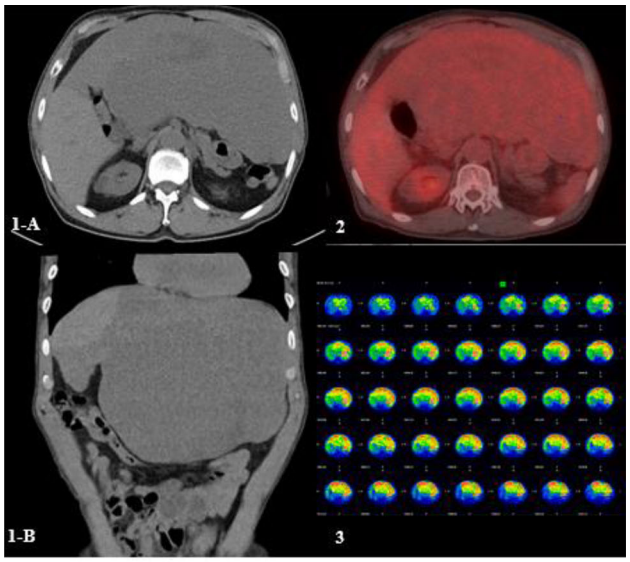

Figure 1. A-P CT scan (without enhance) showed 25cm sized huge hepatic mass in the Lt. lobe.
Figure 2. PET-CT scan showed isometabolic liver mass involving Lt. lobe without extrahepatic uptake.
Figure 3. hemangioma SPECT showed mildly increased RBC accumulation in Lt. hepatic lobe.

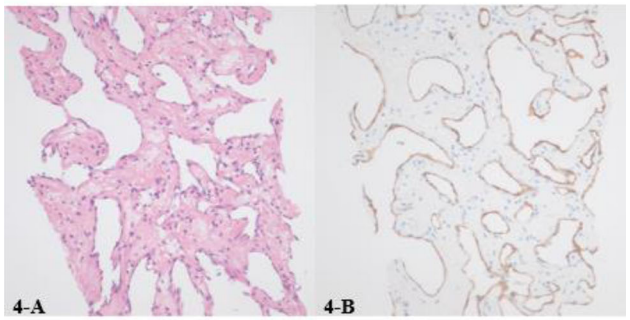

Figure 4. Histology of liver biopsy revealed liver mass was compatible with cavernous hemangioma (4-A H&E stain X100, 4-B immunohistochemistry CD31 positive)

[PP-0722]

Comparison of nab-paclitaxel plus gemcitabine-cisplatin and gemcitabine-cisplatin as a first-line chemotherapy for advanced biliary tract cancers

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Objectives: Recently, administration of nab-paclitaxel plus gemcitabine-cisplatin (nab-P/GP) has been proposed as an effective treatment strategy in advanced biliary tract cancers (aBTCs). However, its superiority over gemcitabine-cisplatin (GP), the current standard regimen, has not yet been fully established. This study therefore sets out to compare the clinical outcomes of nab-P/ and GP as a first-line chemotherapy for aBTCs.
Materials and Methods: Between January 2017 and June 2021, 148 consecutive patients who underwent first-line chemotherapy for aBTCs using either nab-P/GP or GP regimen were enrolled and were propensity-score matched at a 1:1 ratio. The major endpoints involved objective response rate (ORR), disease control rate (DCR), overall survival (OS), progression-free survival (PFS), and adverse events (AEs) $\geq$ grade 3.
Results: There were 33 comparable patients in each group after matching. Of these 66 patients, the mean age was 65.5 $\pm$ 9.1 years and male: female ratio was 1:1. Thirteen (19.7%) had intrahepatic cholangiocarcinoma, 35 (53.0%) had extrahepatic cholangiocarcinoma, and 18 (27.3%) had gallbladder cancer. Patients treated with nab-P/GP had a significantly higher DCR rate (97.0 vs. 60.6%, P = 0.001) than the GP group. ORR was also higher in the nab-P/GP group, but this difference was not significant (42.4% vs. 21.2%, P = 0.113). At the clinical cut-off date of Nov 8, median PFS and OS were both improved in the nab-P/GP group compared with the GP group. (10.2 vs 4.5 months and not reached (NR) vs. 7.7 months, P < 0.001 and P = 0.001, respectively). AEs $\geq$ grade 3 in the nab-P/GP group were 24.2%, which did not differ significantly compared to 33.3% in the GP group.
Conclusion: The present study indicated that aBTC patients treated with nab-P/GP had better OS and PFS, and an acceptable safety profile compared to GP. Nab-P/GP regimen could be considered as an alternative for the treatment of aBTC.

[PP-0915]

Oncologic effects of lymph node dissection for intrahepatic cholangiocarcinoma in the absence of lymph node metastasis on preoperative imaging

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Objectives: It is still controversial whether lymph node dissection (LND) in patients with no evidence of lymph node metastasis is beneficial in long term outcome. We aimed to investigate the clinical significance of LND for those IHCC patients through this study.
Materials and Methods: We retrospectively analyzed 131 patients who underwent surgery for IHCC without lymph node metastasis on preoperative imaging findings between January 2013 and February 2020. The patients were divided into two group according to whether node dissection was performed or not. Clinical outcomes were compared between the two groups.
Results: Among 131 patients, 57 patients underwent surgery with LND and 74 patients underwent surgery without LND. There was no difference of post-operative 30-day morbidity between the two groups while hospitalization period was longer in LND group (11.6 vs 9.8 days, p = 0.042). Both overall survival (OS) and recurrence-free survival (RFS) seemed significantly better in patients without LND (p = 0.017 and p = 0.046, respectively). Age, weight, LND, pos-operative complication, preoperative levels of CA 19–9, tumor size, TNM stage, histologic characteristics of tumor were identified to be associated with OS using univariate analysis. However, LND was not a significant risk factor for OS using multivariate analysis.
Conclusion: In this study, we concluded LND would not be beneficial for the overall outcome of IHCC with clinically negative lymph

node metastasis and should be done with selected patients with significant risk factors.

[OP-0933]

Benefit of MRI with hepatobiliary agent for HCC surveillance according to LI-RADS

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Objectives: To determine the benefit of MRI with HBA for HCC surveillance according to the LIRADS v2018.
Materials and Methods: From 1 April 2009 to 31 January 2020, we retrospectively included patients who had small liver nodules from surveillance ultrasonography, who were proceeded to be evaluated by MRI with HBA. LI-RADS v2018 criteria was assigned to each nodule by two radiologists, who were blinded to the definite diagnosis. Diagnostic performance of MRI with HBA were analyzed.
Results: Of 305 enrolled patients, the mean age was 61.5 ± 10.9 years and 62.3% were male. Among total 330 liver nodules, the median size was 1.5 cm and 190 nodules (57.6%) were diagnosed HCC which mostly caused by chronic hepatitis B infection. The accuracy for diagnosis of HCC by MRI with HBP was significantly higher than MRI without HBP (AUC 0.88 (95%CI, 0.84–0.91) vs 0.81 (95%CI, 0.76–0.84) respectively). In multivariate analysis, two MRI findings, included hyperintensity on T2 weighted and hypointensity on HBP were associated with diagnosis of HCC (odds ratios, 4.06 (1.93–8.54) and 4.36 (1.76–10.83) respectively). Furthermore, isointensity on HBP had high specificity (92.6%) and high positive predictive value (81.6%) for the diagnosis of benign liver nodule.
Conclusion: Imaging of hepatobiliary phase from MRI with HBA improved accuracy for the diagnosis of small liver nodules from HCC surveillance according to LIRADS v2018.

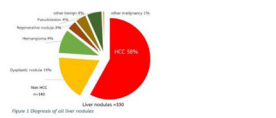

Figure 1 Diagnosis of all liver nodules

Table 1 Characteristics of the study patients

Baseline Characteristics	All patients (n=305)	HCC (n=177)	non-HCC (n=128)	p-value
Age (years, mean)	61.5±10.9	63.9±10.6	58.2±10.7	<0.001
Male, n (%)	190 (62.3)	120 (67.8)	70 (54.7)	0.02
Comorbid disease, n (%)				
DM	90 (29.5)	121 (56.3)	94 (43.7)	0.34
HT	117 (38.4)	79 (67.5)	38 (32.5)	0.008
CKD	41 (13.4)	35 (19.8)	6 (4.7)	<0.001
Cirrhosis, n (%)	259 (84.9)	162 (62.5)	97 (37.5)	0.001
CTP A/B, n (%)	240/19 (92.7/7.3)	150/99 (62.5/37.5)	127 (65.2/34.8)	0.94
MELD, mean	9.1±2.7	9.0±2.8	9.2±2.8	0.59
Etiology of liver disease, n (%)				
CHB	156 (51.2)	83 (66.8)	73 (57.0)	0.29
CHC	79 (25.9)	58 (32.8)	18 (16.4)	0.13
Alcohol	29 (9.5)	20 (11.3)	9 (7.0)	0.21
Other	56 (18.4)	28 (15.8)	28 (21.9)	
Laboratory				
Platelet count (x 10^3cell/mm^3), mean	162.7±79.9	154.3±78.2	174.7±81.1	0.03
Creatinine (mg/dL), median	0.94 (0.3-8.27)	0.99 (0.3-8.03)	0.92 (0.49-8.27)	0.006
Albumin (g/L), mean	4.1±0.5	3.99±0.54	4.22±0.46	<0.001
AFP, median	4.74 (0.7-255,315)	6.05 (0.67-255,315)	3.42 (0.74-1410)	<0.001

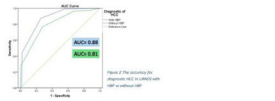

Figure 2 The accuracy for diagnostic HCC in LIRADS with HBP or without HBP

Table 2 Results of the univariate and multivariate logistic regression analysis

MRI features	Univariate analysis OR (95% CI)	p-value	Multivariate analysis Adjusted OR (95% CI)	p-value
Major features				
Nonrim arterial phase hyperenhancement (APHE)	1.79 (1.07-3.01)	0.03	1.69 (0.77-3.68)	0.19
Non peripheral washout appearance "wash out"	1.96 (1.08-3.58)	0.03	1.86 (0.63-3.37)	0.38
Ancillary features (+)				
Hyperintensity on T2 weighted	6.34 (3.59-11.38)	<0.001	4.06 (1.93-8.54)	<0.001
Hyperintensity HBP	7.37 (3.73-15.42)	<0.001	4.36 (1.76-10.83)	0.002
Hypointensity transitional phase	3.93 (1.97-5.86)	<0.001	1.35 (0.85-4.41)	0.12
Restricted diffusion	5.65 (2.95-10.82)	<0.001	1.78 (0.74-4.18)	0.19
Ancillary features (-)				
Isointensity HBP	0.13 (0.06-0.28)	<0.001		

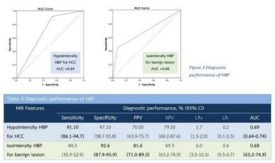

Figure 3 Diagnostic performance of HBP

Table 3 Diagnostic performance of HBP

MRI Features	Diagnostic performance, % (95% CI)						
	Sensitivity	Specificity	PPV	NPV	LR+	LR-	AUC
Hypointensity HBP	91.10	47.50	70.60	74.50	1.7	0.2	0.69
for HCC	(86.1-94.7)	(38.7-55.8)	(63.9-75.7)	(69.2-87.4)	(1.5-2.0)	(0.1-0.3)	(0.64-0.74)
Isointensity HBP	66.3	92.6	81.6	89.3	9.0	0.4	0.68
for benign lesion	(59.9-52.9)	(87.9-95.9)	(75.0-89.5)	(83.2-74.9)	(5.5-10.3)	(0.5-0.7)	(63.2-74.9)

[OP-1063]

Biliary cystadenocarcinoma mimicking hydatid cyst of liver—A case report

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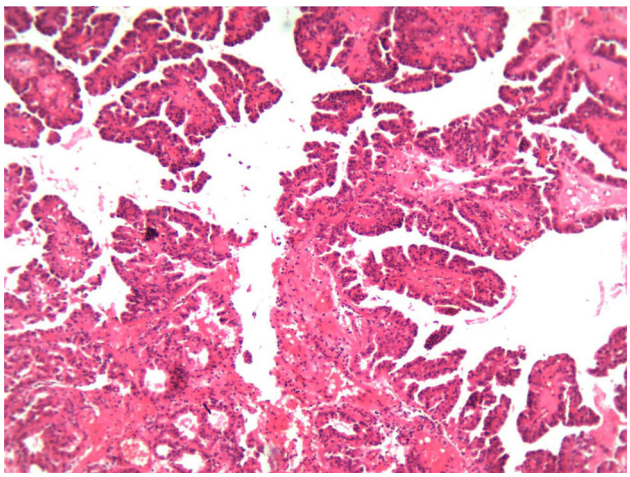
Materials and Methods: 60 year old male with complaint of right abdominal pain since past 2 years which was increasing after intake of meals. He had no history of cough or fever.No history of tuberculosis, diabetes mellitus or hypertension. An ultrasound abdomen revealed moderately enlarged liver and large hypodense mass lesion measuring 20.6 × 12.6 cm in subhepatic region obliterating left lobe of liver with thick internal echos and septations. Differentials rendered were subhepatic abscess and pseudocyst pancreas. CT scan abdomen revealed large bilobed predominantly cystic density mass lesion ms 18 × 16 × 10 cm showing thin irregular enhancing wall, few enhancing thick septations and multiple eccentric nodular lesions along inner surface of wall and along the septa along with tiny foci of wall calcification seen in left lobe of liver and few separate small cystic lesions around primary lesion with possibility of mitotic etiology, Biliary cyst adenocarcinoma more likely than complex hydatid cyst. On USG guided FNAC of epigastric mass 4 ml pus was aspirated. Cytology diagnosis was acute inflammatory abscess. MRI done preoperatively revealed well defined irregular wall cyst in left lobe of liver with few areas of solid mural nodule of wall of cyst compressing the left lobe of IHBR suggestive of benign congenital cyst or hydatid cyst. With a preoperatve diagnosis of hydatid cyst the patient was operated and 12 × 15 cm size cyst in left lobe of liver and about 2 L of cystic fluid aspirated & drain placed in cavity and Morrisons pouch. (Laparoscopic PAIR with deroofing of cyst). Histopathology initially reported as Metastatic papillary adenocarcinoma.
Conclusion: On review of Histopathology slides features showed architectural & cytologic atypia (figure uploaded) & on mucicarmine stain the epithelial cells showed mucin production & on IHC the epithelial cells were immunoreactive to cytokeratins (AE1,AE3) & EMA.The final diagnosis rendered was Biliary Cystadenocarcinoma.



[PP-1153]

A case of aggressive primary hepatic neuroendocrine tumor

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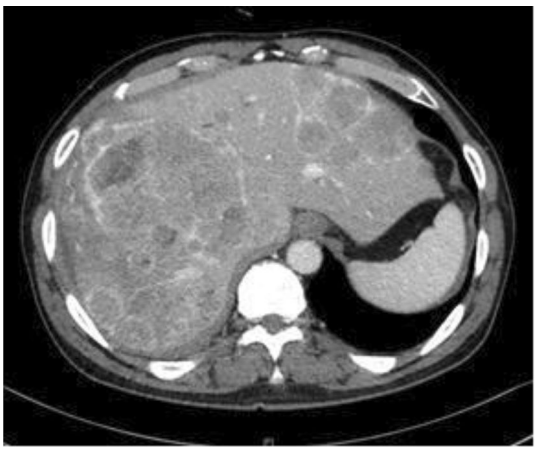
Objectives: Neuroendocrine tumors(NETs) represent approximately 1–2% of all gastrointestinal tumors, and primary hepatic neuroendocrine tumors (PHNETs) are very rare entities accounting for 0.3 cm of all NETs. The first case of such a tumor was reported was by Edmonson in 1958. The surgical resection is main treatment for PHNETs can provide a complete cure, in patient with unresectable disease, 5-FU, transarterial hepatic embolization, and

octreotide therapy can be used for palliative options. In general, NETs are known as slow-growing tumors in the early stage, but, we experienced unresectable primary NETs that deteriorated rapidly in a short period of time.
Materials and Methods: CASE: We describe a case of a 64-year-old male, who presented with abdominal discomfort. He had a history of laparoscopic cholecystomy at our hospital due to acute gangrenous cholecystitis 3 month ago. Abdomen CT showed Newly defined multiple variable sized early arterial hyperenhancing and delayed washout tumor in both lobes of liver, with heterogeneous attenuation due to tumor necrosis compare with abdomen CT 3 month ago.
Results: On hospital 2nd day, we did liver biopsy. On histological examination, it was diagnosed hepatic neuroendocrine tumor with Immunostain.
Conclusion: So, we report a case of primary hepatic neuroendocreine tumor with rapid and aggressive behavior nature which could not be resected.



[L-PP-1213]

Extrahepatic bile duct dilatation, chronic diarrhea, and weight loss caused by a non-hormonal carcinoid tumor of the ampulla of vater

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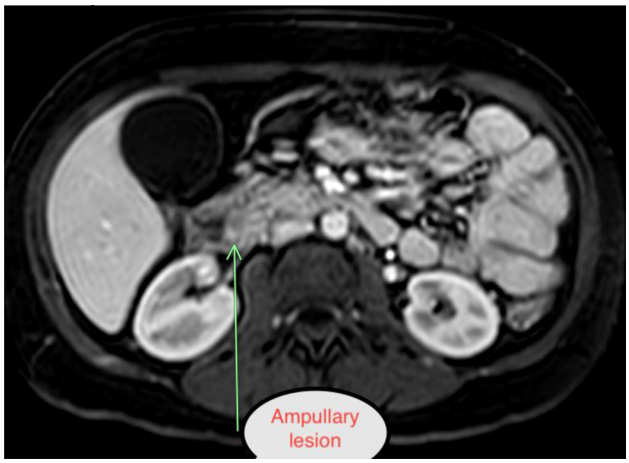
Objectives: CASE REPORT.
Materials and Methods: We describe a 48-year-old, previously healthy, female who weight 62 kg BMI 22. She presents with a 6-month history of diarrhea and moderate abdominal pain. She has not traveled internationally or taken any antibiotics. Oral electrolytes and antidiarrheals partially relieve the symptoms. Posteriorly, bowel movements increase to 10–15 explosive watery stools a day, weight loss of 10 kg, fatigue, and adynamia. Prior testing shows multiple negative stool study results for white blood cells, occult blood, and pathogens. There is no associated bleeding. She had a normal colonoscopy.
Results: Physical examination reveals pallor, normal thyroid, no hepatomegaly or palpable tumors, and no rashes. High doses of loperamide were given to relieve diarrhea and she intermittently improve. Tramadol was given to improve abdominal pain. Laboratory studies reveal: ALT 83/31 U/L, AST 26/32 U/L, LDH 246/214 U/L, Total Bilirubin 0.2 mg/dL, ALP 424/105 U/L, GGT 104/78, U/L, Hct 38.5%, leu 8.6 10⊥3/uL, plt 571 10⊥3/uL. Gastrine, Serotonin and its metabolites and vasoactive intestinal peptide were within normal ranges. The hepatobiliary ultrasound showed: gallbladder hydrops and discrete extrahepatic bile duct dilatation up to the ampullary zone. An MRCP showed dilatation of the common bile duct up to 12 mm in the supraduodenal portion, in the T2 coronal slice, a hypointense image at the ampullary zone, linear, that modified the morphology of the zone, causing also dilatation and irregularity of the pancreatic conduct in its head portion. PET scan was negative for metastases. ERCP was performed and showed extrahepatic bile duct dilatation, pancreatic duct dilatation with incomplete filling, normal intrahepatic bile ducts.
Conclusion: Ampullary cytology showed epithelial neoplasia suggestive of neuroendocrine differentiation. The patient underwent a pancreaticoduodenectomy. The pathology result was a non-hormonal carcinoid tumor of the ampulla of Vater. The patient had a favorable evolution, with no complications and she is still alive.



[L-OP-1242]

A case of hepatic angiomyolipoma that was difficult to make a differential diagnosis from hepatocellular carcinoma in an 8-year-old girl with Li-Fraumeni syndrome

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Objectives: Li-Fraumeni syndrome (LFS) is an autosomal dominant hereditary disease. It is associated with the loss of function of the p53 and an increased risk of malignant tumor development at early age. We report a case of hepatic angiomyolipoma (HAML) that occurred in an 8-year-old girl with Li-Fraumeni syndrome and was difficult to distinguish from hepatocellular carcinoma (HCC).
Materials and Methods: The case was an 8-year-old girl. She developed primary retroperitoneal rhabdomyosarcoma at 1-year-old,

and received surgery and radiation therapy. She developed renal cell carcinoma and received partial nephrectomy at 6-year-old.
Results: When she was 7-year-old, a high echoic nodule whose size were 5 mm found in liver segment 5, and half a year later, it increased to 10 mm. Blood tests showed that the liver function and tumor marker values were within their normal ranges and that hepatitis virus markers were negative. Fat suppression T2-weighted MRI shows high intensity, and diffusion-weighted imaging showed high intensity at the tumor, these findings were suggested malignancy. In Gd-DTPA enhanced MRI, the tumor was enhanced at arterial phase, washed out at portal phase and showed a contrast defect at hepatobiliary phase. These findings suggested HCC, so she was referred to our hospital for receiving radiofrequency ablation (RFA). Under deep sedation, we performed RFA. We biopsied the tumor after RFA. Immunohistochemical stain showed that the tumor was HMB-45 positive, and it was diagnosed histologically as HAML.
Conclusion: HAML is a rare mesenchymal liver tumor assumed to be predominantly benign, although incidental cases with malignant behavior have been reported. We performed RFA because we could not deny HCC, but we need to keep in mind that even if we strongly suspect HAML preoperatively, it has malignant potential in the case of Li-Fraumeni syndrome. We experienced a case of HAML that was difficult to make a differential diagnosis from HCC.

[ABST-0477]

Growing teratoma syndrome affecting hepato-renal space

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Background: Growing teratoma syndrome (GTS), rare condition is related to testis or ovary. It is most commonly seen with testicular non seminomatous germ cell tumors. It is characterized by metastasis from mature teratoma. We present a rare case of growing teratoma syndrome in struma ovarii.
Methods: Case study.
Results: 30-year-old female presented with abdominal distention and adnexal lump. Her CA 125 was 144.9 U/ML along with AFP 212 ng/m. CA-19.9 and CEA were normal. On CT scan, the adnexal mass measuring 16 × 10 cm was encasing uterus and bilateral ovaries. She underwent left salphingo-oopherectomy. Histopathology showed the mass as strumaovarii. She was given 4#TP regimen. After 8 months, the size of mass was increasing. Repeat CT showed bilateral adnexal mass with deposits in bowel & omentum. Her CA-125, α-fetoprotein and b-HCG were normal. Adnexal mass biopsy stated mature teratoma. Patient was operated again. Histopathology showed mature teratoma with deposits on bowel wall, omentum and anterior abdominal wall (IIIc). Repeat CT scan showed loculated collection of fluid in perisplenic, pelvic and left para colic gutter. Small irregular heterogeneous enhancing calcification was seen at pouch of douglas, anterior wall, peritoneal reflection and hepatorenal space. The patient is asymptomatic and doing well.
Conclusions: GTS should also be considered in ovarian germ cell tumor. Early diagnosis, surgery and monitoring to the response to chemotherapy should be done. Involvement of liver from peritoneal spread is categorized as stage III.

Liver Transplantation

[PP-0083]

Cost-effective and time-saving three-dimensional (3-D) printing protocol of intra-abdominal cavity of liver transplantation recipient to minimize risk of large-for-size syndrome

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Objectives: Cost-effective and time-saving Three-dimensional (3-D) printed model of intra-abdominal cavity protocol was utilized in liver transplantation to prevent large-for-size syndrome.
Materials and Methods: 3-D printing of the intra-abdominal cavity were performed on potential adult recipients with small cavity and pediatric patients scheduled for transplantation during the period of July 2020 to July 2021. The printed models of adult patients were used for comparing the size to the graft during deceased donor organ procurement while models of pediatric patients were used for directly comparing the size to the 3-D printed graft of living donors.
Results: Nine adults and five pediatric patients with median height and weight of 162 cm (IQR 158–165) and 58 kg (IQR 46.5–65.0), and 63 cm (IQR 58–104.5) and 7.0 kg (IQR 6.2–17.4), respectively, were included. Median time and filament cost were 584 min (IQR 502–644) and 1.6 US dollars (IQR 1.1–1.7). Reduction graft from deceased donor (n = 1), whole liver after abortion of first matched donor (n = 2), whole liver from first matched donor (n = 4), living donor transplantation using right liver (n = 1) and left liver from living donor after abortion of first matched deceased donor (n = 1) were successfully transplanted in adults. In pediatric patients, reduction (n = 2) and extended left lateral graft (n = 3) transplantations were successfully performed.
Conclusion: Our cost-effective and time-saving 3-D printed model of intra-abdominal cavity was feasible and proved to be useful for preventing large-for-size syndrome in small adult recipients and pediatric patients.

[OP-0204]

The role of complement C4 and Alt level for acute rejection after liver transplantation

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Objectives: Acute liver graft rejection is still a common complication after liver transplantation. Diagnosis of acute cellular rejection (ACR) requires a liver biopsy with attendant expense, and risk, especially for developing country. Measurements of serum complement components C3 and C4 are useful in the diagnosis and monitoring of immune complex disease. The normal adult range of C4 is 20-50 mg/dl. Low levels of C4 strongly suggest immune complex disease. The combination C4 and ALT levels are highly predictive of acute cellular rejection (ACR) in liver transplant recipients. A lowered concentration or the complete absence of C4 occurs in immunocomplex diseases, systemic lupus erythematosus (SLE), autoimmune thyroiditis and juvenile dermatomyositis.

Materials and Methods: The study has two groups, one group comprised 8 liver transplant recipients, who has predictive diagnosis of ACR. The other group comprised 8 liver transplant recipients, who has not prediction of ACR. Pathologist evaluated the ACR by Banff grading schema. Serum C4 was checked Cobas 6000/c501/ analyzer, which made by Roche Diagnostics.
Results: ACR patients had an average of C4 $\leq$ 0.22 gm/L test, ALT $\geq$ 124 IU/ml. The patients without ACR had an average of C4 $\geq$ 0.61 gm/L test, ALT $\leq$ 87 IU/ml. The ACR patients had done needle biopsy, which showed liver rejection.
Conclusion: To detect serum C4 in blood is a relatively non-invasive, inexpensive, easy to measure and quick marker. Especially for developing country like Mongolia, preliminary diagnosis of ACR, which revealed decreasing C4 and increasing ALT convenient to biopsy results.

[PP-0502]

Evaluating the effect of statins on prognosis in patients undergoing liver transplantation for hepatocellular carcinoma

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Objectives: The anti-cancer effect of statins is drawing attention. However, it is unclear whether statin use reduces the risk of hepatocellular carcinoma (HCC) recurrence in patients who undergo liver transplantation (LT) for HCC.
Materials and Methods: Consecutive patients who underwent LT for HCC between 1995 and 2019 were enrolled. The effects of statins on HCC recurrence and mortality were compared between statin user and statin non-user groups. We performed the analyses in a variety of ways, including inverse probability of treatment weighting (IPTW) methods to balance any confounders and the landmark method to avoid immortal time bias.
Results: A total of 430 patients was enrolled, among whom 323 (75.1%) were statin non-users and 107 (24.9%) were statin users. During a median of 64.9 months (IQR, 26.1–122.6) of follow-up, 79 patients (18.4%) had HCC recurrence and 111 (25.8%) died. Among those who died, 53 (47.7%) were identified as HCC-related mortalities. Statin use was a predictor of HCC recurrence (adjusted HR = 0.3, 95% CI, 0.1–0.6; P = 0.002), all-cause (adjusted HR = 0.3, 95% CI, 0.2–0.5; P < 0.001), and HCC-related mortality (adjusted HR = 0.4, 95% CI, 0.2–0.9; P = 0.03). The effects of statin use on clinical outcomes also were identified through IPTW analysis. There was a dose-dependent relationship between statin use and HCC recurrence. The anti-cancer effect of statins on HCC recurrence was consistently significant across multivariable-stratified and sensitivity analyses.
Conclusion: Statin use significantly reduced the risk of HCC recurrence and improved the survival of patients who underwent LT for HCC.

[OP-0529]

Long-term patency of all-in-one sleeve outflow vein venoplasty in living donor liver transplantation using a right liver graft

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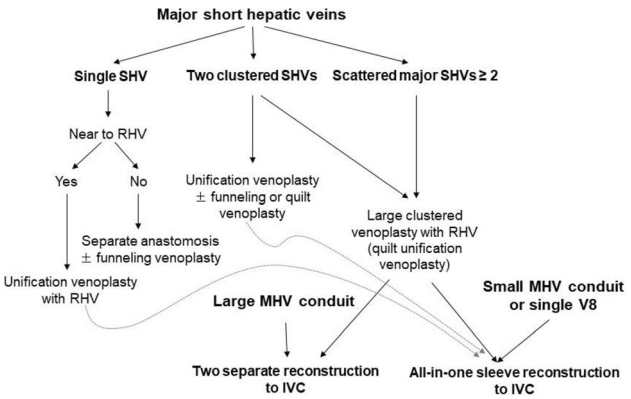
Objectives: Graft outflow vein reconstruction is the most important procedure for successful implantation of a right liver graft (RLG) in living donor liver transplantation (LDLT). All-in-one sleeve venoplasty (ASV) can unify the right hepatic vein (RHV), short hepatic vein (SHV), and middle hepatic vein (MHV) of an RLG. ASV enables wide side-to-side anastomosis to the recipient inferior vena cava (IVC).
Materials and Methods: Of 2,875 patients who underwent LDLT with an RLG from August 2009 to July 2019, 16 (0.5%) patients underwent ASV. The ASV techniques applied to these patients, as well as patient long-term outcomes, were analyzed.
Results: Type 1 ASV unified one RHV, one IRHV, and one MHV conduit (n = 12 [75.0%]). Type 2 ASV unified one RHV, multiple IRHVs, and one MHV conduit (n = 4 [25.0%]). All patients are currently alive with a mean follow-up period of 70.1 $\pm$ 41.9 months. No patient underwent retransplantation. Follow-up computed tomography showed SHV occlusion in one (6.3%) patient at 4 months, resulting in 1-, 3-, and 5-year SHV patency rates of 93.8% each. MHV occlusion was identified in six (37.5%) patients, with the 1-, 3-, and 5-year MHV patency rates being 81.3%, 68.8%, and 68.8%, respectively (p = 0.037). No patient underwent endovascular stenting of the SHV or MHV. Patency rates were significantly higher for SHV than MHV (p = 0.037).
Conclusion: ASV using various vascular patches is a useful technique enabling secure reconstruction of an RLG in grafts with complex hepatic vein anatomy or recipients with poor IVC condition.



[OP-0539]

An analysis of the number of deceased donors and organ transplantations during COVID-19 pandemic in Korea

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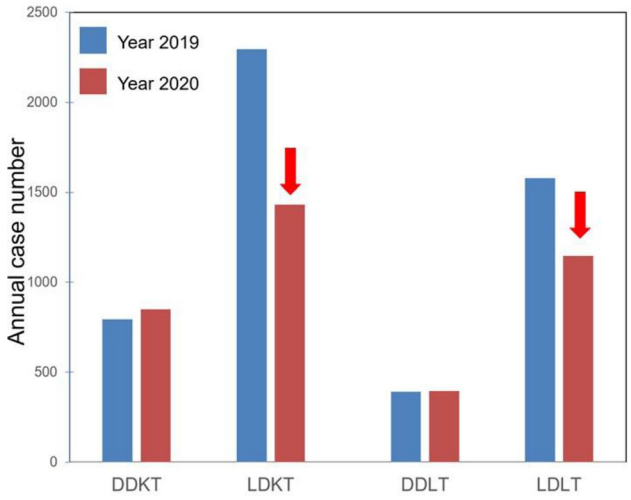
Objectives: Coronavirus disease 2019 (COVID-19) pandemic is severe enough to discourage organ donation. Since prevalence of COVID-19 in Korea was much lower than in Western countries, we decided to determine the real-world impact on organ donation and transplantation in Korea.
Materials and Methods: The annual number of kidney transplantation (KT) and liver transplantation (LT) in 2020 were compared with those in 2019 using Korean Network for Organ Sharing database and Asan Medical Center (AMC) database.
Results: The number of deceased donors (DD) was 450 in 2019 and 478 in 2020. Monthly DD number was 37.5 ± 5.9 in 2019 and 39.8 ± 4.4 in 2020 (p = 0.284). Annual number of DDKT was 794 in 2019 and 848 in 2020, and monthly number was 66.1 ± 10.4 in 2019 and 70.7 ± 9.8 2020 (p = 0.285). Annual number of DDLT was 391 in 2019 and 395 in 2020, and monthly number was 32.6 ± 5.7 in 2019 and 32.9 ± 4.7 in 2020 (p = 0.877). Number of living donor (LD) KT was 2,293 in 2019 and 1,432 in 2020, and monthly number was 191.1 ± 19.5 in 2019 and 119.3 ± 11.7 in 2020 (p < 0.001). Number of LD LT was 1,577 in 2019 and 1,146 in 2020, and monthly number was 131.4 ± 18.1 in 2019 and 95.5 ± 8.0 in 2020 (p < 0.001). In AMC, all types of KT and LT were not significantly changed.
Conclusion: The results of this study indicate that the number of DD organ transplantations remained stable in Korea during 2020, but the number of LD organ transplantations significantly reduced during COVID-19 pandemic. However, organ transplantation number was not changed in AMC.



[OP-0572]

Optimal intervention for initial treatment of anastomotic biliary complications after living donor liver transplantation

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Objectives: This study evaluated the optimal intervention between Endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD) for patients with anastomotic biliary complications (ABC) after living donor liver transplantation (LDLT).
Materials and Methods: Prospectively collected data of patients who were diagnosed with ABC after LDLT between January 2013 and June 2017 were retrospectively reviewed.
Results: There were 57 patients who underwent LDLT with a right liver graft using duct-to-duct biliary reconstruction and experienced ABC. Among the patients with RAD involvement, there were no significant differences in the intervention success (P = 0.271) and patency (P = 0.267) rates between ERCP and PTBD. Similarly, among the patients with RPD involvement, there were no significant differences in the intervention success (P = 0.148), and patency (P = 0.754) rates between the two procedures. Graft bile duct variation (P = 0.013) and a large angle between the recipient and graft bile duct (R-G angle) (P = 0.012) increased the likelihood of failure of ERCP in the RAD. When R-G angle was greater than 47.5°, the likelihood of failure of ERCP was increased.
Conclusion: PTBD would be preferred when graft bile duct variation is presented in the patients with RAD involvement and/or when R-G angle is greater than 47.5°.

[OP-0600]

Pure laparoscopic versus open right hepatectomy in living liver donors: Bench-surgery time

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Objectives: Recently, there have been several reports on pure laparoscopic donor right hepatectomy (PLDRH), but the effect of pure laparoscopy on bench surgery has not been evaluated. This study aimed to compare bench-surgery time between PLDRH and conventional donor right hepatectomy (CDRH).
Materials and Methods: We retrospectively reviewed the medical records of 758 live liver donors between January 2012 and December 2019. We divided the patients into two groups: between January 2012 and September 2015, when we exclusively performed CDRH, and between March 2016 and December 2016, when PLDRH was standardized. We excluded all other types of graft donor hepatectomy, laparoscopic assisted donor hepatectomy, and cases with no recorded data.
Results: In total, 267 donors were included in the PLDRH group and were compared with 247 donors in the CDRH group. Similar

proportions of graft vascular variations were observed between the two groups. The mean bench-surgery time was longer in the PLDRH group than in the CDRH group (49.3 ± 19.9 vs. 39.5 ± 17.5 min; $P < 0.001$).
Conclusion: The bench-surgery time was longer in the PLDRH group than the CDRH group, regardless of whether the vascular network was reconstructed. Expertise in bench-surgery as well as donor surgery and recipient surgery is mandatory for PLDRH to be safe and feasible.

[PP-0640]

Human intrahepatic CD56bright NK cells display a tissue-resident transcriptional profile and enhanced ability to kill allogenic CD8+ T cells

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Objectives: Natural killer (NK) cells are enriched in human liver and are phenotypically distinct from their blood counterparts. Although these cells are capable of rapid cytotoxic effector activity, their role remains unclear. We hypothesise that they may contribute to immune tolerance in the liver during transplantation.
Materials and Methods: Methods. NK cell populations were analysed in liver perfusates from 52 donor organs. RNA sequencing was carried out on FACS sorted NK cells from liver perfusates (n = 5) and blood from healthy controls (n = 5). Hepatic NK cell cytotoxicity against allogeneic T cells was tested using an in vitro co-culture system of liver perfusate-derived NK cells and blood-derived T cells (n = 10–13).
Results: Results. CD56bright NK cells are enriched in human liver, on average accounting for on average 55% of the hepatic lymphoid population, with the frequency varying by age. Liver-resident CD56brightCD16 ± NK cells upregulate genes associated with tissue residency as well as functional surface receptors including, CD160, TIGIT and LY9. In co-culture experiments, hepatic NK cells but not blood NK cells induced significant allogeneic T cell death.
Conclusion: We propose that liver NK cells contribute to tolerogenicity post transplantation.

[PP-0645]

Liver transplantation in children in single center

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Objectives: Liver transplantation is currently the only treatment for terminal liver disease.
Materials and Methods: In our center, from 2014 to 2021, 14 liver transplants from a living donor to pediatric patients were performed. The ages of the children ranged from 6 to 17 months. The causes of terminal liver damage were congenital malformations (atresia of the biliary tract) and intrauterine infections (cytomegalovirus). All transplants were performed according to the group compatibility of the donor and recipient. The donors were relatives of the patients. In all cases, transplantation of the left lateral sector (1 and 2 segments) of the liver was performed. Immunosuppressive therapy included: induction—basiliximab, basic—tacrolimus, MMF, glucocorticoids.
Results: Of the 14 transplants performed, surgical complications were observed in 3 cases (21.4%). All complications were corrected by repeated surgery. Mortality—1 patient (7.2%). The donors had no complications. The duration of surgical intervention in donors was 4 ± 1.5 h, in recipients—7.5 ± 2 h. The average length of hospital stay for donors was 17.3 bed-days, and recipients were hospitalized for an average of 47.7 bed-days.
Conclusion: We consider liver transplantation from a living donor to young children to be a more optimal method of treatment compared to transplantation from a cadaveric donor. Removing the left lateral liver for transplantation is safer for a living donor.

[OP-0721]

Legal issues of Liver transplantation in Nepal: Maximizing benefits of organ transplantation while reducing the risk of organ trafficking

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Objectives: To review existing laws of liver transplantation in Nepal; discuss nuances of these laws for maximizing medical benefit; identifying loopholes in human trafficking laws and proposing recommendations to reduce organ trafficking risk in Nepal and related countries.
Materials and Methods: Extensive review of literature, including legal documents/laws surrounding organ transplantation in Nepal- the Human Organ Transplantation(Regulation and Prohibition) Act,1998; Transplant Act and Regulation 2016; Human Trafficking and Transportation(Control) Act 2007; UN Trafficking Protocol and mandasmus issued by honorable Supreme Court of Nepal,2021.
Results: Liver transplantation is in its initial stages in Nepal and so far,13 live donor transplants have been performed. Impetus for liver transplantation came after its legalization in 2016. Newer laws have extended the criteria for donors with provision of paired exchanges as well as transplantation from deceased donors. While this is a welcome decision and is expected to strengthen transplant medicine in Nepal, it may as well make it a hub for organ trafficking. This is evidenced by recent organ trafficking related prosecution that suggests large-scale, organized trafficking groups running in Nepal. Moreover, new legal provision of financial incentive to donor family and health facilities for increasing brain-dead donors may escalate unethical practices, including premature certification of death; denying patients life-saving treatment and social pressure on economically poor families as an easy way of making money.
Conclusion: While the new transplant laws are aimed to expedite the organ transplant system, the complex socio-economic and geopolitical situation in Nepal poses a unique challenge. These laws, one one hand, will for sure provide medical care to thousands of Nepalese who really need them, but placing millions of Nepalese who are illiterate

and economically backward at risk. Our study aims to find ways to optimize medical care and reducing this vulnerability to improve the field of transplant medicine in Nepal and other low- and-middle-income countries.

[OP-0950]

Vascular reconstruction and outcomes of adult-to-adult right lobe living donor liver transplantations: A single center experience in Vietnam

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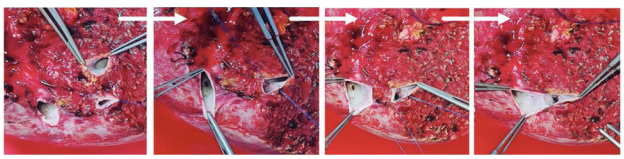
Objectives: Outflow and inflow reconstruction of the liver graft is a key to successful results of living donor liver transplantation (LDLT) using right lobe graft.
Materials and Methods: We prospectively analyzed the data on all right lobe LT adult patients, consecutively performed from January 2019 to December 2020 in Central Military Hospital 108. When the remnant and total liver volume ratio (RLV/ TFLV) less than 35%, we used modified right lobe (MRL) graft. In the case using extended right lobe (ERL) graft (RLV/ TFLV greater than 35%), we conjoined MHV and RHV. Reconstruction of the portal vein (PV) was done by end-to-end anastomosis by using continuous sutures. Reconstruction of the hepatic artery was done by end-to-end anastomosis by using continuous sutures and surgical loupes.
Results: A total of 52 cases of adult-to-adult LDLT using right lobe graft were collected. For hepatic vein reconstruction, there were 10 cases using MRL and 42 cases of ERL. The intervention rate for outflow stenosis was 0/52 case (0%) of a mean follow- up of 11.4 ± 6.5 months (range, 1–28 months). PV stenosis were detected in 2 patients (3,8%) whom were successfully treated with stent placement. No hepatic artery thrombosis and hepatic artery stenosis were found after LDLTs.
Conclusion: The single orifice hepatic vein reconstruction in LDLT using right lobe graft is a simple and feasible surgical technique and it can prevent effectively RHV stenosis. PV stent placement was technically and clinically effective technique in managing PV stenosis after living donor liver transplantation.



[PP-0958]

Human fetal liver cells as a bridge to the liver transplantation in patients waiting for donors

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Objectives: The liver transplantation (LT) a method for treating liver cirrhosis. With a great increase in the death rate of patients with liver disorders, there is a necessity to pursuit for alternative therapeutic implement as a supportive therapy. Recent studies show outstanding results in therapy using human fetal liver-derived stem cells (FLSC) and can deliver potential to conservatively manage end-stage liver diseases. The present investigation aimed to study the safety and efficacy of FLSC transplantation.
Materials and Methods: 115 patients with liver cirrhosis of different etiologies were included in this study. All patients were on the waiting list and they were divided for 2 groups: received FLSC therapy and no treatment. FLSC were obtained from the fetus after abortion by medical indications and were infused into periphery. Liver function scores were chosen as endpoints to assess efficacy.
Results: Child–Pugh score improved in 90 days in the cell therapy group. The model for end-stage liver disease score remained stable in the treated patients, whereas it increased during follow-up in the control group. Bilirubin levels increased among controls, whereas they decreased in the therapy arm during the first 60 days; INR RC differences between groups reached up to 10%. The changes observed did not persist beyond 90 days. There was marked clinical improvement observed in terms of all clinical and biochemical parameters. Further, there was decrease in mean MELD score observed in 6 months follow-up in all patients.
Conclusion: Transplantation of human FLSC into the periphery improved liver function in patients with advanced cirrhosis in the first 90 days. However, larger studies are necessary to define the role of human FLSC therapy in cirrhotic patients. Treatment by means of human FLSC proposals a potentially helpful modality to liver transplantation in the management such diseases.

[OP-1045]

Safety of inactivated SARS-CoV2 vaccines in liver transplantation recipients

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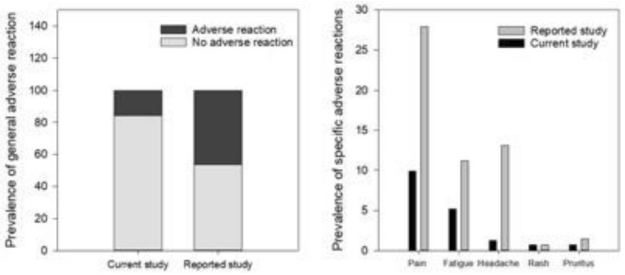
Objectives: To evaluate the safety of inactivated SARS-CoV2 vaccines in liver transplantation recipients.
Materials and Methods: This is a cross-sectional observational study. We enrolled stable liver transplantation recipients who had completed the full course of the covid-19 vaccines in our hospital from March 2021 to October 2021. The general adverse reactions and severe adverse events following immunization reported in the LT group were compared to those reported in the general population receiving inactivated covid-19 vaccine.
Results: We recruited 151 eligible LT recipients, among which 120 (79.5%) were males, and 31(20.5%) were female. The median age was 56.0 (49.0, 63.0) years old. The median period after LT was 8.44 (4.37, 12.39) years, the median trough concentration of tacrolimus was 2.5 (1.8, 3.9) ng/L. 83 (58.9%) subjects received the CoronaVac vaccine (Sinovac Biotech Ltd), the remaining received Sinopharm Covid-19 vaccine (Beijing Institute of Biological), or compound course of CoronaVac and Sinopharm. The reported incidence of

general adverse reaction among LT recipients in the current study was 15.9%, as compared with the reported incidence of 41.7%–46.5% in the general population (Fig. 1A). The prevalence of pain at the injection site, fatigue, headache, pruritus was 9.9%, 5.2%, 1.3%, 0.7% respectively, as compared with the reported 19.4%–27.9%), 10.6–11.2%, 12.6%–13.1%, 1.3%–1.5% in the general population (Fig. 1B). Both inactivated vaccines had similar incidence of adverse reactions. No LT recipients had vaccine related SAE or Covid-19 infection during follow-up despite being residing in areas that had local outbreaks (Beijing, Yunnan, Henan).
Conclusion: Covid-19 vaccine was safe in LT recipients. Only a few participants experienced mild reactions such as pain at the injection site and fatigue.



[PP-1109]

A safe and feasible method for initiating pure laparoscopic living donor right hepatectomy; External traction of the cystic duct

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Objectives: Laparoscopic major hepatectomy is gradually increasing with two consensus meetings. However, pure laparoscopic donor right hepatectomy (PLDRH) is still being performed carefully, because donor safety and quality grafts must be obtained. The external traction of the cystic duct can be helpful for hilar dissection and duct division.
Materials and Methods: From March 2019 to December 2020, 40 patients underwent PLDRH. PLDRH was performed using flexible scope and 5 ports. The gallbladder was not divided from the liver bed for traction after only cutting the cystic duct and artery. After tying the cystic duct stump in a 'Round loop', external traction was performed to the left side of the epigastric area. From the seventh patient with PLDRH, cystic duct traction method was used.
Results: Using external traction of the cystic duct, the exposure of the right hepatic artery and the right portal vein was much easier. Because of the constant traction, it was more stable for hilar dissections, and the common bile duct was lifted to facilitate long dissections of the right hepatic artery. Also, when cutting the right hepatic duct, traction made it easier to divide.
Conclusion: PLDRH still remains a challenging procedure requiring important experiences in both laparoscopic liver surgery and open living donor right hepatectomy. External traction of the cystic duct may be helpful for PLDRH.

[OP-1113]

Surgical outcomes after donor hepatectomy for adult living-donor liver transplants: A single-center experience in Vietnam

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Objectives: Living-donor liver transplantation (LDLT) is a well-established treatment for end-stage liver disease. Even after 2 decades of experiences this approach, data on this approach for donor right hepatectomy in living donor liver transplantation are limited in Vietnam.
Materials and Methods: We conducted a prospective study of surgical outcomes of all living liver donors at in 108 Military Central Hospital from 10/2017 to 10/2021. The characteristics of donors, anatomical variation, techniques, postoperative complications were collected and analyzed.
Results: A total of 88 donors underwent right hepatectomy. 71,5% of patients were performed living donor liver transplantation using extended right lobe graft when the remnant liver volume was greater than 35%. The remaining liver volume was 38,1 ± 4,5%. The mean operating time was 288 min, and the estimated blood loss was 345 ml. A total of 5,6% complications were reported with no donor mortality.
Conclusion: The right hepatectomy in LDLT is a safety and feasible surgical technique.

[PP-1114]

Safety and usefull method in donor hepatectomy; The enhanced recovery after surgery (ERAS) program

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Objectives: Enhanced recovery after surgery (ERAS) programs have been reported to reduce the rate of postoperative complications and shorten hospital stays in liver surgery. However, while these achievements could be expected to improve the safety of donor hepatectomy, relevant research on this issue remains unclear. The aim of this study was to evaluate the outcomes and benefits after implementation of an ERAS program on donor hepatectomy in living donor liver transplantation (LDLT).
Materials and Methods: We analyzed perioperative outcomes of consecutive patients who underwent donor hepatectomy between January 2016 and October 2020. Patients were divided into the ERAS group (N = 42) and the traditional care (TC) group (N = 42), and propensity score matching (PSM) was used to define the independent effect of the ERAS program on donor hepatectomy.
Results: The rate of postoperative morbidity was significantly lower in the ERAS group than in the TC group (11.9% vs. 31%, p = 0.033), and the postoperative length of hospital days were significantly shorter in the ERAS group (10.2 vs. 11.4 days, p = 0.039). The

postoperative pain scores ($p < 0.001$, 0.012 and 0.005 in postoperative day (POD) 1, 3, and 5) and the number of demands for analgesic in POD 3 and 5 ($p = 0.025$ and < 0.001) were lower in the ERAS group. Postoperative nausea and vomiting (PONV) (23.8% vs. 52.4%, $p = 0.027$) and the number of demands for antiemetic (0.4 vs. 1.2, $p = 0.012$) were significantly reduced in the ERAS group.
Conclusion: ERAS programs applied to the patients undergoing donor hepatectomy can safely and effectively reduce the incidence of complications. In addition, ERAS programs improve the donor's quality of life during hospitalization and helps them quickly return to their daily routine.

[PP-1131]

Pediatric liver transplantation with daclizumab induction

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Objectives: A new class of monoclonal antibodies (non-T-cell depleting) has gained favor for induction therapy after transplantation. This study evaluated the non-T-cell depleting antibody to the CD25 cell, daclizumab, as a single-dose induction agent immediately after pediatric liver transplantation to spare the use of the calcineurin inhibitor, tacrolimus, for 7 days in respect to both efficacy and renal function.
Materials and Methods: From January 1998 to November 2001, 81 pediatric orthotopic liver transplant recipients receiving 89 liver grafts were evaluated. The treatment arm (n = 61) received daclizumab 1 mg/kg immediately after liver transplantation along with mycophenolate, steroids, and, on postoperative day 7, tacrolimus. The control group did not receive induction therapy, whereas tacrolimus, mycophenolate, and steroids were started immediately after surgery.
Results: The induction group had fewer patients with rejection within the first 30 days after liver transplantation (9 [14.8%] vs. 10 [50%]; P = 0.003). The mean time to first rejection was similar between groups (12.1 [± 7.8] days vs. 18.5 [± 8.1] days; P = not significant). There was a 3.39 increase in relative risk to develop rejection within the first 30 days after orthotopic liver transplantation if the patient did not receive induction therapy (relative risk = 3.39; 95% confidence interval [1.61, 7.14]). Two-year actuarial survival for the induction group was 93.2% compared with 85% in the control; graft survival was also similar between groups (87.8% vs. 72.7%) at 2 years.
Conclusion: Daclizumab 1 mg/kg given immediately after pediatric liver transplantation and withholding tacrolimus, is safe, efficacious, and reduces rejections within the first 30 days after surgery.

[L-OP-1216]

The role of extracorporeal membrane oxygenation in adult liver transplant patients: A single-center experience

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Objectives: Extracorporeal membrane oxygenation (ECMO) has been often applied in liver transplantation (LT) recipients with acute and potentially reversible life-threatening cardiopulmonary failure that is unresponsive to conventional therapies. This study designed to assess the outcome of the ECMO in LT recipients and identify the predictors of the prognosis.
Materials and Methods: We retrospectively reviewed our experience in ECMO during perioperative period in patients undergoing LT From January 2007 to December 2020, and this study was conducted in 109 patients who received ECMO support for more than 24 h.
Results: Recipients who received ECMO support during perioperative period showed a 32.0% 1-year survival rate and 53.3% success rate for ECMO weaning. Out of 109 recipients, eight patients were administered intraoperative ECMO for cardiopulmonary failure, of whom seven recipients (87.5%) succeeded in ECMO weaning, six patients (75.0%) survived for longer than a year. In case of ECMO treatment prior to 2011, septic shock as an indication of ECMO treatment, and a total bilirubin level of 5 or higher, were independent predictors of in-hospital mortality on multivariable analysis.
Conclusion: Our acceptable outcomes of this study suggest that the ECMO can be considered a viable rescue therapy in highly selected LT recipients with severe, and acute cardiopulmonary failure from reversible cause.

[L-OP-1275]

Adherence to immunosuppression in Indian children after liver transplant

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Objectives: The study was conducted with an aim to study the adherence pattern and factors predicting non-adherence to immunosuppression in pediatric LT recipients.
Materials and Methods: In this prospective observational questionnaire study, all pediatric liver transplant recipients (under-18 years of age) and/or their parents who were discharged from hospital, minimum 6 months of post-transplant period,can communicate in either Hindi or English language were enrolled. Data collection was performed from September 2019 to February 2020 in the form of questionnaire. Medical records were retrieved from the hospital information system and outpatient records. Complete demographic and clinical details were recorded.
Results: Over the study period, 40 children fulfilling inclusion and exclusion criteria were enrolled. There was male preponderance (77.5%) with median age at LT of 60 (24, 129) months – 21 (52.5%) were under-5 year at the time of LT. The indications for LT were pediatric acute liver failure in 12 (30%) and end-stage chronic liver disease in 28 (70%). Eighteen (45%) of these children suffered from 30 (median 1, range 1–5) episodes of rejection – overall 5 children had > 1 rejection episode. At the time of assessment, 12 had past ACR, 3 had LAR and 3 had CR. Presence of > 1 rejection episodes was associated with usage of 3 or more immunosuppression at the time of assessment (OR = 3.11, 95% CI = 1.52–6.35, $p = 0.031$). The study population had a median adherence score of 74 (71, 80) and percentage of 87.6%. Majority of the LT recipients (72.5%) had an average level of adherence (score of 80–95%) while poor adherence (< 80%) was seen in 5.
Conclusion: We concluded that adherence to immunosuppression was above average (> 80%) in 87.5% children and was related to rejection and longer time from transplant. Timely identification of barriers to adherence need identification to ensure the success of an LT program.

Table 1: Characteristics of 40 pediatric liver transplant recipients.

	Numbers (%) or median (IQR)
Demographic variables	
Gender (Male / Female)	31 / 9
Age groups (at time of transplant) (<12 mo / 1-5 y / 5-10 y / 10-18 y)	7 / 14 / 9 / 10
Age groups (at time of assessment) (<12 mo / 1-5 y / 5-12 y / >12 y)	1 / 10 / 16 / 13
Time post-transplant (<12 mo / 1-2 y / 2-5 y / >5 y)	4 / 10 / 18 / 8
Rural / Urban	18 / 22
Type of family (Joint / Nuclear)	31 / 9
Education of mother (None / Primary / High School / XII / Graduate / PG	4 / 1 / 8 / 5 / 13 / 9
Socio-economic status* (1 / 2 / 3 / 4 / 5)	4 / 22 / 11 / 3 / 0
Financial support (Self / Extended family / Govt Beneficiary)	27 / 4 / 9
Access to Medical care (Easy / Difficult)	13 / 27
Distance from transplant center (</=10 km / >10 km)	10 / 30
Relation with donor (Mother / Father / Sibling / Others)	22 / 9 / 4 / 5
Indication for transplantation	
Acute liver failure#	12 (30)
Chronic liver disease	28 (70)
Biliary atresia	11
Progressive familial intrahepatic cholestasis (PFIC)	6
Wilson disease	4
Primary sclerosing cholangitis (PSC)	3
Others^	4
Rejection	18 (45)
Acute	12
Late acute	3
Chronic	3
1 rejection episode	13
>1 rejection episode	5
Type of Immunosuppression	
Prednisolone + Tacrolimus	24 (60)
Prednisolone + Tacrolimus + MMF	10 (25)
Prednisolone + Tacrolimus + MMF + Sirolimus	3
Tacrolimus + Sirolimus	1
Tacrolimus + MMF	1
Tacrolimus	1

IQR = Interquartile range; MMF = Mycophenolate mofetil; PG = Post-graduate.

[ABST-0403]

Living donor liver transplantation in polycystic liver disease: The recipient liver splitting method

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Background: Polycystic liver disease(PLD) can progress to massive hepatomegaly resulting in impaired performance status and quality of life. In PLD patients with diffuse liver cysts with few areas of normal parenchyma, liver transplantation(LT) can be the only curable treatment. But LT can be extremely challenging due to difficulty in resecting a massive native liver. We report our case of liver transplantation for massive hepatomegaly due to symptomatic PLD.
Methods: A 53-year-old man was diagnosed with autosomal dominant polycystic kidney disease in 1998. After 11 years, he was diagnosed also with PLD. The patient developed the end-stage renal disease, starting hemodialysis in 2011. He was first listed for kidney transplantation. While waiting for a deceased donor, abdominal discomfort aggravated due to the huge size of the kidney. So he underwent bilateral nephrectomy sequentially. He underwent several surgeries such as segmental resection of small bowel and ventral hernioplasty. In July 2020, due to an enlargement of liver cysts and massive hepatomegaly, the patient developed severe clinical symptoms; abdominal discomfort due to abdominal distension, dyspepsia, poor oral intake. He was listed for combined LT and KT in September 2020.
Results: Because of his low MELD score (21) and preserved liver function, the probability of liver transplantation in brain death was too sparse. So he decided to proceed with living donor LT (LDLT) first. At the LDLT, the graft mobilization was too hard not only because of the size, weight, and hardness of the organ but also because of inflammation and adhesion due to previous several operations. Careful dissection around the liver was done but the liver was not able to be mobilized. After hilar dissection and all the vasculatures were ligated, the IVC was exposed and could be dissected up to the right hepatic vein. However, the hepatic veins were not able to be identified due to the huge liver. Liver parenchyma was resected and right, middle, and left hepatic veins were isolated after parenchymal resection. The recipient's liver was weighed 10,134 g.
Conclusions: We report our case of LDLT for massive hepatomegaly due to symptomatic PLD, which used a novel recipient liver splitting method.

[ABST-0505]

The feasibility and outcome of patients undergoing liver transplantation for combined hepatocellular-cholangiocarcinoma

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Background: Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare primary liver tumor demonstrating histological features of both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). It remains unclear whether the prognosis of cHCC-CC differs from that of HCC. The present study aimed to evaluate the therapeutic effects of liver transplantation on cHCC-CC and analyze the clinicopathological factors affecting prognosis.
Methods: Retrospective analysis of the clinicopathological data of 8 patients with cHCC-CC who underwent living donor liver transplantation from 2011 to 2020 was performed. Cumulative survival rate and tumor-free survival rate were calculated using the Kaplan–Meier method.
Results: The operative survival rate of the 8 patients was 50%; the 30 day mortality was 0%; 1-, 3-, 5-year overall cumulative survival rates were 75%, 45%, and 45%, respectively; and the corresponding cumulative disease-free survival rates were 54%, 29%, and 29% respectively.
Conclusions: Liver transplantation may be an effective therapeutic method for the treatment of cHCC-CC. Strict preoperative screening of potential liver transplantation candidates with cHCC-CC can help reduce the risks of tumor recurrence and metastasis.

[ABST-0493]

Effect of everolimus rescue therapy for acute cellular rejection following living donor liver transplantation: Report of one case

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Background: Acute cellular rejection (ACR) after living donor liver transplantation (LDLT) is often curable with steroid pulse therapy, but a few patients show steroid-resistant ACR, which is difficult to control.
Methods: The patient was a 61-year-old male who was admitted due to chronic HBV decompensated liver cirrhosis with hepatocellular carcinoma. ABO-incompatible LDLT operation using a modified right liver graft from son was performed. The graft-recipient weight ratio was 1.21. The patient recovered uneventfully with immunosuppression using tacrolimus with mycophenolate.
Results: However, 11 months later, after LDLT, the liver enzyme levels began to increase. The first liver biopsy showed mild ACR with a rejection activity index (RAI) score of 4. At that time, steroid pulse therapy was performed, and the liver enzyme was recovered. But one month later, the liver enzyme levels increased further. The second liver biopsy taken at POD 40 showed moderate ACR with RAI score of 7. At this time, everolimus was administered, and soon after that, liver enzyme levels had gradually improved even after stopping the steroid administration. Currently, the patient has been doing well for five months to date without any abnormal findings. The maintenance target trough concentrations were tacrolimus 4–6 ng/ml and everolimus 4–6 ng/ml. Our case demonstrated the effect of rescue therapy using everolimus for ACR following LDLT.
Conclusions: Further studies are needed to assess the role of everolimus in pediatric liver transplant recipients suffering from ACR.

Hepatobiliary Surgery

[OP-0301]

Accurate right anterior sectionectomy using liver hanging maneuver and one way parenchyma resection

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Objectives: Right anterior sectionectomy is a complicated procedure because: (1) The right intersectional plane has uneven and curved surface. (2) The landmark—right hepatic vein (RHV) is not always fully exposed, (3) The boundary between right anterior section (RAS) and caudate lobe is not clearly. We proposed the using of liver hanging maneuver and one way parenchymal resection to archive accurate right anterior sectionectomy.
Materials and Methods: 2 patients with diagnosis of HCC. First, dissecting the right anterior pedicle to confirm the demarcation line on the liver surface. Using anterior approach, we transect the parenchyma along the Cantlie line to the anterior surface of the IVC, and expose the root of RHV. Then, transecting between segment V and VI along the plane made by the demarcation line to the level of hepatic hilus and expose the distal trunk of RHV. Cutting a groove 0.5 cm in depth along the demarcation line between segment VIII and VII. A tape was put in the groove and pulled to the left. So we transect the liver along 3 landmarks: (A) the IVC, (B) the RHV, (C) the demarcation line on the liver's surface.
Results: In both cases, we could achieve the accurate bending intersectional plane with RHV exposed and take whole RAS with apart of paracaval of caudate lobe with no complication.
Conclusion: The combination of liver hanging maneuver and one way parenchymal resection could achieve accurate right anterior sectionectomy.

[OP-0302]

Four modified liver hanging maneuvers to complicated hepatectomy: A single center experience

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Objectives: The liver hanging maneuver (LHM) is a useful technique enabling a safe anterior approach. Since the first time described by Belghiti, it has been modified many times by different surgeons to be more effective. Thus, we aim to evaluate the short term results of using some modified liver hanging maneuvers (mLHM) for difficult types of Hepatectomy.
Materials and Methods: From February 1,2020 to February 30, 2021, we perform 4 modified techniques of LHM for 4 patients with liver's tumors. mLHM 1: A tape was placed upon the fossa ductus venosi, its cranial tip was passed to the right behind the common trunk of left hepatic vein and middle heptic vein, and its caudal tip passed behind the left Glissonean pedicle to the hepatic hilum. mLHM 2: After transect the caudal part of S1R about 2 cm, a tape was passed through the hepatic hilum and the right hepatic vein – middle hepatic vein pocket along the right border of the paracaval portion. mLHM 3: Instead of a tape, we used 2 fingers to create the tunnel and push the liver forward. mLHM 4: A tape was placed upon the fossa ductus venosi with cranical tip on the left of left hepatic vein and cranial tip passed behind the left Glissonean pedicle to the hepatic hilum.
Results: Among 5 patients, there were 2 right hepatectomy and caudate lobectomy, 1 left hepatectomy and caudate lobectomy, 1 right anterior sectionectomy with reconstruction right hepatic vein for huge tumor and 1 right trisectionectomy with left hepatic duct-jejunostomy. The modified LHMs were performed successfully in all patients, provide adequate cut planes without complications.
Conclusion: The LHM is a safe and effective technique which can be modified to adapt with many types of hepatectomy.

[OP-0626]

Transpancreatic sphincterotomy vs double-guidewire technique in cases of difficult biliary cannulation: Systematic review and meta-analysis

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Objectives: Endoscopic retrograde cholangiopancreatography (ERCP) has become the preferred minimally invasive treatment for a vast array of pancreatobiliary diseases. Despite substantial progress in the optimization of ERCP techniques, selective biliary cannulation is still one of the most challenging of ERCP. To date, there is no study comparing the clinical success and safety profile fortranspancreatic sphincterotomy (TPS) and double guidewire (DG) technique. We aim to review the efficacy and safety profile for TPS and DG.
Materials and Methods: We systematically searched for trials comparing the outcomes of TPS and DGT up until October 2021 on MEDLINE, Cochrane, and Science Direct database for relevant studies. The systematic review was conducted in accordance with the

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Quality and risk of bias assessment of included studies was performed using the GRADE tool. Meta-Analysis of the results were performed with fixed and random effect model (Mantel-Hanszel method) using RevMan to calculate the pooled risk ratio.

Results: In 6 randomized and 1 non-randomized trial, a total 794 patients underwent ERCP procedure with failed standard selective biliary cannulation; in which TPS and DGT technique was employed in 372 and 422 patients, respectively. Success rate for biliary cannulation were comparable (RR 1.18; 95% CI 0.58–2.37, p value 0.65) and overall complications (RR 1.45; 95% CI 0.88–2.41, p value 0.14). We found no statistically significant difference in terms of risk for post-ERCP pancreatitis (RR 1.44; 95% CI 0.90–2.29, p value 0.13); hemorrhage (RR 0.63; 95% CI 0.21–1.89, p value 0.82); and perforation (RR 1.04; 95% CI 0.18–5.99, p value 0.96).

Conclusion: TPS and DGT manoeuvre have comparable clinical success and safety profile. Considering the recent favourable data for the early use of transpancreatic sphincterotomy, updated algorithm for difficult biliary cannulation especially in patients with unintentional passage of the guidewire into the main pancreatic duct is proposed.

[OP-0662]

Extended right hepatectomy with portal vein reconstruction in Biliary tuberculosis with hilar stricture: Feasibility of extensive resection in Benign hepatobiliary disease

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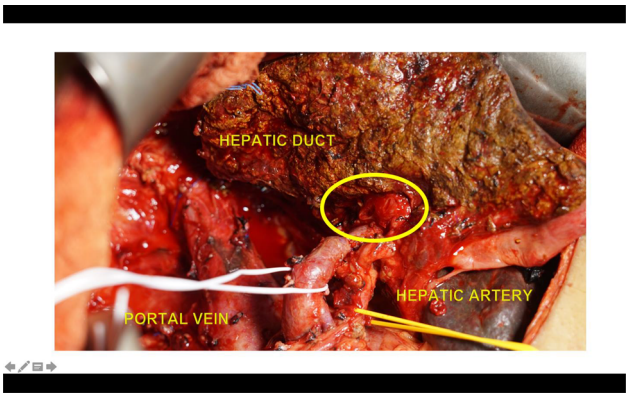
Objectives: Hilar strictures caused by hepatobiliary tuberculosis (TB) is one of the rare manifestation of Mycobacterium tuberculosis infection. Hepatobiliary TB is more frequently encountered in Asian countries, and it has been observed that Filipinos have racial vulnerability to the tubercle bacilli. It is more common in males with a ratio of 2:1, with majority of the patients fall within the age range of 11–50 years old. This is a case of a 31-year-old male with a 2 years history of right upper quadrant associated with symptoms of obstructive jaundice. The patient was previously diagnosed with pulmonary tuberculosis, completed 6 months of recommended treatment with a negative repeat sputum examination.

Materials and Methods: The contrast CT of the chest showed a chronic granuloma infection of the upper airways, whereas the contrast CT of abdomen showed a massive hepatomegaly with diffuse biliary obstruction due to fibrosis with stricture in region of confluence of right and left bile ducts which was consistent with hepatobiliary tuberculosis.

Results: The patient was scheduled for surgery, in which the intraoperative findings revealed a contracted mass at segments 7 & 8, with involvement of right and middle hepatic vein, right anterior portal vein, in addition to hypertrophied left lateral segment and caudate lobe, with complete obstruction of the hilum and common bile duct. Hence, the patient underwent extended right hepatectomy with caudate lobectomy, portal vein resection, ductoplasty, Roux-en-Y hepaticojejunostomy. Postoperatively, patient developed post-hepatectomy liver failure, and eventually improved and was discharged. The patient was advised for follow-up on an outpatient basis.

Conclusion: Hepatobiliary TB is a rare extrapulmonary manifestation of tuberculosis. Diagnosis is often difficult preoperatively, however, it should be suspected in Asian patients presenting with obstructive jaundice with previous history of tuberculosis. This case report highlights that extensive liver resection is feasible in cases of benign hepatobiliary diseases.



[PP-0689]

The choice of the method of treatment of postoperative destructive pancreatitis in patients after surgical interventions on the liver and biliary tract

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Objectives: To determine the most effective method of treatment of postoperative destructive pancreatitis in patients after surgical interventions on the liver and biliary tract.

Materials and Methods: Over the past 15 years, out of the total number of purulent-septic complications of operations on the liver and bile ducts (n = 142), postoperative pancreatic necrosis occurred in 21 (14.8%) patients. There were 16 men (76.2%), 5 women (23.8%). The average age of the patients was 57.3 ± 4.6 years.

Results: Percutaneous drainage interventions with pancreatic punctate were performed in 12 (57.1%) cases. At the same time, in 10 (83.3%) observations, translumbal paravertebral access was performed through the anterior abdominal wall – draining the omentum bag, in 2 (16.7%)—translumbal paravertebral access was performed. Histological examination of pancreatic biopsies showed that the areas of pancreatic tissue necrosis occupy from 20 to 90% of the drug area. In the analysis of microbiological studies of punctates. the growth of bacteria from the foci of pancreatic destruction was 9 (75%) cases in the remaining (n = 3) cases, microflora was not detected. Relaparotomy with omentoburso pancreatostomy was performed in 4 (19%) patients. Relaparoscopy in 5 (23.8%) cases was combined with minilumbotomy and omentobursostomy. Postoperative purulent-septic complications were noted in 5 (23.8%) cases with 3 (14.3%) deaths.

Conclusion: Minimally invasive interventions in postoperative destructive pancreatitis after surgical interventions on the liver and biliary tract, can significantly reduce the number of postoperative complications and mortality.

[PP-0690]

Correction of postoperative intra-abdominal infectious complications of surgical interventions on the liver and biliary tract

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Objectives: To study the effectiveness of videolaparoscopy in the correction of intra-abdominal infectious complications of surgical interventions on the liver and biliary tract.
Materials and Methods: The study is based on the analysis of 78 laparoscopic interventions performed to correct intra-abdominal infectious complications after surgery on the liver and biliary tract. At the same time, pathology requiring relaparotomy was diagnosed in 12 (15.4%) cases, in 66 (84.6%) cases, diagnostic videolaparoscopy was transformed into a therapeutic measure.
Results: Videolaparoscopy made it possible to assess the condition of the abdominal cavity and the omentum by the following criteria: the amount and nature of effusion; the state of the peritoneum and retroperitoneal space; the severity of intestinal paresis and adhesions. The severity of bacterial contamination was determined by the following indicators: low degree, less than 105mt/g—transparent effusion or bile without an odor of serous or serous-fibrinous character; the parietal and visceral peritoneum is covered with gentle, easily relieving fibrinous overlays in a small amount; the small intestine is moderately swollen, but not more than 5 cm in diameter. High degree, more than 105mt/g—effusion, colored brown or greenish, pus with an unpleasant odor; the parietal and visceral peritoneum are covered with massive non-removable fibrinous overlays or stearin plaques; pronounced intestinal paresis, the diameter of the small intestine is 5 cm or more. The presence of postoperative peritonitis was confirmed in 58 (74.3%) cases, and postoperative pancreatic necrosis in 8 (10.2%) patients. At the same time, video laparoscopy allowed to establish intra-abdominal abscesses in 12 (15.4%) observations.
Conclusion: Videolaparoscopy for postoperative infectious complications of surgical interventions on the liver and biliary tract, allows not only to diagnose the nature of complications in a timely manner, but also to choose the most effective ways to treat them and the optimal timing of their implementation.

[PP-0761]

Influence of fluid balance on postoperative outcomes after hepatic resection in patients with left ventricular diastolic dysfunction

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Objectives: Maintenance of low central venous pressure (CVP) during hepatic resection is an effective strategy to minimize intraoperative blood loss. After completion, compensative administration of large amounts of fluid is required, however, this fluid challenge may influence on the postoperative outcomes of patients with left ventricular diastolic dysfunction (LVDD) who cannot tolerate volume adjustment.
Materials and Methods: A total of 190 patients who underwent hepatic resection between March 2015 and February 2021 were evaluated. LVDD was defined according to the American Society of Echocardiography and the European Association of Cardiovascular Imaging 2016 recommendations as left ventricular diastolic dysfunction (group A, n = 37), normal left ventricular diastolic function (group B, n = 127), or indeterminate decision (n = 26).
Results: CVP at the end of surgery was significantly higher in group A than in group B (6.3 ± 3.4 vs. 5.1 ± 2.8, P = 0.030). Postoperative acute kidney injury (AKI, 10.8% vs. 0.8%, P = 0.002) and pleural effusion or edema (48.6% vs. 29.9%, P = 0.035) were more common in group A than in group B. Further, significant increments of creatinine levels from postoperative day 1 to day 7 and decrements of daily urine outputs at postoperative day 1 and day 2 were observed in group A than in group B. LVDD was the only significant risk factor for postoperative AKI after hepatic resection (odds ratio, 20.155; 95% confidence interval, 1.739–233.623, P = 0.016).
Conclusion: Patients with LVDD have significant increment of postoperative morbidity after hepatic resection owing to fluid overload that delicate volume control would be required in these patients.

[PP-0797]

Significance of preoperative volume control for hepatic resection in obese patients

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Objectives: Obese patients requiring hepatic resection are increasing. however, little is known about operative outcomes in such patients. The aim of this study was to investigate clinical outcomes of patients after hepatic resection in relation to obesity.
Materials and Methods: A total of 175 patients who underwent hepatic resection between March 2015 and July 2021 were evaluated. The patients were divided into two groups according to their body mass index (BMI): Obese patients (BMI $\geq$ 25 kg/m^2, n = 84) and non-obese patients (BMI $<$ 25 kg/m^2, n = 91). We compared demographics, operative outcomes and postoperative complications between the groups.
Results: There was no significant difference of demographics between the groups. Operative duration (195.7 ± 62.9 vs. 176.0 ± 53.6, P = 0.027) was longer and estimated blood loss (EBL, 587 ± 694 vs. 430 ± 422, P = 0.022) was increased in the obese patients, compared to non-obese patients. Postoperative complication (47.6% vs. 33.0%, P = 0.048), especially wound infection (8.3% vs. 1.1%, P = 0.022), and postoperative hospital stay (11.7 ± 4.4 vs. 10.6 ± 2.6, P = 0.044) were increased in the obese patients, compared to non-obese patients. Obesity (odds ratio[OR], 0.204; 95% confidence interval[CI], 1.177–4.129; P = 0.014) and central venous pressure (CVP) $\geq$ 5 (OR, 2.733; 95% CI, 1.445–5.170; P = 0.002) at start of surgery were significant risk factors for EBL $\geq$ 500 mL.
Conclusion: Obese patients had increments of operative duration and EBL related with postoperative morbidity and hospital stay and low CVP at start of surgery would be helpful to improve clinical outcomes in those patients.

[PP-0801]

Endoscopic treatment of suppurative liver echinococcos

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Objectives: To improve the endoscopic treatment of liver echinococcosis.
Materials and Methods: Over the past 5 years, the clinic has treated 120 patients with suppuration echtnococcosis of the liver. There were 75 men (62.5%), 45 women (37.5%). The age of patients ranged from 24 to 82 years. In 59 (49.2%) In observations, suppurative echinococcosis of the liver was located in the right lobe of the liver—38 (31.7%) in the left lobe—23 (19.1%) cases in both lobes of the liver.
Results: With suppurative liver echinococcosis, the clinical picture of the disease in 98% of cases was dominated by signs of intoxication syndrome. Of the instrumental research methods, the most informative in terms of diagnosing suppurative liver echinococcosis were ultrasound and CT, which diagnosed the disease in 95–97% of cases. To select the method and scope of surgery for traditional or video laparoscopic intervention They attached importance to assessing the severity of the condition of patients on the APACHE II scale. So, with suppurating liver echinococcosis and severity of the condition of patients according to APACHE II from 0 to 20 points in 74 (61.7%) cases, traditional open methods of echinococcectomy (n = 48), pericystectomy (n = 14) and liver resection (n = 12). In 46 (38.3%) cases with indicators of severity of the condition of patients according to APACHE II more than 20 points whether video laparoscopic and puncture-draining interventions under ultrasound control. After doing nii of traditional open surgical interventions postoperative complications of purulent-septic this character was noted in 27 observations, with 8 deaths, whereas after video laparoscopic interventions and puncture-draining operations postoperative complications were observed in 9 patients ents, with 1 death.
Conclusion: Video laparoscopic interventions and puncture-draining operations under ultrasound control are the operation of choice for suppurating liver echinococcosis in patients with high operational risk.

[PP-0805]

Experience of surgical treatment alveococcosis liver in children

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Objectives: Analysis of the results of surgical treatment of alveococcosis in children.
Materials and Methods: From April 2009 to November 2018 46 children with liver alveococcosis aged 7 to 18 years were treated, 26 are boys and 20 are girls. Of 46 patients, 24 children (52%) had the following complicated forms of liver alveococcosis: obstructive jaundice—4, cavernous forms of alveococcosis—10, invasion into neighboring organs and great vessels (inferior vena cava and portal veins, diaphragm)—18, bilobar lesion—4.
Results: Of 46 patients, 24 children (52%) had the following complicated forms of liver alveococcosis: obstructive jaundice—4, cavernous forms of alveococcosis—10, invasion into neighboring organs and great vessels (inferior vena cava and portal veins, diaphragm)—18, bilobar lesion—4. All 46 children with liver alveococcosis and its complications underwent surgery. The volume of resection was determined by the size and localization of the parasitic node and the functional state of the liver. The following operations were performed: percutaneous transhepatic cholangiostomy, atypical and extensive liver resections. A 42 (91.3%) liver resection was performed in children with liver alveococcosis. Extensive liver resections—20, Atypical liver resections (segmentectomy and bisegmentectomy) – 22 Radical liver resection was performed in 30 (65.2%) patients, 8 (34.8%) patients were operated on palliatively. There was no intraoperative lethality. Postoperative complications occurred in 2 (8.7%) patients.
Conclusion: The relevance of liver alveococcosis is growing every year due to the high infection rate of the population in the endemic regions of Kyrgyzstan. The percentage of complicated forms of the disease among children is high—52%. The only and radical method of treatment is liver resection within healthy tissues. In complicated forms of liver alveococcosis, palliative liver resections and palliative operations (CCS) prolong and improve the quality of life.

[PP-0836]

Laparoscopic redo liver surgery; Indications and results

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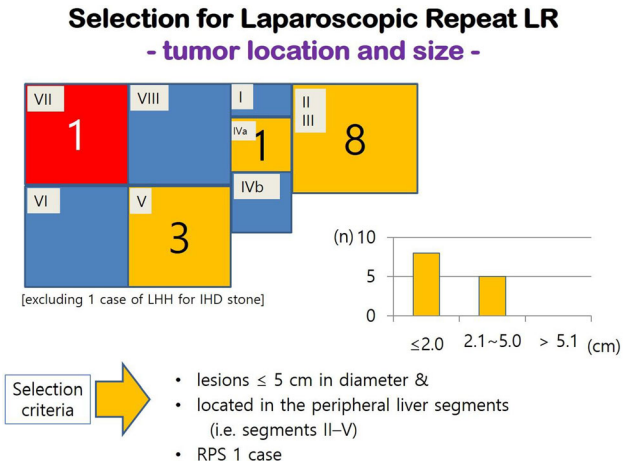
Objectives: The authors conducted this study to identify the most suitable candidates of laparoscopic repeat liver resection (RLR).
Materials and Methods: Among the 817 patients who underwent liver resection from Sep. 2008 to Nov. 2020, 14 and 35 patients who underwent repeat liver resection by laparoscopic (L-RLR or laparoscopic group) and open approach (O-RLR or open group), respectively were compared. The variables investigated were tumor size, location and laterality, underlying liver condition and operative characteristics. and their short-term outcomes were compared.
Results: Hepatocellular carcinoma was the most common indication for RLR, 74% for O-RLR group and 50% for L-RLR group. All the L-RLR were performed for tumors smaller than 5 cm and 57% of L-RLR were performed for tumors 2 cm or smaller (Fig. 1). There was a considerable trend to perform RLR laparoscopically for smaller tumors ($p = 0.055$). 84% of L-RLR were performed for tumors at anterolateral location in contrast to 42% for O-RLR ($p = 0.032$, Fig. 1). There was no significant difference in the rates of major resection and anatomical resection between the 2 groups. Formal anatomical liver resection including posterior sectionectomy was performed in 57% of patients in L-RLR group. There were 2 cases of the 3rd resection and one case of 4th resection performed laparoscopically. Two cases in L-RLR group were open converted, due to poor localization in 1 and bleeding in another 1. There was significant difference in mean operation time, intraoperative bleeding amount and postoperative hospital stay, favoring L-RLR group ($p = 0.014$, 0.028 and 0.005, respectively). The morbidity rate was 28% in open group and 7% for laparoscopy group, but the difference was not significant ($p = 0.098$). One mortality in the O-RLR group was due to liver failure ($p = 0.523$).
Conclusion: For recurrent liver tumors located at anterolateral region, preferably for those less than 5 cm, the laparoscopic approach deserves to be considered first (Fig. 1).



[OP-0955]

Risk factors for hepatic decompensation after surgical resection in patients with hepatocellular carcinoma

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Objectives: Indocyanine green (ICG) clearance test is commonly used for assessment of preoperative risk, and the degree of liver fibrosis might be associated with preoperative liver function. The aim of study was to evaluate the risk factors for postoperative hepatic decompensation in patients with hepatocellular carcinoma (HCC).
Materials and Methods: A total of 62 patients with HCC who performed ICG retention rate at 15 min (R15) and fibroscan before surgery, and underwent surgical resection between April 2007 and August 2021 were retrospectively enrolled. The clinical characteristics, laboratory data, the result of ICG R15 test, and non-invasive fibrosis markers [aspartate aminotransferase to platelet ratio index (APRI), FIB-4 index, and liver stiffness measurement (LSM) on fibroscan] were analyzed for the risk factors of postoperative or persistent hepatic decompensation after surgery.
Results: There was a significant correlation between the results of ICG R15 test and LSM at baseline ($r = 0.498$, $P < 0.001$). Postoperative hepatic decompensation was present in 25.8% (16/62) and persistent decompensation at 3 months after surgery was present in 4.8% (3/62) of patients. In the univariate analysis, LSM [odds ratio (OR): 1.05 (1.01–1.09), P = 0.025], AST [OR: 1.03 (1.00–1.05), P = 0.047], albumin [OR: 0.05 (0.01–0.37), P = 0.004], platelet count [OR: 0.99 (0.98–0.99), P = 0.031], FIB-4 index [OR: 1.80 (1.15–2.83), P = 0.010], and APRI [OR: 9.18 (1.98–42.59), P = 0.005] were risk factors for postoperative decompensation. In the multivariate analysis, albumin [OR:0.06 (0.004–0.846), P = 0.037] was an independent risk factor for postoperative decompensation. In the univariate analysis, LSM [OR: 1.06 (1.01–1.12), P = 0.011], AST [OR: 1.04 (1.00–1.09), P = 0.048], and APRI [OR: 5.57 (1.09–28.31), P = 0.039] were risk factors for persistent decompensation. In the multivariate analysis, LSM [OR:1.06 (1.00–1.13), P = 0.035] was an independent risk factor for persistent decompensation.
Conclusion: Although the results of preoperative ICG R15 are suitable for surgery, careful decision about whether or not to perform surgery may be needed in patients with high preoperative LSM.

[PP-0997]

Surgical treatment of liver alveococcosis complicated with mechanical jarcus

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Objectives: Evaluation of the general condition and laboratory data results before and after CCS, CCC in order to prepare for a radical method of treatment.
Materials and Methods: An analysis of case history was carried out from the Department of Surgical Gastroenterology and Endocrinology, and Purulent Surgery of the National Hospital under the Ministry of Health of the Kyrgyz Republic. 504 patients with liver alveococcosis received inpatient treatment during the period from 2009 to 2020, out of 81 patients there were 34 men (42%) and 47 women (58%) The age of the patients ranged from 15 to 65 years, the average age of the patients was 36.6 ± 3 years.., The standard laboratory and instrumental research methods, such as ultrasound of the abdominal cavity organs, CT, MRI, ChChS, ChChG were used during the diagnostic examination. The results of the blood test for liver tests, characterized the picture of obstructive jaundice.
Results: A large number of patients are hospitalized with a complicated form of liver alveococcosis with jaundice, liver failure (81). In order to decompress the biliary tract, minimally invasive surgery) was performed i.e. percutaneous transhepatic cholangiostamia (CCC. Thus, 81 patients were hospitalized with liver alveococcosis complicated by obstructive jaundice with high levels of bilirubin, which indicates a prolonged obstructive course. The duration of obstructive jaundice affects the individual approach to the patient's treatment and the choice of surgical treatment, i.e., to divide the operation into several stages.
Conclusion: In order to improve the results of major operations and the general condition of patients with alveococcosis of the liver complicated by mechanical, it is recommended to perform decompression of the biliary tract, which will improve the quality of life of patients during preparation for liver transplantation.

[PP-1017]

Advanced liver resections in Alveococcosis

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Objectives: Improving the results of diagnostics and surgical treatment in liver alveococcosis.
Materials and Methods: Analyzed the results of surgical treatment of 478 patients with liver alveococcosis since April 2009. to October 2021 Liver resection was performed in 430 patients. In 7 patients, metastases were found in the brain, in 3 in the lungs, and in 4 in the soft tissues. In 2 cases, a hepatic-bronchial fistula was detected. The average age of the patients was 37 ± 2.3 years. There were 149 (31.2%) men and 329 (68.8%) women.
Results: In total, 430 patients were operated on, surgical interventions of various sizes were performed from diagnostic laparotomies to liver resections: in 210 cases—in the volume of extensive anatomical liver

resections (RPHGE, PHGE, RLHGE, LGGE), in 220 cases—atypical resection. The resectability was 90.0%, 61.8% of them were radically operated on. Characteristics of postoperative complications according to Clavien-Dindo: I degree—21, I degree—22, III b degree—1, IV a degree—17, V degree—4.
Conclusion: The final decision on resectability can be made after intraoperative revision, IOUS, USG, and liver mobilization. Liver resection in case of widespread alveococcosis is extensive, the need to perform resection and prosthetics of large vessels, as well as reconstruction of the bile ducts. R0 liver resection in the absence of distant metastases remains a radical method of treatment. With liver alveococcosis, repeated operations are justified.

[OP-1021]

Operations for liver alveococcosis with involvement of the inferior vena cava

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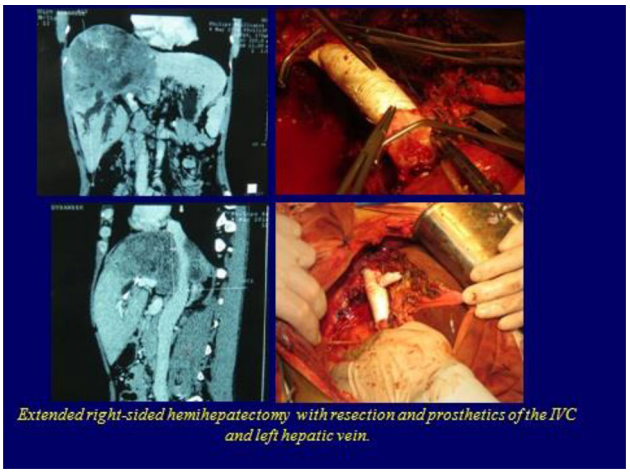
Objectives: to evaluate the results of surgical treatment of liver alveococcosis with lesions the of IVC.
Materials and Methods: Our experience of surgical treatment with liver alveococcosis for the period from 2009 to 2018. amounted to 422 patients, of which in the clinic. I.K. Akhunbaeva was being treated for 224 patients with liver alveococcosis. In 53 (23.6%) patients, the alveolar node grew into the IVC. They were 23 men (43.4%), women—30 (56.6%). The average age of the patients was 33.8 ± 1.9 years. According to the PNM classification, patients were distributed as follows: P4N0M0 (III B stage)—32, P4N0M1 (IV stage)—2 (with lung metastases), P4N1M0 (IV stage)—15 patients, P4N1M1 (IV stage)—1.
Results: Performed operations: extended right-sided hemihepatectomy—15 (with resection and prosthetics of the IVC and left hepatic vein, resection and reconstruction of the portal vein -1, with marginal resection of the IVC—2, left a plate on the inferior vena cava—8); right-sided hemihepatectomy—12 (with marginal resection of the IVC -3, left the plate on the IVC -6); extended left-sided hemihepatectomy -5 (the plate was left on the IVC -2); atypical resections—7 (with marginal resection of the IVC -1, left a plate on the IVC -4); cytoreductive resections—4; S1 resection with marginal IVC resection—1; opening and drainage of the alveolar cyst -3; explorative laparotomies—7; There aer 40 liver resections were performed: 17 (32%) radical liver resections and palliative operations –23 (43.4%).
Conclusion: Despite the circular lesion of the inferior vena cava by alveococcosis of the liver, radical resection of the liver with resection and prosthetics of the affected area of the IVC and portal vein is possible. Reoperations after palliative resections in other clinics are justified.



[OP-1055]

Management of gallstones with periampullary diverticula

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Objectives: Periampullary diverticula (PAD) is extraluminal outpouching of the duodenal mucosa. The incidence of PAD increases with age and is frequently found accidentally in patients while undergoing Endoscopic Retrograde Cholangiopancreatography (ERCP). Therapeutic ERCP can be difficult in patients with PAD since the orientation and location of major duodenal papilla might have changed.
Materials and Methods: This paper presents a case series of two patients from the Endoscopy Clinic in St. Carolus Hospital, Jakarta. Both patients were diagnosed with choledocholithiasis and PAD. ERCP procedures with variations of intervention were done in both patients.
Results: Both patients came primarily to the internal medicine clinic with complaints of right upper abdominal pain, nausea, vomiting, and fever. Laboratory exams showed an increase in bilirubin levels and leukocytes; other results were generally unspecific. Abdominal Magnetic Resonance Imaging (MRI) in both patients showed multiple stones in the gallbladder and common bile duct and dilated intra- and extrahepatic bile duct. ERCP was conducted for both patients and we noticed the presence of PAD. One patient had type IIB PAD and the other one type IIA PAD according to the Li-Tanaka classification. The first patient underwent limited endoscopic sphincterotomy with large balloon dilatation, while in the latter patient, eversion of the diverticula was required with placement of two haemoclips to stabilize the papilla prior to balloon dilation. Cholecystectomy was done subsequently. There were significant clinical improvements and a decrease in bilirubin levels in both patients afterwards.

Conclusion: PAD is commonly found by coincidence at the time of ERCP. The presence of PAD may cause difficulties during therapeutic ERCP procedure and a variety of interventions are needed in patients with PAD.

[PP-1189]

Results of treatment of liver alveococcosis with large vessels involving

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Objectives: To evaluate and compare the results of surgical treatment of AP with lesions of large vessels.
Materials and Methods: We have analyzed the results of treatment of 32 patients with liver alveococcosis for the period from 2009 to March 2018, in whom the alveolar node has grown into large vessels—the IVC and portal vein IV. These patients were divided into two groups; the first group included patients with lesions of the inferior vena cava, and the second group included patients with invasion of the portal portal gate of the liver. The average age of the patients was 46 ± 10.8; it is worth noting that two patients at the time of treatment were grade 11 students. The male/female ratio is 11/21. The average length of inpatient stay is 16.1 ± 3.9 bed days. According to the PNM classification: P4N0M0—18, P4N0M1—2 (with metastases to the lungs), P4N1M0—12 patients.
Results: The first group included 21 patients, the second group included 10 patients. In the first group, the percentage of radical liver resection was 13%, in the second group it was 29%. The following types of surgery were performed: PHGE—13, RHGE—4, RPHGE—9, Atypical resection (AR): AR of the right lobe of the liver—1, AR 3,5,7 and 4a of liver segments with marginal resection of IVC—1. Resection S1 with marginal IVC resections—1. Cytoreductive LELE—1. Explorative laparotomy—2.
Conclusion: Despite the invasion of the IVC and portal vein, it is possible to perform a radial surgery. It is justified to perform palliative liver resection even with repeated surgery. It was determined that the percentage of radical liver resections with IV lesions is higher than with IVC lesions, 13% and 29%, respectively.

[L-PP-1225]

Anatomic liver resection performed by approaching the Umblical plate for perihilar cholangiocarcinoma

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Objectives: The Anatomic right hepatic trisectionectomy with caudate lobectomy for hilar cholangiocarinoma was reported in 2006. This technique need the umblical plate access. With extension of this technique, anatomic central bisectionectomy can be also performed for the Bismuth type 4 of perihilar cholaniocarcinoma (CCA).
Materials and Methods: From 2010 to 2020, anatomic right trisectionectomy (N = 8) and anatomic central bisectionectomy (N = 3) was performed for the patients with the Bismuth type 4 of perihilar CCA. All anatomic liver resection was performed by approaching the umblical plate, in which the bile ducts of the left lateral section were divided at the left side of the umblical fissure following complete dissection of the umblical plate.
Results: Liver resection was successfully performed, and there was no postoperative mortality. All patients were histologically diagnosed as having CCA. Among the patients who underwent anatomic right trisectionectomy, 5 patients received portal vein embolization (PVE) and 3 patients did not. R0 resection rate was 63%. 2 patients performed portal vein wedge resection. 3 patients died of cancer progression and 2 patients died of biliary sepsis. One patients survived without recurrence for 8 years. 4 patients are under follow-up without recurrence. The remaining one patient recurred after 28 months and is undergoing radiation therapy. There were only three patients had biliary leakage.
Conclusion: Anatomic liver resection that is performed by approaching the umblical plate can be safely and effectively proformed even in perihilar CCA.

[L-PP-1226]

Laparoscopic liver resection versus percutaneous radiofrequency ablation for single hepatocellular carcinoma (≤ 3 cm)

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Objectives: Laparoscopic liver resection (LLR) and Percutaneous radiofrequency ablation (RFA) are ideal treatment options for single hepatocellular carcinoma (HCC). As laparoscopic technology advances, LLR is now less invasive and safer than RFA comparable. Therefore, this study aims to compare the long-term survival outcomes of the two treatment and to suggest appropriate treatment criteria.
Materials and Methods: From 2008 to 2019, a total 342 newly diagnosed patients with single HCC ≤ 3 cm underwent RFA or LLR as first-line therapy. A total of 268 patients were analyzed retrospectively, excluding those with a Platelet count less than 100,000.
Results: A total of 122 and 146 patients underwent RFA and LLR, respectively. RFA showed significantly higher marginal recurrence rate than LLR. (21 versus 1, $p < 0.0001$). LLR has better overall survival (OS) and recurrence free survival (RFS) ($p < 0.0001$, $p < 0.0001$). Multivariable analysis found the treatment methods as the unique variable statistically significant for OS [hazard ratio (HR) 0.271, 95% confidence interval (CI) 0.126–0.583, p = 0.001] and RFS (HR 0.507, 95% CI 0.290–0.885, p = 0.017).
Conclusion: LLR showed better outcomes in overall survival and recurrence free survival. In cases where RFA is difficult to perform or if the possibility of local recurrence is high, it is recommended to consider LLR for single HCC (≤ 3 cm).

[L-PP-1238]

Surgical treatment of biliopancreato-duodenal zone tumors

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Objectives: To evaluate the results of surgical treatment of patients with tumors of the biliopancreatoduodenal zone.
Materials and Methods: In the clinic them. I.K. Akhunbaeva NG MH KR from 2009 to 2021. 73 GPDRs were performed for malignant tumors of the biliopancreatoduodenal zone. Among the patients there were 64 men and 9 women. The average age of the patients was 54.5 ± 1.4 years. Of these operations for tumors of the head of the pancreas—53 (72.6%), large duodenal papilla—8 (11.0%), distal common bile duct—7 (9.6%) and duodenum—5 (6.8%). Adenocarcinoma was diagnosed in 95.9% of cases, neuroendocrine tumor—2.7%, solid pseudo-papillary tumor (Franz's tumor)—1.4%. According to TNM classification I and II—9 (39.7%), III-44 (60.3%). In 70 cases, a pancreaticogastroanastomosis was formed and in 3 cases—a pacreaticogastroanastomosis.
Results: Postoperative mortality—2.7%. Postoperative complications were observed in 26 (35.6%) patients. The main and most severe of them were failure of pancreaticogastroanastomosis with the formation of a pacreatic fistula—in 6 patients (23%), failure of biliodhistivny anastomosis—in 1 patient (3.8%), pulmonary embolism—in 1 patient (3.8%), gastrostasis—in 18 patients (69.2%). Repeated surgery was required in 1 observation.
Conclusion: The number of malignant tumors of the biliopancreatoduodenal zone annually increases due to the increased, compared with previous years, cases of early diagnosis of tumors, which is associated with an improvement in the diagnostic algorithm of patients with this pathology. Currently, the only radical operation for the formations of the biliopancreatoduodenal zone is gastropancreatoduodenal resection. The largest number of GADDs in patients was performed for pancreatic adenocarcinoma (95.9% of cases). Postoperative complications are observed in 35.6% of patients. Postoperative mortality is 2.7% of cases.

[L-PP-1252]

Surgical treatment of the liver alveococcosis

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Objectives: to evaluate the results of extensive liver resections in alveococcosi.
Materials and Methods: For the period from April 2009 to August 2016 were on treatment—358 patients with liver alveococcosis. Of 358 patients, 317 were operated on, of which 167 underwent extensive liver resections (52.7%). The average length of inpatient stay is 16.5 ± 0.9 bed-days.
Results: 167 patients had 214 complications: obstructive jaundice—31, cavernous forms of alveococcosis—25, invasion of neighboring organs (lung, kidney, diaphragm, stomach, pancreas, HDS, large intestine, adrenal gland)—54, bilobar lesion—95, MTS in lungs—4, MTS to the brain—2, MTS to soft tissues—3.
167 (100%) extensive liver resections were performed: of them with resection of the bile ducts—9 (5.4%), with resection of the portal vein—22 (13.2%), resection and prosthetics of IVC—7 (4.2): right-sided hemihepatectomies 79 (47.3%), of which with resection of the bile ducts—3, with resection of the portal vein—11, resection and prosthetics of IVC—5; left-sided hemihepatectomies—26 (15.6%), of which with resection of the bile ducts—2, with resection of the portal vein—4; extended left-sided hemihepatectomies—19 (11.4%), of which with resection of the bile ducts—1, with resection of the portal vein—4; extended right-sided hemihepatectomies—43 (25.7%),

Postoperative complications were observed in 24 patients (14.3%): liver failure—16, bile leakage—6, reactive pleurisy—7, bilateral pneumonia—1, gastrointestinal bleeding—1. The mortality rate is 2.4%—2 patients.
Conclusion: The final decision on resectability can be made after intraoperative revision, IOUS, USDG and liver mobilization, liver resection is quite feasible even with invasion of the great vessels and bile ducts, the radical method of treatment remains liver resection R0.

[L-PP-1261]

Endoscopic treatment of suppurative liver echinococcosis

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Objectives: To impruve treatment of suppurative liver echinococcosis.
Materials and Methods: Over the past 5 years, the clinic has treated 120 patients with suppuration echtnococcosis of the liver. There were 75 men (62.5%), 45 women (37.5%). The age of patients ranged from 24 to 82 years. In 59 (49.2%) In observations, suppurative echinococcosis of the liver was located in the right lobe of the liver, in 38 (31.7%) in the left lobe of the liver and in 23 (19.1%) cases in both lobes of the liver.
Results: With suppurative liver echinococcosis, the clinical picture of the disease in 98% of cases was dominated by signs of intoxication syndrome. Of the instrumental research methods, the most informative in terms of diagnosing suppurative liver echinococcosis were ultrasound and CT, which diagnosed the disease in 95–97% of cases. To select the method and scope of surgery for traditional or video laparoscopic intervention They attached importance to assessing the severity of the condition of patients on the APACHE II scale. So, with suppurating liver echinococcosis and severity of the condition of patients according to APACHE II from 0 to 20 points in 74 (61.7%) cases, traditional open methods of echinococcectomy (n = 48), pericystectomy (n = 14) and liver resection (n = 12). In 46 (38.3%) cases with indicators of severity of the condition of patients according to APACHE II more than 20 points whether video laparoscopic and puncture-draining interventions under ultrasound control. After doing nii of traditional open surgical interventions postoperative complications of purulent-septic this character was noted in 27 observations, with 8 deaths, whereas after video laparoscopic interventions and puncture-draining operations postoperative complications were observed in 9 patients ents, with 1 death.
Conclusion: Video laparoscopic interventions and puncture-draining operations under ultrasound control are the operation of choice for suppurating liver echinococcosis in patients with high operational risk.

[L-OP-1269]

Surgical series of large symptomatic cystic neoplasms of liver

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Objectives: Cystic neoplasms of liver are uncommon($\sim$ 5%) and literature regarding management of symptomatic large liver cysts (LC) is rare.We report the outcome following surgical treatment of symptomatic LC from a tertiary centre.
Materials and Methods: A retrospective study was performed on 10 patients diagnosed as large (> / = 4 cm) symptomatic cystic neoplasms of liver who underwent surgical treatment in one high volume Gastro-surgery centre at Kottayam, Kerala, India, during the last 5 year period. An analysis was made using the demographic, tumour related and surgical related variables as well as post-operative outcomes.
Results: Out of the 10 patients, 8 were females (mean follow up-24.3 months). Mean age was 60 years. Median tumour size was 14 cm. Six were in left lobe, three in right lobe and two were central (one patient- multiple-two cysts) in location. Diagnosis were Biliary cystadenoma (BC) in six (one with foci of invasive carcinoma, one in patient with multiple cysts), hydatid cyst (HC) in two, simple cyst(SC) in two (one with intra-cystic rupture, another in patient with multiple cyst) and one with cystic presentation of angiosarcoma (15 cm). Surgical treatment comprised of enucleation in five (four BC, one SC), right hepatectomy in two (one with HC and another SC with intra-cystic hemorrhage), left hepatectomy in one (BC with invasive-foci), left lateral sectionectomy in one (BC), central hepatectomy in one (angiosarcoma with rupture) and abandoned in one with BC due to dense adhesion at hilum. Median blood loss was 100 ml and median hospital stay was 7 days. Most common morbidities were bile leak in two (one HC, one SC with rupture) and pleural effusion requiring drainage in one. There were no peri-operative mortality.
Conclusion: Aggressive surgical resection is safe in symptomatic liver cysts with enucleation feasible in most cases. The incidence is predominant in females and left lobe in symptomatic LC.

[L-OP-1279]

Effectiveness of video assisted teaching on incentive spirometry in terms of skills score and bedside pulmonary function test outcomes of patients undergoing hepatopancreatobiliary surgeries

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Objectives: To assess the effectiveness of Video Assisted Teaching on Incentive spirometry in terms of Skills Score and Bedside Pulmonary Function Test Outcomes of patients undergoing hepatopancreatobiliary surgeries.
Materials and Methods: Using quantative approach a True-experimental study was conducted. Pre-test Post-test control group design was adopted. Simple random sampling technique was used to enrol 50 patients undergoing Hepatopancreatobiliary Surgeries at ILBS, from 10/11/2020 to 12/12/2020. The experimental group received Video Assisted Teaching (VAT) on Incentive Spirometry (IS) by the researcher on the day of pre-test whereas control group received the routine instructions by the physician/nurse. Patients under experimental group were given reminders to perform IS. Post-test was conducted on the third post-operating day. Tools included a structed questionnaire on Socio Demographic and Clinical Variables, structured checklist to assess Skills on IS and Bedside Pulmonary Function Test Assessment tools. Obtained data was analysed using descriptive and inferential statistics.
Results: Both the groups were homogenous and comparable at baseline. The findings related to Skills Score showed that the Skills Score under experimental group increased significantly from pretest (5.20 ± 1.41) to post-test (9.00 ± 1.71) with a p value of < 0.001. The difference in the number of balls lifted during inspiration and expiration was found significantly increased in the experiment group($p < 0.001$). A significant difference was found in the duration of holding the balls at highest level during IS of patients under experimental group during pretest and posttest both during inspiration($p < 0.001$) and expiration($p < 0.001$). Significant difference was found in Breath Holding Test and Single Breath Count Test during IS under experimental group during inspiration($p < 0.001$) and expiration($p < 0.001$). A significant association was found between mean gain in Skills Score with days between appointment and Date of surgery($p = 0.02$) of the patients.
Conclusion: The findings indicate that implementation of VAT on IS was effective in improving Skills Score and Bedside PFT Outcomes of patients undergoing HPB surgeries.

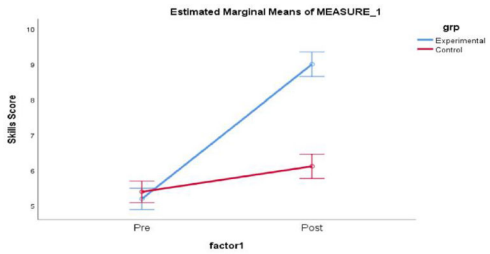

Figure-1 Line graph showing the mean of Skills Scores in performing Incentive Spirometry of experimental and control group

[ABST-0039]

Perioperative and long-term oncological outcomes of laparoscopic right hepatectomy versus open right hepatectomy for hepatocellular carcinoma: A propensity score matching analysis

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Background: Despite of the popularity of laparoscopic hepatectomy, laparoscopic right hepatectomy (LRH) is, however, still in need of further evidence to assess safety and efficacy for the treatment of hepatocellular carcinoma (HCC).

Methods: From 2008 to 2017, total 149 patients (LRH, 28 patients; ORH, 121 patients) were included. Baseline characteristics including tumor characteristics, perioperative outcomes, and survival outcomes were compared between two groups. One-to-one propensity score matching (PSM) was used to minimize selection biases.
Results: After a 1:1 PSM, 25 patients were included in each group. The LRH group had lesser intraoperative blood loss (p = 0.02), lower rate of intraoperative transfusion (p = 0.02), lower overall morbidity rates (p = 0.00), and shorter postoperative hospital stays (p = 0.004). The cumulative 1-, 3-, and 5-year OS rates were 100%, 92.0%, and 92.0%, respectively for the LRH group and 84.0%, 80.0%, and 64.0%, respectively, for the ORH group. Furthermore, the cumulative 1-, 3-, and 5-year DFS rates were 96.0%, 80.0%, and 75.3%, respectively for the LRH group and 72.0%, 48.0%, and 40.0%, respectively, for the ORH group. LRH group showed significantly longer DFS (p = 0.009) and OS (p = 0.028) than ORH group.
Conclusions: LRH can be safely performed for HCC, and it is associated with better oncological outcomes.

[ABST-0095]

Laparoscopic associating liver partition and portal vein ligation for staged hepatectomy for patients with colorectal liver metastases: Experience of a tertiary hospital in South Africa

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Background: ALPPS (Associating Liver Partition and Portal vein ligation for Staged hepatectomy) is becoming more established for the management of colorectal liver metastases where a future liver remnant is not deemed sufficient. Our institute has expanded into performing the challenging procedure laparoscopically.
Methods: A retrospective analysis of all consecutive patients undergoing ALPPS at a single referral center (Dr George Mukhari Academic hospital) for colorectal liver metastases with a small future liver remnant was performed using a prospective database from January 2020 till August 2021. Feasibility was assessed by analysis of conversions. The 90-day mortality and complications were analyzed using the Clavien-Dindo scoring system. Operative time, blood loss, volumetric growth and hospital stay were all studied.
Results: Laparoscopic ALPPS was performed in 3 patients. There was no mortality and no complication grade greater than IIIb was observed. One patient required a relook laparoscopy for sepsis at the site of the liver partition. Liver failure was not observed in any of the patients. The average hospital stay was 20 days.
Conclusions: Laparoscopic ALPPS is a feasible procedure in patients with colorectal liver metastases and a small future liver remnant. It is a complex procedure requiring significant resources and skill, but it is definitely feasible within the South African setting.

[ABST-0108]

Clinical effectiveness and safety of laparoscopic liver resection versus open liver resection for hepatocellular carcinoma in elderly patients: A systematic review and meta-analysis

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Background: With the aging population, surgical treatment in elderly patients with hepatocellular carcinoma (HCC) is increasing. The difference in effectiveness between surgical treatments in elderly patients is unclear to date. This study aimed to compare effectiveness and safety of laparoscopic liver resection (LLR) compared with open liver resection (OLR) in elderly patients with HCC.
Methods: We searched Ovid-Medline, Ovid-EMBASE, Cochrane library, and 3 local medical databases through March 2021 to identify comparative studies on primary HCC in elderly patients ($\geq$ 65 years). The outcomes were over-all survival, disease-free survival, 90-day mortality, 30-day mortality, in-hospital mortality, major post-operative complications, overall complications, post-operative liver failure and length of stay (LOS). Two independent reviewers extracted data from each study using a standardized form. The quality of the selected studies was assessed using Methodological index for non-randomized studies (MINORS).
Results: Five eligible comparative cohort studies representing 653 patients were identified. The two groups did not show statistical difference for overall survival and disease-free survival in 2 studies. 90-day mortality, 30-day mortality, in-hospital mortality (n = 4 studies, OR 0.38, 95% CI 0.07–1.99, I2 = 11%; n = 2 studies, OR 0.33, 95% CI 0.03–3.20, I2 = NA; n = 1 study, OR 0.19, 95% CI 0.02–1.69, I2 = NA, respectively) were not significant different between two groups. Overall and major post-operative complications (n = 5 studies, OR 0.43, 95% CI 0.26–0.70, I2 = 27%; n = 5 studies, OR 0.36, 95% CI 0.17–0.77, I2 = 14%; n = 2 studies, OR 0.41, 95% CI 0.19–0.91, I2 = 0%, respectively); the incidence of liver failure were significantly fewer in LLR than in OLR. The LOS was consistently reported to be shorter in the LLR with 5 studies.
Conclusions: LLR may be a generally safer and better option than open surgery in elderly patients with HCC. Laparoscopic LR is associated with significantly fewer complications, major complications, post-operative liver failure; and shorter LOS than OLR. Further prospective studies with long term follow-up in elderly patients are needed.

[ABST-0110]

Multifocal hepatic epithelioid haemangioendothelioma: Extended resection or liver transplant

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Background: Hepatic epithelioid haemangioendothelioma (HEHE) is a rare malignant vascular tumour. It's unique tumour biology behaves on a spectrum of aggressiveness between haemangiomas and angiosarcomas. First described in 1982 by Weiss and Enzinger, it has a reported incidence of 1–2 cases per 1 million. It's rarity, multifocal disease combined with usually a young female population makes management challenging. Liver resection and liver transplant have been well described as effective treatment options with good long-term outcomes.
Methods: Case report: a 26-year-old female presented to the emergency department with acute severe abdominal pain. An ultrasound revealed an indeterminate liver lesion in segment VII measuring

10 × 10x16mm. Her pain resolved and an outpatient CT multiphase revealed three hypodense nonenhancing lesion within the right lobe of the liver and one 4 mm hypodense nodule in segment II. No other metastatic lesions or primary malignancy were identified. Endoscopy and colonoscopy were normal. A diagnostic laparoscopy and excisional biopsy was performed. At laparoscopy, multiple liver lesions were evident but there was no metastatic disease. Successful excisional biopsy of a segment VII lesion using intra-operative ultrasound demonstrated HEHE on histopathology.
Results: Given the multifocal disease, a multidisciplinary team decision opted to proceed for liver transplant in which she is currently being worked up for.
Conclusions: HEHE is a rare neoplasm that warrants a multidisciplinary approach. Liver resection and liver transplant have been reported successfully in the literature. This case highlights the complexities in managing HEHE and should encourage clinicians to report their experience.

[ABST-0273]

Usefulness and performance of portal vein stent insertion following hepatobiliary and pancreatic surgery

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Background: Portal vein (PV) stenosis after hepatobiliary and pancreatic (HBP) surgery is an emergent and severe complication requiring immediate intervention, especially for patients undergoing portal vein anastomosis, including liver transplant recipients. There are three routes to access the portal vein: trans-hepatic, trans-splenic, and intraoperative inferior mesenteric vein routes. This study retrospectively evaluated the usefulness and performance of portal vein stents following three different approaches after HBP surgery.
Methods: This study enrolled patients who underwent PV stent insertion after HBP surgery between 2010 and 2020. The portography and PV stent insertion criteria were as follows: pre-to-post anastomotic velocity ratio > 3 on doppler sonography with significant PV stenosis for patients undergoing portal vein anastomosis, kinking of PV with partial of complete PV thrombus. Prospectively collected clinical characteristics, perioperative outcomes, and patency of PV stents were evaluated.
Results: The study cohort comprised of 32 patients: 14 (43.8%) patients underwent liver transplantation, 15 (46.9%) with major liver resection, 3 (9.4%) with pancreaticobiliary surgery. In terms of routes for portal vein stent, the transhepatic approach was performed for 20 (62.5%) patients, transsplenic approach for 7 (21.9%), and intraoperative approach for 5 (15.6%). Median PV stent patency was 342 (7–3437) days in the transhepatic group, 120 (8–673) in the transsplenic group, and 125 (1–3314) in the intraoperative group ($P < 0.001$). Partial stent obstruction was observed in 7 (35.0%) in transhepatic group, 1 (14.3%) in transsplenic group, and 0 (0.0%) in intraoperative groups ($P = 0.358$). Only one patient experienced a procedure-related complication, and she died due to severe splenic bleeding after transsplenic PV stent insertion.
Conclusions: PV stent insertion was needed following a multitude of HBP surgery. Since there was no significant difference in stent performance with regard to the routes of stent insertion, PV stent insertion should be performed if necessary according to the bleeding tendency of each patient and the feasibility of the procedure.

[ABST-0319]

A combined large-cell neuroendocrine carcinoma and hepatocellular carcinoma tumor in the liver: A rare case report

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Background: Primary hepatic neuroendocrine carcinoma is extremely rare, with only a few cases reported to date. Hence, preoperative diagnosis is difficult and most are postoperatively diagnosed. In accordance with the general principle of surgical indication applied in liver tumors, resection of the primary hepatic neuroendocrine tumor is also suggested as the mainstay of treatment. Large-cell neuroendocrine carcinoma is poorly differentiated neuroendocrine carcinoma that has been rarely reported in liver. Generally, biological behavior of neuroendocrine carcinoma more aggressive than that of adenocarcinoma We report a rare case of combined primary tumor (large-cell neuroendocrine carcinoma (90%) and hepatocellular carcinoma (10%)) of the liver that was treated curative resection.
Methods: This study reviewed a retrospective database of the patient who was diagnosed combined primary tumor (large-cell neuroendocrine carcinoma (90%) and hepatocellular carcinoma (10%)) of the liver. A 73-year-old female with chronic hepatitis B disease presented suspected with a malignant hepatic mass (segment 3, sized 4.5 cm) and lymph node metastasis on computed tomography and magnetic resonance imaging. Despite Child–Pugh class A, esophageal varices were presented. The paitent underwent left lateral sectionectomy and lymph node dissection. The pathological examination of the resected specimens revealed large cell neuroendocrine carcinoma (90%) and hepatocellular carcinoma (10%) in the form of collision tumors.
Results: Metastasis of large-cell neuroendocrine carcinoma was found in one of the three lymph nodes obtained. She recovered without any postoperative abnormal events and discharged in good condition on postoperative day 13. She did not receive adjuvant chemotherapy and had no recurrence during a follow-up of 14 months.
Conclusions: Since combined tumor based on neuroendocrine carcinoma in liver is a very rare disease, there is no guideline for adjuvant treatment for them. In order to improve the therapeutic effect of combined tumor in liver, it is necessary to discuss each individual's clinical experience and consider an appropriate method for preoperative diagnosis and treatment.

[ABST-0346]

Pure single-port robotic left lateral sectionectomy using the Da Vinci SP system

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Background: Since its first appearance in the early 1990s, laparoscopic hepatic resection has become increasingly accepted and recognized as safe as laparotomy. The recent introduction of robotic surgery systems has brought new innovations to the field of minimally invasive surgery, such as laparoscopic surgery. The da Vinci line of

surgical systems has recently released a true single-port platform called the da Vinci SP system, which has three fully wristed and elbowed instruments and a flexible camera in a single 2.5 cm cannula. We present the first case of robotic liver resection using the da Vinci SP system and demonstrate the technical feasibility of this platform.
Methods: A 63-year-old woman presented with elevated liver function test results and abdominal pain. Computed tomography (CT) and magnetic resonance cholangiopancreatography showed multiple intrahepatic duct stones in the left lateral section and distal common bile duct (CBD) stones near the ampulla of Vater.
Results: The docking time was 8 min. The patient underwent successful da Vinci SP with a total operation time of 135 min. The estimated blood loss was 50.0 ml. No significant intraoperative events were observed. The numerical pain intensity score was 3/10 in the immediate postoperative period and 1/10 on postoperative day 2. The patient was discharged on postoperative day 5 after verifying that the CT scan did not show any surgical complications.
Conclusions: We report a technique of left lateral sectionectomy, without the use of an additional port, via the da Vinci SP system. The present case suggests that minor hepatic resection is technically feasible and safe with the new da Vinci SP system in select patients. For the active application of the da Vinci SP system in hepatobiliary surgery, further device development and research are needed.

[ABST-0349]

Clinical impact of surgical treatment for the spontaneously ruptured resectable hepatocellular carcinoma

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Background: Spontaneously ruptured hepatocellular carcinoma (srHCC) is a fatal complication of hepatocellular carcinoma (HCC). In addition, emergency treatment is frequently fraught with difficulties. The aim of this study was to investigate the prognosis and recurrence pattern in patients undergoing hepatectomy for the srHCC.
Methods: This retrospective study included 11 patients with srHCC treated using either emergency hepatectomy or emergency transarterial embolization (TAE) followed by staged hepatectomy between January 2015 and December 2019. The patients visited the emergency room because of sudden rupture of HCC without being diagnosed with HCC. We analyzed the prognosis, recurrence rate and survival in patients after hepatectomy.
Results: Four of the 11 patients in this study were classified as Child–Pugh class A and 7 as Child–Pugh class B. Nine patients were visited for sudden onset of abdominal pain, and two for sudden onset of shock. The median hemoglobin level at the time of the visit was 11.5 g/dL (interquartile range: 9.8–12.7). Five patients underwent one-stage hepatectomy and six underwent emergency TAE hemostasis followed by staged hepatectomy. Median survival and disease-free survival were 23 and 15 months, respectively. Recurrence occurred in seven patients (four in the one-stage group and three in the staged group). Among patients with recurrence, six had intrahepatic recurrence and three peritoneal metastases.
Conclusions: Hepatectomy for srHCC could achieve compare good prognostic outcomes, especially for staged hepatectomy. The most common locations of recurrence after hepatectomy are intrahepatic and peritoneal. Peritoneal metastases are more likely to occur after one-stage hepatectomy.

[ABST-0401]

Surgical techniques of laparoscopic right hepatectomy after right portal vein embolization

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Background: Portal vein embolization (PVE) is a very useful and widespread tool to reduce the risk of postoperative liver failure by increasing the future remnant liver volume. When it comes to the laparoscopic right hepatectomy, PVE has an additional benefit by making it easier to extract the atrophied and so smaller right liver than the original one. This good strategy, however, also entails some untoward drawbacks like increased difficulties in the surgical procedures. These include; 1. decreased visibility of the liver hilum due to the hypertrophied segment 4, 2. difficulty in isolation of the right portal vein due to tight fibrous adhesion around the embolized right portal vein, and 3. need for the verification of no remnant embolic material in the main and left portal vein, often by opening of the portal vein confluence. The authors will show how these problems can be managed during laparoscopic right hepatectomy with video.
Methods: A 79 years old man was referred for surgery for 2 HCC's. A 4.0 cm sized HCC was located at segment 6. Direct invasion of right posterior portal vein from this mass was suspected. Another HCC was 1.1 cm in size and located at S8. He had a history of treated HCC that was 2.4 cm in size and located between S6 and S7 and underwent radiofrequency ablation 6 years and 10 months ago. AFP and PIVKA-II level were 28.0 ng/ml and 134 mAU/ml, respectively. HBsAg was positive but HBV DNA was not detected on PCR examination. He was on Entecavir. Child class was A. Liver stiffness E was 7.8 kPa on Fibroscan. He had taken medication for DM and hypertension. He was 79 years old but fit for major hepatectomy. Preoperative right portal vein embolization was performed. and laparoscopic right hepatectomy was followed in 18 days.
Results: The operation took 310 min. Intraoperative blood loss was estimated to be 300 ml. There was no postoperative complication. Postoperative hospital stay was 6 days. Two HCC's were confirmed pathologically. There was no portal vein invasion and the liver showed chronic hepatitis on pathologic examination.
Conclusions: By carefully preparing for the technical difficulties that may follow right portal vein embolization in advance, misadventures that may occur during laparoscopic right hepatectomy can be prevented.

[ABST-0527]

Proximal splenorenal shunt for symptomatic hypersplenism with EHPVO

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Background: Extrahepatic portal vein obstruction represents major cause for non-cirrhotic portal hypertension in India.Patient have varied clinical presentation like hematemesis, splenomegaly, portal biliopathy and hypersplenism. Treatment options includes endoscopic therapy and surgery based on the clinical conditions. We present an operative video of proximal splenorenal shunt for a patient with hypersplenism and extrahepatic portal vein obstruction.
Methods: Surgical Video exhibition.
Results: Case Report An adolescent girl presented with complaints of hematemesis and passing dark coloured stools. On abdominal examination, massive splenomegaly was noted. Blood investigations revealed thrombocytopenia and leukocytopenia. Upper GI endoscopy showed grade II esophageal varices and portal gastropathy. Abdominal computed tomography reported massive splenomegaly with extrahepatic portal vein obstruction and multiple collaterals. Patient diagnosed with hypersplenism with bicytopenia and extrahepatic portal vein obstruction and she underwent proximal splenorenal shunt. Post operative course uneventful and on two months followup.
Conclusions: In non-cirrhotic portal hypertension due to extrahepatic portal vein obstruction, proximal splenorenal shunt is worthwhile option for patients with symptomatic hypersplenism.

[ABST-0532]

Unpleasant surprise after atypical liver resection using ICG

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Background: Hepatocellular carcinoma remains a global health problem, as being the most common type of liver cancer. Even if the risk factors are known, still a small percentage of cases have no comorbidities at the time of diagnostic.
Methods: We present the case of a 32-year-old female patient hospitalized in the Monza Oncology Hospital Bucharest. Prior to intervention, the patient was diagnosed incidentally by abdominal CT scan with a tumor in the segment 6 of the liver. The patient had no risk factors for liver disease or biochemical abnormalities.
Results: The CT scan revealed a tumor of 4,8/3,5/4cmm imagistically suggestive for an adenoma. The tumor did not invade the liver, but it had a mass effect on the right kidney. Considering the fact that the patient was young and without comorbidities, the treatment of choice was atypical segment 6 resection performed laparoscopically after intravenous injection of ICG (0,25 mg/kg, in total 3 ml). ICG staining helped guiding the resection in order to achieve negative edges. The patient was discharged without complications in the 3rd day. The unpleasant surprise was the pathology report that showed that the tumor was a WHO grade 2/3, Edmondson-Steiner grade III/IV hepatocarcinoma. ICG staining proved to be an useful tool for the surgical treatment, in this case.
Conclusions: Early detection of hepatocarcinoma is important in achieving effective treatment with good survival rate. Surgery guided by ICG staining combined with complementary treatment remains the best option for this patients.

[ABST-0533]

Difficulties of an HPB surgery team during the SARS-CoV–2 pandemic

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Background: The SARS-CoV-2 pandemic has put pressure on the entire medical system and has made it difficult to provide healthcare and optimal treatment to patients with hepato-pancreato-biliary pathology. Surgeons had to adapt to these changes and hospitals underwent a systematic reorganization of their activity.
Methods: The cases with HPB onco-surgical pathology treated between March 2020—December 2021 in the General Surgery Clinic within the Saint John Emergency Clinical Hospital Bucharest and Monza Oncology Hospital Bucharest have been analyzed.
Results: At the beginning of the SARS-CoV2 pandemic, there was a sudden decrease in HPB treated by the team due to the decrease in general addressability to health services, most likely generated by the fear of hospitalization in pandemic conditions. In the following months, the activity was gradually resumed, but did not reach the average number of cases treated before the onset of the pandemic. There has been an increase in the severity of cases compared to the current period. As of November 2020, Saint John Hospital has been transformed into a COVID-19 support unit and the entire work has focused on treating patients with SARS-CoV2 infection. A solution for treating the patients was to perform surgeries in the private medical network.
Conclusions: Discontinuation of surgical and oncological activity during the pandemic has led to an increase in the number of terminal cases from a surgical point of view with patients presenting with more advanced stages of the disease, treatment being limited and the postoperative evolution has been longer.

Biliary and Pancreatic Disease

[OP-0023]

Young woman with colic and obstructive jaundice due to ascariasis treated with endoscopic retrograde cholangiopancreatography (ERCP)

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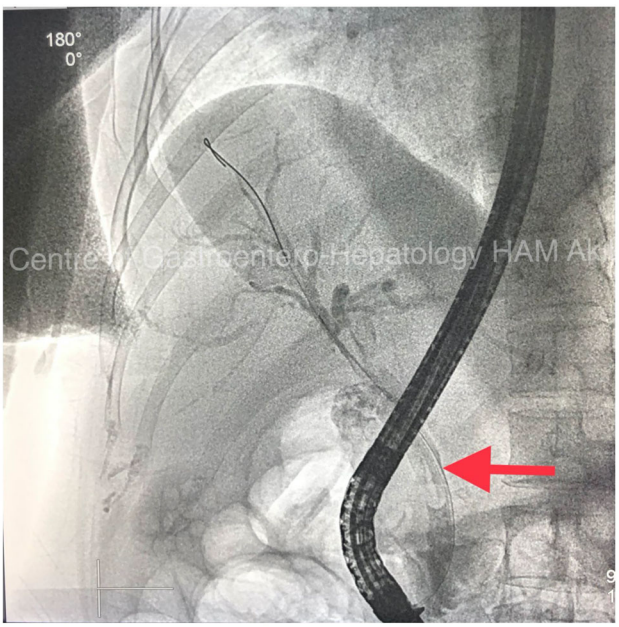
Objectives: It is estimated that 1.4 billion people worldwide are infected by Ascaris lumbricoides and 10–19% are manifested as biliary ascariasis especially in endemic regions. The worm migration into the biliary tree leads to wide clinical symptoms such as biliary colic and obstructive jaundice. Formerly, most cases were diagnosed either during surgery or post-mortem which making the diagnosis could be missed in significant number. The improvement of the diagnostic equipments has led to an increased of the parasite detection. The therapeutic principles of biliary ascariasis are conservative, administration of antihelminth drugs, as well as ERCP and surgery. The diagnostic and therapeutic of ERCP has 90—100% successful rate with low complication.
Materials and Methods: Case Study.
Results: A-34-y.o woman presented with intermittent abdominal pain in the upper right quadrant since 3 months, followed by jaundice in the last 1 month with history of fever. Dark brownish urine was noted. Investigations include increasing in ALT 191 U/L; AST 276 U/L; Total bilirubin 9,16 mg/dl; Direct bilirubin 6,60 mg/dl. MSCT Scan abdomen show distended and thickening of the gallbladder wall, cholelith with highly suspected choledocolithiasis. The patient then underwent Endoscopic Retrograde Cholangiopancreatography (ERCP), which revealed dilatation of common bile duct (CBD), multiple gallstones, and filling defect linier on CBD wall. Ascaris Lumbricoides were seen after extraction. The patient received single dose of pyrantel pamoat then discharged 3 days after ERCP in improved condition.
Conclusion: ERCP is the main therapy of choice for biliary ascariasis.



ERCP : Dilatation of CBD, multiple gallstone and 2 layers shadow (filling defect linier) on the CBD wall as pointed

[OP-0030]

A follow-up study of the patients with biliary tract cancer who underwent portal vein embolization but not resectable

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Objectives: The Japanese guidelines for the management of biliary tract cancer recommend preoperative portal vein embolization (PVE) in patients who are scheduled to undergo hepatic resection of more than 50–60% of the liver. However, some cases cannot be resected after PVE for various reasons other than inadequate residual liver volume, but the outcome and prognosis of these cases have not been reported. The aim of this study is to clarify the outcome and prognosis of patients with biliary tract cancer who underwent PVE but were not resected.
Materials and Methods: Of the 31 cases of PVE in our department from January 2011 to March 2021, 8 cases of biliary tract cancers that cannot be resected after PVE were included. The clinical background, reasons for unresected, and prognosis of the patients were retrospectively reviewed.
Results: The median age was 69 (61–77) years. The primary diseases were hilar cholangiocarcinoma and gallbladder cancer in 4 patients each. Reasons for unresected cases were as follows: 4 patients underwent exploratory laparotomy (dissemination: 2, positive lymph node #16: 1, liver metastasis: 1), liver metastasis, worsening Indocyanine green clearance test, insufficient volume of the residual liver, and withdrawn because of concerning about liver failure in one patient each. All patients were treated with chemotherapy, and the number of cancer-related deaths and that of other causes of death was 1 case in each. The 2-year OS and PFS were 75% and 62.5%.
Conclusion: Even if the tumor is unresectable after PTPE, the prognosis is relatively maintained with chemotherapy and other therapies.

[OP-0064]

Evaluation of the effectiveness of antegrade methods of direct contrast of biliary tract in the diagnosis of diseases of the biliary tract complicated by mechanical jaundice

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Objectives: Direct contrast of the biliary tract of the gastrointestinal tract with antegrade access is the method of choice in cases where the performance of endoscopic retrograde cholangio-pancreatography is uninformative.
Materials and Methods: Percutaneous transhepatic cholangiography was performed in 82 patients. Repeated percutaneous transhepatic cholangiography was performed in 20 patients, who were treated at the clinical base of the Department of Surgery № 1 of Kharkiv National Medical University—State Institution "Zaycev V.T. Institute of General and Emergency surgery of the National academy of medical sciences of Ukraine" (Kharkiv, Ukraine).

Results: The nature and level of obstruction found in most patients—80 (97.6%) and only 2 (2.4%) patients interpretation of percutaneous transhepatic cholangiography was incorrect. Significantly positive conclusions about the etiology of mechanical jaundice, according to percutaneous transhepatic cholangiography, were made in 97.5%. In 36 (43.9%) patients with percutaneous transhepatic cholangiodrainage or percutaneous transhepatic cholecystostomy (82 patients) control fistulocholangiography was performed 5–7 days after drainage. The data of the radiological picture at percutaneous transhepatic cholangiography and fistulography coincided. Strictures of the biliodigestive anastomosis by percutaneous transhepatic cholangiography were detected in 5 (6.1%) cases.
Conclusion: In our observations, the diagnosis made by percutaneous transhepatic cholangiography was correct in 97.5% of patients. Incorrect diagnosis was made in 2 (2.5%) patients, with false-positive conclusions made in 8 (9.8%) patients, false-negative—in 5 (6.1%) patients. Analyzing the results of the use of percutaneous transhepatic cholangiography in 82 patients, it was determined that this method allows to diagnose cholangiocarcinomas, strictures of hepaticocholedoch, choledocholithiasis.

[OP-0087]

New Approach towards pancreatic cancer by amalgamation of therapies targeting in synergistic action

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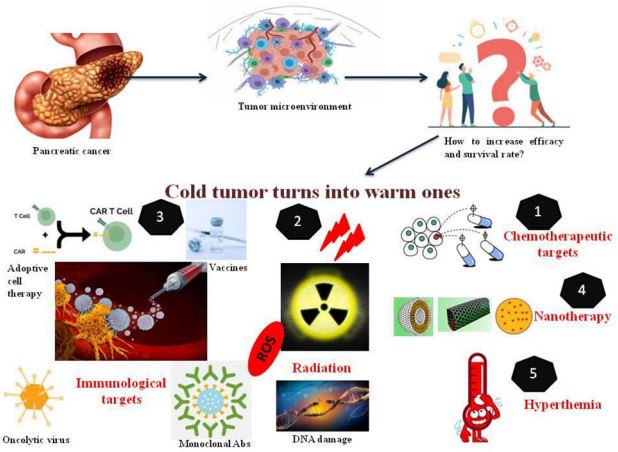
Objectives: Pancreatic cancer is the seventh leading cause of cancer death across the world, which shows 5- year overall survival rate to be below 5% and 1-year overall survival rate to be at 24% with the conventional treatments. It has been expected that it would become second cause of cancer death by 2030 which makes an immediate need to alter, modify the therapies. To achieve low toxicity and improve immunotherapeutic response in the combined treatment regimen. To improve the efficacy and overall survival rate in the combined therapies compared with monotherapy alone.
Materials and Methods: Many of the patients are offered with the first line treatment; chemotherapy followed by radiotherapy or the surgery but during the past few years, there has been research performed on immune checkpoint inhibitors but due to dense stromal tissue and tumor microenvironment it's still challenging to achieve efficacy. Some other treatment options which could be considered are the molecular targeted therapy, combination of immunotherapy, radiotherapy with nano-therapy or combination of immunotherapy, radiotherapy with hyperthermia.
Results: Immunotherapy when combined with radiotherapy and hyperthermia, it has shown improvement in the killing of tumor cells. Hyperthermia can increase the temperature around the tumor tissues and with radiotherapy induce DNA damage. The immunotherapy combined with cytotoxic drugs has synergistic effect and improved the overall survival rate.
Conclusion: There is an urge to treat pancreatic cancer due to its poor prognosis and survival rate. The combination therapies could make the cold tumor turn into warm one by the use of immunological therapy with the conventional therapies.



[PP-0127]

Assessment of contractility by hepatobiliary scintigraphy can be misinterpreted in segmented gallbladder

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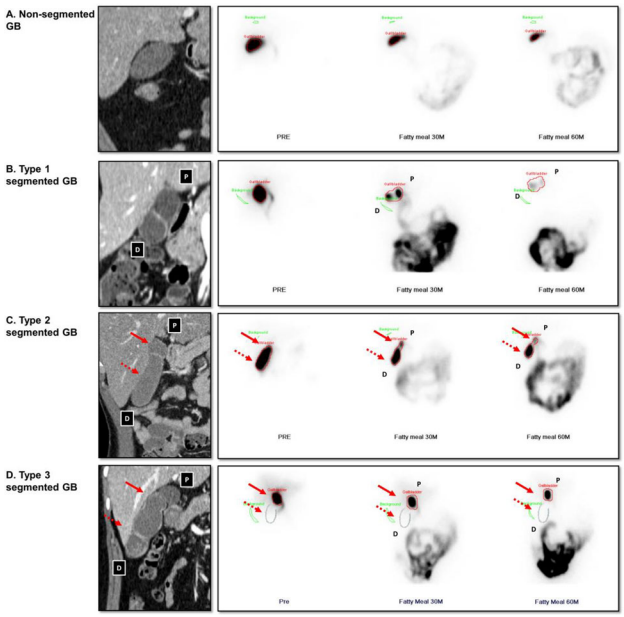
Objectives: Hepatobiliary scintigraphy (HBS) is a useful diagnostic imaging technique that uses radiotracers to evaluate the function of the gallbladder (GB) and biliary system. However, some scanned images of HBS can reveal a discordant GB boundary compared with anatomical images. To evaluate the characteristics of HBS images in the segmented GB and to determine the clinical relevance of the technique.
Materials and Methods: A total of 268 patients with chronic cholecystitis or GB stones who underwent HBS from 2011 to 2020 were enrolled. Segmented GB was defined as segmental luminal narrowing of the GB body in CT or MR images. Segmented GB was classified into 3 types based on the filling and emptying patterns of proximal and distal segments.
Results: The segmented GB accounted for 63 cases (23.5%) including 36 patients (57.1%) with normal filling and emptying pattern (type 1), 18 patients (28.6%) with defective emptying in the distal segment (type 2), and 9 patients (14.3%) with a filling defect involving the distal segment (type 3). No remarkable differences in baseline characteristics, radiologic or pathologic findings were detected depending on the type. Interestingly, the measured ejection fraction of GB via HBS in types 2 and 3 was higher than in type 1.
Conclusion: Approximately 40% of the scanned images of HBS showed a discordant pattern compared with anatomical images in segmented GB. Filling or emptying defects detected via HBS may overestimate the GB function. Therefore, the HBS results in segmented GB should not be misinterpreted.



[PP-0141]

Risk factors associated with the recurrence in patients underwent percutaneous transhepatic gallbladder drainage and catheter removal in non-malignant acute cholecystitis

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Objectives: Percutaneous transhepatic gallbladder drainage (PTGBD) is an important bridging treatment option in acute cholecystitis (AC) for patients unsuitable for early cholecystectomy. If interval cholecystectomy cannot be performed, removal of the PTGBD catheter should be considered. However, AC often recurs after catheter removal. This retrospective study investigated outcome and recurrence factors after catheter removal in AC patients who underwent PTGBD.
Materials and Methods: Patients who treated with PTGBD for AC from January 2014 through December 2018 were reviewed. 780 patients underwent PTGBD, of which 214 patients did not undergo interval cholecystectomy and had catheter removed or were not reinserted after unintentional removal by the physician's decision, excluding patients with biliary tract obstruction due to tumor. Acute cholecystitis and recurrence were diagnosed through clinical symptoms, blood tests and radiologic evaluation.
Results: The mean age of patients who underwent PTGBD was 79.5 ± 9.3 years old, and the 95 males (44.4%). The median follow-up period was 492 (range: 21–2493 days) days. The recurrence rate of acute cholecystitis after PTGBD tube removal was 18.2% (39/214), and the median time to recur was 165 (range: 1–1274 days) days. During the observation period, 18/214 (8.4%) patients died, of which only 3(1.40%) died related to recurrence. The multivariable logistic regression analysis model was used to identify factors associated with an increased risk of recur of cholecystitis. Calculous cholecystitis (OR: 2.630; CI: 1.015–6.813; P = 0.046), history of CBD stone (OR: 2.245; CI: 1.088–4.634; P = 0.029) and catheter retention duration of less than 28 days (OR: 2.254; CI: 1.073–4.739; P = 0.032) were positively correlated with recurrence.
Conclusion: Although our study is limited to a small number of cases in single institution, cholecystectomy is more recommended or maintenance of the catheter should be considered in patients with calculous cholecystitis, history of CBD stones and catheter retention duration of less than 28 days.

Table. Multivariable logistic regression analysis of recurrence factors after catheter removal in acute cholecystitis patients who underwent percutaneous transhepatic gallbladder drainage.

Variable	OR	95% CI	P value
Calculous cholecystitis	2.630	1.015-6.813	0.046
History of CBD stone	2.245	1.088-4.634	0.029
Catheter retention duration ≤ 28 days	2.254	1.073-4.739	0.032

CBD: Common bile duct; ERCP: Endoscopic retrograde cholangiopancreatography; OR: odds ratio; CI: confidence interval

[OP-0181]

Subclinical, histopathological and immunohistochemical characteristics of intrahepatic cholangiocarcinoma

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Objectives: The purpose of this study was to describe subclinical manifestations, histopathological and immunohistochemical characteristics of intrahepatic cholangiocarcinoma (iCCA) patients.
Materials and Methods: This retrospective study was conducted on 52 iCCA patients. Diagnosis of iCCA was made based on histological assessment of liver biopsy specimen. Immunohistochemical staining of markers CK7, P40, CK19, CK20, CDX2, Hep par-1, AFP, TTF1, CEA, PSA, CA125, WT1, NapsinA, CD34 with a color indicator. Assessment of staining result was positive when yellow–brown color was expressed in the cytoplasm and plasma membrane or nucleus. TNM stage classified according to AJCC 2010.
Results: This study included 52 patients (male 59.6%), mean age was 60.9 ± 10.3. The most common risk factor for the disease was hepatitis B 21.2%. Regarding immunological tests, the increased CA 19–9 rate was 63.5%, increased CEA rate was 44.2%. On abdominal CT scan, the mean tumor diameter was 6.7 ± 3.5 cm (1.3–13.6 cm). Organ metastases included lymph node 32.7%, bone metastases 11.5%. TNM stage II and IV together had the highest rate of 32.7%. The histopathological type of iCCA was mainly well-differentiated adenocarcinoma, accounting for the highest proportion with 40.4%. CK7 was positive in 100% of patients. CK19 was simultaneously positive with CK7 in 94.2% of patients. A low positive rate was found in markers CK20, CDX2, P40.
Conclusion: Simultaneous staining of multiple immunohistochemical markers is now very useful to accurately diagnose iCCA.

[OP-0200]

Carbohydrate antigen 19-9 and carcinoembryonic antigen serum markers are associated with some factors of cholangiocarcinoma

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Objectives: To evaluate the relationship between serum Carbohydrate Antigen 19–9 (CA 19–9), Carcinoembryonic Antigen (CEA) levels, and some factors in Cholangiocarcinoma (CCA) patients.
Materials and Methods: A prospective study was carried out on 52 CCA patients. Patients were tested Carbohydrate antigen 19–9 (CA 19–9), Carcinoembryonic antigen (CEA); computed tomography scan, endoscopy, bone scintigraphy to assess metastases. Diagnosis of CCA was determined by histopathological examination.
Results: The rate of increased CA 19–9 was 63.5%. The CEA increased rate was 44.2%. CA 19–9 was highest (756.2 ± 871.3 IU/ml) in TNM stage 3, p = 0.9. The highest CEA (184.6 ± 371.2 ng/ml) in TNM stage 3, p = 0.3. Mean CA 19–9 of intrahepatic CCAwas 715.3 ± 605.7, this of extrahepatic CCA 436.2 ± 517.5, p = 0.2. The mean CEA of intrahepatic CCA was 88.0 ± 268.9, this of extrahepatic CCA was 17.6 ± 23.4, p = 0.4. CA 19–9 serum level and tumor size had a weak linear correlation, r = 0.22 (r < 0.3), p = 0.11. CEA serum level and tumor size had a weak linear correlation, r = 0.19 (r < 0.3), p = 0.17. Mean CA 19–9 of resectable patients was 278.4 ± 522.6, much lower than that of unresectable patients 756.8 ± 582.4, p = 0.02. The mean CEA of resectable patients was 49.8 ± 122.1, lower than that of unresectable patients 82.6 ± 268.0, p = 0.7.
Conclusion: CA 19–9 levels in resectable patients were lower than patients treated with chemotherapy, radiation, and palliative care. No association between CEA and TNM stage, biliary cancer classification, indications for treatment.

[OP-0430]

Diagnostic significance and prognostic role of the PTEN gene in periampullary cancer

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Objectives: Periampullary Adeno Carcinoma (PAC) is a heterogeneous and rapidly growing carcinoma that arises near the duodenal papilla and is identified in its advanced stages. In periampullary tumours, the influence of a PTEN (phosphatase and tensin homolog) gene mutation on prognosis is unknown. The effect of PTEN downregulation and hypermethylation of the promoter region on survival in periampullary cancer has yet to be investigated. As a result, the goal of this work was to look into the expressional value of PTEN gene methylation as a potential biomarker.
Materials and Methods: One hundred and one tumour tissues and their non-adjacent tissues from patients were investigated for the mutational, expressional, and apoptotic state of the PTEN gene. Sanger sequencing was used for molecular profiling, immunohistochemistry for protein expression, methylation specific PCR for methylation status, and a terminaldeoxynucleotidyltransferase biotin–dUTP nick end labelling test for programmed cell death (apoptosis). The changes were linked to clinicopathological features, overall survival (OS), and recurrence-free survival (RFS).
Results: In ampullary tumours, the clinicopathological relationship was significantly downregulated (p = 0.06), although hypermethylation (p = 0.08) and apoptosis loss (p = 0.06) were dramatically elevated in patients under 50 years of age. The ampullary tumour had a higher survival rate than the bile duct, duodenum, and pancreatic head cancers (p = 0.00). Furthermore, early stage T1 patients have a better prognosis than later stage T1 patients (p = 0.017). Patients who got adjuvant CTRT had a greater survival rate than those who did not (p = 0.010).
Conclusion: The absence of PTEN gene expression is detected in the ampullary subgroup of periampullary tumours. Those who have positive hypermethytion but modest expression has a poor overall survival. PTEN apoptosis-negative patients, on the other hand, had a higher survival rate.

Table 3: Different factors affecting survival of periampullary cancer patients

Survival analysis (n=101)								
S. No.	Parameters	Deaths	Median survival	3 Year survival	5 Year survival	95%CI Lower bound	95% CI Upper bound	*p*- Value
1	Age							
	≥60	37	46	64.4	0.00	33.2	58.7	0.476
	<60	64	40	51.7	33.9	31.5	48.4	
2	Sex							
	Male	74	45	59.5	27.6	35.9	54.0	0.271
	Female	27	36	46.0	0.00	25.8	46.1	
3	T Stage							
	T1	5	-	0.00	0.00	-	-	
	T2	34	-	72.2	0.00	-	-	0.000
	T3	59	-	56.0	0.00	-	-	
	T4	3	-	0.00	0.00	-	-	
4	LN Positivity							
	Yes	59	36	45.4	0.00	25.7	46.2	0.004
	No	42	-	0.00	59.4	32.2	47.7	
5	Adjuvant CTRT							
	Yes	64	36	51.7	28.6	26.4	45.5	0.010
	No	37	-	0.00	62.2	-	-	
6	Tumor Site							
	1	68	45	68.0	42.7	38.1	51.8	
	2	20	43	53.6	0.00	23.6	62.3	0.000
	3	05	16	0.00	0.00	9.3	33.6	
	4	08	11	0.00	0.00	0.7	21.2	
7	Differentiation							
	Well	40	38	51.6	27.9	27.8	48.1	
	Moderate	52	45	60.5	0.00	21.2	68.7	0.811
	Poor	09	46	71.4	0.00	30.6	61.3	
8	Perineural Invasion							
	Yes	25	20	16.5	0.00	8.9	31.0	0.000
	No	76	45	69.7	56.5	36.4	53.5	
9	Recurrence							
	Yes	31	26	21.7	0.00	21.8	30.1	0.000
	No	70	-	90.4	78.0	-	-	
10	Expression							
	Yes	48	40	61.8	42.2	33.3	46.6	0.430
	No	53	40	68.2	0.00	27.4	52.5	
11	Methylation							
	Positive	55	36	66.6	0.00	22.7	49.2	0.761
	Negative	46	40	64.2	0.00	37.4	42.6	
12	Apoptosis							
	Yes	48	40	57.5	0.00	30.3	49.6	0.481
	No	53	43	64.5	0.00	30.8	55.1	

[OP-0786]

Hyperechoic pancreas on ultrasonography: An analysis of its severity and clinical implications

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Objectives: This study investigated risk factors for hyperechoic pancreas (HP) on ultrasonography (US) according to HP severity.
Materials and Methods: Between December 2008 and February 2014, 1459 subjects who underwent abdominal US as part of health

examinations were retrospectively included. Two radiologists assessed and categorized the severity of HP as normal, mild, moderate, and severe. Subjects were allocated to two groups as follows: FP1 (fatty pancreas 1, normal vs. ≥ mild HP) and FP2 (normal and mild HP vs. ≥ moderate HP). Clinico-metabolic parameters such as the body mass index and blood test profile of subjects with normoglycemia and prediabetes/diabetes were compared. Logistic regression analysis was used to evaluate the associations between HP, non-alcoholic fatty liver disease (NAFLD), and diabetes/prediabetes with adjustment for clinico-metabolic parameters.
Results: Of the 1459 subjects, 71.2% and 40.4% showed HP and NAFLD on US, respectively. Normoglycemia and prediabetes/diabetes were present in 74.3% and 25.7% of subjects, respectively. Univariable analysis revealed that all the clinico-metabolic parameters were significantly associated with HP (all $P < 0.05$). In the adjusted multivariable analysis, prediabetes/diabetes, NAFLD, age, and body mass index were significantly associated with HP with the FP1 and FP2 criteria. The independent factor with the strongest association with HP was NAFLD using the FP1 criterion (odds ratio [OR] = 7.93, $P < 0.001$) and prediabetes/diabetes using the FP2 criterion (OR = 6.96, $P < 0.001$).
Conclusion: NAFLD and prediabetes/diabetes were associated with US-diagnosed HP. The F2 criterion (≥ moderate HP) was a better predictor of prediabetes/diabetes than the F1 criterion (≥ mild HP), suggesting that evaluating HP severity may be useful in clinical practice.

[PP-0787]

Severity of hyperechoic pancreas on ultrasonography as a risk factor for glycemic progression

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Objectives: The aim of this study was to evaluate the association between the severity of hyperechoic pancreas (HP) on ultrasonography (US) and glycemic progression.
Materials and Methods: In total, 1,386 participants who underwent abdominal US as part of health examinations between December 2008 and May 2014 were included in this retrospective study. We classified pancreatic echogenicity on a 4-point scale, and compared it using two distinct criteria: fatty pancreas (FP) 1 criterion (normal vs. ≥ mild HP) and FP2 criterion (normal/mild HP vs. ≥ moderate HP). According to the presence of nonalcoholic fatty liver disease (NAFLD), participants were subdivided into four groups: non-NAFLD and non-HP, isolated NAFLD, isolated HP, and HP with NAFLD. Glycemic progression was defined as progression from normoglycemia to prediabetes or diabetes or progression from prediabetes to diabetes.
Results: During the follow-up (median, 5.9 years), 262 of the 1,386 participants developed glycemic progression. Using FP2, the probability of glycemic progression across the four subgroups showed cumulative aggravation for NAFLD and HP (all $P < 0.05$). Isolated HP showed a higher probability of glycemic progression than isolated NAFLD according to FP2 ($P < 0.001$). The highest probability of glycemic progression was observed in patients with both NAFLD and HP ($P < 0.001$). The hazard ratio for glycemic progression increased with the severity of HP.
Conclusion: Increasing severity of HP on US was found to be significantly correlated with glycemic progression. Moreover, isolated HP of moderate or greater severity predicted glycemic progression independent of NAFLD.

[PP-0846]

Carcinosarcoma originating from the pancreas that mimicked a pancreatic cystic neoplasm: A case report

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Objectives: To present a rare case of Pancreatic carcinosarcoma patient that mimics pancreatic cyst.
Materials and Methods: A 54-year-old man visited our hospital with abdominal pain and uncontrolled blood sugar.
Results: Computed tomography were performed, and a lobulated pancreatic cystic neoplasm about size of 16.0 × 10.0 cm with extensive enhancing mural nodules and hemorrhagic component in cystic portion was detected. So, we performed Magnetic Resonance Imaging (MRI) and Positron emission tomography-computed tomography (PET-CT) after a presumptive diagnosis of malignant change of pancreatic cystic neoplasm. The tumor was not diagnosed histologically, so surgical resection was planned and performed. As a result of MRI and PET-CT, it was presumed to be a malignant lesion and the transverse colon was invaded, but distant metastasis was not confirmed, so distal pancreatectomy with splenectomy and segmental resection of colon was performed. The histopathologically confirmed mass size was 13.0 × 12.0 × 8.0 cm, and a pancreatic carcinosarcoma was identified.
Conclusion: Pancreatic carcinosarcomas are exceedingly rare tumor. This disease may be confused with other pancreatic cystic neoplasm, so we think that the possibility of pancreatic carcinosarcoma should be kept in mind when clinically approaching this disease.

[OP-0985]

A functional MSC-derived liver on a chip for modelling liver diseases

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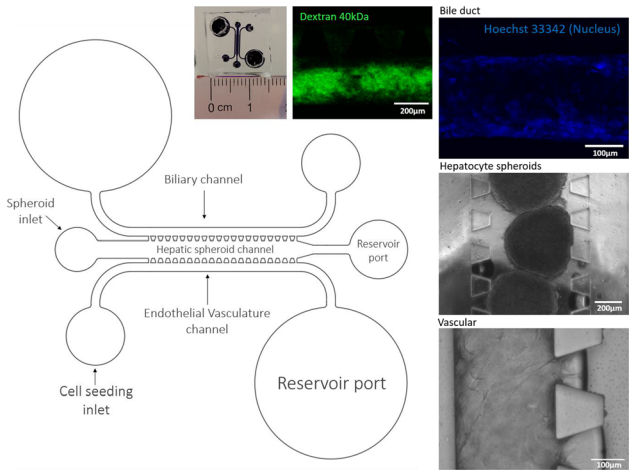
Objectives: Current study of liver diseases and drug development is hampered by the lack of an appropriate model. Most current liver models are unable to replicate the complex liver structure and function due to a lack of optimal co-culture systems which can include all the parenchymal and non-parenchymal cells found in the liver. Microfluidics offers a new potential platform for creating an in vivo like environment to better study and understand disease and drug development. Using patient derived mesenchymal stem cells (MSCs), we aim to derive a liver-on-a-chip which houses a hepatic vasculature, a bile duct, and a hepatic compartment.

Materials and Methods: The microfluidic chip was designed using standard soft lithography procedure. MSCs were cultured and differentiated into hepatocytes, endothelial cells and cholangiocytes. The cells were seeded into three independent but interconnected channels. Cell culture conditions were optimised by modifying channel surface coating, cell seeding density, and cell rotation to yield the idealised bile duct, endovasculature and hepatic spheroids.
Results: MSC-derived functional hepatic cells including hepatocytes, endothelial cells and cholangiocytes have been successfully differentiated and characterised. MSC-derived cholangiocytes and endothelial cells successfully formed a dense tube with a functional lume. The cholangiocyte tube had low dextran permeability and high rhodamine 123 uptake. MSC-derived hepatocytes cultured into functional spheroids which were successfully loaded into a hepatic compartment.
Conclusion: The microfluidic device designed was capable of creating a functional liver-on-a-chip that could serve as a reliable model replica of a simplified liver in structure and organ-level functions. With this model, personalised drug testing, analysis and disease modelling could be further developed and investigated. The independent channels allow for targeted disease modelling such as biliary disease, alcoholic liver disease, cancer, disease treatment and stem cell therapy studies.



[OP-1054]

Adenoma of the ampulla of vater

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Objectives: Adenoma of the ampulla of Vater is a rare cause of obstruction of the biliary duct. It is a premalignant lesion that may undergo malignant transformation into ampullary adenocarcinoma. It carries a significant rate of morbidity and mortality.
Materials and Methods: This paper is a case series of two patients diagnosed with adenoma of the ampulla of Vater. Both cases are documented in St. Carolus Hospital, Jakarta. Patients presenting with obstructive symptoms underwent Endoscopic Retrograde Cholangiopancreatography (ERCP). Presence of any masses were documented and biopsies were done.
Results: Both patients presented primarily with abdominal pain, nausea, and vomiting. Laboratory exams showed a slight increase in bilirubin levels; other results were generally unremarkable. Magnetic Resonance Cholangiopancreatography (MRCP) showed dilated intra- and extrahepatic biliary duct and pancreatic duct, and prominent ampulla of Vater. Both patients underwent ERCP and stent placement, and samples were taken for histopathology examination. The histological analysis showed mild dysplastic tubular adenoma of the ampulla of Vater with foci of severe dysplasia. Afterward, the first patient went through Whipple procedure, while the second patient underwent pylorus-preserving pancreaticoduodenectomy.
Conclusion: ERCP is the modality of choice to confirm the diagnosis of adenoma of the ampulla of Vater, which can be difficult to assess from MRCP.

[OP-1188]

Pancreatic cancer—How does indonesian management this disease?

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Objectives: Pancreatic cancer is cancer that's found anywhere in the pancreas. How serious pancreatic cancer is depends on where it is in the pancreas, how big it is if it has spread, and your general health. Pancreatic cancer is one of the deadliest and highly aggressive cancer. According to the latest WHO data published in 2018, Pancreas Cancer Deaths in Indonesia reached 6,554 or 0.38% of total deaths. Its incidence and mortality are highest in developed countries. In 2020, Pancreatic cancer will be the eleventh cause of cancer death in Indonesia (Rikarni, 2021). This study aims to identify how does Indonesia management this disease.
Materials and Methods: Articles from 2011–2021 were collected from an electronic database. Then eleven reputable selected papers were reviewed to answer the purpose of this study.
Results: Based on the literature study conducted, there are many treatments that Indonesia does. The first one has computed tomography, which has considered the best method of choice for diagnosing and determining the stage of pancreatic cancer. Another one is nutrition management; there are few considerations in acute pancreatitis nutrition. Nutrition should give adequate calories, protein, minerals, and vitamins. Nutrition should not stimulate autodigestive in the pancreas. Another one doing management strategy in advanced pancreatic carcinoma is important due to the poor prognosis nature. Identifying hereditary and genetic factors in the Indonesian population can help in the targeted screening of high-risk individuals.
Conclusion: From the literature search conducted, computed tomography, nutrition management, management strategy, and identification of hereditary is an activity that Indonesia was doing to prevent and treat pancreatic cancer.

[L-PP-1258]

An unusual cause of a polypoid lesion in the extrahepatic bile duct

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Objectives: Here we present a rare case of a biliary adenomyoma with raised Ca19-A that mimics a biliary neoplasia.
Materials and Methods: A case report and brief literature review.
Results: Adenomyomas are benign lesions that are most frequently found in the gallbladder but can also be rarely found in the biliary tract. Although benign, they present very similarly to malignant lesions and thus pose an important clinical consideration. We present a case of a 74-year-old Chinese man who presented acutely with fever and painless obstructive jaundice. CT imaging showed a large calculus within a dilated common bile duct (CBD) and despite undergoing a endoscopic retrograde cholangiopancreatography (ERCP) with stone clearance, there was a persistent filling defect that was adherent to the wall of the proximal common bile duct. Intraductal ultrasonography (IDUS) showed a polypoid mass with papillary-like projections and ERCP forcep biopsies were unable to exclude a lesion with neoplastic potential. The patient subsequently underwent cholecystectomy with open CBD excision and Roux-en-Y hepaticojejunostomy and histology showed features consistent with a biliary adenomyoma.
Conclusion: In conclusion, as biliary adenomyoma is frequently associated with obstructive jaundice and mimics a neoplastic lesion, invasive surgery often follows. Importantly, it was noted that the recurrence rate of such benign lesions (22%) are 4 times greater after local excision compared to a more radical procedure. In our patient, the raised serum Ca 19–9 made the suspicion for a neoplastic lesion even higher although on hindsight, the raised Ca 19–9 is likely related to cholangitis. Following biliary drainage surgery, our patient made a complete recovery with resolution of symptoms and jaundice.

[L-OP-1262]

Progression of pancreatic branch duct-type intra-ductal papillary mucinous neoplasms (BD-IPMNs) after surgery for extra-pancreatic malignancies

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Objectives: The natural course of pancreatic branch duct-type intraductal papillary mucinous neoplasms (BD-IPMNs) is still not fully known. The objective of the present retrospective study is to assess the morphological changes of BD-IPMNs, especially after a history of surgical resection of extra pancreatic malignancies.
Materials and Methods: 134 cases who suffer from BD-IPMN at the Osaka Medical College in the period from January 20,014 to December 2020, were recruited in the present study. Factors predicative of BD-IPMN progression based on morphological variations were assessed using multivariate as well as univariate analyses. Furthermore, the clinical characteristics of BD-IPMNs with progressive lesions were meticulously investigated during the follow-up period.
Results: The average follow-up interval was estimated of 35.8 months (range, 12.1 – 157 months). Disease progression happened in 6 cases (4.5%). Of these, IPMN-derived invasive carcinoma has been detected in two cases (1.5%). Multivariate analysis revealed that the surgical resection for extra-pancreatic malignancies could be an important predictive factor for BD-IPMN progression.
Conclusion: History of surgery for extra-pancreatic malignancies should be kept in our mind throughout the follow-up time of pancreatic BD-IPMN.

[L-OP-1289]

High time to revisit choledochal cyst classification-cystic duct variants with Type 1- Type 1D vs 6B

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Objectives: Choledochal cysts are cystic dilatation of the biliary tree involving extra-hepatic or intra-hepatic biliary radicals or both, most commonly involving the main portion of the common bile duct (CBD). Cystic duct variants with type 1 Choledochal cysts (CDC) are being reported nowadays, making a confusion in the literature whether to classify it as Type 1D or 6B.
Materials and Methods: Here we present two cases with concomitant cystic duct and focal type variant CDC. Thorough literature search was done to identify to which sub-group of Modified Todani's classification these variants to be included- whether type 1 or 6.
Results: First case was a 42 year old lady presented with right upper quadrant pain (RUQ) and Magnetic Resonant Cholangio-Pancreatography (MRCP) revealed focal dilatation of mid CBD with dilated cystic duct. Patient underwent Complete extra hepatic bile duct excision (EHBDE) along with cholecystectomy and reconstruction with Roux en Y Hepatico-jejunostomy. Patient had an uneventful recovery and is on follow up since 3 years. Second case was a 37 year old lady presented with right upper abdominal pain and jaundice. MRCP revealed focal upper CBD dilatation with dilated cystic duct with suspicious sludge in lower normal common bile duct (CBD). Further EUS evaluation revealed absent sludge in lower CBD with clinical improvement with conservative management. Patient had been discharged in a stable condition and is now awaiting surgery. Thorough literature review revealed less than 10 cases reported yet and most associated with focal subtypes and in females.
Conclusion: Focal subtypes more associated with cystic duct variant CDC and it is better to redefine these as Type 6B rather than 1D. Need reevaluation of retrospective data from high volume centres to rule out under reporting of this entity.

[L-OP-1342]

Measurement of pancreas damage status after intervention of synbiotic drink of stelechocarpus burahol with Lactobacillus casei and Lactobacillus plantarum isolates: A dyslipidemic rats model study

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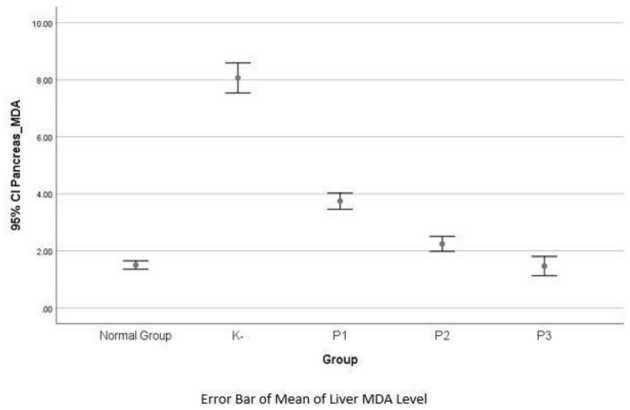
Objectives: Dyslipidemia may promote systemic oxidative stress-induced pancreas damage. Malondialdehyde (MDA) level is commonly known as a marker of oxidative stress. Recently, many studies revealed that synbiotic has potency as an anti-dyslipidemic agent. This study focused on measuring MDA levels in pancreas dyslipidemic rats after the intervention of synbiotic drink of Stelechocarpus burahol with Lactobacillus casei and Lactobacillus plantarum isolates.
Materials and Methods: A randomized controlled group was conducted on twenty-five rats divided into five groups. The negative control group (K-) and interfered group (P1, P2, P3) were fed a high-fat diet for four weeks, while the normal group was given a standard diet. Lipid profile measurement was conducted on the rats to ensure that the rats (negative control group, P1, P2, and P3) had contracted dyslipidemia. Then, synbiotic drinks were given to the interfered group at various dosages (P1 = 1.2; P2 = 1.8; P3 = 2.4) ml/day for four weeks. At the end of the study, the rats were terminated, then MDA level measurement was conducted on pancreas tissue.
Results: The mean of pancreas MDA level (nmol/gram) were 1.51 ± 0.12 (normal group); 8.07 ± 0.43 (K-); 3.75 ± 0.23 (P1); 2.24 ± 0.21 (P2); 1.47 ± 0.27 (P3). One-way ANOVA with post hoc bonferroni test showed significant differences between all groups (p-value < 0.05) except the pancreas MDA level between normal group and P3 group (p-value = 1).
Conclusion: This study suggests that the synbiotic drinks reduced pancreas damage status.



[ABST-0076]

Safety evaluation of early drain removal following pancreatic resections: Meta-analysis and single-center retrospective cohort study

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Background: No consensus was reached with regard to whether to place prophylactic intraperitoneal drainage, when to remove drainages after pancreatic resections. The meta-analysis and single-center retrospective cohort study were designed to explore the safety of early drain removal (EDR).
Methods: For meta-analysis, the stratified analyses of pancreaticoduodenectomy (PD) and distal pancreatectomy (DP), and subgroup analyses of RCTs and NO RCTs were conducted to investigate the effect of EDR on postoperative outcomes. We also conducted the meta-analyses for the studies with the same inclusion criteria and drain removal criteria separately. For single-center study, a total of 112 patients undergoing PD with drain fluid amylase (DFA) on POD 1 and $3 < = 5000$ were divided into EDR and late drain removal (LDR). Propensity Score Matching (PSM) was used. We compared postoperative outcomes between two groups and explore the risk factors of total complications using univariate and multiple logistic regression analyses.
Results: The meta-analysis of RCTs showed that there was no statistical difference in Grade B/C POPF (postoperative pancreatic fistula) rate (RR = 0.47, 95% CI: 0.06—3.46; P = 0.46). However, the meta-analysis of No RCTs and all studies indicated EDR group had lower Grade B/C POPF rate (RR = 0.21, 95% CI: 0.15—0.29; $P < 0.00001$; and RR = 0.23, 95% CI: 0.15—0.37; $P < 0.00001$). In the single-center study, no statistical differences were found in primary outcomes, including Grade B/C POPF (Original cohort: 5.71% vs. 3.90%; P = 1.000; PSM cohort: 3.33% vs. 6.67%; P = 1.000), and total complications (Original cohort: 17.14% vs. 32.47%; P = 0.093; PSM cohort: 13.33% vs. 33.33%; P = 0.067). For both meta-analysis and single-center study, EDR was associated with shorter in-hospital stay.
Conclusions: The meta-analysis demonstrates EDR is safe for patients following pancreatic resections, and single-center study demonstrates EDR on POD 3 is safe for patients following PD with low risk of POPF.

[ABST-0197]

Berne modification procedure in a patient diagnosed with distal common bile duct stricture and pancreatic duct stricture with pancreatoliths secondary to chronic pancreatitis: A case report

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Background: Pancreatolithiases occurs as a sequela to a chronic pancreatitis. It presents most commonly with epigastric pain radiating to the left scapula. This occurs from repeated inflammation, which leads to an irreversible destruction of pancreatic parenchyma and subsequent fibrosis which eventually obstructs the pancreatic ducts.
Methods: There is a relatively lack of data on the appropriate treatment for chronic pancreatitis, which differs between specialties and centers, however surgical intervention remains to be the superior management for patients with pancreatolithiases secondary to chronic pancreatitis.
Results: This report presents a case of a 32 year old male with 1 month history of jaundice, with an imaging of distal common bile duct stricture and pancreatic duct stricture with pancreatoliths on top of chronic pancreatitis.
Conclusions: This case was managed by performing Berne modification procedure which was done in Vicente Sotto Memorial Medical Center for the first time.

[ABST-0228]

Is central pancreatectomy an effective alternative for distal pancreatectomy for low-grade pancreatic body tumors: A 20-year single-center propensity score-matched case–control study

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Background: Central pancreatectomy (CP) is associated with a higher rate of postoperative pancreatic fistula (POPF) rate and is less preferred to distal pancreatectomy (DP). The study was done to compare the short and long-term outcomes between the CP and DP in low-grade pancreatic body tumors.
Methods: It was a propensity score-matched case–control study including patients who underwent either CP or DP for low-grade pancreatic body tumors from 2001 to 2020 in a tertiary care unit in South India. Patients with tumor > 10 cm or length of distal stump < 3 cm were excluded. The demography, clinical profile, intraoperative, post-operative parameters, the long-term postoperative outcome for exocrine insufficiency, endocrine insufficiency, weight gain, and SF-36 questionnaire for quality of life were compared.
Results: Eighty-eight patients [CP = 37(cases), DP = 51(control)] were included in the unmatched group after excluding 22 patients (< 3 cm distal stump length, > 10 cm tumor, or both = 15, 2, and 5 patients respectively). After propensity score matching both groups had 37 patients. The clinical and demographic profiles were comparable between the two groups. Blood loss and POPF rates were significantly higher in the CP group. However, Clavien-Dindo's grades of complications were similar between the two groups (p = 0.27). On median follow-up of 38 months (range = 187), exocrine sufficiency was similar between groups. Endocrine sufficiency, Weight gain, SF36 pain control score, and general health score were significantly better in the CP group.
Conclusions: The short-term outcomes of CP were similar to DP but have statistically better long-term outcomes for low-grade pancreatic body tumors.

[ABST-0280]

Extra-Abdominal neuroendocrine tumor, a rare case report

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Background: The most common site of Neuroendocrine tumor (NET) gastrointestinal tract, large intestine (20%), small intestine (19%), and appendix (4%) (1). It rarely affects the cervix. Cervical NET management is difficult and is associated with uncertainty. We present a rare case of mixed adenocarcinoma and high-grade neuroendocrine carcinoma, with widespread metastasis.
Methods: Case study.
Results: A 67 year old postmenopausal woman presented with vaginal bleeding for one year. Pap smear showed squamous cell carcinoma. Biopsy showed invasive non keratinising squamous (basaloid) cell carcinoma, high grade; immunopositive for chromogranin, synaptophysin, pancytokeratin and TTP 1 diffusely, while negative for p40. MRI showed a mass in cervix with umbilical hernia. Cytoreductive surgery was done. Histopathology showed adenocarcinoma with neuroendocrine tumor. Non neuroendocrine portion comprises of endocervical adenocarcinoma usual type; immunopositive for CEA and negative for oestrogen receptor. The neuroendocrine portion was high-grade and immunopositive for synaptophysin and chromogranin. Following Carboplatin (400 mg) and Etoposide (150 mg) #3, clinical remission was achieved. After one year mass recurred in uterus and cervix with metastasis to lung, liver & ribs. Repeat three cycles of carboplatin (240 mg) and etoposide (100 mg) was followed by palliative radiotherapy 28 cycles of EBRT and 3 cycles of ICRT. Partial improvement was seen. The patient had progressive disease and expired 3 months later.
Conclusions: During histological examination, a diagnosis of small cell NET may be misdiagnosed as non-keratinized squamous cell carcinoma; because it contains neuroendocrine components in only limited nested areas. Immunohistochemistry is the gold standard for its diagnosis. Early and accurate diagnosis is essential so as to begin therapy earlier and prevent potentially lethal metastasis.

[ABST-0312]

Diagnostic yield of EUS-guided FNA for pancreatic lesions. A case series

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Background: EUS-guided fine-needle aspiration (EUS-FNA) has gained increasing popularity worldwide in the diagnosis and management of pancreatic lesions, including both cystic and solid. Several technologies are emerging to increase the diagnostic yield and risk stratification to guide subsequent management. The aim of this study was to audit and evaluate the diagnostic yield, safety of EUS-FNA of pancreatic lesions in Yan Chai hospital.
Methods: All cases of pancreatic lesions with EUS-guided FNA performed in Yan Chai Hospital from Jan 2018 to Jun 2021 were reviewed. Among which, pattens who underwent cytological or histological sampling with either FNA needle or FNB needle were identified. In patients who underwent surgery, operative histopathological findings were compared with cytological findings from EUS-FNA. Otherwise, EUS-FNA cytology findings were compared with clinical outcome upon follow-up.
Results: There were 38 patients identified with pancreatic lesions detected on computer tomography (CT) and confirmed by diagnostic endoscopic ultrasound. There were 24 cases using 19G/20G/22G FNB needle and 12 cases using 22G FNA needle. There were 18 cases using fanning technique during sampling. There were 9 cases with more than 3 passes of needles during procedure. There were 2 cases on macroscopic on-site evaluation performed. The overall sensitivity, specificity, PPV and NPV of FNA (all 38 cases) were respectively 70.3%, 90.9%, 95% and 55.5%. For complication. There was 1 cases of subclinical pancreatitis and 1 cases of sepsis.
Conclusions: This case series demonstrated that EUS-FNA is feasible and reliable method for diagnosis of pancreatic lesions. We are expecting the usage of different adjunct technique including fanning, suction, MOSE to increase the diagnostic yield in the future.

[ABST-0347]

Feasibility and efficacy of pure single-port robotic cholecystectomy using the Da Vinci SP surgical platform

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Background: Single-incision laparoscopic cholecystectomy, first introduced in 1995, features acceptable cosmetic outcomes and postoperative pain control. The outcomes of single-port cholecystectomy by laparoscopy and robots were recently examined in many studies owing to surgeon and patient preference for minimally invasive surgery. A next-level single-port da Vinci system platform was recently released that features three fully wristed and elbowed instruments and a flexible camera in a single 2.5-cm cannula. This study aimed to evaluate the feasibility and efficacy of robotic cholecystectomy (RC) using the new da Vinci SP system.
Methods: In this retrospective observational single-center study, we analyzed the medical records of 304 patients who underwent RC between March 2017 and May 2021.
Results: Of the 304 patients, the da Vinci Xi (Xi) was used in 159 and the da Vinci SP (SP) was used in 145. The mean age was 44.9 years in the SP group and 39.8 years in the Xi group. In both groups, the dominant sex was female. Most patients were asymptomatic in both groups, followed by the complaint of abdominal pain. The mean operation time was 45.7 min in the SP group versus 49.8 min in the Xi group. The mean docking time of the SP group was shorter than that of the Xi group (5.7 min vs 8.8 min; $p = 0.024$). The mean immediate postoperative numerical rating scale (NRS) score was 4.0 in the SP group and 4.3 in the Xi group, showing a significant difference ($p = 0.003$). A separate analysis of only patients with acute cholecystitis treated with the da Vinci SP showed that the immediate postoperative NRS score in the acute group was higher than that in the non-acute group, but those for the next 24 h did not differ significantly between groups.
Conclusions: This study demonstrated acceptable results of single-site cholecystectomy using da Vinci SP. Thus, pure single-port RC using the da Vinci SP for various benign gallbladder diseases may be an excellent treatment option.

[ABST-0350]

Segmentectomy 5 and hepaticojejunostomy for strasberg type E5 bile duct injury during laparoscopic cholecystectomy

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Background: The authors experienced a case of Strasberg type E3 (Injury at the confluence; confluence intact) + E5 (Injury to aberrant right hepatic duct) injury that was treated by segmentectomy 5 and hepaticojejunostomy and report here with an operative video.
Methods: A 36 years old female patient was referred to UUH due to jaundice after laparoscopic cholecystectomy (LC). She underwent LC 9 days ago at other hospital and suffered from jaundice and AST/ALT elevation from the day after LC. Serum bilirubin level rose to 7.7 mg/dl on day 7. She was transferred to another hospital. MRCP revealed complete disconnection of extrahepatic bile duct at the hilar level. Communication between the right and left ducts was preserved only at the roof of the bifurcation. There was no common hepatic duct stump. PTBD was tried. But only the bile duct of one segment of right liver where no communication exist with other segments was puncture and drained. Trial to puncture the left bile duct was failed. She was transferred to UUH and 2nd PTBD was inserted into the left liver on the day. On cone-beam CT, the isolated bile duct was identified as B5. This was a case of Strasberg type E3 + E5 injury where complete transection of the confluence happened with concomitant separate transection of the aberrant B5. Since early (within 6 weeks) bile duct repair is reported to be associated with increased rates of repair failure, postoperative complications, and biliary stricture, delayed repair was decided.
Results: After waiting 7 weeks after the LC, she underwent open segmentectomy 5 and hepaticojejunostomy. The mucosa of the B5 (the separated duct) was destroyed so deeply (by 2 large metal clips) that a safe mucosa-to-mucosa anastomosis to the jejunum was impossible. Segmentectomy 5 was performed by Glissonean approach guided by the first PTBD. The aberrant B5, P5 and A5 were separately closed. After removing all the scar tissues surrounding the previous clipped site on common hepatic duct, hepaticojejunostomy was done with some extension (3 mm) of the left hepatic duct. Operation time was 375 min. Estimated blood loss was 100 ml. There was no postoperative complication. Postoperative hospital stay was 11 days.
Conclusions: For injury of an aberrant right duct with concomitant injury of main bile duct, delayed repair after more than 6 weeks of the injury seems offer a good chance of sound repair if on-table repair was not possible. When the injured aberrant right segmental duct is not repairable, Glissonean approach guided by the PTBD make precision segmentectomy possible.

[ABST-0447]

Duodenal gangliocytic paraganglioma

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Background: Gangliocytic paraganglioma (GP) is an extremely rare neoplasm originating in the hindgut, predominantly arising in the second part of the duodenum, with rare local recurrence or metastasis to regional lymph nodes.
Methods: The authors reported the case of gangliocytic paraganglioma in duodenum.
Results: A male-62 year old patient underwent routine check for gastroduodenoscopy. The tumor was 2.8 cm size in the 2nd portion of duodenum. The overlying mucosa was intact. The mass was arterial enhancing lesion on abdominal CT exam, hypermetabolic mass in PET CT scan. The authors had a plan for transduodenal ampullectomy and proceeding for pancreaticocduodenectomy in case of malignancy on frozen biopsy. However, the mass was proximal to ampulla, transduodenal tumor resection was performed, ganglioblastoma was suspicious on frozen biopsy. Final pathology was GP with the triphasic cellular differentiation; epithelioid neuroendocrine cells,

spindle cells with Schwann cell–like differentiation, and ganglion cells.
Conclusions: Duodenal Gangliocytic paraganglioma is the most common among the periampullary GP. Local excision or endoscopic resection is the treatment of choice without evidence fo metastasis wheras pancreaticoduodenectomy is recommended for those with features suggestive of malignancy such as large tumor size, submucosal extent, or pancreatic GP.

[ABST-0497]

Cancer mimicking schwannoma in CBD: A case report

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Background: Benign schwannomas arise in neural crest-derived Schwann cells which usually occur from all parts of the body, but the most common sites are the upper extrimities. Schwannoma in the digestive organ is rare, and most such tumors are reported in the stomach, followed by the colorectum and esophagus. Biliary schwannomas are extremely rare. We present the case of a patient with biliary schwannoma that required differentiation from extrahepatic bile duct cancer.
Methods: A 69-year old man was admitted to out institution for gastrectomy due to gastric cancer. Abdominal CT for pre-operative evaluation revealed a incidental hyperdense mass in the remnant cystic duct. He had undergone laparoscopic cholecystectomy for gallstone 30 tears previously. There was no evindence of jaundice or abdominal symptoms. Laboratory studies revealed within normal. The tumor markers including CEA and CA 19–9 were within normal. We planned surgical treatment without additional biliary radiology examination and intervention because he already planned gastrectomy for gastric cancer. We performed extrahepatic bile duct resection. A hard mass was palpable in the hepatoduodenal ligament, but the tumor was noninvasive and mobile. After extrahepatic bile duct resection, biliary reconstruction was performed by the Roux-en-Y hepaticojejunostomy.
Results: A histopathologic examination of the resected specimen revealed that the tumor consisted of spindle cells with wavy nuclei and exhibited a palisading arrangement. Immunohistochemical staining was positive for protein S-100 and negative for SMA, desmin, CD 34, p53 and c-kit. Based on these pathologic findings, we diagnosed the patient with schwannoma of extrahepatic bile duct.The surgical margin was negative, including complete resection. The patient's postoperative course was uneventful, and he has been doing well without any complications.
Conclusions: Biliary schwannomas are rare tumors which can be successfully treated surgically. The preoperative diagnosis is difficult, especially when associated with other malignancies.

[ABST-0509]

Pure laparoscopic pancreaticoduodenectomy with radical cholecystectomy for gallbladder cancer

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Background: Hepatopancreatoduodenectomy (HPD) is an aggressive surgery for treatment of gallbladder cancer, because of high risk of perioperative morbidity and mortality. Furthermore, pure laparoscopic HPD is an extremely complex procedure. Laparoscopic HPD in gallbladder cancer has recently been reported in only one case worldwide. We will present a case who received a laparoscopic HPD.
Methods: A 66 year old male was transferred for treatment of mass forming lesion in pancreas head. During pre-operative further evaluation, gallbladder wall thickening was also identified. Gallbladder cancer with invasion into peri muscular connective tissue was confirmed by intra-operative frozen biopsy. PPPD with extensive regional lymph node dissection and radical cholecystectomy including partial hepatectomy of segment V and IVb was performed by totally laparoscopic approach. And, portal vein at the confluence of superior mesenteric vein and splenic vein was segmentally excised and reconstructed by end-to-end anastomosis due to the risk of cancer invasion. Five ports were used for PPPD and one port was added for hepatectomy. Total operation time was 470 min and there was no transfusion.
Results: Patient was discharged at 20 days after surgery with uneventful post-operative course. The patient's final pathology was advanced gallbladder cancer with pancreas head invasion by lymph node metastasis.
Conclusions: Conclusively, we present a successful laparoscopic HPD in gallbladder cancer. Laparoscopic HPD is still a technically challenging procedure, but can be considered a feasible procedure in advanced gallbladder cancer, based on sufficient experience with laparoscopic PPPD and hepatectomy.

[ABST-0547]

Double pursue string techinique of pancreaticogastrostomy—an easier and simplified pancreatic reconstruction

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Background: One of the most serious complications after pancreatic resection is the development of a post-operative pancreatic leak or fistula, with resulting morbidity such as abdominal pain, ileus, fever.Importantly, patients with post-operative pancreatic fistula (POPF) leak, or abscess have been found to have a 90-day mortality of 5% in a single-institution report of pancreatectomy in a large worldwide literature search, the incidence of pancreatic fistula after pancreaticoduodenectomy was found developing in approximately 13% of pancreaticoduodenectomies.
Methods: During a period of 6 months, from July 1st to dec 31 -2021, whipples procedure was done for 16 cases for various indications.we used the technique of double pursue string for pancreatic reconstruction by pancreaticogastrostomy. 2–0 prolene and 3–0 prolene suture material was used as double pursue string from 3 o clock to 6-o clock and 6 o clock to 3 o'clock.PD is stented with IFT tube based on size and PG done by dunking. Intra op leak test after PG is done by metheylene blue dye mixed with 500 ml normal saline.
Results: pancreatic reconstruction done by double pursue string method in our study group of 16 cases had no POPF in any of the case. The average time to complete this type of PG was 15.5 min done by three different surgeons. No leak of methylene blue dye was

found intraoperatively to prevent post op.post of PPH was found in 3 cases, 2 cases were managed conservatively and one case required laparotomy, DGE was identified in 5 cases and was managed conservatively.
Conclusions: double pursue string techinique of PG can be easily performed by surgical resident simplifing the complexity of pancreatic anastomosis and less time consuming than any other type pancreatic reconstruction with acceptable outcomes.

[ABST-0386]

Large cell neuroendocrine carcinoma of the extrahepatic bile duct: A case report of two cases

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Background: Neuroendocrine carcinoma originating from extra hepatic bile duct is very rare and only a few cases have been reported. Because of its scarcity of incidence, not much is known about the disease but for its aggressiveness and poor prognosis. Herein we report two cases of large cell neuroendocrine carcinoma (LCNEC) originating from extrahepatic bile duct (hilum and common bile duct (CBD)).
Methods: CASE 1. A 60-years-old woman was preoperatively diagnosed a perihilar cholangiocarcinoma, and a left hepatectomy and caudectomy with hepaticojejunostomy was performed. From the histopathological findings, we diagnosed the tumor as a LCNEC (pT2aN1Mx, pStage IIIB) with focal proportion of an adenocarcinoma component. The postoperative course was uneventful, and she was administered etoposide and cisplatin every 3 weeks (6th cycles) as an adjuvant chemotherapy. She has remained recurrence-free for 7 months.
Results: CASE 2. A 67-years-old man was diagnosed a cholangiocarcinoma of mid-CBD and underwent laparoscopic pylorus-preserving pancreatoduodenectomy (PPPD). The pathological findings showed a LCNEC (pT1N1Mx, pStage IIB) with focal proportion of an adenocarcinoma component in the extrahepatic bile duct with lymph node metastases. After recovery, he was administered etoposide and cisplatin every 3 weeks (currently 6th cycle) as an adjuvant chemotherapy. At 7 months after surgery, there was no recurrence of the disease.
Conclusions: Neuroendocrine carcinoma of the extrahepatic biliary tracts is a very rare and highly malignant disease with a poor prognosis. To establish the definite treatment approach, more cases should be found and reviewed. Until then, a multidisciplinary approach could improve the prognosis for this neoplasm.

Pediatric Hepatology

[OP-0245]

Rapidly decreased HBV RNA predicts HBeAg seroconversion in children with chronic hepatitis B

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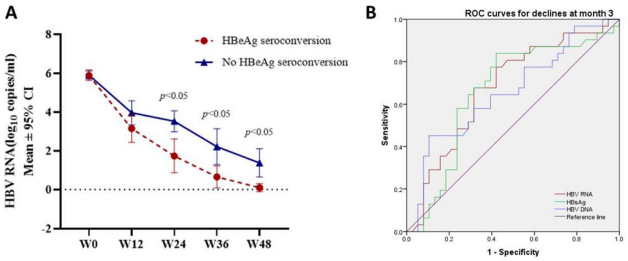
Objectives: The purpose of this study was to explore the role of HBV RNA predict the HBeAg seroconversion in children with chronic hepatitis B(CHB).
Materials and Methods: A total of 175 children with HBeAg-positive CHB aged 1 to 17 years, treated with interferon α (IFNα) 48 weeks. Based on the results of HBeAg seroconversion at treatment week 48, the patients were divided into HBeAg seroconversion group and without seroconversion group. Univariate and multivariate regression was used to identify the impact factors associated with HBeAg seroconversion. The area under the receiver operating characteristic curve (AUROC) was used to assess the prediction for HBeAg seroconversion.
Results: The HBeAg seroconversion rate was 36.0%(63/175) at week 48. HBV RNA levels decreased more rapidly than HBV DNA and HBsAg. Patients with HBeAg seroconversion showed a significantly larger HBV RNA decline levels from baseline to week 12, 24, 36 and 48, respectively, in comparison to the patients without HBeAg seroconversion ($p < 0.05$). Univariate and multivariate analysis showed that age, HBV RNA decreased levels at week 12 were independent predict factors for HBeAg seroconversion. AUROC of HBV RNA decreased levels at week 12 was 0.677(95%CI 0.549–0.806), which was significantly better than the decreased levels of HBV DNA (AUROC 0.657, 95% CI 0.527–0.788, $p = 0.025$) and HBsAg (AUROC 0.660, 95% CI 0.526–0.795, $p = 0.023$). HBV RNA levels decreased above 1.385 $\log_{10}$ copies/ml from baseline to week 12, the positive predictive value (PPV) and negative predictive value(NPV) for HBeAg seroconversion were 53.2% and 72.2%, respectively, with a sensitivity of 77.4% and specificity of 57.9%.
Conclusion: The decreased levels of HBV RNA at treatment week 12 could be used as an early predictor of HBeAg seroconversion. Using the index, clinicians can choose more reasonable therapeutic strategy and reduce the waste of medical resources.



[OP-0254]

The Etiology of genetic neonatal/infantile cholestasis and usefulness of the molecular genetic testing

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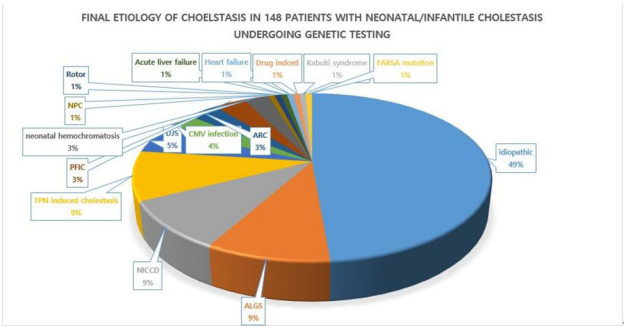
Objectives: Advances in molecular genetics have uncovered a previously unexplained gene responsible for neonatal/infantile cholestasis, previously classified as "idiopathic". In particular, next-

generation sequencing(NGS) is frequently being used to test various candidate genes for neonatal cholestasis. The aim of this study is to evaluate the etiology of genetic neonatal/infantile cholestasis and the usefulness of neonatal cholestasis gene panel and single gene testing.
Materials and Methods: In the past 11 years, 148 patients suspected with genetic neonatal/infantile cholestasis at Seoul National University Hospital were tested. If there was a clinically suspected disease, single gene testing(JAG1 sequencing, SLC25A13 sequencing, ATP8B1/ABCB11 sequencing, and VPS33B sequencing) was performed, and if clinically difficult to differentiate, neonatal cholestasis gene panel containing 34 genes was performed. Then we compared clinical data of genetically confirmed neonatal/infantile cholestasis patients.
Results: A total of 49 patients were confirmed by genetic analysis, including 14 with Alagille syndrome(ALGS), 14 with neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD), 7 with Dubin-Johnson syndrome(DJS), 5 with Arthrogryposis-renal dysfunction-cholestasis (ARC) syndrome, 5 with ABCB11 mutation(PFIC II), 1 with Rotor syndrome, 1 with Niemann-Pick disease type C(NPC), 1 with Kabuki syndrome, and 1 with FARSA mutation. Through neonatal cholestasis gene panel, 14 of 69(23.2%) were genetically confirmed, including 6 with DJS, 4 with NICCD, 1 with Rotor syndrome, 1 with ALGS, 1 with ABCB11 mutation, and 1 with NPC. In patients with NICCD, AST/ALT ratio and INR were significantly higher and total protein and albumin were significantly lower. GGT levels were significantly lower in the patients with ABCB11 mutation and ARC syndrome.
Conclusion: ALGS and NICCD are most common disease in genetic neonatal/infantile cholestasis. NICCD could be considered when prothrombin time and AST/ALT ratio are increased. Single gene testing and neonatal cholestasis gene panel are necessary and complementary to the diagnosis of genetic neonatal/infantile cholestasis.



[OP-0280]

Myopenia and impaired performance status affect outcomes of children undergoing living donor liver transplantation

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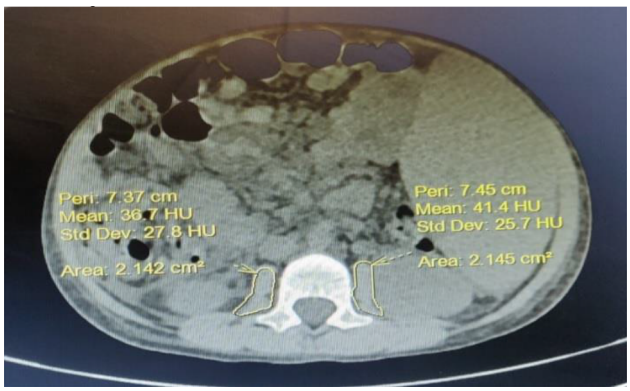
Objectives: The current study was aimed at exploring the ability of myopenia assessment based on computed tomography (CT) scan measurement of total psoas cross sectional area (TPSA) and previously published pediatric performance scores in predicting outcomes of children undergoing LDLT and to establish CT based TPSA measurement as an effective subjective tool for assessing pediatric myopenia.
Materials and Methods: All children aged 6 months to 10 years undergoing LDLT in our center between November 2018 and June 2020 were included. Children receiving deceased donor liver or those undergoing LT for acute liver failure were excluded. Children were followed up for a minimum of 3 months post-LT. Demographic data, PELD score, need for pre-LT organ support, operative details, complications, post-operative course and outcomes were retrieved. TPSA at lower border of L3 measured on 5 mm cuts of plain abdomen CT scan on both sides and the average was used to calculate Z scores for each child by comparing with age matched control cohorts.
Results: Median age, weight & PELD score at LT were 14 months, 8.1 kg and 18. 36(43.9%) had Z-TPSA < -2.0 suggestive of significant myopenia. 18(22%) and 16(19.5%) had moderate and severe IPS respectively. Median ICU and hospital stay were 5 and 15.5 days. 27(32.9%) had major complications (Clavien-Dindo Grade > 2). 90-day and overall survival were 92.7% and 90.2%. On multivariable regression, Z-TPSA was an independent predictor of major morbidity (OR:0.68(0.51,0.90),p = 0.008) and prolonged ICU stay (OR:0.67 (0.48,0.92), p = 0.015). Pre-transplant IPS alone was an independent predictor of survival. Post-LT survival was 98%, 84.3% and 76.5% in children with mild, moderate and severe pre-transplant IPS respectively (Log rank test, p = 0.024).
Conclusion: Pre-transplant myopenia expressed as z score of TPSA was an independent predictor of major morbidity and prolonged ICU stay, whereas pre-transplant impaired performance status[IPS] was an independent predictor of survival.



[OP-0359]

Clinical and laboratory risk predictive factors for mortality in HLH with associated liver dysfunction in pediatric age group

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Objectives: Hemophagocytic lymphohistiocytosis is a life-threatening hyperinflammatory disorder that is associated with high morbidity and mortality.
Materials and Methods: This was a retrospective observational study. Medical records of 38 pediatric patients (range 0.2–15 years) with non-malignancy associated HLH were retrospectively reviewed.

Treatment strategies included methyl prednisolone, IVIg, etoposide and plasmapheresis.
Results: In the last 7 years from 2014 to 2021, we have admitted 38 cases of HLH with liver dysfunction under Department of Pediatric Hepatology. Median age of the children was 50 (IQR 9.5–120) months and 32 (84.2%) were males. Twenty-six (68.4%) patients presented with jaundice and INR was deranged in 18 (47.3%) with Hepatic Encephalopathy present in 13 (34.2%). The definition of pediatric acute liver failure (PALF) was fulfilled by 14 (36.2%) cases. Thirteen out of 38 (34%) children with HLH did not survive with median hospital stay of 10 days; none received liver transplantation. On univariate analysis, PALF (9/14 versus 4/24, OR 2.60 95% CI 1.12–6.04, p value = 0.005) and INR (2.9 ± 2.5 versus 1.4 ± 0.4, p value = 0.009) were the risk predictive factors showing a significant association with death. Younger age and AST/ALT ratio also showed borderline association with death in these children. On logistic regression analysis, PALF was only independent predictor of death (Adjusted OR 9, p = 0.005) improving the correctness of classification of the model from 65 to 75%. On removing PALF from the model, usage of steroid (Adjusted OR 17, p = 0.033), AST/ALT ratio (Adjusted OR 2.05, p = 0.066) and INR (Adjusted OR 2.86, p = 0.047) were found to be independently associated with survival which also improved the correctness of classification to 78.9%.
Conclusion: There is a 9-folds increase of death in HLH who present as PALF but the usage of steroids, lower INR and lower AST/ALT ratio can improve the likelihood of survival by 17, 2.8 and 2 times respectively.

[OP-0378]

Epidemiology data of pediatric patients in liver diseases department

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Objectives: The epidemiology of pediatric liver disease in Azerbaijan has not been studied extensively. There has been a lack of sufficient research. Therefore, the development of such a science as pediatric hepatology is very important.
Materials and Methods: During period since October 2019 to October 2021, 571 (302 (52,9%) male and 269 (47,1%) female) children from birth to 18 years old (mean age is 6 ± 1) were admitted to our department of liver diseases. All of them were observed for Hemogram, Biochemical examinations (ALT, AST, ALP, AFP, Bilirubin fractions, Albumin), Abdominal ultrasound, Endoscopy and Fibroscan.
Results: As a result of research, the following diseases have been identified 38 pts (6,66%) with Genetic diseases, 82 pts (14,37%) with Disease of the gallbladder and biliary tract, 85 pts (14,88%) with Steatohepatitis, 38 pts (6,66%) with Fetal hepatitis, 13 pts (2,28%) with Autoimmune liver disease, 27 pts (4,72%) with Toxic hepatitis, 188 pts (32,92%) with Viral hepatitis, 100 pts (17,51%) with Gastrointestinal diseases. Figure 1
Conclusion: · Among pediatric patients who applied to the Liver disease department from October 2019 to October 2021 prevalence of viral hepatitis. · It means that pediatric population should be examined to viral hepatitis depending of anamnesis, and should be more intensive control to vaccination against viral hepatitis. To another side—constantly control to pregnant woman with viral hepatitis, to prevent mother-to-child transmission. · The second one main problem among pediatric patients is Disease of the gallbladder and biliary tract. · Treating a pediatric patient offers a unique opportunity to prevent progressive liver injury and to develop novel therapeutic regimens that reduce the need for liver transplantation.

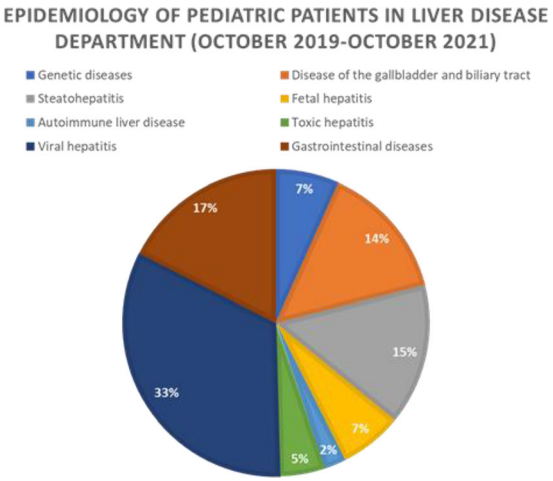

Fig.1

[OP-0550]

The role of B lymphocytes in HBsAg seroconversion in children with chronic hepatitis B

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Objectives: To explore the role of B lymphocytes predict the HBsAg seroconversion in children with HBeAg-positive chronic hepatitis B(CHB).
Materials and Methods: A total of 273 children aged 1 to 17 years, treated with interferon α (IFNα) combinated with nucleus(t)ide analogues 96 weeks. Based on the results of HBsAg seroconversion at treatment week 96, the patients were divided into HBsAg seroconversion group and without seroconversion group. Univariate and multivariate regression was used to identify the factors associated with HBsAg seroconversion. The area under the receiver operating characteristic curve (AUROC) was used to assess the role of HBsAg seroconversion.
Results: The HBsAg seroconversion rate was 34.43%(94/273) at week 96. Univariate and multivariate analysis showed that age, B cell values at baseline were independent predict factors for HBsAg seroconversion. AUROC of B cell at baseline was 0.762(95%CI

0.693–0.831), B cell values at baseline above 2.865 $\log_{10}$ cells/uL, the positive predictive value (PPV) and negative predictive value(NPV) for HBsAg seroconversion were 55.77% and 87.0%, respectively, with a sensitivity of 81.7% and specificity of 64.9%.
Conclusion: B cell values at baseline could be used as a predictor of HBsAg seroconversion in children with chronic hepatitis B.

[OP-0558]

Follow up of 24-h urinary copper excretion in pediatric Wilson disease patients under chelation plus zinc therapy: Experience from a tertiary pediatric liver care unit

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Objectives: 24 Hour Urinary copper excretion (UCE) is a recommended biochemical tool for diagnosis of Wilson disease, however its role in follow-up is not well studied especially in Pediatric population. Hence, this present study is planned with a primary objective to evaluate UCE in pediatric Wilson patients on long-term follow-up.
Materials and Methods: Clinical and laboratory data of all Wilson patients < 18 years age diagnosed at our institute from 2014 to 2021 were reviewed retrospectively. Patients on combination therapy (D-penicillamine/ Trientine along with Zinc) and had at least one UCE value available after first year of treatment were included. UCE assessed at baseline, 1, 2 and 3 years after starting of therapy.
Results: During study period, 93 of 133 newly diagnosed Wilson patients had survived with native liver. After exclusion of 27 (8: zinc monotherapy, 13: follow-up data unavailable, 6: < 1 year of chelation), total 66 patients (Male: 41, Female: 25) were included with median follow up of 3 years (IQR: 2–6 years). Poor compliance was reported in 15 (22.7%). UCE (mcg/day) before, after 1 year and 2 years of chelation was 625 ± 796, 409 ± 321 and 310 ± 165 (ANOVA p = 0.001). UCE (mcg/day) at 1 year was < 200 in 19.7%, 200–500 in 57.6% and > 500 in 22.7%. Non ceruloplasmin bound copper (NCC) (mcg/dl) was 36 (IQR: 23.4–49.3) before chelation, which reduced to 0.7 (IQR: -4.6 to 8.3) at 1 year and 0.1 (IQR: -2.4 to 5.6) at 2 years after treatment (ANOVA p = 0.00). NCC was comparable between those with UCE (mcg/day) < 200, 200–500 and > 500 at 1 year. Furthermore, UCE and NCC were comparable between compliant and non-compliant patients.
Conclusion: UCE by 1 year normalises or is even lower than normal in 77.3% with combination therapy. NCC was comparable in various grades of cupriuresis. Both of these markers do not differentiate between compliant and non-compliant patients.

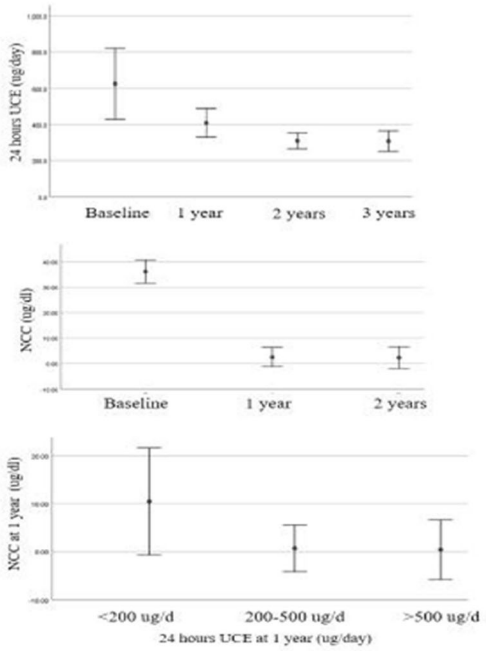

Figure:
(A) Trends of 24 hours urinary copper excretion (UCE) from baseline to 3 years; value at baseline significantly higher than at other time points.
(B) Trends of NCC (Nonceruloplasmin bound copper) from baseline to 2 years;value at baseline significantly higher than at other time points.
(C) Comparison of NCC (Nonceruloplasmin bound copper) at various levels of cupriuresis at 1 year follow up. All values comparable.

Table: Albumin, INR, AST and ALT at baseline, 1 year and 2year post combination therapy: Albumin improved and INR/AST/ALT declined significantly at 1 year and 2year post treatment as compared to baseline

	Baseline (Median, IQR)	1 year post Combination therapy (Median, IQR)	2 year post Combination therapy (Median, IQR)
Albumin (mg/dl)	2.4 (2.1-3.3)	4 (3.8-4.2)	4.2 (3.9-4.39)
INR	1.89 (1.38-2.40)	1.26(1.12-1.38)	1.18(1.09-1.28)
AST (IU/L)	101 (70-150)	42 (35-55)	41 (33-46)
ALT (IU/L)	45 (31-78)	39 (27-54)	38 (28-50)

[OP-0597]

A set of new genes and its coding proteins associated with short-term native liver survival time in post-Kasai biliary atresia

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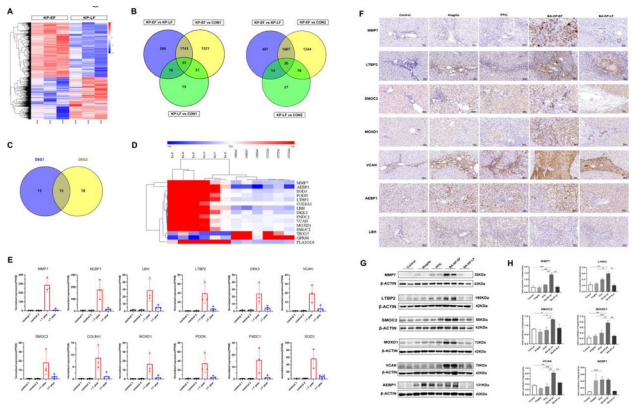
Objectives: To screen molecular markers associated with one year of native liver survival time (NLST) after Kasai procedure (KP) in biliary atresia (BA).
Materials and Methods: RNA-sequencing of liver tissues were performed and compared in patients with KP early failure (KP-EF group, NLST ≤ 1-year, n = 3), KP late failure (KP-LF group, NLST > 1-year, n = 3) and non-cholestastatic controls (CON group, methylmalonic acidemia and urea circulation disorder, n = 6 in each group). The differential expression genes were further verified by qRT-PCR, immunohistochemistry and Western blot. We also collected plasma samples from BA patients in KP-EF (n = 25), KP-LF (n = 25), non-BA cholestatic control (Non-BA group, n = 20) and CON group (n = 10) and the coding proteins in plasma were determined by enzyme-linked immunosorbent assays.
Results: We identified 12 genes (MMP7, MOXD1, VCAN, LTBP2, SMOC2, AEBP1, LBH, DKK3, COL8A1, PODN, FNCD1 and SOD3), which was closely correlated with KP-EF. Five of them (MMP7, MOXD1, VCAN, LTBP2 and SMOC2) were further validated and significantly higher in KP-EF group (n = 13) in comparison to the KP-LF (n = 13) and non-BA groups (n = 16). The plasma MMP7 level in KP-EF group was 1.81 (1.44–3.21)ng/ml, which were also significantly higher than that of those in KP-LF group 0.82(0.52–1.08) ng/ml and non-BA group 0.21(0.18–0.26) ng/ml and CON group 0.49 (0.43–0.84) ng/ml, all $P < 0.05$]. The area under receiver operating characteristic curve (AUROC) of plasma MMP7 in differentiating KP-EF and KP-LF patients was 0.920(0.837–1.000), the sensitivity and specificity were 96% and 80% respectively. Furthermore, the AUROC of LTBP2 was 0.685(0.536–0.833), the sensitivity was 52% and the specificity was 80%.
Conclusion: The expression of 5 genes (MMP7, MOXD1, VCAN, LTBP2 and SMOC2) were significantly unregulated in the liver of BA. Plasma MMP7 and LTBP2 levels are associated with the short-term NLST, which underscore its possible clinical usefulness for the prediction of NLST in post-Kasai BA patients.



[PP-0666]

Correlation antineutrophil cytoplasmic antibody or antinuclear antibody with severity and prognosis in biliary atresia

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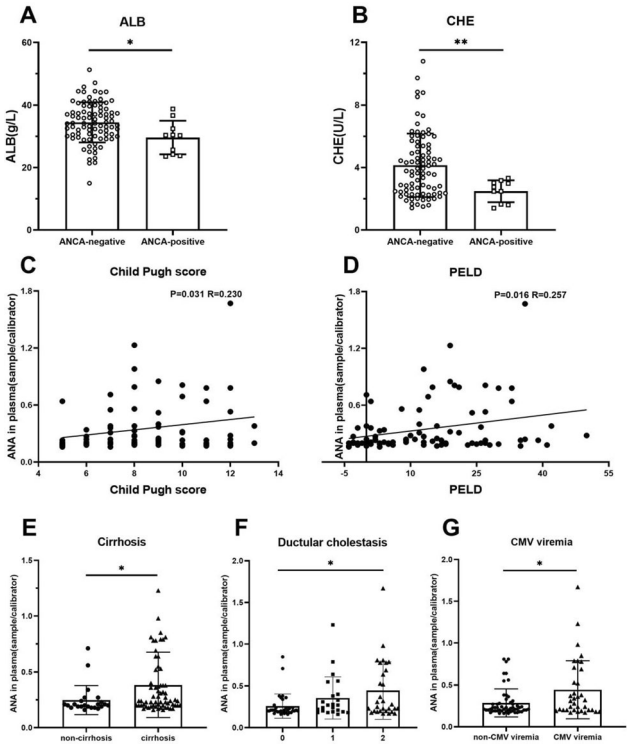
Objectives: To investigate the positive rate and clinical significance of plasma antineutrophil cytoplasmic antibody (ANCA) and antinuclear antibody (ANA) in patients with biliary atresia (BA).
Materials and Methods: The clinical data and samples of BA patients undergoing liver transplantation (LT) from April 2017 to October 2020 were retrospectively collected. The plasma ANCA were qualitatively detected by indirect immunofluorescence and ANA semi-quantitatively measured by enzyme linked immunosorbent assay. ANCA positive was defined as a titer of antibodies > 1:10, and ANA positive was defined as ANA ratio (sample/calibrator absorbance) ≥ 1.0. Correlation ANCA or ANA with laboratory parameters, severity, pathological histological features and post-LT complications were analyzed.
Results: The ANCA positive rate was 10.2% (10/98) in BA, one case was cytoplasmic ANCA, nine cases were perinuclear ANCA. Prior-LT, plasma albumin [30.35 (24.10, 33.55), Fig A.] and cholinesterase level [2.62 (1.64, 3.06),Fig B.] in ANCA-positive patients was significantly lower than that in ANCA-negative patients [albumin: 34.25 (30.23, 39.18), P = 0.018; cholinesterase: 3.86 (2.40, 5.39), P = 0.009]. The positive rate of ANA was 3.3% (3/90). There was a weak positive correlation between the ANA ratio and Child–pugh score (P = 0.031, R = 0.230, Fig C.), as well as pediatric model of end-stage liver disease score (P = 0.009, R = 0.257, Fig D.). Histopathologically, the ANA ratio was significantly higher in patients with cirrhosis (P = 0.016, Fig E.) and the ratio increased with higher degree of ductular cholestatis (P = 0.040, Fig F.). In addition, the ANA ratio was significantly higher in patients with CMV viremia post-LT (P = 0.036, Fig G.).
Conclusion: The positive rate of ANCA and ANA of patients with BA is low, but it correlates with liver synthetic function, fibrosis stage and post-LT CMV infection. Autoantibodies may be of clinical value for the assessment of BA severity and post-LT prognosis.



[PP-0895]

Effectiveness of transcutaneous bilirubin measurement in managing neonatal jaundice

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Objectives: Neonatal jaundice is a common cause of concern in immediate newborn period for parents. Obtaining blood bilirubin samples is a painful procedure; it predisposes the baby to infections and requires skilled health personnel. Moreover, laboratory tests are costly and time consuming, leading to unnecessary delays in commencing phototherapy and discharge from hospital.
Materials and Methods: Ninety newborns with jaundice were referred to the postnatal ward of Dornod Medical center from 2017 august to 2019 January. For patients, we used breastfeeding, intravenous fluid and phototherapy. Before and after the treatment, transcutaneous bilirubin meter were checked.
Results: From the 180 participants of the age (day) 1–35 (mean 17), male were 106 (58.9%), female were 94 (41.1%), body mass were 1.1–4.9 kg (mean 3.7). Phototherapy and nursing care had significantly decreased bilirubin level from 129.0–469.0 (mean 295.1) mmol/l to 97–298 (mean 173.4) mmol/l (T test, $p \leq 0.05$).
Conclusion: In conclusion, specially of transcutaneous bilirubin measurement is safe and effective in neonatal jaundice.

[PP-0967]

Extending the clinical spectrum of familial Mediterranean fever: A case report of Armenian child with liver involvement

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Objectives: To describe the isolated cytolysis in FMF patients.
Materials and Methods: Clinical and laboratory findings are presented.
Results: With a nine-year old girl (seven years ago) was established FMF with M694V/M694V mutation. Colchicine was started 0.25 mg/day and gradually increased up to 1.0 mg/day. The level of transaminase was increased – AST, ALT (3.0xn.v.) after five years. Echography pattern reveled "starry sky liver" with high echogenicity without dilation of vessels. The attacks of FMF was continue, we increased dose of colchicine up to 1.2 mg/d, at the same time rule out Wilson disease, autoimmune, viral, toxic hepatitis (colchicine dose 0.04–0.05 mg/kg). However, the combination of ursodeoxycholic acid with the 1.25 mg/d of colchicine showed it dramatic results with clinical and laboratory (including SAA) improvement.
Conclusion: We can suspect that liver involvement in FMF could be one of the clinical features of FMF (based upon transaminase elevations without liver biopsy). It is assumed, that patients with the M694V/M694V mutation could be the risk factors not only for the development of complications (amyloidosis, intestinal obstruction) of FMF but also play a favorable role for the development of liver involvement in FMF. Hence, for the understanding pathogenesis of isolated cytolysis and liver involvement in general in FMF patients, should be further studies with more patients for a providing precise interpretations.

[PP-1013]

Efficacy and safety of D-penicillamine, Trientine and Zinc in Pediatric Wilson disease patients

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Objectives: Wilson's disease (WD) is a rare genetic disease that requires lifelong medication to avoid mortality. Data on the long-term outcome of treatment are limited. This study aims to evaluate the effectiveness and safety of D-penicillamine, trientine and zinc in patients diagnosed with WD in childhood.
Materials and Methods: We retrospectively reviewed the records of the patients diagnosed with WD before the age of 18 at Seoul National University Hospital from 2005 to 2021. The type of drug, the duration of administration, and the reason for medication change were assessed. When a drug was changed due to treatment failure or side effects, Kaplan–Meier analysis was used.
Results: Ninety patients were enrolled (median age at diagnosis: 8.3 years, median follow up period: 7.9 years), and a total of 148 treatment cases were used in the analysis (37 D-penicillamine, 50 trientine, 61 zinc). Treatment change due to ineffectiveness was most common in patients receiving trientine (44%), and this was reach significantly difference compared in patients receving D-penicillamine (5%) and zinc (25%). D-penicillamine (5%) and zinc (25%) also reach statistical significance. Discontinuation due to side effects was significantly more frequent in patients receiving D-penicillamine (43%) than in patients receiving trientine (4%) and zinc (23%).
Conclusion: In pediatric WD, D-penicillamine, zinc, and trientine have therapeutic effects in that order, but D-penicillamine has more side effects than trientine and zinc.

[OP-1034]

Extra-hepatic portal vein obstruction in infants and young children: Does early onset imply poorer growth indices?

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Objectives: Extrahepatic portal vein obstruction (EHPVO) is the most common cause of portal hypertension in children. We studied the profile of infants and young children with EHPVO in under-five age group and compared the burden of growth failure with older children and adolescents.
Materials and Methods: Data of EHPVO patients from September 2000 to September 2021 with index presentation at < 5 years were analysed from a prospectively maintained liver clinic database. Anthropometric data were compared with those presenting between 5–18 years.

Results: 181 patients were identified with diagnosis of EHPVO at < 18 years of age. Of these, 61(33.7%) were < 5 years. After excluding for paucity of data, 40[21(52.5%) male] under 5 years formed the study cohort and 32[20 (62.5%) male] in 5–18 years as comparison cohort. Median age at presentation in study group was 40.5(1–60) months. 9(22.5%) were preterm(< 40 weeks gestation), 14(35%) had low birth weight(LBW, < 2500 g). Of those with LBW, 8(57%) had a neonatal intensive care unit stay for > 7 days and 5(35.7%) had early or late neonatal sepsis. Index presentation was upper gastrointestinal bleed [24(60%)], abdominal lump [7(17.5%)], left hypochondriac discomfort [6(15%)] or incidentally detected [3(7.5%)]. In < 5 years, 16(40%) had weight < 3rd centile [(wasted),WHO MGRS charts 2006], 13(32.5%) had height < 3rd centile(stunted), while both stunting and wasting was seen in 12(30%). The LBW subgroup had significantly more wasting at presentation compared to normal birth weight cohort (p = 0.003).) Among 5–18 year olds, weight < 3rd centile was seen in 15.6%[vs. 40% in < 5y, p = 0.023] and height < 3rd centile in 6.25%[vs. 32.5% in < 5y, p = 0.006].
Conclusion: EHPVO in infants and children less than 5 years has more severely affected growth indices, possibly due to early deprivation of adequate portal blood flow. A significant impairment in catch-up growth may result in infants with low birth weight developing EHPVO.

Characteristic	< 5 y (n=40)			p value^	>5 y (n3 =32)	p value$
	NBW (n1=26)	*LBW (n2=14)*	Total (n=40)	(n1 *vs* n2)		(n *vs* n3)
Index presentation				*0.97*		*0.47*
➢ Upper GI bleed	16 (61.5%)	8 (57.1%)	24 (60%)		24(75%)	
➢ Lump abdomen	4(15.4%)	3(21.4%)	7(17.5%)		2(6.25%)	
➢ Left hypochondriac pain	4(15.4%)	2(14.3%)	6(15%)		4(12.5%)	
➢ Incidental detection	2(7.7%)	1(7.1%)	3(7.5%)		2(6.25%)	
Median (range) age at presentation(mo)	56 (1-60)	29 (1-60)	40.5 (1-60)	*0.09*	162(72-204)	*NA*
Nutritional assessment at presentation						
➢ Weight for age< 3rd centile(wasting)	6(23.1%)	10(71.4%)	16(40%)	***0.003***	5(15.6%)	***0.023***
➢ Height for age< 3rd centile (stunting)	5(19.2%)	8(57.1%)	13(32.5%)	***0.03****	2(6.25%)	***0.006***
➢ Both Stunting and wasting	4(15.4%)	8(57.1%)	12(30%)	***0.01****	2(6.25%)	***0.01***
➢ Anemia	22(84.6%)	12(85.7%)	34(85%)	*0.93*	26(81.25%)	*0.67*

Data represented as median(range) for continuous variables and frequency (%) for categorical data.
^ p value between normal birth weight (NBW) and low birth weight (LBW)
$p value between < 5 year and > 5-year-olds
**Fisher exact test*

[OP-1138]

Influencing factors for clinical cure in children with chronic hepatitis B

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Objectives: To investigate the influencing factors for clinical cure in children with chronic hepatitis B.
Materials and Methods: A total of 273 HBeAg-positive children aged 2–17 with CHB received a 106 ± 46 week interferon alone or combined with nucleoside analogues. Serum levels of HBV DNA, HBsAg, degree of inflammatory and fibrosis et al. were measured according to routine laboratory methods. Univariate and multivariate regression was used to identify the impact factors associated with clinical cure.
Results: 38.1%(104/273) of patients exhibited clinical cure during observation. Univariate and multivariate analysis showed that age, degree of inflammatory and baseline B cell absolute value were the influencing factors of clinical cure. The patients under 4.87 years old, degree of inflammatory under A2, baseline B cell absolute value above 2.865 $\log_{10}$ cells/uL had high clinical cure rate in children with CHB.
Conclusion: Age, inflammatory activity and baseline B cell absolute value were the influencing factors of clinical cure in children with CHB. The goal of clinical cure can be achieved through selecting the dominant population.

[OP-1143]

Extended therapy is critical for clinical cure in children with chronic hepatitis B

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Objectives: To investigate the influencing factors for clinical cure in children with chronic hepatitis B.
Materials and Methods: A total of 273 HBeAg-positive children aged 2–17 with CHB received a 96 week interferon alone or combined with nucleoside analogues and followed up 24 week. Serum levels of HBV DNA, HBsAg, degree of inflammatory and fibrosis et al. were measured according to routine laboratory methods.
Results: HBsAg loss rate was only 27.11% at 48 weeks, while it reached to 38.1% after treatment of 96 weeks.
Conclusion: Extended therapy is critical for clinical cure in children with chronic hepatitis B.

[OP-1151]

Role of age dependent innate immune cells in children with chronic hepatitis B

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Objectives: To study the role of age dependent innate immune cells in children with chronic hepatitis B(CHB).
Materials and Methods: In previous studies, we found that age is an important factor affecting the clinical cure in children with CHB. Age under 4.87 years old had high HBsAg serum clearance rate. We divided the patients into two groups according to their age, the immunological differences between them were compared.
Results: There were significant differences in degree of liver inflammatory and fibrosis, amount of monocyte, amount and percentage of lymphocyte, amount and percentage of T cell, amount of CD4 cell, amount and percentage of CD8 cell, amount and percentage of B cell, amount of NK cells, HBsAg and HBV DNA levels between the under 4.87 and above 4.87 years old. Further analysis showed that there were significant differences in monocytes and NK cells number in younger than 4.87 years old group compared to above 4.87 years old group. The younger the age, the higher the number of monocytes and NK cells, and the higher HBsAg serum clearance rate after antiviral treatment.
Conclusion: Monocytes and NK cells is critical for clinical cure in children with chronic hepatitis B.

[L-OP-1313]

HBV RNA and HBeAg levels at baseline are important predictors of HBsAg loss in children with chronic hepatitis B

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Objectives: To evaluate whether HBV RNA and HBeAg could act as an early predictor for HBsAg loss.
Materials and Methods: A total of 175 children with HBeAg-positive CHB aged 1 to 17 years received a 48 week treatment of IFNα was studied and followed up 24 week. Univariate and multivariate regression was used to identify the impact factors associated with HBsAg loss.
Results: The HBsAg loss rate was 36.6% at the end of observation. Univariate and multivariate analysis showed that age, HBV RNA and HBeAg levels at baseline were independent predictors for HBsAg loss. The cutoff value under 6.32 $\log_{10}$ IU/mL of HBV RNA levels or above 2.37 $\log_{10}$ IU/mL of HBeAg levels at baseline, the positive predictive value (PPV) and a negative predictive value (NPV) for HBsAg loss were 47.1% and 84.6%, respectively, with a sensitivity of 86.0% and specificity of 48.0%.
Conclusion: The levels of HBV RNA and HBeAg at baseline could be used as an early predictor of HBsAg loss treated with interferon in children with CHB.

[L-OP-1314]

HBV RNA profiles of different disease phases in children with chronic hepatitis B

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Objectives: To study HBV RNA profile of different disease phases and its correlation with other viral markers in children with chronic hepatitis B(CHB).
Materials and Methods: A total of 189 children with CHB aged 1 to 17 years treatment-naïve were enrolled and categorized into HBeAg positive group(n = 169) and HBeAg negative group(n = 20). Then, all enrolled patients were further divided into HBeAg-positive chronic infection (n = 12), HBeAg-positive chronic hepatitis (n = 157), HBeAg-negative chronic hepatitis (n = 20). HBV RNA and biomarkers were measured in these patients receiving IFN at baseline, week 12, week 24 and week 48. Patients were followed up every 3 to 6 months for clinical assessment, blood tests monitoring. Kinetics of HBVRNA were compared with HBV-DNA and HBsAg during antiviral treatment.
Results: In HBeAg positive group(n = 169), HBV RNA both showed good correlation with HBV DNA and HBsAg at baseline($r = 0.589$, $p = 0.021$; $r = 0.481$, $p < 0.0001$, respectively). In HBeAg negative group(n = 20), HBV RNA also showed good correlation with HBV DNA and HBsAg at baseline($r = 0.790$, $p < 0.0001$; $r = 0.588$, $p = 0.021$, respectively). In HBeAg positive chronic hepatitis group(n = 157), HBV RNA showed good correlation with HBV DNA and HBsAg at baseline($r = 0.581$ and 0.477, respectively, all $p < 0.0001$). The correlation between HBV RNA and HBV DNA, HBsAg was still preserved at 12 weeks of antiviral treatment($r = 0.642$ and 0.634, respectively, both $p < 0.0001$) in HBeAg positive chronic hepatitis group. However, there was no correlation was observed between HBV RNA and HBV DNA, HBsAg in HBeAg negative chronic hepatitis group at 12 weeks for those receiving antiviral treatment($r = 0.540$, $p = 0.108$; $r = 0.407$, $p = 0.205$).
Conclusion: HBV RNA can be used as an indicators of virus replication for children with HBeAg positive CHB. HBV RNA levels were inconsistent with HBV DNA and HBsAg levels during antiviral therapy in children with HBeAg negative CHB.

[L-OP-1315]

Analysis of influencing factors of HBV RNA in children with chronic hepatitis B

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Objectives: To explore the influencing factors of HBV RNA in children with chronic hepatitis B(CHB).
Materials and Methods: A total of 87 HBeAg-positive children with CHB, the average age was 4.64 ± 3.60 years treatment naive was studied. Serum levels of HBV RNA, HBV DNA, and HBsAg were measured according to routine laboratory methods, HBV PC/BCP mutants was measured by HBV DNA sequencing experiment.
Results: Univariate analysis showed that baseline ALT level ($p = 0.003$), baseline HBV DNA ($p < 0.001$), HBeAg($p = 0.033$), HBV BCP variation ($p < 0.001$) and baseline HBsAg levels ($p < 0.001$) were closely related to serum HBV RNA levels. Multivariate linear regression analysis showed that HBV BCP variation, ($p = 0.041$), HBV DNA ($p < 0.001$) and HBsAg levels ($p = 0.003$) are important factors affecting serum HBV RNA levels.
Conclusion: In this 87 HBeAg-positive with CHB untreated children, factors associated with serum HBV RNA levels were HBV BCP variation, serum HBV DNA levels and HBsAg levels. If using serum HBV RNA as a clinical marker in the future, it seems that these factors must be considered.

Other

[PP-0004]

An autopsy case of multicentric Castleman disease presenting with severe jaundice

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Objectives: Castleman disease is an uncommon lymphoproliferative disease described in the 1950s by Dr. Benjamin Castleman. Castleman disease has two types, namely, unicentric Castleman disease and multicentric Castleman disease (MCD). MCD often presents with generalized lymphadenopathy, fever, weight loss, fatigue, edema, anemia, and hypoalbuminemia. Severe patients may develop hepatosplenomegaly, massive ascites, pleural effusions, or organ failure, but severe jaundice or liver failure can occur in rare cases.
Materials and Methods: We present an autopsy case of MCD presenting with severe jaundice.
Results: A 70-year-old man with multicentric Castleman disease (MCD) was admitted to our hospital with jaundice and ascites. Elevations in bilirubin and interleukin-6 were noted, and computed tomography revealed the hepatic atrophy and the portal vein and bile duct disorders. Steroid therapy was started for MCD, but he died of hepatic failure. An autopsy revealed that MCD activity was mild, but advanced fibrosis and cholestasis were observed in the liver. Mild infiltration of IL-6-positive plasma cells was noted in the highly fibrotic area of the liver.
Conclusion: We experienced an autopsy case of MCD with severe jaundice. We speculated that intrahepatic cholestasis due to inflammation and severe fibrosis in the liver caused by chronic hyper-IL-6emia might be the main cause of severe jaundice. Although rare, liver and biliary tract damage, such as liver injury and cholestasis, may be also considered organ disorders of MCD.

[OP-0011]

Cell Phones and its association with liver disease

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Objectives: Cell phones (mobile) release radiofrequency waves (RFW) which is a kind of non-ionizing radiation. Although it is too weak to damage DNA to cause cancer in human, but its association with other diseases can't be ruled out. Ionizing radiations (X-rays, gamma rays & UV rays) can damage DNA to cause cancer.
Materials and Methods: Literature review with few studies is being discussed below.
Results: Interphone Study (2007): It involved 13 countries engaging 5,000 people for > 10 years showed no link of brain tumors with RFW. Danish cohort study (2007): conducted between 1982 and 1995 (400,000 people) showed no link head & neck tumors with RFW. Million Women Study: 800,000 women in UK were studied for 7-year on self-reported cell phone use for any health effect, which showed encouraging results. American Cancer Society monitors the health effect of cell phone with International Agency for Research on Cancer (IARC) & National Toxicology Program. IARC classifies RFW as possible carcinogen (2011). Ragy MM et al. studied on rat, showed increased MDA and decreased total antioxidant capacity in brain, liver and kidneys. Serum ALT, AST, urea, creatinine and corticosterone were increased, were corrected by withdrawal of phone. Siddiqi N et al. 2017 studied on fertilized eggs & embryos, revealed that RFW led to altered development & fatty change in liver. Ma HR et al. 2015 showed high MDA and hepatic necrosis.
Conclusion: Future health effects can't be ruled out, because of constantly changing variants of mobile for last 20 years.

[OP-0049]

2D-Shear wave elastography (2D-SWE) and transient elastography (TE) are poorly correlated in fontan-associated liver disease (FALD): A head-to-head comparison

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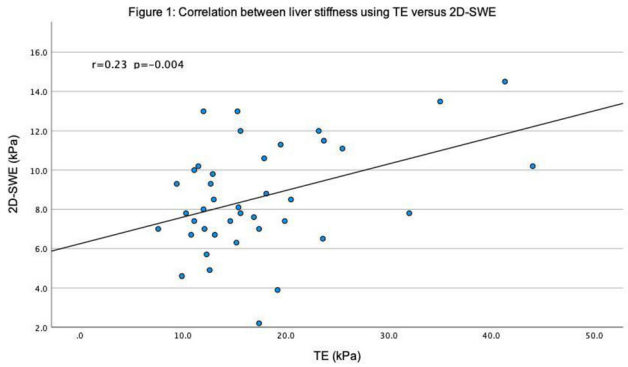
Objectives: To evaluate the relationship between TE and 2D-SWE in FALD.
Materials and Methods: Retrospective cohort study including all Fontan patients managed in a specialist clinic from 2018–2021. Trained clinicians performed 2D-SWE (GE Logiq-E9®) and TE (FibroScan 503 Touch®) on the same day, fasting for 4 h.

Laboratory, echocardiography and imaging data were collected. The atrioventricular systolic to diastolic duration (AVV S/D ratio) was calculated as measure of cardiac function. Pearson's correlation and Wilcoxon signed rank test were used.
Results: We analysed 40 paired measurements from 25 patients. Median age was 22 years (18–29). Ultrasound evidence of cirrhosis (ie. irregular liver contour and nodularity) was found in 6/40 (15%); none had evidence of portal hypertension. Median liver stiffness (LSM) by TE was 15.4 kPa (12.1–19.6) and 8.0 kPa (7.0–10.3) ($p = 0.001$) by 2D-SWE. There was a weak but significant correlation between modalities ($r = 0.23$, $p = 0.004$), Fig. 1. The median difference between TE and SWE was 7.3 kPa (3.7–12.1). There was no correlation between time since Fontan and LSM by TE ($r = 0.15$, $p = 0.19$) or 2D-SWE ($r = 0.19$, $p = 0.13$). There was no difference in LSM if sonographic cirrhosis was present or absent by TE (17.4 kPa (15.9–23.6) vs 14.9 kPa (12.0–19.4) respectively, $p = 0.6$) or 2D-SWE (9.0 kPa (2.8–10.5) vs 8.0 kPa (6.7–10.1), $p = 0.46$). There was no correlation between AVV S/D ratio and LSM by TE ($r = 0.16$, $p = 0.18$) or 2D-SWE ($r = 0.02$, $p = 0.45$).
Conclusion: TE and 2D-SWE are poorly correlated. Neither modality is associated with known risk factors for histological liver fibrosis or global Fontan function. Based on these data, the role of elastography in FALD is uncertain.



[OP-0078]

Anaerobe coverage is important for the prognosis of pyogenic liver abscess: A population-based study in Korea

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Objectives: Gram-negative bacteria such as Klebsiella pneumoniae and Escherichia coli are the most common cause of pyogenic liver abscess (PLA). We investigated whether the use of anaerobic-covering antibiotics is essential for the treatment of pyogenic liver abscess.
Materials and Methods: We analyzed the Health Insurance Review and Assessment Service data in Korea between 2007 and 2017. We classified PLA into two groups: a group using antibiotics that inhibited only aerobic strains (anaerobe (-) group) and a group using antibiotics that inhibited both aerobic and anaerobic strains (anaerobe (+) group). The primary outcome was the difference in in-hospital mortality between the two groups.
Results: During this period, a total of 30,690 PLA patients were obtained. There were 6,733 patients in the anaerobe (-) group and 23,957 patients in the anaerobe (+) group. In-hospital mortality was significantly lower in the anaerobe (+) group than the anaerobe (-) group (7.9% vs. 15.6%, $p < 0.001$). In multivariate analysis, the use of anaerobic antibiotics reduced the in-hospital mortality by 42% (odds ratio 0.42, 95% confidence interval 0.38–0.46, $p < 0.001$) after adjusting for age and comorbidities. Furthermore, the improvement of in-hospital mortality was present regardless of the presence of cancer or diabetes.
Conclusion: The use of broad spectrum empirical antibiotics covering anaerobic strains is important for the treatment of pyogenic liver abscess.

[OP-0149]

The relationship between chronic kidney disease stage and liver function in chronic kidney disease patients at the general hospital of Dr. Soedirman Kebumen, Central Java, Indonesia

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Objectives: Chronic kidney disease can lead to hypoxia condition and an increase of oxidative stress in the body. This condition can stimulate liver injury condition. The previous research showed there is a relationship between kidney disease and liver injury called hepatorenal syndrome. This research aims to know the relationship between Chronic Kidney Disease Stage and Liver Function in Chronic Kidney Disease Patients at The General Hospital of Dr. Soedirman Kebumen, Central, Java, Indonesia.
Materials and Methods: This research is using a cross-sectional study method with a total of subjects consisted of 88 patients in The General Hospital of Dr. Soedirman Kebumen from January 2020 until December 2020. Subjects were male and female, aged 17–80 years old who only had a primer diagnosis of chronic kidney disease and had completed medical record data. The data taken were the stage of chronic kidney disease (CKD I, CKD II, CKD III, CKD IV, and CKD V) that is based on WHO diagnostic criteria and the patient's liver enzyme (Serum glutamic oxaloacetic transaminase/SGOT and serum glutamic pyruvic transaminase /SGPT).
Results: There are 32 patients with CKD I and the mean of SGOT/SGPT (U/L) were $24 \pm 1.6/18.8 \pm 2.9$. There are 16 patients with CKD II and the mean of SGOT/SGPT (U/L) was $21.75 \pm 8.83/21.258 \pm 11.67$. There are 16 patients with CKD III and the mean of SGOT/SGPT (U/L) was $83 \pm 16.34/41.258 \pm 11.38$. There are 12 patients with CKD IV and the mean of SGOT/SGPT (U/L) was $61 \pm 15.04/113 \pm 56.50$. There are 12 patients with CKD V and the mean of SGOT/SGPT (U/L) was $351.33 \pm 18.98/114 \pm 47.12$. The result of statistical analysis showed there was a relationship between CKD and liver function (SGOT and SGPT) with a p-value < 0.001.
Conclusion: There is a relationship between CKD stage and liver function that is the sign by decreasing the level of liver enzyme (SGOT/SGPT) with a p-value < 0.001.

[OP-0170]

The impact of portal T cell infiltration on the response of corticosteroid therapy and survival in patients with chronic hepatitis GVHD after allogenic stem cell transplantation

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Objectives: The chronic hepatic GVHD after allogeneic hematopoietic stem cell transplantation has not been studied in detail. In this study, we investigated the impact of histological characteristics of chronic hepatic GVHD on clinical outcomes.
Materials and Methods: Thirty-eight patients with biopsy-confirmed, chronic hepatic GVHD patients were enrolled. Immunohistochemical staining for CD3, CD68, CD38, CD20, and CK19 was performed to identified immune cell types infiltrated in the liver. The primary outcome was biochemical response at 4 weeks (early) and 12 weeks (late) after corticosteroid treatment. Biochemical response was defined as bilirubin normalization + ALP $< 1.5 \times$ ULN + AST $< 1.5 \times$ ULN (Paris-II criteria in PBC was adopted). The secondary outcomes were the overall survival (OS) and liver-related event-free survival (EFS). Liver-related event were defined as liver failure or liver transplantation (LT).
Results: Pathologically, two separate patterns of chronic hepatic GVHD were identified: the hepatitic group (n = 19) and cholestatic group (n = 19). In the hepatitic group, periportal areas demonstrated prominent inflammation with a main population of T cells. In the cholestatic group, dutulitis and ductopenia was predominantly identified. Median ALT was marginally higher in the hepatitic group, although median bilirubin was higher in the cholestatic group. The hepatitic group demonstrated significantly higher early (52.6% vs. 10.5%; P = 0.015, respectively) and late (73.7% vs. 36.8%; P = 0.05, respectively) than the cholestatic group. Moreover, the hepatitic group showed significantly better OS (P = 0.026) and liver-related event EFS (P = 0.036) than the cholestatic group. There was no liver-related event in the hepatitic group, whereas three patients in the cholestatic group died from liver-related event (n = 2, liver failure; n = 1, LT). In patient with LT, the explant showed diffuse necrosis of hepatocytes with extensive CK19 + bile ductules proliferation and fibrosis.
Conclusion: In chronic hepatic GVHD, hepatitic variants with portal T cell infiltration shows better outcomes than cholestatic variants.

[OP-0183]

Diagnostic value of color doppler ultrasonography in diagnosis of hepatic hemangioma

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Objectives: To evaluate the value of color Doppler ultrasound in the diagnosis of hepatic hemangioma.
Materials and Methods: This was a retrospective study on 53 patients with a liver tumor. The sensitivity and specificity of color Doppler ultrasound in the diagnosis of liver hemangioma were determined by comparing with contrast-enhanced computed tomography (CT)/magnetic resonance imaging (MRI) or histopathology.
Results: This study included 49.1% male and 50.9% female, mean age was 54.7 ± 16.9 years. The rate of right liver tumor accounted for the highest rate 67.9%. The number of solitary tumors accounted for a higher rate at 71.7%. Tumor size $\geq$ 4 cm accounted for a higher rate with 58.5%, tumor size $<$ 4 cm was 41.5%. The mean tumor size was 5.1 ± 2.6 cm, the smallest tumor size was 1 cm, the largest tumor was 10.7 cm. The mixed echoic image on ultrasound was most common with 50.9%, the hypoechoic rate was 7.5% and the hyperechoic rate was 41.5%. The sensitivity of color Doppler ultrasound in the diagnosis of a hepatic hemangioma was 42.9%, the specificity was 75.0%, the positive predictive value was 95.5%, the negative predictive value was 9.7%, diagnostic accuracy was 41.5%.
Conclusion: Color Doppler ultrasound is the initial imaging method in the diagnosis of hepatic hemangioma. For a definitive diagnosis, additional methods such as contrast-enhanced CT/MRI or liver biopsy should be performed.

[OP-0250]

Association between serum liver enzymes and cardiovascular diseases: A cross-sectional study in Nepali adults with cardiovascular disease

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Objectives: Cardiovascular diseases (CVDs) are the main leading cause of global morbidity and mortality. Several studies conducted elsewhere have identified that a certain liver enzymes in serum could predict incident CVDs in adults. However, such predictors of incident CVDs have not been explored and verified for Nepali population. Hence, the main objective of this study was to explore the best predictor by determining the association between liver enzymes and CVDs in Nepali adults.
Materials and Methods: This was a hospital-based cross-sectional study conducted among 400 adult subjects (200 healthy controls and 200 CVD patients). Socio-demographic, physiological, and biochemical variables were collected with structured questionnaires and appropriate standardized and validated measurement methods. P-value (two-tailed) < 0.05 was considered statistically significant.
Results: The frequency of smoking ($p < 0.001$) and drinking habits ($p < 0.001$), and mean values of BMI ($p < 0.001$), WHR ($p < 0.001$) and SBP (p = 0.006), AST, ALT, ALP, FBS, HbA1C, CK-MB, troponin-I, TC, and TG were significantly higher in CVDs patients than in healthy controls. The HDL-C, on the other hand, was significantly lower in CVD patients. Only the AST showed significant correlation with the cardiac markers CK-MB and TpI. Logistic regression analysis revealed that AST was the best predictor among others for incident CVDs in the adult population.
Conclusion: Our study verifies that liver enzymes, particularly aminotransferases, are significantly associated with the incident CVD

and thus could potentially be measured together with established cardiac biomarkers for the staging and differential diagnosis of CVDs in Nepali adults.

[PP-0289]

Hypoxic hepatitis: Incidence, biochemical markers, and risk factor of mortality: A cohort study

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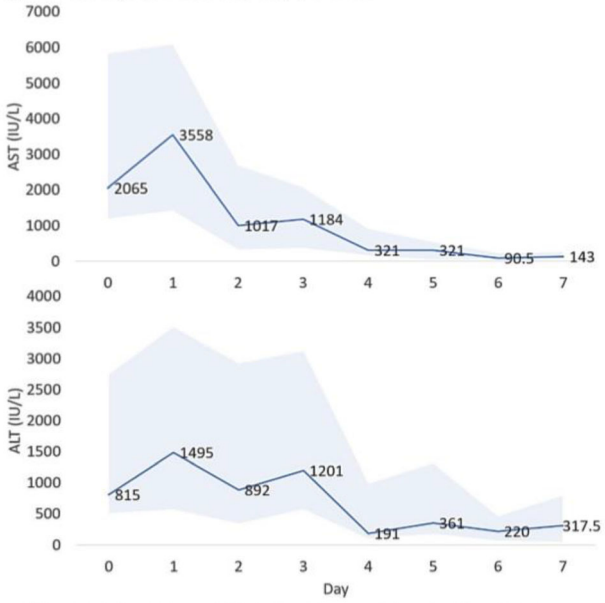
Objectives: Hypoxic hepatitis is an acute severe liver injury, usually associated hemodynamic instability. Diagnosis is usually made by exclusion with clinical setting compatible with hypoxic hepatitis. Prior studies reported the incidence of hypoxic hepatitis in the range of 0.9–2.4% in all admission. There is no specific treatment for hypoxic hepatitis and mortality rate is about 50–70%. This study is aimed to evaluate incidence of hypoxic hepatitis and to study clinical course and outcome of these patients.
Materials and Methods: This study is a retrospective cohort study conducted at Siriraj hospital from October 30, 2019 to January 25, 2021. Data were retrieved from hospital admission chart of the patients who were admitted at Siriraj Hospital from January 1, 2008 to December 31, 2018. Hypoxic hepatitis was defined by the following criteria: serum AST and/or ALT levels of more than or equal to 20 times ULN in the absence of evidence of drug, toxic, or acute viral hepatitis.
Results: Of 4,000 admission, there were 29 cases (0.73%) who met the criteria of hypoxic hepatitis. Mean age was 68.2 years old and median serum AST and ALT levels at the time of diagnosis were 2,065 and 815 IU/L, respectively (Fig. 1). Underlying diseases of these patients included hypertension (69%), diabetes mellitus (48.3%), chronic kidney disease (37.9%), and atrial fibrillation (31%). Comorbidities included acute kidney injury (93.1%), sepsis (79.3%), hypotension (75.9%), requirement of vasopressor (65.5%), acute respiratory failure (55.2%), heart failure (41.4%), unstable arrhythmia (41.4%). Mortality rate at day 28 was 72.4%, none of which was liver related. The only significant risk factor of mortality was lower bicarbonate level ($p = 0.012$).
Conclusion: Hypoxic hepatitis was uncommon with incidence of 0.73% of admission, most patients associated with multiple organ failure and had high mortality rate of 72.4%. The only predictor of high mortality was lower bicarbonate level.

Figure 1. Change of serum AST and ALT levels



* Day 0 defined as the day of serum AST and/or ALT more than 20 times of UNL
* The line and number showed median of serum AST/ALT and the area around the line showed P_{25}-P_{75} of serum AST/ALT

[PP-0370]

Development of a high sensitivity elisa for HDV-AB detection

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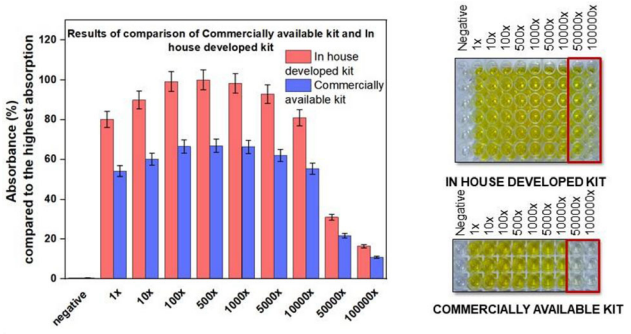
Objectives: Sophisticated diagnostic assays are not well developed for HDV due to very limited prevalence of the virus in most countries in the world. In this study we have developed a high sensitive ELISA for detection of hepatitis delta virus antibody (HDV-Ab) in human serum.
Materials and Methods: Recombinant His-tagged HVD-Ag protein (23 kDa) was produced in E.Coli and subsequently purified by Ni–NTA metal-affinity chromatography. We used self assembled monolayer method, which is considered as much better than the conventional physical absorption method in terms of sensitivity and specificity. First, surface of polystyrene plates were functionalized by treating with sodium hydroxide for binding of APTES, EDC/NHS crosslinking agents. Then HDV-Ag proteins were immobilized on the functionalized surface via the crosslinking agents by self-assembled manner. Using the plates, we performed ELISA by comparing with a commercially available ELISA kit (Beijing Wantai Biological Pharmacy), which is used extensively in Mongolia. HDV infected (HDV-RNA positive) human serum was serially diluted by 1x, 10x, 100x, 500x, 1000x, 5000x, 10000x, 50000x, 100,000 × and applied for analyzing of sensitivity.

Results: The result showed that our in house developed ELISA assay is able to detect HDV-Ab sufficiently at highest dilution rates (50,000 × and 100000x), which is not able to be detected by Wantai kit. This result indicates that ELISA assay developed by cross-linker mediated self assembled monolayer method is apparently good option for HDV-Ab detection. In practice, high rate of dilution of serum sample is not necessary, especially in qualitative purpose. But high dilution of serum sample should be very important for quantitative detection of HDV-Ab, which can be used for RNA positivity prediction and analysis of disease prognosis.
Conclusion: Therefore, simple and cost-effective ELISA microwell plates holds promise in clinical applications.



Name	Negative	1x	10x	100x	500x	1000x	5000x	10000x	50000x	100000x
In house developed kit	0.38	80.11	89.91	99.17	100	98.29	92.82	81.01	31.03	16.45
Commercially available kit	0.44	54.16	60.05	66.49	66.80	66.32	61.95	55.27	21.71	10.93

Absorbance percentage at 450 nm

[PP-0371]

Development of surface plasmon resonance biosensor for detection of HDV antibody

Nomin Ariungerel[1,5], Nomin-Erdene Erdenebat[2], Badmaarag Munkhjin[1], Saruul Enkhjargall[1], Purevjargal Bat-Ulzii[4,5], Sumiya Byambabaatar[4,5], Naranjargal Dashdorj[4,5], Erdene Norov[3], Davaasambuu Jav[2], Odgerel Oidovsambuu[1,5]

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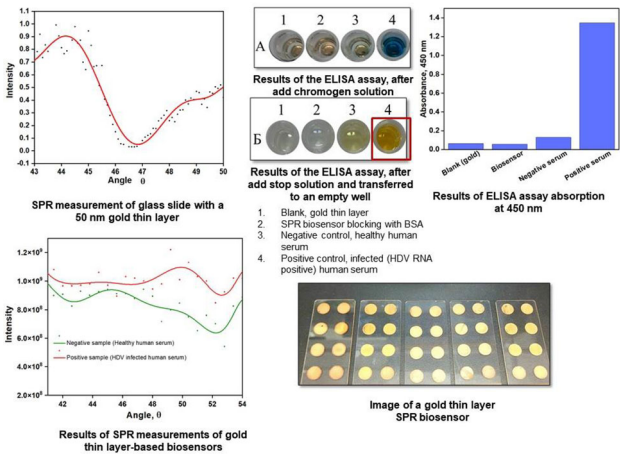
Objectives: HDV prevalence is very limited in most countries, but in Mongolia it is known that the overall prevalence of HBV is 10,62% in adult Mongolian population and about 70% of them are infected with HDV. Serological diagnostic option is limited by only few numbers of ELISA kits and rapid diagnostic tests or full automatic serological tests are not yet developed for this virus. Biosensors using the surface plasmon resonance (SPR) technology are promising for their many advantages high-sensitivity, real-time monitoring availability. In this work, we have developed a biosensor for detection of HDV-antibody using gold thin film and laser detection setup based on Kretschman's configuration.
Materials and Methods: Thin gold films (50 nm) were vapor-deposited onto microcscope slides and the slides were treated by piranha solution for further steps. The detection surface was fabricated by binding chemically to self-assembly monolayer (SAM) of 10 mM ethanolic 11-mercaptoundecanoic acid (MUA) for at least 24 h. We use 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and N-Hydroxysuccinimide (NHS) crosslinkers in this study. The NHS ester was formed via exposure of the MUA SAM to 75 mM EDC and 15 mM NHS for 1 h. MUA–NHS estermonolayers were reacted for 1 h with a solution of HDVAg in carbonate- bicarbonate buffer. The confirmation the activity of the assembling biosensor, colorimetric transformation and absorption intensity were initially measured using the enzyme-linked immunosorbent assay (ELISA) method. The laser inducing SPR instrument was newly set-up using Kretschmann configuration.
Results: Comparative measurements of the positive and negative samples yielded different results of absorption intensity and angular displacement.
Conclusion: This result confirmed that our newly developed SPR based biosensor is able to detect HDV antibody in the human serum sample without any use of probe or conjugate.



[OP-0372]

Spatial analysis of colorectal cancer incidence in West of Iran

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Objectives: Colorectal Cancer (CRC) is ranked the third most common cancer in women and the fourth in men in Iran. Many factors contribute to CRC occurrence, and most of them are interrelated. The present study aimed to explore the spatial pattern of CRC incidence in Hamadan province, Iran.
Materials and Methods: We collected and analyzed data on patients' location, gender, age, and date of diagnosis recorded in the CRC registry between 2007 and 2014 in Hamadan province. The Anselin Local Moran's I statistic was conducted to identify clusters and outliers of CRC distribution.
Results: There were 805 recorded CRC cases in Hamadan province during 2007–2014, with an incidence of 45.89 patients per 100,000 people. Three significant clusters of both high and low incidence rates were found in the study area.
Conclusion: This research demonstrated significant geographical disparities in CRC incidence in Hamadan province. The spatial analysis of CRC incidence pattern generates a new hypothesis on the

effect of location in disease clusters. These findings may shine a light on underlying risk factors in areas where the CRC risk is greater and how contextual factors may play a role in CRC geographic disparity.

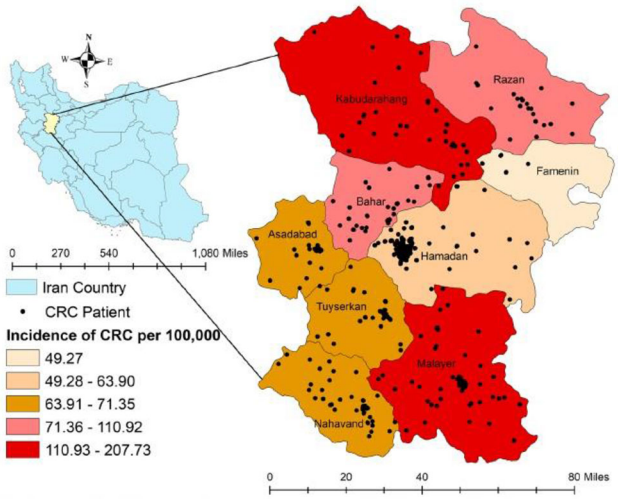

Fig. 1 Geographical distribution of CRC patients at county level in Hamadan Province, Iran

[OP-0390]

Clinical study of pyogenic liver abscess in patients with history of COVID 19

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Objectives: SARS COVID-19 was associated with thrombosis and vascular events, also associated with liver injuries but data and study of liver pathologies in relation to COVID-19 is scarce. The aim of this study was to evaluate the incidence of pyogenic liver abscess in patients with history of COVID-19.
Materials and Methods: A current retrospective observational study is done during study period of 6 months (march 2021- august 2021) duration on patients diagnosed with pyogenic liver abscess on ultrasound or computed tomography, which was conformed with pus culture sensitivity reports from fluid obtained with fine needle aspiration or during pigtail catheter insertion. History of COVID-19 and incidence of pyogenic liver abscess was evaluated according to age, gender, comorbidities, severity of covid19.
Results: Total 78 patients with pyogenic liver abscess History of COVID-19 in 64 patients 27 males, 37 females Age wise distribution $< 20 = 9$,20–40 = 8,40–60 = 22, 60–80 = 19, $> 80 = 6$ 13 patients were diabetics, 24 patients were hypertensive. Distribution according to severity of COVID-19, asymptomatic = 23, mild illness = 11, moderate illness = 19, severe illness = 8, critical illness = 3.
Conclusion: The study concluded that high incidence rate of pyogenic liver abscess in post COVID-19 infection which may require further study.

[PP-0395]

Assessment of knowledge on liver cirrhosis among college students from western region of Nepal

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Objectives: Liver cirrhosis is a chronic progessive condition and common health problem in Nepal. The common risk factors are chronic hepatitis B & C, chronic heavy alcohol use, drug and toxins. Liver cirrhosis is presented with scarr tissue which blocks blood flow through the liver. The aim of study was to assess the knowledge of college students on liver cirrhosis.
Materials and Methods: A total of 450 college students were enrolled in this study. The students of school of health and allied sciences, Pokhara University and Manipal College of Medical Sciences, Pokhara, Nepal were involved in this study. The knowledge was assessed with the help of questionaire and data were analysed using SPSS.
Results: All the participants were of age group between 19–25 years. Most of the participants were female (71.1%) and 28.9% were male. Maximum participants were Hindu and belong to nuclear family. All the participants had good knowledge on definition of liver cirrhosis. The majority of subjects had moderate knowledge on the causes, prognosis, treatment and management of liver cirrhosis. More than half of the participants (58%) had good knowledge on liver cirrhosis while 42% had poor knowledge.
Conclusion: The levels of knowledge on liver cirrhosis were good among the college students. Therefore, it is necessary to increase the knowledge of college students on liver cirrhosis to decrease the cases of liver cirrhosis patients.

[PP-0426]

Study of liver enzyme status among type 2 diabetic patients attending tertiary care hospital, Chitwan, Nepal

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Objectives: To study the status of Liver enzymes in type 2 diabetes patients attending tertiary care hospital, Bharatpur, Chitwan, Nepal.
Materials and Methods: This was cross sectional study conducted at tertiary care hospital, Bharatpur, Chitwan, Nepal. 5 ml of blood samples were collected from all the participants and liver enzymes were measured. Data were analyzed with the help of Statistical Package for Social Service (SPSS) version 16. $p < 0.05$ was considered to be statistically significant.
Results: A total 275 subjects (155 DM and 120 healthy) were included. The age of the diabetic subjects ranges from 27–86 years with a mean of 57.00 ± 12.00 years while Age of Healthy subjects ranges from 31–85 years with the mean of 54.27 ± 12.21. Among the Diabetic population 9.67% had raised AST, 17.42% have raised ALT, 12.94% had raised ALP, and 19.60% had raised GGT. The level of liver enzymes were showed statistically significant ($p < 0.005$).
Conclusion: In this conclude that liver enzymes were increased in patients with diabetic patients.

[PP-0638]

Prognostic implication of elevated transaminases among adult COVID 19 patients

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Objectives: Elevated transaminases has been inconsistently associated with mortality in COVID-19 patients. There may be regional variations because of differences in concomitant liver diseases. We aimed to determine the prognostic implication of elevated transaminases among hospitalized adult COVID-19 patients.
Materials and Methods: Clinical and laboratory parameters were determined from consecutive COVID-19 patients hospitalized in a tertiary hospital in Manila from March 2020 to March 2021. Binary logistic regression analysis was used to determine independent predictors of peak COVID-19 severity and 60-day mortality.
Results: A total of 289 patients were included of which 135 (47%) and 158 (55%) had elevated baseline alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, respectively, with peak ALT at 82.7 IU/mL (7–2,381) and peak AST at 106.5 IU/mL (10–9,826). Concomitant liver disease was very low (1.3%) and was not related to transaminase elevation. Peak COVID-19 severity was: mild (13.1%), moderate (26.6%), severe (43.9%), and critical (16.3%). Baseline and peak ALT, and baseline AST and CRP were independent predictors of peak severe-critical versus mild-moderate disease. The 60-day mortality rate was 12.1% and on univariate analysis was associated with elevated peak AST, older age, presence of co-morbidities, higher COVID-19 severity, elevated inflammatory markers, and the need for more intensive care. Only peak ALT ($p = 0.032$) and peak AST ($p = 0.026$) were independently associated with 60-day mortality.
Conclusion: Elevated liver enzyme levels were associated with worse peak COVID-19 severity and 60-day mortality. However, the association of peak instead of baseline liver enzymes with 60-day mortality highlights the importance of serial enzyme monitoring in hospitalized patients.

[PP-0692]

A case of renal cell carcinoma occurred in a young man with extremely high gamma-glutamyltransferase

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Objectives: Gamma-glutamyltransferase (GGT) is a well-known serum marker for alcohol-related liver disease. In addition, a number of studies have reported that GGT is an early predictive marker for atherosclerosis, heart failure, metabolic disease, and various cancers. In terms of carcinogenesis, several experimental models demonstrated that cellular GGT modulates crucial redox-sensitive functions such as antioxidant/antitoxic defenses and cellular proliferative/apoptotic balance. Also, high GGT level was reported to be significantly associated with increased cancer incidence of digestive organs, respiratory system/intrathoracic organs, and urinary organs. Herein, we report a case of renal cell carcinoma occurred in a young man with markedly elevated GGT.
Materials and Methods: A 30-year-old man was referred to our institution for right renal mass which was detected on health screening exam. On preoperative evaluation, his blood chemistry was normal except strikingly high GGT level (4,200 U/L, normal 10–71 IU/L). He had no liver disease, and denied alcohol drinking or medications. He stated his father and older brother also had very high GGT level.
Results: He underwent right partial nephrectomy and was diagnosed with renal cell carcinoma. After surgery, he has been being followed up for 8 years without recurrence. During follow-up, his serum GGT level has been persistently elevated between 2,000 and 6,466 U/L.
Conclusion: This case implicates that high GGT may play a role in carcinogenesis at young age and need to be paid attention.

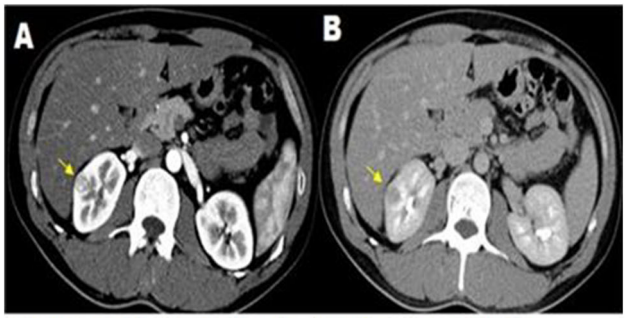

Fig. 1 Computed Tomography showing 1.4cm sized mass (yellow arrow) in the right kidney, arterial (A) and venous (B)phase

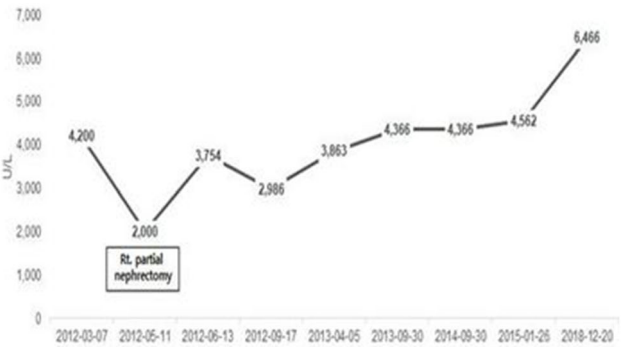

Fig. 2 Change in Gamma-GT during follow up period

[OP-0703]

Covid-19 infection and hepato-biliary surgeries: From diamond princess cruise ship toward the daily routine at the end of 2021

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Objectives: Since the admission of the critically ill American patients from Diamond Princess on February 11, 2020, our hospital has accepted a total of 300 Covid-19 infected patients.
Materials and Methods: On January 29, 2020, we established our own PCR test method based on the SARS-CoV-2 genome data (Hirotsu Y, et al. J Virol Methods. 2020). In the PCR test for screening of all hospitalized patients, the minimum detection limit was determined based on the data of positive sample dilution experiments, and a method for testing multiple samples at once was established using the "Pooling Strategy" (Hirotsu Y, et al. Sci Rep. 2020). To date, the total number of PCR tests performed at our hospital has exceeded 25,832 cases. In addition, we have established a system that allows us to perform antigen/antibody testing and PCR testing at the same time for urgent hospitalization and emergency surgery cases without interfering with the emergency system.
Results: With these systems in place, we have been able to achieve zero nosocomial infections and no staff waiting at home, and have been able to perform surgical operations as usual.
Conclusion: Currently, the Genome Analysis Center has resumed genome analysis of the accumulated liver cancer resection specimens. Panel analysis of hepatocarcinoma-associated mutated genes (72 SMGs) using next-generation sequencers has shown a trend toward early recurrence and poor prognosis after hepatic resection in cases of multinodular hepatocarcinoma that share multiple oncogenic mutations.

[OP-0720]

Abdominal tuberculosis: Diagnosis and antimicrobial susceptibility of mycobacterium tuberculosis in a tertiary care hospital

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Objectives: To determine the yield of various diagnostic modalities and antimicrobial susceptibility in abdominal tuberculosis patients.
Materials and Methods: Cross sectional observational study was employed among 73 adult patients with abdominal TB (Based on positive AFB culture, Gene Xpert, histopathology, ascitic fluid ADA and response to anti TB trial) met selection criteria, attended in GHPD of DMCH from May 2016 to April 2018. Demographic profile, clinical features, family and past history of TB, laboratory & MT test, chest and abdominal imaging results, histopathology, Gene Xpert,acid fast bacilli (AFB) culture(MGIT 960) and DST reports, ascitic fluid analysis including ADA, findings of UGIT endoscopy, colonoscopy, laparotomy, abdominal site involved (Intestinal, Peritoneal and Nodal) were collected by structured questionnaire.
Results: Mean age was 33.90 ± 15.14 years with a range of 18–70 years. Frequent symptoms were weight loss(96.9%), abdominal pain(75%) and fever(75%). Frequent signs were anaemia(34.4%),ascites(27.9%). 8.21% patients had concomitant active PTB. Diagnostic yield were 59.6%,46.3%,13.7% and 94.7% respectively in histopathology, Gene Xpert, AFB culture and ADA in ascitic fluid. Basis of diagnosis were: histolopathogy in 46.3%, Gene Xpert in 26.02%, Positive AFB on culture in 4.7%, ADA value in ascitic fluid in 24.6% and good clinical response to therapeutic trial of anti-TB in 15.06% patients. Predominant site of involvement was intestinal in 64.3%,peritoneal in 24.6%, nodal in 9.5% and splenic abcess in 1.36% patients. Drug sensitivity pattern was analyzed in all three culture positive patients; resistance was detected in one(3.12%) of all patients and 33.33% of the patients in whom sensitivity was done) which showed multidrug resistance (MDR TB).
Conclusion: The study results highlighted diagnostic yield of various investigation modalities including newer modalities(Gene Xpert, culture sensitivity in Bactec MGIT 960) and basis of diagnosis in abdominal TB. This study also determined the MTB culture positivity rate from tissue biopsies and demonstrated drug-resistant MTB in culture confirmed abdominal TB.

[OP-0742]

Relative frequency of acute pancreatitis from dengue outbreaks as a late complication, in Egypt

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Objectives: Patients with dengue virus infection have a different symptoms range from asymptomatic to sever form depending on primary and secondary immune status of host, infecting genotype and patient's age. The current study aimed to describe the clinical and laboratory profile of dengue fever outbreak and acute pancreatitis as a late complication, in Egypt, as two case reports only were available in literature regarding this issue.
Materials and Methods: This prospective cohort study was carried out on 100 patients confirmed to have dengue disease out of 200 clinically suspected patients. Clinical, laboratory (serology for dengue specific IgM, real-time PCR for dengue virus, serum amylase and lipase) and abdominal multi-slice CT were done to all included patients.
Results: All patients presented with fever, headache and fatigue, which are the main clinical manifestations of dengue fever. The mean age of studied patients was 40.34 ± 15.74 years. Thirteen patients (13%), with their mean age 44.57 ± 11.53, presented after 3 months with typical clinical, laboratory and radiological manifestations of acute pancreatitis with positive serum dengue virus IgM, antibodies and negative serum dengue virus PCR.

Conclusion: So, acute pancreatitis as a late complication of dengue fever disease should be keep in mind for its early diagnosis and management, thus minimize the morbidity and mortality from dengue fever.

[OP-0745]

Olfactory disturbances as presenting manifestation among egyptian patients with COVID-19: Possible role of zinc

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Objectives: COVID-19 is a severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2). Deficiency of zinc has been supposed to contribute to loss of smell and taste in COVID-19 patients. Our study aimed to assess the serum zinc levels among patients with COVID-19 of various severities, with and without olfaction dysfunction, and to evaluate the effect of zinc therapy in recovery of smell dysfunction among such patients.
Materials and Methods: This study included 134 patients; real-time reverse transcription-polymerase chain reaction (rRT-PCR) proved SARS-CoV-2. Serum zinc levels were measured for all infected patients. One hundred and five patients were detected to have anosmia and/or hyposmia and were categorized randomly into 2 groups; the first group included 49 patients who received zinc therapy and the second group included 56 patients who did not received zinc. All patients were followed up for the recovery duration of olfactory and gustatory symptoms and duration of complete recovery of COVID-19.
Results: Olfactory dysfunction was reported in 105 patients (78.4%). Serum zinc levels were not significantly different between the patient subgroups regarding disease severity or the presence or absence of olfactory and/or gustatory dysfunction (p ? 0.05). The median duration of recovery of gustatory and/or olfactory function was significantly shorter among patients who received zinc therapy than those who did not received zinc ($p < 0.001$), while the median duration of complete recovery from COVID-19 was not significantly different among the two groups (p ? 0.05).
Conclusion: Although the zinc status of COVID-19 patients did not exhibit a significant role in development of anosmia and/or hyposmia or disease severity, zinc therapy may have a significant role in shortening the duration of smell recovery in those patients without affecting the total recovery duration from COVID-19.

[PP-0755]

A newly diagnosed Budd-Chiari Syndrome with thrombotic thrombocytopenia after BTN162b2 vaccination

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Objectives: Worldwide, Pfizer/BioNTech (BTN162b2) mRNA vaccine is now under massive use to be protected from COVID-19, although it may cause thrombotic thrombocytopenia in rare cases. Budd-Chiari syndrome (BCS) is a rare condition and is defined as the obstruction of hepatic venous outflow.
Materials and Methods: A 34-year-old woman who was vaccinated with first dose of BTN162b2 6 weeks ago newly developed ascites, liver dysfunction, and thrombocytopenia.
Results: Contrast-enhanced CT scan, doppler ultrasound, and hepatic venography showed complete obstruction of three major hepatic veins without membranous structure and without any collaterals, causing portal hypertension and liver dysfunction. Percutaneous liver biopsy showed diffusion dilation of sinusoids with extensive hepatocyte dropout, although there was no portal inflammation or fibrosis. The patient was treated with anticoagulants and intravenous immunoglobulin. After 6 weeks of anticoagulation, hepatic venous outflow became well detectable by doppler ultrasonography and ascites disappeared.
Conclusion: This is a rare case of acute BCS with thrombotic thrombocytopenia after BNT162b2 mRNA vaccination.

[OP-0849]

Landscape of cell death pathways in ballooned hepatocytes: Finding from bioinformatic analysis

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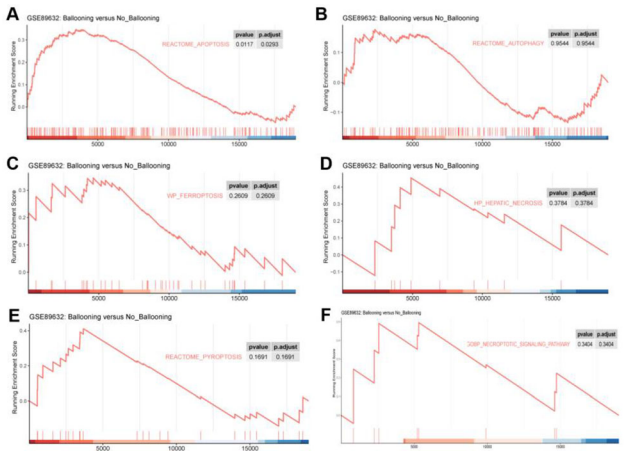
Objectives: Nonalcoholic steatohepatitis (NASH) is the severe form of nonalcoholic fatty liver disease (NAFLD). Hepatocellular ballooning is an important hallmark of NASH, characterized by substantial accumulation of fat droplets, dilation of the endoplasmic reticulum, and injury to the cytoskeleton. However, the cell death pathways of ballooned hepatocytes remain unclear. Therefore, we performed bioinformatics analyses to get further insight into the underlying pathophysiological alterations in ballooned hepatocytes.
Materials and Methods: We used open-source dataset (GSE89632) of biopsy-proven NAFLD patients. Bioinformatic analyses such as gene set enrichment analysis were all performed.
Results: Among 38 patients with NAFLD, 19 patients were defined as NASH (coexisting of significant steatosis, lobar inflammation and hepatocellular ballooning). By gene set enrichment analysis of the six cell death pathways, we observed that hepatocellular ballooning was only significantly associated with increased apoptosis ($p = 0.012$), but not necroptosis, autophagy, ferroptosis, pyroptosis, and necrosis. In

terms of subcellular alterations, pathway of apoptotic mitochondrial changes was significantly activated (p = 0.005). In addition, GSEA-based gene expression similarity score of apoptosis pathway was increased with lobular inflammation (R = 0.38; p = 0.019) and NAFLD activity score (R = 0.37; p = 0.023), whereas it was not associated with liver fibrosis (R = 0.12; p = 0.48). Finally, five B-cell lymphoma (BCL) inhibitors (gossypol, ABT-737, navitoclax, TW-37, and obatoclax) were predicted by Connectivity Map to inhibit cell apoptosis in ballooned hepatocytes.
Conclusion: These results suggest that apoptosis might be the predominant mode of cell death in ballooned hepatocytes. Considering that at least 2 points of NAFLD activity score reduction with at least 1-point from hepatocellular ballooning is one of the essential endpoints for phase 2b trials of NASH, BCL inhibitors might be an attractive option to achieve superior efficacy on resolution of NASH.



[PP-0898]

Vitamin D deficiency in chronic liver disease patients

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Corresponding author: Bayarjargal Altankhuyag, Internal Medicine, Dornod Medical Center, Choibalsan, Mongolia

Objectives: One of the most nutritional deficiency in the world is the deficiency of 25-hydroxyvitamin D [25(OH)D]. Study assessed that there are more than 1 billion people living in the world that has serum 25(OH)D < 20 ng/ml deficiency. Vitamin D deficiency is widespread in individuals irrespective of their age, gender, race and geography. Deficiency of 25(OH)D not only causes children's arthritis but to a range of common chronic diseases in adulthood such as diabetes, cancer, infectious diseases, cardiovascular disease, and autoimmune disease, this continuous to be a major public health problem in the world.
Materials and Methods: Study participants were 204 chronic liver disease over the age of 18 from the citizens of "Choibalsan" city, "Dornod" province, who were referred to the outpatient of Dornod Medical center, Dornod, Mongolia. Overnight fasting blood samples were collected. All patients had tests for blood 25(OH)D were measured by ELISA and 56 patients who took 6 questionnaire tests.
Results: Of all patients, 132 were men (68.1%) and 68 were women (31.9%). The mean age was 49 (between 18 and 89 years). There were 110 patients with cirrhosis (54%), and were 94 patients with chronic hepatitis B and C in the study group. 188 (92%) participants had 25(OH)D < 20 ng/ml deficiency. Age and season had no correlation on the 25(OH)D level. From the results of the questionnaire test we can see that 5 have efficient 25(OH)D, 34 had the possibility of deficiency of 25(OH)D, and 12 had to reapply for the tests but these participants had 25(OH)D < 10 ng/ml and this has no relevance on the level 25(OH)D (Pearson r = 0.07, p = 0.5).
Conclusion: In conclusion, our pilot results show that patients as in 92% have 25(OH)D deficiency.

[PP-0901]

Oral administration of hydrolyzed casein based supplements on chronic liver disease patients

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Objectives: Medical conditions that may lead to malnutrition include: gastrointestinal disease, chronic kidney disease, cardiovascular disease, after surgery and infections such as cancer. Malnutrition—hypoalbuminemia can present edema, appetite loss, muscle weakness, ascites, plural effusion and several other complications. Regardless of its cause, hypoalbuminemia has strong predictive value on mortality and morbidity.
Materials and Methods: Thirty adult patients with liver cirrhosis Child Pugh classification B and C were referred to the outpatient of NB clinic Choibalsan, Mongolia. Hydrolyzed Casein Based Supplements is a breakthrough nutritional formulation that is specially formulated with hydrolyzed casein and calcium 198 mg, potassium 270 mg etc. For patients, we dissolved Hydrolyzed Casein Based Supplements (55 g) into 210 ml of warm water to prepare a 250 ml drink during the period of 30 days. Before and after the treatment, overnight fasting blood samples were collected. All patients had tests for blood chemistries ALT (0–45 u/l), AST (0–35 u/l), total protein (66.0–83.0 g/l), albumin (35.0–50.0 g/l), potassium (3–3.5 mg/dl), calcium (8.5–10.2 mg/dl), and abdominal ultrasound.
Results: Oral supplement had significantly increased total level of protein from 70,34 ± 6.8 to 75.25 ± 6.2 ($P < 7.1*10^{-16}$), albumin from 33.38 ± 4.61 to 38.37 ± 4.62 ($P < 4.6*10^{-11}$), potassium from 3.5 ± 1.0 to 4.7 ± 0.7 ($P < 1.631*10^{-08}$), calcium from 8 ± 1.1 to 9.2 ± 1.6 (0.007). Eight patients had ascites, and after oral supplement, in two cases ascites were removed, in four case sascites fluid were decreased, and in two cases they were not increased.
Conclusion: In conclusion, specially formulated with hydrolyzed casein supplement is safe and effective in improving serum protein, albumin, potassium, calcium in patients with liver cirrhosis.

[OP-0965]

Prevalence of chronic hepatitis virus infection in depressive disorder: A population-based study

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Objectives: To estimate the prevalence of hepatitis B, hepatitis C, and hepatitis D virus infection in depressive adults in the United States.
Materials and Methods: From the US Center for Disease Control's National Health and Nutrition Examination Survey, we obtained data about depression status, exposure to hepatitis B, hepatitis C, and hepatitis D in the institutionalized civilian population between 1999 to 2018. Data were weighted according to the age–sex–residence distribution data from census population survey to adjust for differential probabilities of selection and differential response, as well as to post-stratify the sample to match the population distribution. The data were entered into Python and analyzed by the statistical package.
Results: Of the 43,052 institutionalized civilian aged $\geq$ 18 years old enrolled in the study, 38,476 (89.4%) completed the Composite International Diagnostic Interview Version2.1(CIDI-Auto2.1) or Patient Health Questionnaire-9 (PHQ-9). The weighted prevalence of chronic hepatitis virus infectious diseases including hepatitis B surface antigen (HBsAg) positive、hepatitis C RNA positive or hepatitis delta virus antibodies(anti-HDV) positive in depressive patients was 3.1% (95% CI 2.5–3.7%), compared with 1.1% (95% CI 1.0–1.2%) in non-depressive adults. HBsAg positive were reported for 0.6% (95% CI 0.3–0.9%) of depressive adults, hepatitis C RNA positive for 5.6% (95% CI 4.4–6.8%), and anti-HDV positive for 0.1% (95% CI 0.1–0.2%). Population fractions of HBsAg positive, hepatitis C RNA positive, and anti-HDV positive in non-depressive adults were 0.4% (95% CI 0.3–0.5%)、1.9% (95% CI 1.7–2.1%)、0.1% (95% CI 0.0–0.1%), respectively.
Conclusion: The likelihood of chronic hepatitis virus infection was greater among depressive patients than patients without depressive disorders. Efforts on multiple fronts are needed to combat the symptoms of depression in patients with current hepatitis virus infection, including increasing capacity for and access to testing, mental health service, and cure.

[OP-0969]

Diagnostic value of fecal calprotectin and serum MMP-9 in diagnosing disease activity of ulcerative colitis

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Objectives: Ulcerative colitis (UC) is a chronic, idiopathic inflammatory bowel disease characterized by remission of disease activity. Searching for laboratory markers which are simple, sensitive, specific an non-invasive is fundamental to assess the extent of inflammation, activity of the disease, evolution and prognosis which can be used to assess response to treatment and the possibility of relapse. Our aim of the work was to investigate the diagnostic role of fecal calprotectin and serum MMP-9 in determining the activity of ulcerative colitis.
Materials and Methods: 71 patients were included in the study and fecal calprotectin, serum MMP-9, ESR and CRP were measured in these patients to determine the disease activity of ulcerative colitis.
Results: Fecal calprotectin concentration in the patients with active UC was significantly higher than that in inactive disease and in controls (387.21 ± 44.07 μg/g vs 103.62 ± 119.67 μg/g, 12.44 ± 3.65 μg/g, $p = 0.000$). Serum MMP-9 was found to be higher in patients with active UC than in patients with inactive disease (11.02 ± 5.29 vs 4.01 ± 1.72 ng/ml, $p = 0.000$). A significant difference was also found in the patients with active UC of mild, moderate and severe degrees. Also, strong positive correlation was found between fecal calprotectin and serum MMP-9 and the severity of the disease. The area under the curve of the receiver operating characteristics (AUCROC) was 0.949 and 0.941 for fecal calprotectin and serum MMP-9 respectively.
Conclusion: Fecal calprotectin and serum MMP-9 can be used to differentiate between active and inactive forms of UC.

[OP-1023]

Analysis of serum bilirubin changes pattern after endoscopic retrograde cholangiopancreatography drainage in patients with chronic liver disease

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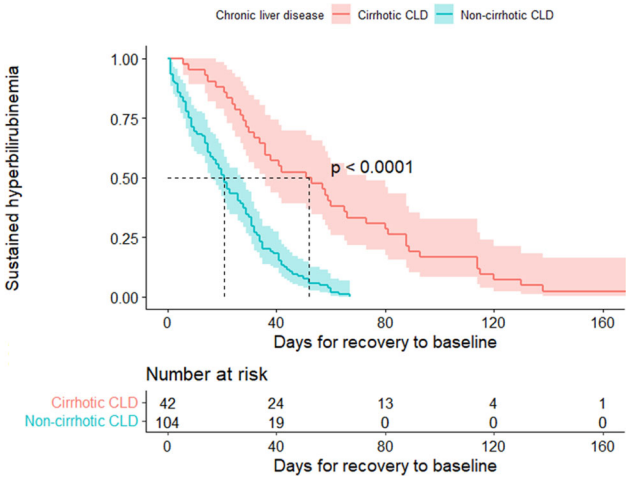
Objectives: When following up on serum bilirubin after ERCP, most ERCP doctors are aware of the fact that bilirubin in patients with chronic liver disease does not improve well, but there is a lack of research on how much it is. This study aimed to evaluate a pattern of serum bilirubin after bile drainage with ERCP in patients with chronic liver disease.
Materials and Methods: In a single tertiary center, 726 patients with or without chronic liver disease, divided by propensity score matching, who underwent ERCP were enrolled in a retrospective analysis. We recorded the serum bilirubin change after the ERCP procedure with drainage and analyze the pattern of serum bilirubin. First, patients were divided into groups with or without chronic liver disease groups and further analyzed depending on whether the chronic liver disease group had cirrhosis or not.
Results: 480 patients without chronic liver disease showed a higher ratio of normalized serum bilirubin compared to 246 patients with chronic liver disease (376/387, 97.16% vs. 120/193, 62.18%, $p < 0.001$). The non-chronic liver disease group showed a lower crescendo-decrescendo pattern of serum bilirubin than the chronic liver disease group (88/480, 18.33% vs. 120/246, 48.78%, $p < 0.001$), and bilirubin improved earlier in the crescendo-decrescendo pattern (1.48 ± 0.79 days vs. 5.48 ± 4.75 days, $p < 0.001$). Subgroup analysis to compare between non-cirrhotic and cirrhotic groups of chronic liver disease patients revealed differences in days for recovery to baseline serum bilirubin, showing delay in the cirrhotic group (23.20 ± 16.77 days vs. 59.21 ± 39.75 days, $p < 0.001$).
Conclusion: This study provides additional information about the slowness to improve on the post-ERCP serum bilirubin conducted to assess the successfulness of ERCP drainage in patients with chronic liver diseases.



[OP-1026]

Liver function test pattern as a means for predicting Covid-19 pneumonia related severity

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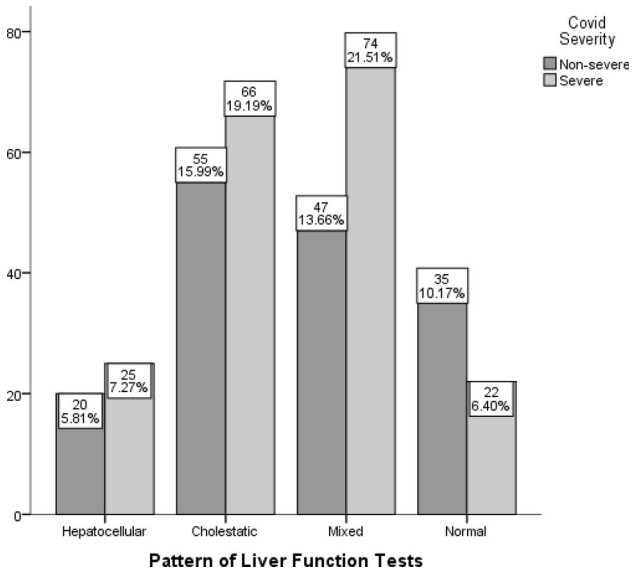
Objectives: After being declared a pandemic, SARS CoV-2 causing Covid-19 pneumonia has been rampant in affecting the world population and causing heightened morbidity & mortality across all age groups. SARS CoV-2 was found to affect many organs systems of the human body, from lungs to brain, kidneys, coagulation system & also involving gastrointestinal system & liver respectively. It exerts effects on the liver via complex incompletely understood processes including, directly utilizing ACE- II receptors & mitochondrial protein complexes and indirectly via exaggerating the immune response via cytokine storm and drug effects, to include a few. We have conducted our research to see the prevalence of liver function (LFT).
derangement, its pattern of derangement, and the association of LFT pattern to the severity of.

Covid-19 pneumonia.

Materials and Methods: A retrospective, consecutive data analysis was conducted at Dow University hospital & OICD. All patients above 18 years of age with positive rRT-PCR on the nasal swab for Covid-19, admitted at our institute were enrolled after excluding patients with previous liver disease. Patients' demographic, co-morbidities, addictions, laboratory, and baseline data were collected from electronic & paper records. The severity of Covid-19 was defined by WHO protocols.

Results: Mixed and cholestatic pattern of liver function derangement is prevalent in patients with Covid-19 pneumonia, whereas mixed pattern derangement of LFT is associated with the development of Severe Covid-19 pneumonia along with higher age of patient population and presence of hypertension are risk factors for developing severe covid-9 pneumonia. However, individually deranged AST is statistically associated with the development of severe covid-19.
pneumonia.

Conclusion: Liver function derangement seems to be an integral part of widespread abnormalities occurring in Covid-19 pneumonia affected patients, which ought to be overlooked. Moreover, mixed pattern derangement with raised AST levels may aid in identifying patients needing watchful monitoring till the disease subsides.



[OP-1029]

Frequency & severity of atrophic gastritis in patients undergoing gastroscopy for dyspepsia as assessed by Olga

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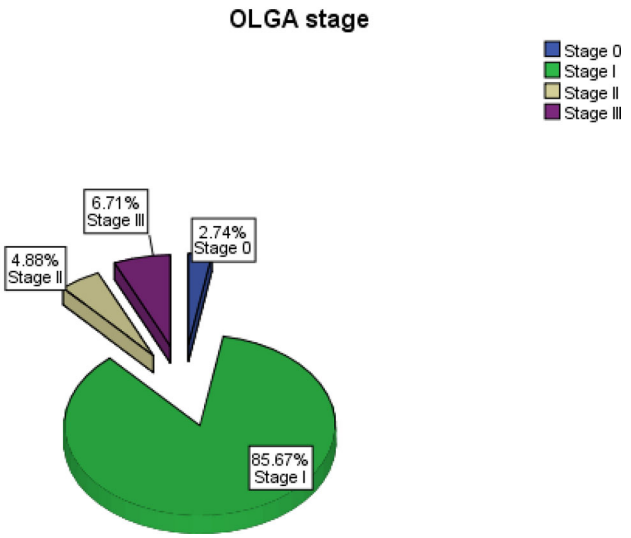
Objectives: The third most common cancer-related death is caused by gastric cancer (GC). Atrophic gastritis plays a vital role in the development of early gastric cancer (EGC), that's why it has been called the field of cancerization in literature. OLGA staging reports gastric atrophy based on five stages.
with the lowest risk in OLGA stage 0/I/II with the highest risk of development of EGC in OLGA stages III/IV. Hence we have conducted our research to see the frequency of atrophic gastritis and its severity based on the OLGA staging system in our population presenting with dyspepsia which is a common presenting symptom of patients with GC.

Materials and Methods: Total 328 patients with dyspepsia were enrolled. Biopsy samples from all patients were taken from the gastric body and gastric antrum (including incisura angularis) in two containers & histology was reported as per the OLGA staging system. Data were analyzed and descriptive statistics were calculated. Effect modifiers were controlled through stratification. The post- stratification chi-square test was applied. P-value ≤ 0.05 was considered significant.

Results: The mean age of the patient population was 37.59 ± 13.92, with predominantly females (n = 55.2%) than male counterparts

(n = 44.8%), 32.9% had previously been treated for H. pylori infection. Out of 328 patients, 97.3% had atrophic gastritis with 85.7% having a milder form of the severity of atrophic gastritis & corresponding OLGA stage I. Around 6.7% of patients had OLGA stage III atrophic gastritis. We found a significant association of atrophic gastritis & its severity with the duration of PPI use, previous H. pylori eradication & OLGA stage.
Conclusion: 6.7% of the study population had OLGA stage III atrophic gastritis and should be surveyed for development of EGC.



[PP-1050]

Autophagy increases collagen degradation in activated hepatic stellate cells

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Objectives: Hepatic stellate cells (HSCs) are the major players during liver fibrogenesis. Upon liver injury, normally quiescent HSCs become activated, into contractile and proliferative myofibroblast like cells, that are responsible for secreting much of the collagen that characterizes liver fibrosis. Autophagy is an intracellular metabolic process that degrades and recycles its own components to maintain homeostasis and supply substrates. In this study, we investigated the effects of autophagy on collagen degradation in activated HSCs.
Materials and Methods: We isolated and cultured mouse primary hepatic stellate cells and activated human hepatic stellate cell line (LX2). We used MG132, Rapamycin, carbamazepine as an autophagy activator. Collagen mRNA expression were measured by Real Time RT-PCR analysis. The expression levels of collagen, LC3, p62, p-smad3 and p-ERK were evaluated by western blot analysis.
Results: To determine whether autophagy regulates collagen levels in activated HSCs. Treatment with autophagy activator decreased collagen expression in primary hepatic stellate cells. Consistently, autophagy activator reduced collagen expression in LX2 cells without altering collagen mRNA. There was no change in the expression of p-smad3 or p-ERK by autophagy activator.
Conclusion: Our results showed that autophagy induction reduced collagen expression in activated HSCs. It also indicates that the decrease in collagen expression by autophagy is due to autophagy degradation independent of other pathways.

[PP-1052]

Lobeglitazone inhibits hepatic fibrosis through inhibition of inflammatory pathway

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is a liver manifestation of metabolic syndrome, and it is a disease accompanied by steatohepatitis due to hepatocyte damage and liver fibrosis due to a long-term inflammatory response. Lobeglitazone, activator of PPAR-γ is known to improve steatosis, inhibited renal fibrosis and ameliorated inflammation of white adipocytes. However, much less is known about whether Lobeglitazone inhibits the progression from liver inflammation to fibrosis. Therefore, this study aims to investigate whether there is a protective effect against liver inflammation and fibrosis.
Materials and Methods: To study the liver inflammation effect of lobeglitazone, we used a mouse (C57BL/6) primary Kupffer cell and primary hepatocyte. We induced inflammation using lipopolysaccharide (LPS), gut derived bacterial endotoxin and fibrosis using transforming growth factor (TGF)-β. Pro-inflammatory cytokine expressions were measured by Real Time RT-PCR analysis and ELISA. The expression levels of CTGF and p-smad3 were evaluated by western blot analysis.
Results: Lobeglitazone decreased LPS-stimulated induced expression and production of iNOS, IL-1β and TNFα in primary Kupffer cell and primary hepatocyte. In addition, lobeglitazone decreased LPS-stimulated TGFβ. Lobeglitazone decreased TGF-β induced CTGF and PAI-1 expression and phosphorylation of Smad3.
Conclusion: In conclusion, lobeglitazone has protective effect on hepatic fibrosis through inhibition of inflammation pathway and the smad pathway.

[PP-1061]

Effect of virtual education of abdominal ultrasonography for internal medicine resident in COVID-19 era; Multi-center analysis

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Objectives: The aim of this study was to compare the effect of online education of abdominal ultrasonography(USG) with off-line

education and evaluate the effectiveness of one-time abdominal USG education for internal medicine resident and gastroenterology fellow.
Materials and Methods: A 25-min lecture on the upper abdomen was carried out online or off-line, and a test with 38 short-answer question was conducted before and after the lecture. Then, theses scores were analyzed for each education method and participant group.
Results: A total of 48 physicians were included in this study. The study population included 25 physicians (13 internal medicine residents and 12 gastroenterology fellow) with online-education and 23 physicians (20 internal medicine residents and 3 gastroenterology fellow) with off-line education. The mean of pretest score in on-line and off-line education group was 16.7 ± 8.6 and 7.3 ± 6.1, respectively (P = 0.003). The rate of USG experience in on-line and off-line education was 52% and 8.7%, respectively (P < 0.001). However, there was a significant increase of test score after one-time USG education regardless in all internal resident group and gastroenterology fellow with on-line education (P < 0.0001, < 0.0001, and 0.0035, respectively). In addition, there was no significance difference in delta-score after education between two groups (7.8 ± 3.7 vs 8.8 ± 4.3, respectively; P = 0.406). In addition, on comparison of the score in internal medicine resident and gastroenterology fellow in online and off-line education group, there was no significant difference in delta-score after education, respectively (8.3 ± 3.6 vs 7.3 ± 3.8, P = 0.485; 9.0 ± 4.5 vs 7.3 ± 3.0, P = 0.537).
Conclusion: The effectiveness of online USG education may not be inferior to off-line education. Additionally, the short-term effect of basic ultrasound education seems to be significantly observed in both the internal medicine resident and gastroenterology fellow group. Besides, there was no significant difference between the two groups.

[PP-1097]

Protein phosphatase 2 regulatory subunit B''Alpha silencing inhibits tumor cell proliferation in liver cancer

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Objectives: Liver cancer ranks sixth among the most common cancers worldwide, with more than 850 000 new cases diagnosed each year, at a ratio of about five males to one female.1 It is the fourth leading cause of cancer?related mortality in the world,2 and the annual mortality rate in China is as high as 55%0.3 Hepatocellular carcinoma (HCC) is the most common primary malignancy in the liver, accounting for 85%–90% of primary liver cancer cases. The oncogenic alterations of gene function, due to gene mutations (such as in TERT, TP53, and CTNNB1), epigenetic changes, or altered transcriptional regulation can lead to the tumorigenesis of liver cancer and therefore represent potential drug targets for cancer therapy.
Materials and Methods: Liver cancer specimens were collected at the General Hospital of Chinese People's Armed Police Forces. All cases were histologically confirmed to be primary HCC. This study was approved by the Ethics Committee of the General Hospital of the Chinese People's Armed Police Force. All procedures involving human participants were performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.
Results: To explore the potential role of PPP2R3A in liver cancer, we examined the expression of PPP2R3A via immunohistochemical staining in eight liver cancer tissue specimens from HCC patients. Positive PPP2R3A expression was found in HCC cells in six of eight specimens, while negative or very low level PPP2R3A expression was observed in the liver cells in the adjacent paratumor tissues (Figure (Figure 1A,B).1A,B). In these cancerous lesions stained with the antiPPP2R3A antibody, a diffuse and strong pattern was observed in four specimens, and a partial pattern in two specimens. In addition,
Conclusion: PPP2R3A may play a role in liver cancer via the regulation of tumor cell proliferation and invasion.

[OP-1112]

Evaluation of prognostic markers in patient infected with SARS-CoV-2

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Objectives: Prognostic markers used to measure the disease progression and patient outcome regardless of treatment in COVID-19. We aim to analyze and evaluate the prognostic markers for early identification of severe patients.
Materials and Methods: During a 3-month period (November 2020 to January 2021), a total of 165 patients attending Sukraraj Tropical and Infectious Disease Hospital with laboratory-confirmed COVID-19 were enrolled and divided into non-severe and severe groups. The demographic data, underlying co-morbidities and laboratory findings were analyzed. Correlation, Regression analysis and ROC curve was performed to determine the risk factors and cut-off values for critically ill patients were speculated.
Results: Disease severity was significantly associated with age (r = 0.359, p < 0.001), RBC (r = -0.163, p = 0.037), AEC (r = -0.300, p < 0.001), ALC (r = -0.239, p < 0.001), ANC (r = 0.228, p < 0.001), NLR (r = 0.336, p < 0.001), PLR (r = 0.286, p < 0.001), glucose (r = 0.155, p = 0.046), urea (r = 0.282, p < 0.001), creatinine (r = 0.194, p = 0.012), AST (r = 0.169, p = 0.030), ferritin (r = 0.359, p < 0.001) and CRP. Whereas Increasing age (AOR = 3.611), positive CRP (AOR = 2.930), high ferritin (AOR = 2.754), decreased AEC (AOR = 3.415) was found to be independent risk factors for COVID-19 severity. Similarly, ROC (Receiver Operating Characteristics) curve analysis showed age (AUC = 0.724), NLR (AUC = 0.710), PLR (AUC = 0.678), ferritin (AUC = 0.735), AEC (AUC = 0.661) can be used to monitor the disease severity.
Conclusion: Our study revealed severe COVID-19 is associated with increased markers of innate immune response such as neutrophil count, NLR, CRP and serum ferritin; decreased markers of adaptive immune response such as lymphocyte and increased markers of major organ damage including AST, urea, and creatinine compared to COVID-19.

[OP-1124]

Clinical application of liver biopsy in the era of non-invasive techniques: A retrospective, multi-center study

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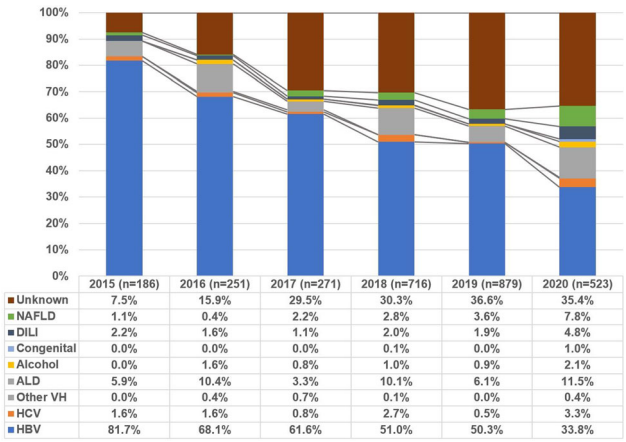
Objectives: Liver biopsy (LB) is widely used to help clarify diagnosis, determine severity and predict prognosis in patients with liver diseases. However, the indications for LB have changed with the development of non-invasive assessments including imaging modalities and serological tests. We aimed to evaluate the changing trend of LB indications.
Materials and Methods: This retrospective, multi-center study collected clinical data of 2,826 patients who had undergone ultrasonic-guided percutaneous LB in four hospitals from 2015 to 2020.
Results: The distribution of indications for LB were as follows: 52.2% of hepatitis B virus (HBV) infection, 30.4% of unknown etiology, 8.2% of autoimmune liver diseases (ALD), 3.6% of non-alcoholic fatty liver disease (NAFLD), 2.4% of drug-induced liver disease (DILI), 1.7% of hepatitis C, 1.1% of alcoholic fatty liver disease (AFLD), 0.2% congenital liver diseases, and 0.2% other viral hepatitis. Over time, the proportions of LB for HBV-infected patients decreased significantly from 81.7% to 33.8%, while the proportions of unknown etiology (from 7.5% to 35.4%) and NAFLD (from 1.1% to 7.8%) increased from 2015 to 2020. In patients with liver diseases of unknown etiology, 62.8% of patients were definitively diagnosed. ALD (28.1%) was the most common etiology, followed by NAFLD (15.0%) and DILI (11.8%), while the etiologies of 37.2% patients remained unclear after LB.
Conclusion: The indication of LB for HBV-infected patients decreased dramatically, while liver diseases of unknown etiology has gradually become the main indication of LB. There are still a substantial proportions of liver diseases can not be definitively diagnosed after LB.



	2015 (n=186)	2016 (n=251)	2017 (n=271)	2018 (n=716)	2019 (n=879)	2020 (n=523)
Unknown	7.5%	15.9%	29.5%	30.3%	36.6%	35.4%
NAFLD	1.1%	0.4%	2.2%	2.8%	3.6%	7.8%
DILI	2.2%	1.6%	1.1%	2.0%	1.9%	4.8%
Congenital	0.0%	0.0%	0.0%	0.1%	0.0%	1.0%
Alcohol	0.0%	1.6%	0.8%	1.0%	0.9%	2.1%
ALD	5.9%	10.4%	3.3%	10.1%	6.1%	11.5%
Other VH	0.0%	0.4%	0.7%	0.1%	0.0%	0.4%
HCV	1.6%	1.6%	0.8%	2.7%	0.5%	3.3%
HBV	81.7%	68.1%	61.6%	51.0%	50.3%	33.8%

[PP-1140]

The chronological changes in the seroprevalence of IgG anti-hepatitis A virus from 2005 to 2019: Experience at four centers in capital area of South Korea

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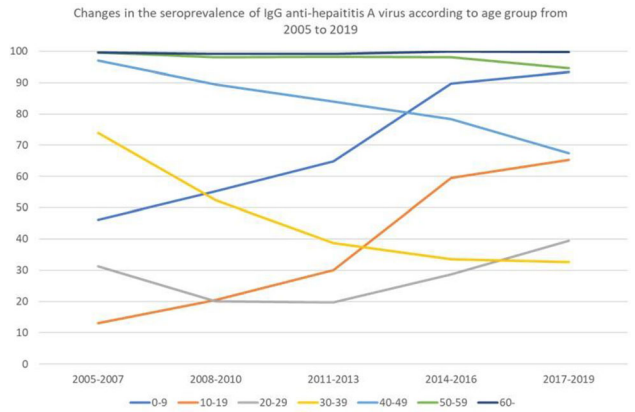
Objectives: Although universal vaccination has been performed, there have been periodic nationwide outbreaks of acute hepatitis A in South Korea since late 2000s. We examined the changes in the chronological changes in the seroprevalence of IgG anti-hepatitis A virus (HAV) over the past 15 years (2005–2019).
Materials and Methods: We collected retrospectively 45,632 subjects who underwent IgG anti-HAV without evidence of HAV infection at four centers in capital area of South Korea between January 2005 and December 2019. The seroprevalence of IgG anti-HAV was analyzed according to age and compared among 7 age groups and among the following 5 time periods: 2005–2007, 2008–2010, 2011–2013, 2014–2016 and 2017–2019. The chi-square test for trend was used for statistical analysis.
Results: The mean age of the enrolled subjects was 39.2 ± 19.2 years and the male-to-female ratio was 1:0.71. During the 15 years period, the seroprevalence of HAV in people aged 0–19 years significantly increased over time ($P < 0.001$). In those aged 20–29 years, the seroprevalence was slightly decreased to that of the early 2010s (31.3% in 2005–2007 to 19.7% in 2011–2013), but it rebounded to 39.5% in 2017–2019. On the other hand, the

seroprevalence of HAV in those aged 30–49 years decreased over time ($P < 0.001$). However, seroprevalence of HAV in those aged 20–39 years in 2017–2019 was still less than 40% (39.5% in those aged 20–29 years and 32.6% in those aged 30–39 years, respectively). Also, the seroprevalence of HAV in those 50–59 years has recently begun to decrease.
Conclusion: Since the introduction of universal vaccination, the seroprevalence of HAV in children and young adults has gradually increased. However, the seroprevalence of HAV in their 20 s was still low and the seroprevalence of HAV in their 30 s and 40 s was gradually decreasing. Therefore, a new strategy for HAV vaccination is needed for adults in their 20 s to 40 s.



[OP-1149]

Engaging, educating, enabling and empowering the clinicians towards liver diseases: A comprehensive training program

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Objectives: Chronic liver diseases (CLDs) accounts for significant morbidity and mortality throughout the world. It is important to empower the clinicians for better management of liver disease patients. A comprehensive program on liver diseases was conceptualised under ILBS-ECHO (Institute of Liver and Biliary Sciences—Extension for Community Healthcare Outcomes). The present study aims at assessing the advancement in knowledge of the clinicians related to liver diseases after attending 6-months virtual training program.
Materials and Methods: A 6-month training program titled 'Liver & Infections' was designed for physicians practicing across India. A total of 69 questions distributed across 8 modules was shared with the registered participants before the start of each module using an online link. An online link consisting of similar questions was shared at the end of the sessions to assess change in knowledge after the session. One mark was allotted for each correct response. At the end of the program an online exit exam consisting of 50 marks was conducted among participants who have attended 80% of the program. The data was analysed using IBM-SPSS version-22.
Results: A total of 84 clinicians across 16 states attended the virtual training on liver diseases with mean age of 40.8 ± 11.90 years and approximately 76% were males. The mean pre-knowledge score of the participants was found to be 42.71 ± 9.1 whereas the post-knowledge score was 54.02 ± 10.6 out of 69. The difference between overall pre and post knowledge score was found to be statistically significant (< 0.001) as seen in Table 1. Approximately, 73% of the clinicians scored above 60% in the exit exam, indicative of learning from the comprehensive training program.
Conclusion: Similar comprehensive training programs on liver diseases should be encouraged in developing countries as they play an important role in strengthening the clinicians for better management of liver disease patients.

Table 1: Overall and module-wise pre and post scores of the participants.

Modules	Mean Pre-Score (SD)	Mean Post Score (SD)	t-test	Mean diff (95% CI)	p-value
Module 1	6.60 (2.1)	8.25 (1.9)	6.85	1.65 (1.17 - 2.14)	<0.001
Module 2	5.89 (2.2)	7.89 (2.2)	8.42	1.99 (1.52 - 2.46)	<0.001
Module 3	6.80 (1.9)	8.22 (1.7)	5.63	1.43 (0.92 - 1.93)	<0.001
Module 4	7.07 (2.5)	8.26 (2.0)	4.61	1.19 (0.68 - 1.70)	<0.001
Module 5	6.7 (1.9)	7.85 (2.2)	4.55	1.14 (0.64 - 1.64)	<0.001
Module 6, 7 and 8	9.64 (3.5)	13.56 (4.1)	7.89	3.92 (2.93 - 4.90)	<0.001
Overall	42.71 (9.1)	54.02 (10.6)	11.8	11.32 (9.41 - 13.23)	<0.001

SD: standard deviation; CI: confidence interval

[OP-1152]

Gastrointestinal, hepatic manifestations, and outcomes of COVID 19 infection among end stage renal disease patients: A retrospective cohort study

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Objectives: The study aimed to determine the prevalence of gastrointestinal and hepatic manifestations of COVID-19 among end-stage renal disease patients on renal replacement therapy and its association with the clinical outcomes.
Materials and Methods: The group utilized a retrospective cohort design. A total of 501 adult with end-stage renal disease patients on renal replacement therapy diagnosed with moderate-to-severe COVID-19, admitted at the National Kidney Transplant Institute from 2020 to 2021 were included.
Results: Overall prevalence of gastrointestinal and hepatic manifestations were 58.08% and 95.94%, respectively. Cerebrovascular disease, systolic blood pressure, diastolic blood pressure, and oxygen saturation significantly differ by presence of gastrointestinal manifestations, while none of the characteristics differ by presence of hepatic manifestations. Intubation, intensive care unit admission, and in-hospital mortality rates did not significantly differ by the presence of either gastrointestinal or hepatic manifestations. However, patients with gastrointestinal manifestation had a longer hospital stay. In-hospital mortality was 31.14%. Gastrointestinal (Odds Ratio = 0.98, $p = 0.91$) or hepatic (Odds Ratio = 2.07,$p = 0.457$) manifestation were not associated with in-hospital mortality. On multiple logistic regression analysis, age, diabetes mellitus, coronary artery disease, encephalopathy, diastolic blood pressure, and intubation were found to be predictors of in-hospital mortality.
Conclusion: Gastrointestinal and hepatic manifestations were common among end-stage renal disease patients with moderate-to-severe COVID-19. The in-hospital mortality rate was high; however, the presence of gastrointestinal and hepatic manifestations was not associated with this outcome.

[OP-1167]

Liver diseases in pregnancy: Trends and their consequence in mother and child

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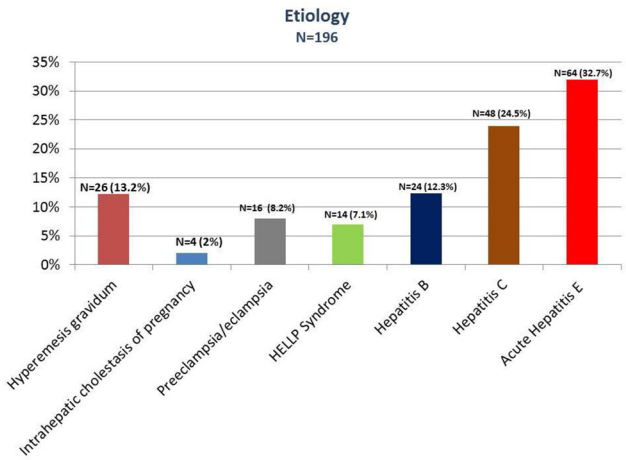
Objectives: To determine the etiologies and outcome of liver diseases in pregnancy.
Materials and Methods: This prospective study was conducted at Gastroenterology department, ward 23 and Gynecology and Obstetrics department, Jinnah postgraduate medical center Karachi, Pakistan.
Results: In our study, a total number of patients were 210 in whom causes of liver disease during pregnancy were evaluated along with their outcomes. 14 patients were excluded due to lost follow up. They had mean age of 27.49 ± 6.02 years. Among all the 196 evaluated pregnant women the most common etiological factor was acute hepatitis E virus (HEV) (33%) followed by acute hepatitis C virus (HCV) (22%), pre-eclampsia & eclampsia (11%), and HELLP syndrome (7%). Fortunately, most of the women survived and discharged without any complication (63%) while 11% were died due to pregnancy associated liver disease. Unfortunately, a significant number of fetal deaths were observed in pregnant women suffered from liver disease 36.4%).
Conclusion: Liver diseases in pregnancy impose a major burden which is a significant problem when occurred in developing country like Pakistan. The mortality rates of mother and fetal are observed significantly higher in our study.



[OP-1179]

Risk factors and outcomes of upper gastrointestinal bleeding in hospitalized patients in a tertiary care hospital

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Objectives: Gastrointestinal bleeding in hospitalized patients is an important cause of morbidity and mortality. By determining the common risk factors of upper gastrointestinal bleeding in admitted patients, due to the availability of better modalities of treatment, such events can be prevented. This study is conducted to evaluate such cases and to provide a better understanding and predictability of risk in hospitalized patients. To determine different etiologies and outcomes of upper GI bleeding in patients while in hospital.
Materials and Methods: This retrospective study was conducted on patients admitted to Aga Khan Hospital during 2019–2021. All patients admitted for non-gastrointestinal disorders who developed upper GI bleeds as 'inpatient bleeds' were considered cases. They were reviewed for clinical characteristics, cause of bleeding, and clinical outcomes.
Results: In hospitalized gastrointestinal bleeding was identified in 147 patients. 84% presented with overt GI bleeding and 16% with a drop in Hemoglobin level. Amongst all these patients, 23% were on aspirin, 24% on dual antiplatelets, 27% on therapeutic anticoagulation, 55% on prophylactic anticoagulation, 4% on NSAIDS, 8% on steroids. Independent risk factors for bleeding included age > 60 years, male sex, acute coronary syndrome, renal insufficiency, sepsis, being on a medicine service, and coagulopathy. 24.4% underwent endoscopy, out of which 5.4% had therapeutic measures to control bleeding. 9.5% of the patients had bleeding for more than 48 h of duration leading to prolonged hospitalization, 60% stepped-up to special care stay. Mortality was seen in 24% of the patients.
Conclusion: Hospital acquired gastrointestinal bleeding is uncommon in hospitalized patients. In this study, we identified several independent risk factors for gastrointestinal bleeding in hospitalized patients. Larger scale studies assessing the role of increased comorbidities and antithrombotic use in this setting are warranted.

[L-OP-1243]

Sarcopenia risk factor for frequent hospitalization and short-term mortality in liver cirrhosis

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Objectives: Sarcopenia is common in chronic liver disease (CLD) and is associated with poor prognosis. Aim of this study was to study the prevalence of sarcopenia in Indian patients with cirrhosis and its impact on their morbidity and short-term mortality.
Materials and Methods: Patients with cirrhosis were prospectively evaluated for presence of sarcopenia using CT abdomen. Cross-sectional area of the right psoas muscle was measured at L3 and the Psoas muscle index (PMI) was calculated. Sarcopenia was defined as PMI < 295 mm^2/m^2 for females and < 356 mm^2/m^2 for males. Normative values of PMI were obtained from patients undergoing CT scan for non-specific abdominal pain.
Results: Out of 156 patients with liver cirrhosis, 47.4% had sarcopenia. Sarcopenia was more common in males (M: F = 61:13) & alcohol related liver disease (70%). Patients with sarcopenia had lower serum albumin (2.51 ± 0.47 vs. 3.01 ± 0.53) (p = 0.001), higher bilirubin (± vs. 2.7 ± 4.19) (p = 0.001), higher MELD (18.8 ± 7.6 vs. 11.45 ± 4.2) (p = 0.0001) and Child–Pugh scores (9.8 ± 1.7 vs. 7.2 ± 1.2) (p = 0.001) as compared to those without sarcopenia. There was a linear correlation (negative) between PMI and severity of liver disease as assessed by Child–Pugh and MELD scores (r = -0.591 and -0.465 respectively). Patients with encephalopathy, ascites and coagulopathy had higher prevalence of

sarcopenia. On 6 months follow up, sarcopenic patients had higher readmission rates (74.3% vs. 22%; p = 0.0001) and higher mortality (24.3% vs. 3.7%; p = 0.002). MELD score and PMI were independently associated with higher mortality. PMI cut off value for predicting mortality obtained was 305.9 mm^2/m^2 with a sensitivity of 76.2% and a false positivity of 22.2%. (AUC was 0.805; 95% confidence interval: 0.69–0.91, p = 0.001).
Conclusion: Sarcopenia is seen in about 50% patients with liver cirrhosis & commoner in males, alcoholic liver disease and those with advanced liver disease. Patients with sarcopenia have worse prognosis, require more frequent hospitalization and negatively impacts short term survival.

Figure 3: Risk of readmission in sarcopenic and non-sarcopenic patients

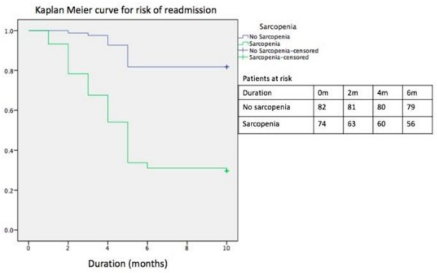
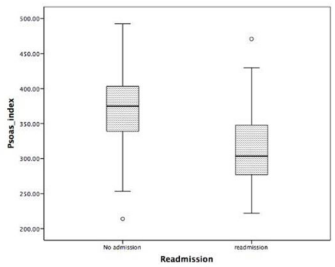


Figure 4: Psoas muscle index in patients readmitted and those without readmission



[L-PP-1260]

Liver abnormalities in patients with COVID-19

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Objectives: To determine the liver function abnormalities in COVID 19 patients and study possible correlation of liver function tests with severity of disease.
Materials and Methods: In a prospective study, we recruited 185 hospitalized patients with COVID 19. The diagnosis of COVID 19 was made on the basis of a positive RT-PCR report. Their clinical characteristics and the laboratory parameters were recorded in a proforma.
Results: The mean age of patients was 52.7 + 16.2 years (66 females), 66 (34.2%) of whom were of age more than 60 years. Based on the clinical criteria 70.4%, 20.9% and 8% patients had mild, moderate and severe COVID-19 infection, respectively. The mean haemoglobin was 12.4 + 2.1 g/dL. 57.8% patients had elevated levels of either alanine aminotransferase (ALT) or aspartate aminotransferase (AST). 35.1% had an elevation of ALT and 32.4% had an elevation in both ALT and AST. Serum bilirubin was elevated in 10.6% and 48.9% had low serum albumin. While a correlation was observed between low albumin and severity of COVID-19, there was no correlation between severity of COVID-19 and hypertransaminasemia.
Conclusion: One third of patients with COVID-19 had raised transaminases and half of them had low albumin. There was a correlation between low albumin and severity of COVID 19 infection.

[L-OP-1264]

When heart meets gut- novel insights for gastrointestinal physicians

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Objectives: We seek to characterize the association between atrial fibrillation and irritable bowel syndrome.
Materials and Methods: We identify 11,642 cases (atrial fibrillation) and 46,487 sex-, age-, and index year-matched controls (non-atrial fibrillation) from Longitudinal Health Insurance Database. Kaplan–Meier, Cox proportional hazards regression methods and competing risk analysis methods were used to assess the association of atrial fibrillation with outcome of irritable bowel syndrome.
Results: After adjustment for gender, age, comorbidities and medications, patients with atrial fibrillation had a significant higher risk (adjusted hazard ratio = 1.12, $p < 0.01$) to develop irritable bowel syndrome than patients without atrial fibrillation. Compared to participants without atrial fibrillation, those with atrial fibrillation had 1.13-fold ($p < 0.05$) and 1.11-fold ($p < 0.05$) risk of irritable bowel syndrome in female and male subgroup, respectively. Among subjects aged $\geq$ 65 years, those with AF had 1.11-fold risk of irritable bowel syndrome than non-AF cohort ($P < 0.01$). Among participants with any one of the comorbidities, those with atrial fibrillation had 1.10-fold risk of irritable bowel syndrome than non-atrial fibrillation cohort ($p < 0.05$).
Conclusion: We report that the presence of atrial fibrillation is associated with greater incidence of irritable bowel syndrome and the association is stronger among female gender, age 65 years or above, and with comorbidities.

[L-OP-1265]

Novel link between ischemic bowel disease and atrial fibrillation-the known, the unknown, and the unforgettable

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Objectives: This study aimed to evaluate the predictive role of CHA2DS2-VASc score specifically for the development of ischemic bowel disease (IBD) among atrial fibrillation (AF) patients.
Materials and Methods: Using a nationwide dataset, an AF cohort was established. The study participants were followed up from the

index date until they withdrew from the health insurance system, the occurrence of IBD or until the end of 2011. The hazard ratios (HRs) and 95% confidence intervals (CIs) were examined by Cox models to present the subsequent risk of IBD among AF patients by CHA2DS2-VASc score. The area under the receiver operating characteristic (ROC) curve was used to assess the predictive power of CHA2DS2-VASc score for IBD development among AF patients.
Results: The cumulative incidence of IBD was higher for AF patients with a CHA2DS2-VASc score ≥ 2 than those with a CHA2DS2-VASc score < 2 by 2.30% ($p < 0.001$) at the end of follow-up. After adjustment for hyperlipidemia, chronic obstructive pulmonary disease, and chronic kidney disease, the AF patients with a CHA2DS2-VASc score ≥ 2 had a 3.35 times higher risk for IBD development compared to those with a CHA2DS2-VASc score < 2 [adjusted HR (aHR) = 3.35, 95% CI = 2.71–4.13]. Among AF patients, the C-statistic of the CHA2DS2-VASc score as a predictor of IBD was 0.56 (95% CI = 0.55–0.57).
Conclusion: In conclusion, the study is? the first to investigate the predictive role of CHA2DS2-VASc score specifically for IBD development among AF patients. However, the predictive power was relatively low; further studies are necessary to confirm our findings.

[L-OP-1267]

Step up approach and late emergency Whipples Pancreatico-duodenectomy in Pancreatico-duodenal trauma

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Objectives: Role of interventional radiology (IR) and damage control procedures in the management of pancreatico-duodenal injuries are rarely described.
Materials and Methods: Here we present a case of pancreatico-duodenal complex injury which was managed as step up approach in a tertiary care centre at Kottayam.
Results: 17 year old boy was admitted with blunt trauma abdomen with grade-2 duodenal injury with duodenal hematoma, grade-2 pancreatic injury and grade-2 hepatic injury. Conservative management was initiated and subsequent repeat imaging on first week revealed doubtful contrast extravasation with ? contained collection in pancreaticoduodenal groove region with luminal narrowing. After nutritional optimization, he was taken up for laparoscopic Gastrojejunostomy + feeding jejunostomy when he developed gastric outlet obstruction despite conservative management on day 14. He developed duodenal bleed due to extravasation from one branch of gastroduodenal artery which was angioembolised on Post-operative day (POD)2. Biliary diversion (percutaneous transhepatic biliary drainage) was done on POD6 when he developed obstructive jaundice with cholangitis. He had another bout of intraluminal bleed with extravasation from an arterial branch from superior mesenteric artery on POD9, and was angioembolised. When he developed repeat luminal bleed on POD15 (after 28 days of trauma), he was taken up for emergency whipple's pancreatico-duodenectomy. He tolerated the procedure well. He had grade A post pancreatectomy fistula, Grade C post post pancreatectomy hemorrhage (late, severe, intraluminal) and grade B delayed gastric emptying which were managed conservatively. Percutaneous drainage of retrogastric collection which he developed in the post-operative period was done and he was discharged in a stable condition on POD20. Now he is healthy at one-year follow up.
Conclusion: With the aid of IR, conservative management initially with step up approach procedures and subsequent minimally invasive damage control surgeries, can be done to post-pone definitive major surgery to a later healthy state after prehabilitaion.

[L-PP-1272]

Changing features of liver injury in COVID-19 patients: Impacts of Infection with the SARS-CoV-2 Delta (B.1.617.2) variants

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Objectives: In many studies, abnormal liver function test has been reported in more than half of the COVID-19 patients. However, it is not known for the liver involvement of the virus according to the strain. We investigated the features of liver injury in the COVID-19 patients with the SARS-CoV-2 Delta (B.1.617.2) variants.
Materials and Methods: We performed a retrospective study that included 375 patients between 1 February 2020 and 31 November 2020 (pre-Delta period (PDP) group) and 125 patients between 1 August 2021 and 31 August 2021 (Delta period (DP) group) hospitalized for COVID-19 at National Medical Center in Korea. Initial liver injury was defined as ALT or AST levels $\geq 3 \times$ upper limit of normal (ULN), or ALP or total bilirubin $\geq 2 \times$ ULN within 3 days from admission. Severe COVID-19 was defined as respiration rate ≥ 30, oxygen saturation $\leq 93\%$, or oxygen requirement with pneumonia.
Results: Of 500 patients with COVID-19, 301 (60.2%) had abnormal liver test and 43 (8.6%) had liver injury within 3 days. The patients with abnormal liver test were similar in both groups. (58.4%vs60.8% P = 0.635). On the other hand, the DP group had a significantly higher proportion of liver injury than the PDP group (15.2% [n = 19]vs.6.4%[n = 24], P = 0.002). The DP group (Odds ratio (OR), 2.539; 95% confidence interval (CI), 1.211–5.325; P = 0.014), patients with pneumonia involvement over 50% of lung field at admission (OR, 4.982;95% CI, 1.966–12.625;P = 0.001), younger patients (OR,0.963;95%CI,0.940–0.988;P = 0.003), lower creatinine at admission (OR,0.132;95%CI,0.028–0.631;P = 0.011), higher CRP at admission (OR,1.009;95%CI,1.003–1.015;P = 0.002) were independently associated with liver injury. During hospitalization, 164 patients had severe COVID-19. The DP group and initial liver injury were high odds of progressing to severe COVID-19 (OR 2.867;95%CI 1.244–6.608, and OR 3.229;95% CI 1.131–9.219, respectively).
Conclusion: Initial liver injury is more common in COVID-19 patients with Delta variants. Also, Delta variants is associated with poor clinical outcomes. Therefore, careful monitoring in COVID-19 patients with Delta variants is needed.

[L-OP-1274]

An experimental study to assess the effectiveness of gum chewing on polyethylene glycol (PEG) related intake adherence, GI side effects and bowel preparation among patients undergoing colonoscopy

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Objectives: This study aimed to reduce the common discomfort of colonoscopy patients when taking a bowel cleansing solution.
Materials and Methods: This was an experimental study utilizing a randomized control group post-test design. This study was conducted in ILBS, New Delhi from November- December 2021. Patients were randomly allocated into two groups; an experimental group (n = 30) or a control group (n = 30). In the control group, patients drank a polyethylene glycol solution according to the general protocol. For the gum-chewing group, patients had to chew one stick of sugarless gum during the pause interval of drinking the polyethylene glycol solution. Results were analyzed using the t-test, Chi-square test or Fisher's exact test, ANOVA test, Pearson's correlation.
Results: The mean and standard deviation of abdominal discomfort score in experimental group was 1.54 ± 1.17 and in control group was 6.21 ± 1.25. The p value was found to be highly significant at $p < 0.001$ level. The mean and standard deviation of INVR score in experimental group was 3.21 ± 2.57 and in control group was 5.36 ± 1.70. The p value was found to be highly significant at $p < 0.001$ level. The mean and standard deviation of BBPS score in experimental group was 7.07 ± 1.30 and in control group was 5.21 ± 1.47. The Pearson's Correlation was used to find the relationship between total amount of fluid taken and INVR score. The computed 'r' value was negative and significant, as evident from the respective p value below 0.01 level of significance.
Conclusion: Gum chewing when consuming PEG solution does not reduce the resulting colon cleanliness but does relieve the abdominal discomfort, nausea and vomiting associated with this procedure, leading to a better intake adherence. Future repeat trials aimed at normalizing the application of gum chewing in this clinical setting are warranted.

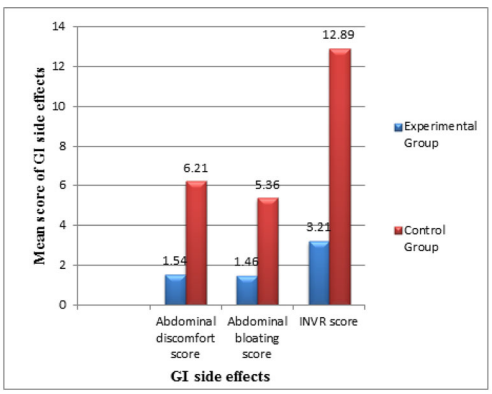

Figure 4: Bar graph showing the mean score of GI side effects of patients in experimental and control group.

[L-PP-1280]

Predictors anf frequency of readmission on decompensated liver cirrhosis with a view to developan educational bookelt

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Objectives: To determine the predictors and frequency of readmission with a view to develop an educational booklet on selfcare for patients with decompensated liver cirrhosis at ILBS,New Delhi.
Materials and Methods: A Retrospective cohort design was adopted on decompensated liver cirrhosis patient hospitalized at ILBS from 1st January 2018 to 31st December 2018. Patients were identified from the Hospital Information System database by typing keywords of any (ICD-9) associated with cirrhosis and complications of cirrhosis.The test of significance used in the study was independent t test, Chi square test, univariate and multivariate analysis.
Results: Among 504 records abstracted, 73.4 percent of patients had no case of readmission,16.9 percent of patients were readmitted on 30 days, 6.1 percent of patients readmitted on 90 days, 3.4 percent of patients readmitted on 6 months, 0.2 percent of patients readmitted on 1 year after hospital discharge. Majority 83.9% of records mentioned nurses documentation on discharge parameters as explained. Only 2.2% of patients records mentioned avoidance of alcohol. None of the records mentioned that avoidance of NSAIDS/Sedatives and avoidance of complementary /Alternatives medicine was explained and exercises were not explained to any of the patient with decompensated liver cirrhosis patients. The study reported that the independent predictors for 30 days readmission were male gender and MELD score at the time of discharge from index hospitalization The independent predictors for 90 days readmission were reported as MELD score and serum ALT at the time of discharge from index hospitalization and the independent predictors for 6 months readmission were reported as MELD score and patient with comorbidities CVA at the time of discharge from index hospitalization. None of the variables found significant on multivariate analysis for 1 year readmission.
Conclusion: 45% decrease in the odds of readmission at 30 days in patients who had been explained discharge advices by nurses.

[L-OP-1281]

Effectiveness of progressive muscle relaxation therapy on physical symptoms among cancer patients receiving chemotherapy admitted in cancer unit of ILBS, Delhi

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Objectives: This study aimed to evaluate the effectiveness of Progressive Muscle Relaxation Therapy (PMRT) on Physical Symptoms among Cancer Patients receiving Chemotherapy admitted in Cancer Unit of Institute of Liver and Biliary Sciences, Delhi.
Materials and Methods: Quasi experimental with pre-test post-test control group design was used. A total of 40 GI cancer patients were enrolled with 20 patients each in experimental and comparison groups by lottery method. Tools used namely- Universal Pain Assessment Tool to assess Pain; Insomnia Severity Index Scale to assess Insomnia; Common Toxicity Criteria for Adverse Events Version-5 to assess Fatigue, Nausea/Vomiting and Anorexia; and Karnofsky Performance Status Scale to assess Performance status.

Results: This showed that mean pre-test insomnia score was 11 which was significantly reduced to 5.17 after the PMRT in the experimental group with p value 0.02. Similarly, there was a significant difference between mean pre-test and post-test grades of fatigue in the experimental group at 0.01 level. There was a significant difference in mean post-test scores of insomnia as well as post-test grades of fatigue in the experimental group and comparison groups at 0.05 level. There was statistically significant association of performance status with gender and educational status among patients in experimental group.
Conclusion: Hence, PMRT is effective in decreasing the physical symptoms of insomnia and fatigue in cancer patients receiving chemotherapy admitted in cancer of Institute of Liver and Biliary Sciences.

[L-OP-1309]

Association between gastrointestinal and liver manifestations and laboratory abnormalities with disease severity and clinical outcomes in COVID-19 confirmed patients in a tertiary hospital

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Objectives: The general objective is to determine the prevalence of gastrointesinal manifestations and corresponding laboratory abnormalities and its association with clinical outcomes among COVID-19 confirmed cases admitted at Baguio General Hospital and Medical Center. Specific objectives would include determining clinico demographic profiles of patients with gastrointestinal and liver manifestations, determine and associate it with disease severity and to determine association of GI and liver manifesations and corresponding laboratory abnormalities with mortality, recovery, need for ICU admissiona and length for hospital stay in COVID-19 patients.
Materials and Methods: Cross sectional study design was used. A 340 sample population was computed at 95% confidence interval. Population was randomly selected. Patients aged > 19 years old admitted for COVID-19 infection from May 1, 2020 to July 31, 2021 was obtained. Data were collected. Frequencies, means, percentages, standard deviations were used. Statistical analyses used were Kruskal–Wallis H test, Chi Square and one Way ANOVA test with alpha level of significance of < 0.01 depicting strong associations.
Results: 18.23% of COVID-19 patients had GI and liver manifestations, with most cases belonging to the severe COVID-19 disease group. Presence of GI and liver symptoms increased risk for developing abnormal liver function tests. Symptoms and laboratory abnormalities were associated with severe COVID-19 infection and deranged laboratory parameters were found to be associated with worse outcomes on mortality, need for ICU stay and length of hospitalizations. Mild elevations of ALT (Mild acute liver injury) were associated with better recovery in patients infected with COVID-19.
Conclusion: In conclusion, these symptoms and laboratory tests provided signifciant associations which can be used by clinicians in prognostication, in improving diagnostics and therapeutic regimens for COVID-19 patients.

Table 1. Clinico-demographic Characteristics and Outcomes of the Sample Population

Clinicodemographic Factor		Mean (SD)	n (340)	%	With GI Symptoms n = 62 Mean (SD)	n	%	Without GI Symptoms n = 278 Mean (SD)	n	%	p-value
Age (Years)		53 (±18)			56 (±17)			51 (±18)			0.076
Sex	Male		147	43.2		32	51.6		115	41.4	0.141
	Female		193	56.8		30	48.4		163	58.6	
Exposure	HCW		15	4.4		3	4.8		12	4.3	<0.01*
	Symptomatic		220	64.7		55	88.7		165	59.4	
	Contact Traced		46	13.5		3	4.8		43	15.5	
	Travel		59	17.4		1	1.6		58	20.9	
	Others		0	0		0	0.0		0	0.0	
Smoking history	Non-smoker		245	72.1		43	69.4		202	72.7	0.851
	Current		6	1.8		1	1.6		5	1.8	
	Former/Quit		89	26.1		18	29.0		71	25.5	
Employment	Unemployed		159	46.8		25	40.3		134	48.2	0.878
	Professional		53	15.6		12	19.4		41	14.7	
	Clerical		44	12.9		10	16.1		34	12.2	
	Agriculture		17	5.0		4	6.5		13	4.7	
	Craft		24	7.1		4	6.5		20	7.2	
	Elementary		34	10.0		5	8.1		29	10.4	
	Armed Forces		8	2.3		2	3.2		6	2.2	
	Others		1	0.2		0	0.0		1	0.4	
Co-morbidities	Hypertension		149	48.8		31	50.0		118	42.4	0.278
	Diabetes Mellitus		88	25.9		17	27.4		71	25.5	0.760
	Heart Disease		75	22.1		16	25.8		59	21.2	0.431
	Chronic Kidney Disease		28	8.2		4	6.5		24	8.6	0.572
	Cancer		16	4.7		2	3.2		14	5.0	0.543
	Cerebrovascular Disease		14	4.1		0	0.0		14	5.0	0.071
	Pregnancy		45	13.2		1	1.6		44	15.8	0.003*
	Liver Disease		12	3.5		3	4.8		9	3.2	0.537
	Hematologic Disorder		4	1.2		1	1.6		3	1.1	0.742
	Respiratory Disease		30	8.8		6	9.7		24	8.6	0.739
Severity	None		35	10.3		12	19.4		24	8.6	0.452
	Mild		82	24.2		7	11.3		75	27.0	0.023*
	Moderate		98	28.8		16	25.8		82	29.5	
	Severe		125	26.8		30	48.4		95	34.2	
	Critical		35	10.2		9	14.5		26	9.4	
Clinical Outcomes	ICU admission		34	10.0%		9	14.5		25	9.0	0.190
	Mortality		26	7.6%		6	9.7		20	7.2	<0.01*
Recovered	With Clinical Improvement		267	85.0%		46	74.2		221	79.5	0.504
	With Residual Organ Damage		47	15.0%		10	16.1		37	13.3	
Days of Illness		15.27 (±5.93)			15.79 (±5.99)			15.15 (±5.92)			0.446
Length of Hospital Stay (Days)		11 (±7.24)			10.73 (±5.5)			11.20 (±7.6)			0.641

[L-OP-1332]

Empowering patients undergoing hepatectomy with standardized health education improves recovery process and mental health

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Objectives: In order to investigate the application of standardized health education based on the empowerment theory in patients with hepatectomy, we conducted this study evaluating the recovery process and mental health status between the patients with traditional treatment and standardized health education.
Materials and Methods: From February to October 2021, patients from our single center were randomly allocated to either control group and empowerment group, in which they received the traditional treatment or standardized health education. The baseline characteristics, health knowledge tests, quality of life, indexes related to surgery recovery and mental health were compared between the two groups.
Results: A total of 170 patients with hepatectomy were enrolled into this study with 82 cases in control group and 88 cases in empowerment group. Patients in empowerment group obtained high scores in health knowledge tests and satisfaction on health service provided ($p < 0.05$). The evaluation of indexes related to surgery recovery and mental health indicated beneficial effects of standardized health education. There was no significant difference in baseline characteristics or and quality of life between two groups.
Conclusion: This study of patients undergoing hepatectomy demonstrated the standardized health education improved the health knowledge related to liver diseases, patient satisfaction, recovery process and mental health. Further studies related to long-term effects with subgroup analysis is needed.

[ABST-0330]

Liver function tests in recovered COVID-19 patients with acute heart failure and associated outcomes

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Background: The objective of this study characterize abnormal liver function test after recovered coronavirus in patients with heart failure (HF) as they are commonly encountered yet poorly defined.
Methods: Clinical Effectiveness of nesiritide in decompensated Heart Failure use data from SCEND-HF to characterize associations with baseline liver function tests (LFTs). each LFT was analysed as both a continuous and dichotomous variable [normal vs. abnormal; bilirubin $>$ 1.0 mg/dL; aspartate aminotransferase (AST) and alanine aminotransferase ALT $>$ 35 mmol/L.
Results: Mean Logistic regression assessed the association of LFTs and 30-day all-cause mortality and HF rehospitalization, and Cox proportional hazards assessed the association with 180-day all-cause mortality among patients alive at a 30-day landmark. In SCEND-HF, 2128 (48%) had complete admission LFT data. Of these, 39% had abnormal bilirubin, 22% had abnormal ALT, and 29% had abnormal AST. Patients with abnormal LFTs were younger, had lower body mass index, and lower left ventricular ejection fraction. In multivariable models, increased total bilirubin was associated with increased 30-day mortality or HF rehospitalization [hazard ratio (HR) 1.17 per 1 mg/dL increase 85% confidence interval (CI) 1.04, 1.32; P = 0.012], but not with an increase in 180-day mortality (HR 1.10, 95% CI 0.97, 1.25; P = 0.13) per 1 mg/dl increase. Compared with normal bilirubin levels, abnormal bilirubin was associated with increased 30-day mortality or HF rehospitalization (HR 1.24, 95% CI 1.00, 1.54; P = 0.048) and 180-day mortality (HR 1.32, 95% CI 1.08, 1.62; P = 0.007). We found no association with AST or ALT and outcomes.
Conclusions: More than 40% of patients Hospitalized with acute HF had abnormal LFTS.After multivariable regulation, only High bilirubin was independently related with worse clinical outcomes and may represent an important prognostic variable.

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- ✓ Improvement of Sarcopenia[3]
- ✓ Improvement of Nutrition status for patients with Liver cirrhosis[4]

References **1.** Nutr Clin Pract. 2013 Oct;28(5):580-8 **2.** Muto Y et al. Clinical Gastorenterology and Hepatology 2005;3:705-713 **3.** Hanai T, Shiraki M, Shimizu M, Moriwaki H et al. Nutrition. 2015;31:193-9, Koya et al.,Hepatol Res 2017;47;E22-34 **4.** J Gastroenterol (2016) 51:629-650

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Maximum change in tumour size by mRECIST[1]*

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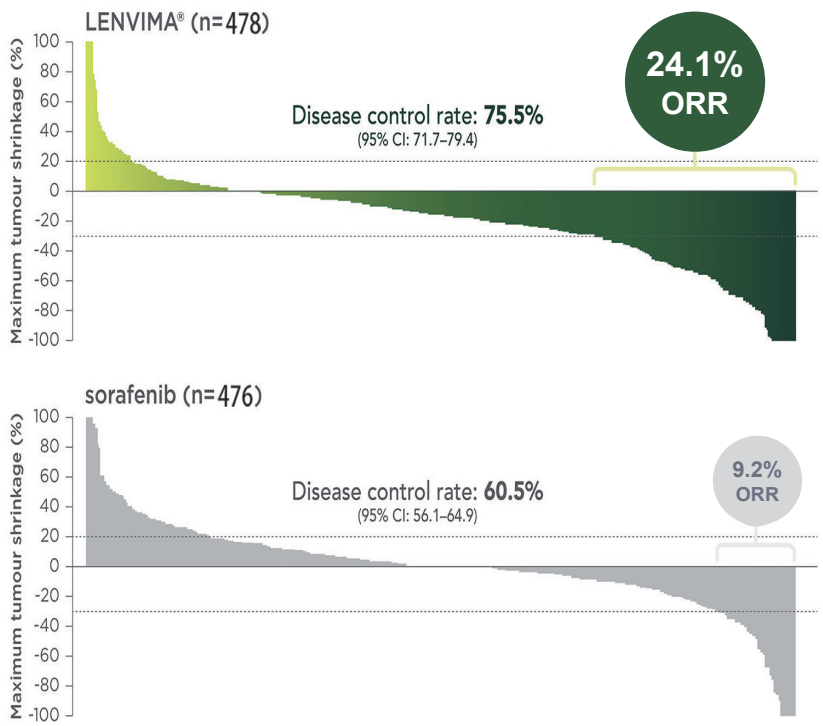

Change in tumour size truncated at 100%. Disease control rate and tumour shrinkage are % of total study groups, including unknown/not evaluable patients not included on these graphs.
*By investigator assessment.
CI: confi dence interval,**mRECIST**: modifi ed Response Evaluation Criteria In Solid Tumours. **ORR:** objective response rate.
uHCC : unresectable hepatocellular carcinoma
Reference 1 : Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. Lancet. 2018 Mar 24;391(10126):1163-1173.

~1 in 4 patients achieved **>30% tumour shrinkage** with **LENVIMA®** compared to ~1 in 10 with sorafenib

[ORR: LENVIMA 24.1%(95% CI 20.2-27.9) vs Sorafenib 9.2%(6.6-11.8) OR 3.13(95% CI 2.15-4.56), p<0.0001, Investigators' review according to mRECIST]

【Study Design】This was an Open-label, phase 3, multicenter, non-inferiority trial that recruited patients with uHCC. Patients were randomly assigned (1:1) via an interactive voice-web response system-with region; macroscopic portal vein invasion, extrahepatic spread, or both; Eastern Cooperative Oncology Group performance status; and body weight as stratification factors-to receive oral Lenvatinib 12mg/day for bodyweight≥60kg or 8mg/day for bodyweight <60kg)or Sorafenib 400mg twice-daily in 28-days cycles. The Primary endpoint was overall survival, measured from the date of randomization until the date of death from any cause. The efficacy analysis followed the intention-to-treat principle, and only patients who received treatment were include in the safety analysis. Lenvatinib(median OS 13.6month,95%CI12.1-14.9)was non-inferior to Sorafenib (median OS 12.3month, 95%CI 10.4-13.9) in overall survival in untreated advanced HCC(HR 0.92, 95%CI 0.79-1.06)1

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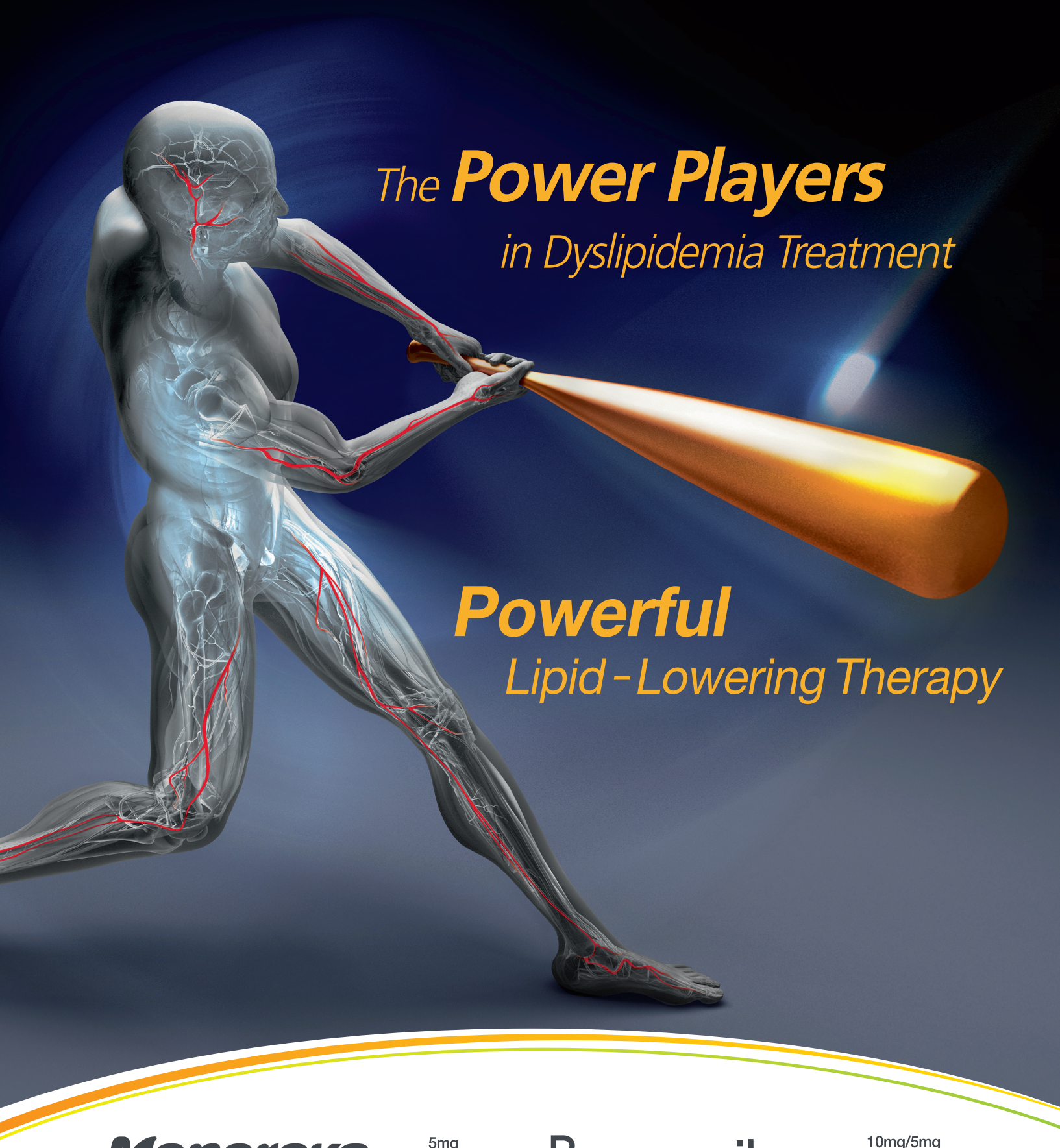

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마비렛®정 제품요약정보

[효능·효과] 만성 C형 간염 바이러스(hepatitis C virus; HCV) 유전자형 1, 2, 3, 4, 5, 또는 6 형에 감염된 성인 및 만 12세 이상 청소년 환자의 치료 **[용법용량]** 이 약은 글레카프레비르와 피브렌타스비르가 함유된 고정 용량 복합 정제이다. 이 약의 권장 경구 투여 용량은 1일 1회 동일한 시간에, 3정을 음식과 함께 복용하는 것이다. 이 약은 씹거나, 부수거나, 자르지 말고 통째로 삼켜야 한다. 표 1과 2에 간경변을 동반하지 않거나 대상성 간경변을 동반하고 신장애(투석 환자 포함)가 있거나 없는 HCV 단독 감염 환자 집단 및 HCV/HIV-1 동시 감염 환자 집단에 근거한 이 약에 대한 권장 치료 기간이 제시되어 있다.

표 1. 치료 경험이 없는 환자들에 대한 권장 치료 기간

유전자형	권장 치료 기간	
	간경변 없는 경우	대상성 간경변 있는 경우
1, 2, 3, 4, 5, 6형	8주	8주

표 2. 치료 경험이 있는 환자들에 대한 권장 치료 기간

유전자형	이전 치료 경험	권장 치료 기간	
		간경변 없는 경우	대상성 간경변 있는 경우
1, 2, 4, 5, 6형	인터페론, 페그인터페론, 리바비린 및/또는 소포스부비르	8주	12주
1형	이전 NS5A 저해제 치료경험이 없고, NS3/4A 단백분해효소 저해제1 치료경험이 있을 경우	12주	
	이전 NS3/4A 단백분해효소 저해제 치료경험이 없고, NS5A 저해제2 치료경험이 있을 경우	16주	
3형	인터페론, 페그인터페론, 리바비린 및/또는 소포스부비르	16주	

1. 임상시험에서, 시메프레비르 및 소포스부비르 또는 시메프레비르, 보세프레비르 또는 텔라프레비르와 페그인터페론 및 리바비린의 병용요법으로 투여받음
2. 임상시험에서, 레디파스비르 및 소포스부비르 또는 다클라타스비르와 페그인터페론 및 리바비린의 병용요법으로 투여받음

간장애 환자에 대한 투여: 경증 간장애(Child-Pugh A)가 있는 환자들의 경우, 이 약의 용량 조절은 필요하지 않다. 이 약은 중등증 또는 중증 간장애(Child-Pugh B 또는 C) 또는 비대상성 간경변(hepatic decompensation) 병력이 있는 환자에게는 투여 금기이다. 신장애 환자에 대한 투여: 경증, 중등증 또는 투석을 받고 있는 환자를 포함한 중증 신장애 환자에서 이 약의 용량 조절은 필요하지 않다. 간 또는 신장 이식 환자에 대한 투여: 이 약은 간 또는 신장 이식 환자에 12 주 동안 투여할 수 있다. 이전 NS3/4A 단백분해효소 저해제 치료경험이 없고, NS5A 저해제 치료경험이 있는 유전자형 1 형, 인터페론, 페그인터페론, 리바비린 및/또는 소포스부비르 치료 경험이 있는 유전자형 3 형의 이식환자에서는 16 주의 치료기간을 고려해야 한다. (용법용량 표 2 및 11, 전문가를 위한 정보 2) 임상시험 정보 항 참고) 알몰 복용을 놓친 경우: 약물 복용을 놓치고:
• 일반적으로 이 약을 복용하는 시간으로부터 18시간 이하 경과한 경우 - 환자에게 해당 용량을 즉시 복용하고, 다음 용량을 원래 복용하던 시간에 복용하도록 조언한다. • 일반적으로 이 약을 복용하는 시간으로부터 18시간 초과 경과한 경우 - 환자에게 놓친 용량을 복용하지 말고 다음 용량을 원래 복용하던 시간에 복용하도록 조언한다. **[주요 사용상 주의사항] 1. 경고** B형 간염 재활성화 위험: HBV/HCV 동시 감염 환자에서 B형 간염 바이러스(hepatitis B virus; HBV) 재활성화 사례(일부에서 간부전이나 사망이 유발됨)가 HCV에 직접 작용하는 항바이러스제로 치료하는 동안 보고되었다. HBV 재활성화는 혈청 HBV DNA 수치 증가로 발현되는 급작스런 HBV 복제 증가가 특징이다. HBV 감염이 해결된 환자들(HBsAg 음성이고 항-HBc 양성)에서, HBsAg가 다시 나타날 수 있다. HBV가 재활성화되면 중증 간기능 검사 수치 이상(즉, 아미노기 전이효소 및/또는 빌리루빈 수치 상승)이 나타날 수 있으며 심할 경우 간부전 또는 사망이 유발될 수 있다. 치료를 시작하기 전에 모든 환자에 대하여 HBV 선별검사를 실시해야 한다. 현재 또는 이전 HBV 감염 환자는 이 약의 치료 중 및 치료 후 간염의 급성 악화(hepatitis flare) 또는 재활성화 확인을 위해 임상적 및 실험실학적 검사(예. HBsAg, HBV DNA, ALT, 빌리루빈 등)로 주기적으로 모니터링해야 한다. HBV의 재활성화가 나타난 경우, 전문가와 상의한다. 당뇨병 환자에서의 사용: 당뇨병 환자는 HCV에 직접 작용하는 항바이러스 치료를 시작한 후, 포도당 조절이 개선되어 잠재적으로 증상이 있는 저혈당을 경험할 수 있다. 직접 작용하는 항바이러스제 치료를 시작하는 당뇨병 환자의 혈당 수준을 특히 처음 3개월 동안 면밀히 모니터링 해야 하며, 필요 시 당뇨병 치료제를 수정해야 한다. 직접 작용하는 항바이러스제 치료가 시작될 때 환자의 당뇨 관리 담당 의사에게 알려야 한다. 간질환이 진행된 환자의 비대상성 간경변/간부전 위험: 이 약을 포함한 HCV NS3/4A 단백질분해효소억제제 함유 요법으로 치료받은 환자에서 치명적인 결과를 가진 환자를 포함하여 비대상성 간경변 및 간부전의 시판 후 사례가 보고되었다. 이러한 사례는 특정할 수 없는 집단에서 자발적으로 보고된 것이었기 때문에, 신뢰할 수 있는 해당 사례의 발생빈도나 약물의 노출과의 상관관계를 확인하는 것이 모두 가능하지는 않았다. 중증의 결과를 보이는 환자의 대다수는 이 약으로 치료를 시작하기 전에 중등증 또는 중증 간 장애(Child-Pugh B 또는 C)로 진행된 간 질환이 있었다. 일부 환자들은 베이스라인에서 경증 간장애(Child-Pugh A 등급)가 동반된 대상성 간경변이 보고되었으나, 기존에 비대상성 간경변의 사례(예. 복수, 정맥류 출혈, 뇌병증)을 경험한 바 있었다. 간경변이 없거나 대상성 간경변(Child-Pugh A)을 가진 환자에서 비대상성 간경변 및 간부전이 드물게 보고되었으며, 이들 중 다수에서 문맥고혈압이 있었다. 병용이 권고되지 않는 병용 약물을 복용하는 환자 또는 심각한 간 관련 내과 또는 외과적 동반 질환과 같은 교란요인이 있는 환자에서도 사례가 보고되었다. 보고된 사례는 통상적으로 치료 시작 후 4 주 이내에 발생하였다(중간값 27일). 대상성 간경변(Child-Pugh A)이나 문맥고혈압 등 간 질환이 진행된 환자에서 임상적으로 필요한 실험실적 간 검사를 시행하고, 황달, 복수, 간성뇌병증, 정맥류 출혈과 같은 비대상성 간경변의 징후와 증상이 나타나는지 모니터링 한다. 비대상성 간경변 및 간부전으로 진행된 증거가 있는 환자는 치료를 중단한다. 중등증 또는 중증 간장애 환자(Child-Pugh B 또는 C) 또는 비대상성 간경변(hepatic decompensation) 병력이 있는 환자에게는 투여 금기이다. **2. 다음 환자에는 투여하지 말 것** 1) 이 약의 주성분 또는 구성성분에 과민증이 있는 환자 2) 중등증 또는 중증 간장애 환자(Child-Pugh B 또는 C) 또는 비대상성 간경변(hepatic decompensation) 병력이 있는 환자 3) 아타자나비르, 아토르바스타틴, 심바스타틴, 에티닐에스트라디올 함유제제, 강력한 P-gp 및 CYP3A 유도제[리팜핀, 카바마제핀, St. John's Wort(hypericum perforatum), 페니토인 등]와의 병용 4) 이 약은 유당을 함유하고 있으므로, 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency) 또는 포도당-갈락토오스 흡수장애(glucose-galactose malabsorption) 등의 유전적인 문제가 있는 환자에게는 투여하면 안 된다. **[제조원] (제조의뢰자)** AbbVie Deutschland GmbH & Co, KG, 독일, Knollstrasse 67061 Ludwigshafen (제조 및 포장) **(제조자)** Fournier Laboratories Ireland Limited, 아일랜드, Anngrove Carrigtowhill Co, Cork. **[수입원]** 한국애브비㈜, 서울특별시 강남구 영동대로 421 삼탄빌딩 6층, 전화: (02)-3429-9300 www.abbvie.co.kr **[허가변경일]** 2021년11월16일 *의약품 부작용 신고 및 피해구제 신청: 한국의약품안전관리원 (1644-6223, www.drugsafe.or.kr) *자세한 제품정보는 제품설명서를 참조해 주십시오.

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An effective protease inhibitor-free HCV treatment[1-3] means prescribing with confidence[1-4,a-c]

EPCLUSA is indicated for the treatment of adults and pediatric patients 12 years of age and older or weighing at least 30 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection, as monotherapy or in combination with ribavirin.[3] See the prescribing information for complete dosing information.

Indications: EPCLUSA is indicated for the treatment of adults and pediatric patients 12 years of age and older or weighing at least 30 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection, as monotherapy or in combination with ribavirin.

Adverse events: Headache, fatigue and nausea were the most common AEs associated with EPCLUSA in clinical trials. Headache, fatigue and nausea (incidence ≥10%), as well as other AEs, were reported at a similar frequency in placebo-treated patients. Cardiac disorders, skin rashes and angioedema have been identified during post approval use of sofosbuvir. EPCLUSA should not be administered concurrently with other medicinal products containing sofosbuvir.

Footnotes: a Despite unknowns in baseline characteristics of some patients such as: HCV genotype, fibrosis stage, former/current IV drug use, PPI use at baseline and treatment history. Based on a retrospective, pooled analysis of SVR12/24 in adult patients treated for 12 weeks with EPCLUSA without RBV in 12 real-world cohorts in Canada, Europe and the US (N = 5,552). Patients were treated in different clinical settings, including university hospitals, academic centres, community centres, outpatient clinics and private practices. Treatment and patient monitoring were based on local clinical practice and standard of care, at the discretion of the treating physician. Treatment-naïve patients and patients who have previously received IFN-based therapy (Peg-IFN + RBV with or without telaprevir, boceprevir or simeprevir) were included. Patients who had previously failed other DAA treatments and patients with current or prior decompensated cirrhosis or hepatocellular carcinoma were excluded. SVR12/24 in the effectiveness population (n = 5,196; excluding patients who did not achieve SVR12/24 due to non-virologic or unknown reasons) was 98.9%. SVR12/24 in the overall population was 92.6%. All patients with unknown genotype (n = 42), unknown fibrosis score (n = 82) and unknown treatment history (n = 33) achieved SVR12/24 with EPCLUSA for 12 weeks.[4] Please note, that coadministration of PPIs with EPCLUSA is not recommended. If it is considered necessary to co-administer, then EPCLUSA should be administered with food and
taken 4 hours before a PPI at a dose comparable to omeprazole 20 mg.[3] **b** Hepatitis B virus (HBV) reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct acting antivirals, and who were not receiving HBV antiviral therapy. Test all patients for evidence of current or prior HBV infection by measuring HBsAg and anti-HBc before initiating HCV treatment with this drug. In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during HCV treatment with this drug and during post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.[3] **c** The addition of RBV is recommended for the treatment of patients with decompensated cirrhosis. For further information on restrictions, please refer to the prescribing information.[3]

Abbreviations: DAA = direct-acting antiviral; GT = genotype; HBV = hepatitis B virus; HCV = hepatitis C virus; IFN = interferon; IV = intravenous; PPI = proton-pump inhibitor; RBV = ribavirin; SVR = sustained virologic response; USPI = US Prescribing Information.

References: 1. Feld J *et al. N Engl J Med* 2015;373(27):2599–2607. **2.** Foster G *et al. N Engl J Med* 2015;373(27):2608–2617. **3.** EPCLUSA® Prescribing Information. Gilead Sciences Korea (2022. 2. 17.). **4.** Mangia A *et al. Liver Int* 2020;40:1841–1852.

Epclusa Tablet [PHARMACEUTICAL FORM] Pink, diamond-shaped, film-coated tablet, debossed with "GSI" on one side and "7916" on the other side **[INDICATION]** Treatment of adults and pediatric patients 12 years of age and older or weighing at least 30 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection, as monotherapy or in combination with ribavirin **[DOSAGE AND ADMINISTRATION]** One tablet taken once daily with or without food. Patients without cirrhosis and with compensated cirrhosis (Child Pugh A): This drug 12 weeks. Patients with decompensated cirrhosis (Child Pugh B or C): This drug + ribavirinb 12 weeks. (Refer to full PI for more information including instructions for ribavirin dosage in pediatric patients or patients with CrCl less than or equal to 50 mL/min.) **[PRECAUTIONS IN USE] 1. Warnings** 1) Risk of Hepatitis B Virus Reactivation in Patients Coinfected with HCV and HBV, who were not receiving HBV antiviral therapy: Test for evidence of HBV infection before initiating HCV treatment. Monitor for signs of hepatitis flare or HBV reactivation. 2) Serious Symtomatic Bradycardia When Coadministered with Amiodarone: Coadministration of amiodarone with this drug is not recommended. (Refer to full PI for more information) **2. Do not administer in the following situations** 1) This drug and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated. 2) In combination with ribavirin, pregnant women and their partners, or women of childbearing potential. 3) Patients who are hypersensitive to the active substances or to any of the excipients. **3. Adverse Reactions** Subjects without Cirrhosis or with Compensated Cirrhosis: From three Phase 3 clinical trials (ASTRAL-1, ASTRAL-2, and ASTRAL-3) which evaluated a total of 1035 subjects who received this drug for 12 weeks, the most common adverse reactions (at least 10%) were headache and fatigue. Adverse reactions, all grades, observed in greater than or equal to 5% in ASTRAL-1 include headache (22%), fatigue (15%), nausea (9%), asthenia (5%), and insomnia (5%). The adverse reactions observed in subjects treated with this drug in ASTRAL-2 and ASTRAL-3 were consistent with those observed in ASTRAL-1. Subjects with Decompensated Cirrhosis: In Phase 3 trial (ASTRAL-4) including 87 subjects who received this drug with ribavirin for 12 weeks, the most common adverse reactions (all grades with frequency of 10% or greater) were fatigue (32%), anemia (26%), nausea (15%), headache (11%), insomnia (11%), and diarrhea (10%). Less Common Adverse Reactions Reported in Clinical Trials: rash, depression (Refer to full PI for more information) **4. General Precautions** 1) Risk of reduced therapeutic effect due to concomitant use of this drug with inducers of P-gp and/or moderate to strong inducers of CYP. 2) Refer to the ribavirin prescribing information for risks associated with ribavirin and this drug combination treatment **5. Drug Interactions** 1) Drugs that are inducers of P-gp and/or moderate to strong inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., rifampin, St. John's wort, carbamazepine) may decrease plasma concentrations of this drug, leading to reduced therapeutic effect. 2) Velpatasvir is an inhibitor of drug transporters P-gp, breast cancer resistance protein (BCRP), OATP1B1, OATP1B3, and OATP2B1. Coadministration of this drug with drugs that are substrates of these transporters may increase the exposure of such drugs. (Refer to full PI for more information) **6. Use in Pregnant Women and Nursing Mothers** 1) Pregnancy: If this drug is administered with ribavirin, the combination regimen is contraindicated in pregnant women and in men whose female partners are pregnant. 2) Lactation: It is not known whether the components of this drug are present in human breast milk, affect human milk production, or have effects on the breastfed infant. 3) If this drug is used in combination with ribavirin, special care should be taken to avoid pregnancy in female patients and female partners of male patients. **7. Use in Specific Populations** 1) The safety and effectiveness of this drug have not been established in pediatric patients less than 12 years of age. 2) No dosage adjustment of this drug is warranted in geriatric patients. 3) No dosage adjustment of this drug is required for patients with mild, moderate, or severe renal impairment, including ESRD requiring dialysis. 4) No dosage adjustment of this drug is required for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C). **[Storage Condition]** Store in a tight container at room temperature (1-30°C) **[Package Unit]** 28 tablets **[Importer]** Gilead Sciences Korea Ltd., West Tower 15F, Center 1, 26, Euljiro 5-gil, Jung-gu, Seoul, Korea (Representative phone: 02-6030-3300, Medical information: 0079-814-800-9172) **[Date of Preparation]** 2022.02.17 (EPC-2202-01) ※ Please refer to full prescribing information (www.gilead.co.kr or nedrug.mfds.go.kr) before prescription for detailed information. This abridged PI might not include some latest information after the date below.

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[효능 · 효과] 1. HIV-1 감염: 성인 및 12세 이상의 소아에서 HIV-1감염의 치료(다른 항레트로바이러스제제와 병용투여) 2. 만성 B형간염:성인 및 12세 이상 소아의 만성 B형간염을 치료 **[용법 · 용량]** 1. 성인 및 12세 이상의 소아(35 kg 이상): 음식물의 섭취와 상관없이 1일 1회 1정 복용 2. 신장애 환자: 이 약을 중등도-중증의 신장애 환자에게 투약할 경우 약물 노출이 유의하게 증가하므로 기저 크레아티닌 청소율이 <50 mL/min인 환자의 경우 이 약의 복용 간격을 조절해야 함 **[경고]** 1. 이 약의 구성성분인 테노포비르를 포함한 뉴클레오사이드 유사체를 기타 항레트로바이러스 치료제와 병용요법으로 사용한 경우에 치명적인 사례를 포함한 유산증 및 지방증을 동반한 중증의 간비대증이 보고됨 2. 이 약을 포함한 항HBV 치료의 중단은 간염의 중증 급성 악화와 관련이 있을 수 있음 3. 이 약은 원칙적으로 신장에서 배설되므로 급성 신부전증 및 판코니 증후군(중증의 저인산혈증을 동반한 신세뇨관 손상)을 포함한 신장애가 보고됨. 치료를 시작하기 전 및 이 약의 치료를 받는 동안 임상적으로 적절하게 모든 환자의 크레아티닌 청소율을 계산하는 것이 권장됨 4. 이 약은 테노포비르가 포함된 복합제 또는 아데포비르와 병용투여하지 말 것 5. HIV-1 내성 발생의 위험 때문에 이 약은 HIV-1와 HBV에 동시 감염된 환자에게 적절한 항레트로바이러스 병용요법의 일환으로만 사용할 것 6. 골절의 병력을 가지고 있거나 골감소증의 위험이 있는 환자에서는 골밀도(BMD) 모니터링을 실시할 것 7. 중심 비만증, 뒷목 지방 확장(버팔로 혹), 말초 소모증, 안면 소모증, 유방 확장 및 쿠싱양을 포함한 HIV 감염 환자의 체지방 재분포/축적이 항레트로바이러스 병용치료를 받는 환자에게서 관찰됨 8. 항레트로바이러스 병용 치료를 받는 환자에게서 면역 재구성 증후군이 보고됨 9. HIV 감염 환자에서 삼중 뉴클레오사이드 요법을 수행할 경우 초기 바이러스학적 부전 및 높은 저항성 치환율이 보고되었으므로 주의해야 하며, 주의 깊게 모니터 하며 치료 방법의 수정을 고려해야 함 **[금기]** 1) 이 약의 성분에 과민증이 있는 환자 2) 이 약은 유당을 함유하고 있으므로, 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency) 또는 포도당-갈락토오스 흡수장애(glucose-galactose malabsorption) 등의 유전적인 문제가 있는 환자 **[이상반응]** 1. 성인 HIV-1 감염 환자에 대한 임상 시험: 가장 흔한 이상반응(발병률 10% 이상, 등급 2-4)으로 발진, 설사, 두통, 통증, 우울증, 무력증 및 구역질이 확인됨 2. 만성 B형간염 및 대상성 간 질환을 앓고 있는 성인 환자에 대한 임상 시험: 대조군(아데포비르 디피복실 제제) 대비 테노포비르디소프록실의 푸마르산염 치료를 받은 대상자가 더 많이 구역을 경험하였고, 테노포비르 치료를 받은 환자 중 5% 이상이 보고한 기타 치료 관련 이상반응으로는 복통, 설사, 두통, 현기증, 피로, 코인두염, 요통, 피부 발진이었음 **[약물상호작용]** 다음 약물과 병용 시 주의 1. 디다노신 2. 아타자나비르 3. 로피나비르/리토나비르 4. 신장 기능에 영향을 주는 약물 **[임부]** 임신 여성에 대한 충분하고 잘 통제된 조사는 없었으므로 이 약은 임신 중에 확실히 필요한 경우에만 사용하도록 함 **[수유부]** 산모로부터 얻는 유즙 샘플에서 테노포비르가 사람의 유즙으로 분비되는 것이 관찰되었으나 이러한 노출이 모유 수유를 받는 유아에 미치는 영향은 알려지지 않았음. 수유중인 유아에게 HIV-1 전이 및 중증의 이상반응이 생길 수 있으므로 이 약을 투약 받고 있는 산모는 수유하지 않도록 함 **[고령자]** 고령자에 대한 충분한 조사가 없었으므로 노인 환자에 대한 복용량 선택은 주의해야 하며 간, 신장 및 심장 기능 저하, 동반질환 또는 기타 약물 치료의 빈도가 더 많아진다는 것을 유념해야 함 **[제조자]** 동아에스티 **[판매자]** 동아에스티

※ 자세한 사항은 허가사항 전문을 참조하여 주시기 바랍니다.

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- Restoration of Hepatic Mitochondrial Dysfunction by **Carnitine Complex**
- **Rapid Normalization** of ALT Level
- Improving effect for **NAFLD** as Evidenced by CT scans

Product Information

Description | Reddish brown colored hard gelatin capsule containing yellowish brown colored powder | **Composition** | Each capsule contains Carnitine Orotate 150mg (73.8mg as orotic acid, 76.2mg as carnitine), Liver Extract Antitoxic fraction 12.5mg, Adenine HCl 2.5mg, Pyridoxine HCl 25mg, Riboflavin 0.5mg, Cyanocobalamin 0.125mg, Biphenyl dimethyl dicarboxylate 25mg | **Indication** | 1) General therapeutics for the following hepatic disease - Acute, Subacute and Chronic Hepatitis, Hepatic cirrhosis, Fatty liver, Drug or chemical induced hepatitis 2) Acute, chronic hepatitis involving high transaminase value | **Dosage & Administration** | Usually, each time 2 capsules, 2~3 times a day as adult dosage. Dosage unit can be changeable depending on symptom or age of patient. | **Special caution** | 1) Severe state of chronic hepatitis 2) Severe state of hapatic cirrhosis | **General caution** | 1) Rarely skin rash can be represented, in this case general antihistamin therapy will be required. 2) In severe case, sometimes intermittent jaundice can be occur in this case, discontinue administration for awhile and other adjuvant therapy for jaundice shall be required. 3) Rarely nausea, gastric discomfortness can be represented. 4) Rarely itching or reddness can be occur, in this case, discontinue administration and follow physician's instruction. | **Insurance Code** | 693900080 | **Packing Unit** | 100, 300 caps. (bottle)/ 100 caps. (PTP) | **Storage** | Tight closed container, room temperature (1~30℃) in dry place. Expiry - 60 months from Manufacturing date.

Diagnostic Codes

B15-19 Viral hepatitis **K70.0** Alcoholic fatty liver **K71.0** Toxic liver disease **K73.0** Chronic persistent hepatitis, NEC **K74.0** Hepatic fibrosis **K75.8** Other specified inflammatory liver disease, Nonalcoholic steatohepatitis **K77.0** Liver disorders in disease classified elsewhere

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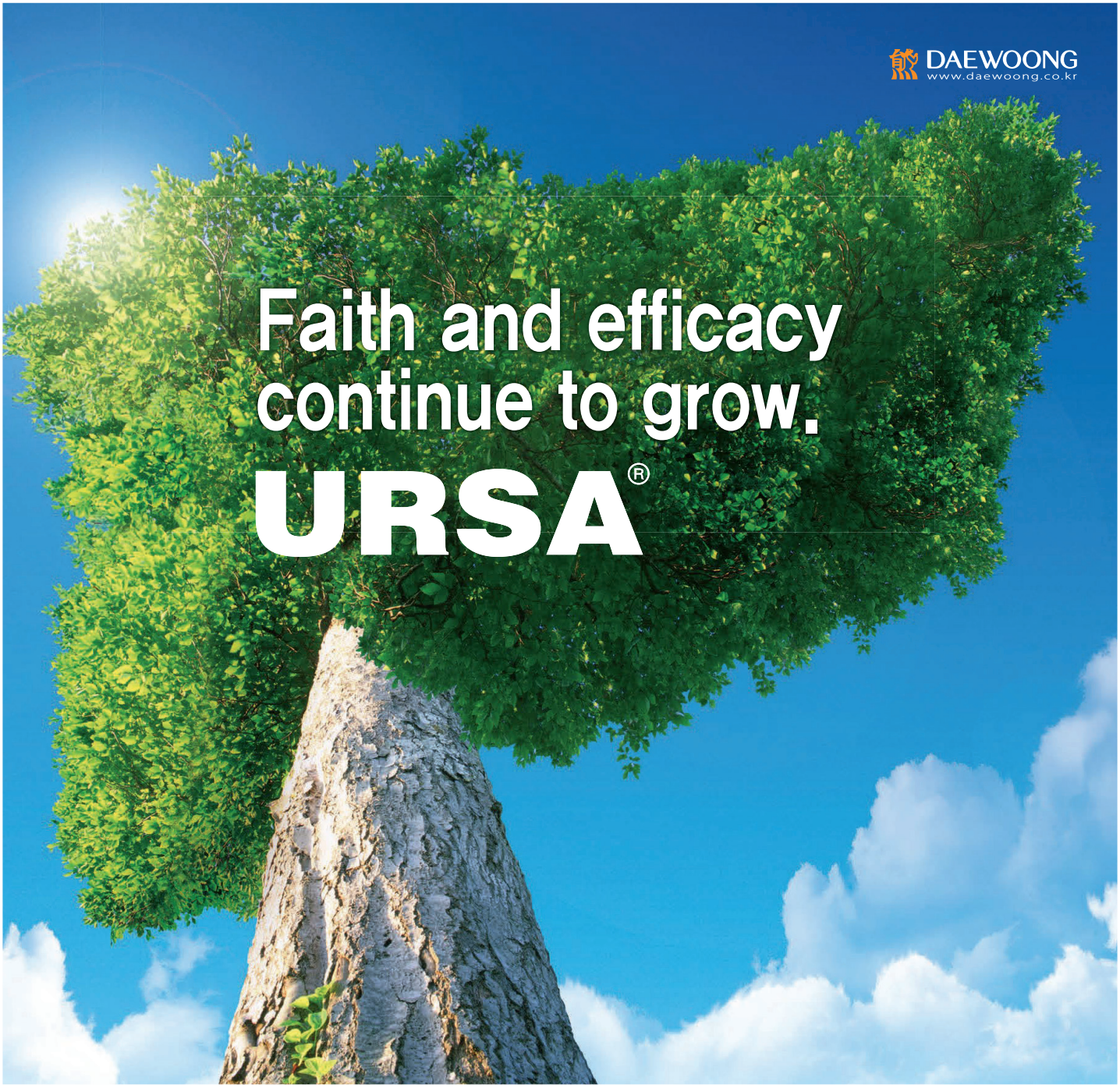

- Displacement of toxic bile acid
- Cytoprotective effects
- Immunomodulatory effects
- Stimulation of bile secretion

Component·Content

- Each tablet contains – Ursodeoxycholic acid(KP) ····· 100mg, 200mg, 300mg

Indication/Dosage and administration

■100mg Tab. :
1. Supplementary treatment for the following conditions
   1–1) Liver disease caused by bile secretion failure
   1–2) Biliary (biliary, gallbladder) system disease
2. Improving liver function in chronic liver disease
3. Indigestion of aftereffects of resection of the small intestine and inflammatory small intestine diseases / 50–100 mg once, 3 times a day.

■200mg Tab. :
1. gallbladder disease / 200-250 mg once, 3 times a day.
2. Improving liver function of primary gallbladder cirrhosis (PBC) / 200 mg once, 3 times a day (take with meal)
3. Improving liver function in patients with chronic hepatitis C / 200–300 mg once, 3 times a day.

■300mg Tab. :
1. Improving liver function of primary gallbladder cirrhosis (PBC) / 300 mg once, 3 times a day (take with meal)
2. Prevention of gallstones in obese patients who have experienced rapid weight loss / 300 mg once, twice a day (non–salary)
   ※ However, it is possible to be paid if the operation for high obesity (activity) is performed.
3. Prevention of gallstones in stomach cancer patients with gastrectomy / 300 mg one time, once a day.

※Inquiry calls: +82–80–550–8329

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14년간의 입증된 증거와 임상 경험을 보유한 CHB 치료제[1]

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VIEW
Values In Evidence and real-World-data

바라 보다. 바로 보다.

• 간경변을 동반한 경우에도[2,3] • HBV DNA 레벨에 관계 없이[4] • 신질환, 골질환의 위험이 있거나 동반한 경우에도[2,5,6]

Reference 1. 바라크루드정 국내허가사항. 식품의약안전처. 의약품통합정보시스템. Available at https://nedrug.mfds.go.kr/searchDrug. Accessed Feb 01, 2021 **2.** 대한간학회. 만성 B형간염 진료 가이드라인 2018. **3.** Chang TT, et al. Hepatology 2010;52:886-93. **4.** Wu IT, et al. Clin Microbiol Infect 2017;23:464-469. **5.** AASLD. Practice Guidance. 2018. **6.** EASL. Clinical Practice Guidelines on the management of hepatitis B virus infection. 2017.

[원료약품의 분량] [0.5mg] 1정(206mg) 중 엔테카비르(별규) 0.53mg(엔테카비르무수물로서 0.5mg) [1.0mg] 1정(412mg) 중 엔테카비르(별규) 1.06mg(엔테카비르무수물로서 1.0mg) [시럽 0.05mg/mL] 100mL 중 엔테카비르(별규) 5.3mg(엔테카비르무수물로서 5.0mg) **[주의]** 제품설명서의 사용상의 주의사항 참조 **[효능·효과]** 활동성 바이러스의 복제가 확인되고, 혈청 아미노전이효소(ALT 또는 AST)의 지속적 상승 또는 조직학적으로 활동성 질환이 확인된 성인(16세 이상)과 2세 이상의 소아 환자의 만성 B형간염 바이러스 감염의 치료 **[용법·용량]** 1. 성인(16세 이상)의 권고 용량: 1일 1회 엔테카비르로서 0.5mg(시럽제의 경우 10mL) 경구투여. 라미부딘 저항성 환자, 즉, 라미부딘 치료에도 불구하고 B형간염 바이러스의 지속적 증식을 경험하였거나, 라미부딘 저항성 변이가 있는 16세 이상의 환자: 1일 1회 공복시 엔테카비르로서 1mg(시럽제의 경우 20mL) 2. 소아의 권고 용량: 제품설명서 참조 *신부전 환자의 용량 조절 및 자세한 내용은 제품설명서를 참조하십시오.

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Stivarga® (regorafenib) tablets

References: 1. Finn RS, Merle P, Granito A, et al. Outcomes of sequential treatment with sorafenib followed by regorafenib for HCC: additional analyses from the phase III RESORCE trial. J Hepatol. 2018;69(2):353-358. **2.** Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med. 2008;359(4):378-390. **3.** Bruix J, Qin S, Merle P, et al; on behalf of the RESORCE Investigators. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2017;389(10064):56-66.

[제품명] 스티바가정40밀리그램(레고라페닙) **[주성분]** 레고라페닙일수화물(별규) 41.49밀리그램(레고라페닙으로서 40.00밀리그램) **[효능·효과]** 1. 이전에 플루오로피리미딘 계열 약물을 기본으로 하는 항암 화학 요법과 항 VEGF 치료제, 항 EGFR 치료제(RAS 정상형 (wild type)의 경우)로 치료를 받은 적이 있는 전이성 직장결장암 환자의 치료 2. 이전에 이매티닙과 수니티닙으로 치료 받은 적이 있는 전이성 또는 절제불가능한 국소진행성 위장관기질종양(GIST) 환자의 치료 3. 이전에 소라페닙으로 치료 받은 적이 있는 간세포암 환자의 치료 **[용법·용량]** 1일 권장 투여 용량은 레고라페닙으로서 160 mg (이 약 40 mg 정제 4정에 해당)이며, 1일 1회 경구 복용한다. 투여 주기는 4주로, 3주 투약하고 1주 휴약한다. 이 약은 매일 같은 시간에 가벼운 식사 후 복용한다. 정제를 물과 함께 통째로 삼켜야 한다. 복용을 잊은 것을 기억하는 즉시 이 약을 복용하되, 전날의 투여량을 보충하기 위해 하루에 2회 용량을 복용해서는 안된다. 이 약의 투여는 질병이 진행할 때까지 또는 수용할 수 없는 독성이 발생할 때까지 지속되어야 한다. 환자 개개인의 안전성 및 내약성에 따라, 일시적 투여 중단 및/또는 용량 감소가 필요할 수도 있다. 용량 변경은 40 mg 1정씩 적용한다. 최소 1일 권장 투여 용량은 80 mg이다. 최대 1일 투여 용량은 160 mg이다. 용량 조절에 대한 자세한 내용은 제품설명서 전문을 참고해주시기 바랍니다. **[사용상의 주의사항] 1. 경고** 1) 임상시험에서 이 약으로 치료 받은 환자에서 치명적인 결과를 동반한 심각한 약물유발 간손상이 발생했다. 대부분의 사례에서, 간 기능 부전은 치료 시작 후 2개월 이내에 발생했으며 간세포 손상 양상으로 특징지어졌다. 2) 임신한 여성에게 이 약 투여 시 태아에게 해로운 영향을 미칠 수 있다. 랫트 및 토끼에서 이 약은 사람의 권장 노출량보다 적은 용량에서 기형 및 배태자 독성을 유발하는 것으로 나타났다. 임신 가능성이 있는 여성 및 남성은 이 약 투여 중 및 투여 후 8주까지 효과적인 피임법을 실시하여야 한다. 임신 중에 이 약을 사용하거나 이 약을 복용하는 동안 임신이 되면, 태아에 미치는 잠재적 위험에 대해 환자에게 알려주어야 한다. **2. 다음 환자에는 투여하지 말 것** 1) 이 약 또는 이 약의 구성성분에 과민증인 환자 **3. 다음 환자에는 신중히 투여 할 것** 1) 간 기능 장애 환자(1. 경고항 참조) 2) 감염 3) 출혈 4) 심장 허혈 및 경색 **4. 이상반응** 이 약의 가장 중대한 약물 이상 반응은 중증의 간 손상 및 출혈, 위장관 천공 및 감염이었다. 임상시험에서 매우 흔하게 나타난 약물이상반응(10% 이상): 감염, 저혈소판증, 빈혈, 식욕 및 음식섭취 감소, 출혈, 고혈압, 발성장애, 설사, 구내염, 구토, 오심, 고빌리루빈혈증, 트랜스아미나아제 상승, 손발피부반응, 발진, 무력증/피로, 통증, 고열, 근육염증, 체중감소 흔하게 나타난 약물이상반응(1%이상 10%미만): 백혈구감소증, 갑상선기능저하증, 저칼륨혈증, 저인산혈증, 저칼슘혈증, 저나트륨혈증, 저마그네슘혈증, 고요산혈증, 탈수, 두통, 떨림, 말초신경병증, 미각이상, 입안건조, 위식도역류질환, 위장염, 탈모, 피부건조, 박리성 발진, 근육 경련, 단백뇨증, 아밀라아제 상승, 리파아제 상승, INR치 비정상 **[전문의약품] [수입 및 판매자]** 바이엘코리아㈜ **[개정년월일]** 2021.12 **보다 자세한 사항은 제품설명서 전문 또는 바이엘 웹사이트, http://www.bayer.co.kr를 참고하시기 바랍니다. 부작용 또는 품질과 관련된 불만사항을 보고하고자 하는 경우 의약전문가(예: 의사 또는 약사), 식품의약품안전처 또는 한국의약품안전관리원에 연락하시기 바랍니다. 혹은 바이엘코리아로도 보고하실 수 있습니다.**

[제품명] 넥사바정 200밀리그램(소라페닙토실레이트(미분화)) **[주성분]** 소라페닙토실레이트(미분화) (별규) 274.0밀리그램(소라페닙으로서 200밀리그램) **[효능·효과]** - 이전의 cytokine 치료에 실패 경험이 있거나, 이러한 치료요법이 적절치 않은 진행성 신장세포암 - 간세포성 암 - 방사성 요오드에 불응한, 국소 재발성 또는 전이성의 진행성 분화 갑상선 암 **[용법·용량]** 권장투여용량은 1회 400mg, 1일 2회이며, 공복상태(최소 식전 1시간 또는 식후 2시간)에 복용한다. 본 약제는 환자에게 더 이상 임상적인 유익성이 없거나 수용할 수 없는 독성이 발생할 때까지 계속 투여해야 한다. 피부착적 독성에 따른 권장용량의 예시는 제품설명서 전문을 확인해 주십시오. **[사용상의 주의사항] 1. 경고** 이 약의 적응 기전 및 임상 사용량보다 훨씬 적은 용량을 투여한 동물시험에서의 관찰 사항에 근거할 때, 이 약을 임부에 투여했을 때 태아에 유해할 것으로 예측된다. 임신부에서는 이 약에 대한 적절한 임상연구를 실시하지 않았다. 임신 가능성이 있는 여성은 이 약을 투여하는 동안에는 임신하지 않도록 해야 한다. 임신 가능성이 있는 환자에게는 중증의 기형(최기형성), 성장 장애, 태아 사망(배아독성)을 포함하여 이 약의 태아에 미치는 잠재적 위험성에 대해 알려주어야 한다. 이 약은 임신 중에는 투여하지 않는다. 임신 중에 이 약을 사용하려면, 태아에 미치는 유익성이 위험성 보다 더 클 때에만 투여토록 한다. 이 약을 투여 받는 동안 수유를 중단해야 한다. **2. 다음 환자에는 투여하지 말 것** 이 약의 주성분이나 부형제에 대해 중증의 과민증이 있는 환자 **3. 주요 이상반응** (1) 간세포암 환자 297명과 신장세포암 환자 451명과 분화갑상선암 환자 207명을 대상으로 하여 총 955명의 환자에 대한 위약 대조 시험한 임상연구의 결과 가장 흔한 이상반응: 설사, 피로, 탈모증, 감염, 수족피부반응, 발진 (2) 여러 임상연구 및 시판 후 조사로부터의 추가 안전성 데이터 중 매우 흔한 이상반응(10% 이상): 감염, 림프구 감소증, 식욕부진, 저인산혈증, 출혈(위장관계, 호흡기계 및 뇌출혈 포함), 고혈압, 설사, 오심, 구토, 변비, 피부건조, 발진, 탈모증, 수족피부반응, 가려움, 홍반, 관절통, 피로, 통증(구강, 상복부, 뼈, 암 통증 및 두통 포함), 발열, 체중감소, 아밀라아제 증가, 리파아제 증가 **[전문의약품] [수입 및 판매자]** 바이엘코리아㈜ **[개정년월일]** 2021.12 **보다 자세한 사항은 제품설명서 전문 또는 바이엘 웹사이트, http://www.bayer.co.kr를 참고하시기 바랍니다. 부작용 또는 품질과 관련된 불만사항을 보고하고자 하는 경우 의약전문가(예: 의사 또는 약사), 식품의약품안전처 또는 한국의약품안전관리원에 연락하시기 바랍니다. 혹은 바이엘코리아로도 보고하실 수 있습니다.**

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* TDF: Tenofovir disoproxil fumarate, ** Ishak modified HAI(Histologic Activity Index) score

REFERENCE
1. MFDS Label (2020.10) **2.** Besivo Phase III Clinical Trial. Protocol No. ID_BVCL011 Clinical Study Report. **3.** Ahn SH, et al. Clin Gastroenterol Hepatol. 2019 Aug;17(9):1850-1859. **4.** Yim HJ, et al. Am J Gastroenterol. 2020 Aug 1;115(8):1217-1225.

ILDONG

Besivo® Tab. (Besifovir dipivoxil maleate 183mg [Besifovir dipivoxil 150mg])[1]

ETC

[Indication and Usage] Treatment of chronic hepatitis B in adults [DOSAGE AND ADMINISTRATION] One tablet containing 150 mg besifovir dipivoxil once daily orally with or without food in adults. When taking this medicine, take 660mg of L-Carnitine together to prevent a decrease in serum L-Carnitine level. [WARNINGS AND PRECAUTIONS] 1) Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs alone or in combination with other antiretrovirals. Treatment should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations). 2) Discontinuation of anti-HBV therapy may be associated with severe acute exacerbations of hepatitis. Patients infected with HBV who discontinue Besivo should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted.3) HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with Besivo. Limited clinical experience suggests there is a potential for the development of resistance to HIV if Besivo is used to treat chronic hepatitis B virus (HBV) infection in patients with HIV infection that is not being treated. Therapy with Besivo is not recommended for HIV/HBV co-infected patients. 4) Since this drug contains lactose, it should not be administered to patients with genetic problems such as galactose intolerance, Lapp lactose deficiency, or glucose-galactose malabsorption.

BES2010A2.2210

GC 녹십자

Human Serum Albumin

알부민주

- Maintenance of Plasma Colloid Osmotic Pressure
- Intravascular Volume Expansion

H_2O

H_2O

Indications

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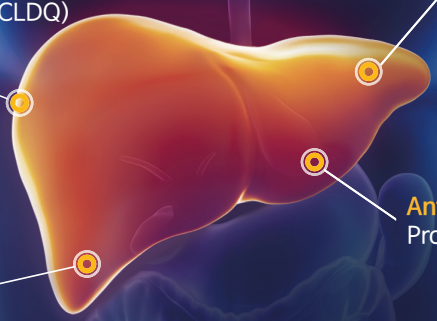

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Quickly Reduces and Helps You Maintain Optimal Level of Alanine Transaminase (ALT)
Contains Garlic Oil Which is Known to Have Strong Antioxidative and Anti-Inflammatory Effects

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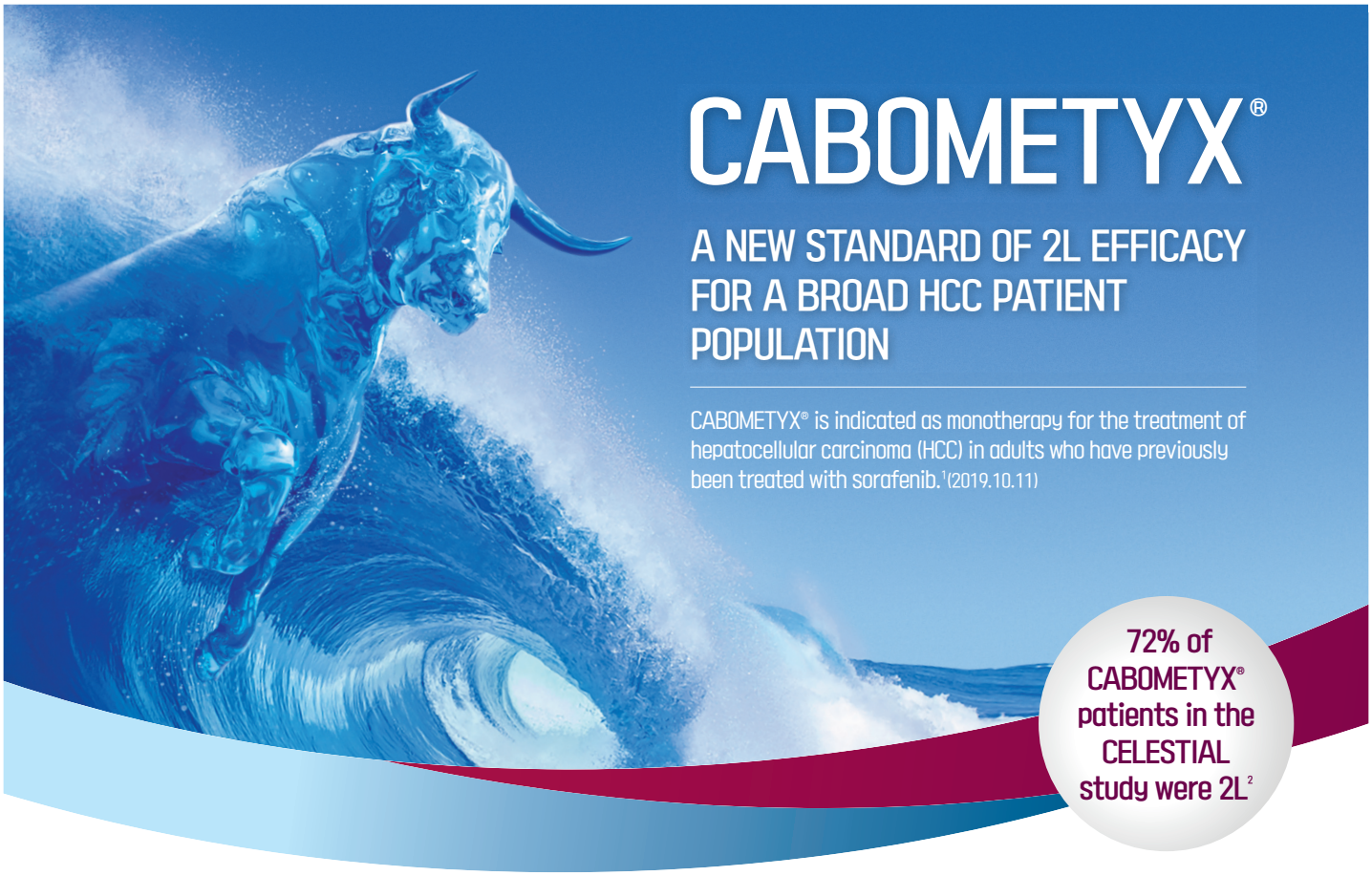
[Ingredients] Chronics hepatitis with continuously elevated ALT level
[Directions] Take 1 or 2 capsules each time, 3 times a day, after meals

Diagnostic Code
B15-19 Viral hepatitis K70.0 Alcoholic fatty liver K71.0 Toxic liver disease K73.0 Chronic persistent hepatitis, NEC
K74.0 Hepatic fibrosis K75.8 Other specified inflammatory liver disease,
Nonalcoholic steatohepatitis K77.0 Liver disorders in disease classified elsewhere



CABOMETYX®

A NEW STANDARD OF 2L EFFICACY FOR A BROAD HCC PATIENT POPULATION

CABOMETYX® is indicated as monotherapy for the treatment of hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib.[1](2019.10.11)

72% of CABOMETYX® patients in the CELESTIAL study were 2L[2]

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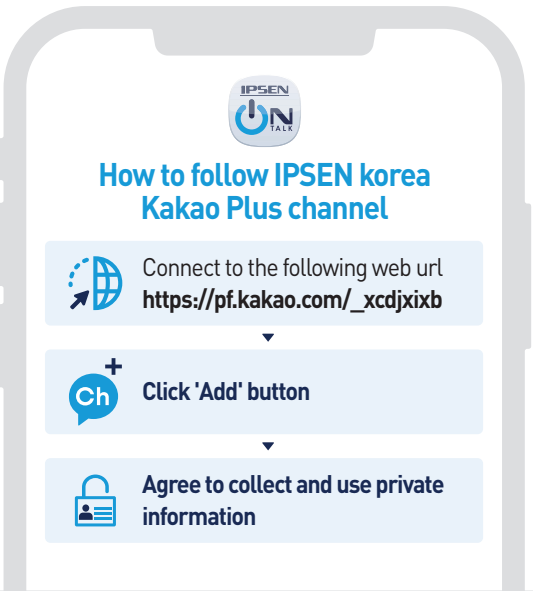

References. 1. Cabometyx® Product Information (2019.10.11) 2. Abou-Alfa GK, *et al. New England Journal of Medicine*. 2018; 379(1): 54-63.

CABOMETYX® HIGHLIGHT OF PRESCRIBING INFORMATION [INGREDIENTS] cabozantinib (S)-malate **[APPEARANCE]** Film-coated tablets: 20mg/ 40mg/ 60mg **[INDICATION]** 1) Renal Cell Carcinoma (RCC): The treatment advanced renal cell carcinoma (RCC) in adultsfollowing prior vascular endothelial growth factor (VEGF)-targeted therapy 2) Hepatocellular Carcinoma (HCC): Treatment of hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib **[DODSAGE AND ADMINISTRATION]** Therapy withCABOMETYX should be initiated by a physic ian experienced in the administration of anticancer medicinal products. The recommended dose of CABOMETYX is 60 mg once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy oruntil unacceptable toxicity occurs. Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of CABOMETYX therapy. When dose reduction is necessary, it is recommended to reduce to 40 mg daily, and then to 20 mg daily.Dose interruptions are recommended for management of CTCAE grade 3 or greater toxicities or intolerable grade 2 toxicities. Dose reductions are recommended for events that, if persistent, could become serious or intolerable. If a patient misses a dose, the missed doseshould not be taken if it is less than 12 hours before the next dose. [Please refer to full SmPC for further information.] **[SPECIAL POPULATIONS]**: <Patients with renal impairment> Cabozantinib should be used with caution in patients with mild or moderate renal impairment.Cabozantinib is not recommended for use in patients with severe renal impairment as safety and efficacy have not been established in this population. <Patients with hepatic impairment> Dose adjustment in patients with mild hepatic impairment is not necessary. In patientswith moderate hepatic impairment the recommended dose is 40 mg once daily. Patients should be monitored for adverse events and dose adjustment or treatment interruption should be considered as needed [see section 'Special warnings and precautions for use']. Cabozantinib is not recommended for use in patients with severe hepatic impairment as safety and efficacy have not been established in this population. Please refer to full PI for further information.] **[SPECIAL WARNINGS AND PRECAUTIONS FOR USE]** Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **[ADVERSE EVENTS]** As most events can occur early in the course of treatment, the physician should evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications are warranted. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmar-plantar erythrodysaesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events [abdominal pain, mucosal inflammation, constipation, diarrhoea, vomiting]. [Please refer to full SmPC for further information.] [STORAGE CONDITION] Tight container, room temperature(1-30℃) [NATURE AND CONTENTS OF CONTAINER] 30 film-coated tablets/ bottle **[MARKETING AUTHORISATION HOLDER]** Ipsen Korea, 11F KAMCO Tower, Gangnam-daero 262, Gangnam-gu, Seoul 06265, South Korea **[DATE OF REVISION]** 2019. 10. 11

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Originality & Worldwide

- The original silymarin for treatment of liver disease by numerous Clinical trials since 1960's.[1-2]

Treatment of Liver disease

- Proven efficacy in improvement of liver function [5-11]
  * NAFLD, NASH, ALD, cirrhosis

Various MoA & All stages

- Multi-therapeutic targets in all-stage of liver disease by various MoA.[3-4]
  * Improvement of insulin resistance
  * Anti-oxidative stress, Anti-inflammation, Anti-fibrosis

Safety & Good tolerance

- Good tolerance and safety with lower side effects [5-9]

[Reference] 1. Bijak M. Molecules 2017 Nov 10;22(11). / 2. LEGALON Cap. 140 – Insert Paper(KOREA) / 3. Federico A, et al. Molecules 2017 Jan 24;22(2). / 4. Hellerbrand C, et al. Clinical Phytoscience 2017 Jan;2:7. / 5. Zhong S, et al. Medicine (Baltimore) 2017 Dec;96(49):e9061. / 6. Hajaghamohammadi AA, et al. Hepatitis Monthly 2008;8(3):191-5. / 7. Hashemi SJ, et al. Hepatitis Monthly 2009;9(4):265-70. / 8. Wah Kheong C, et al. Clin Gastroenterol Hepatol 2017 Dec;15(12):1940-9.e8. / 9. Saller R, et al. Drugs 2001;61(14):2035-63. / 10. Velussi M, et al. J Hepatol 1997 Apr;26(4):871-9. / 11. Mastron JK, et al. Anticancer Drugs 2015 Jun;26(5):475-86.

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Tacrolimus

Wiebe C, *et al.* Class II Eplet Mismatch Modulates Tacrolimus Trough Levels Required to Prevent Donor-Specific Antibody Development. *J Am Soc Nephrol* 2017 Nov;28(11):3353-3362.

For HCP

Chong Kun Dang Pharm. Seoul, Korea

Replacing salt form of Tenofovir by Chong Kun Dang technology[1]

Tenofobell® tab.

Tenofovir Disoproxil Aspartate 308.04mg

Stability Up[1]

The Tenofobell® makes ESCape ways from HBV

ESC

Evidence Conducted a phase III trial with 158 patients in 20 domestic centers[2]

Stability Improved stability, hygroscopicity and solubility with new salf form[1]

Clinical study Completed a phase IV trial in patients with chronic hepatitis B virus

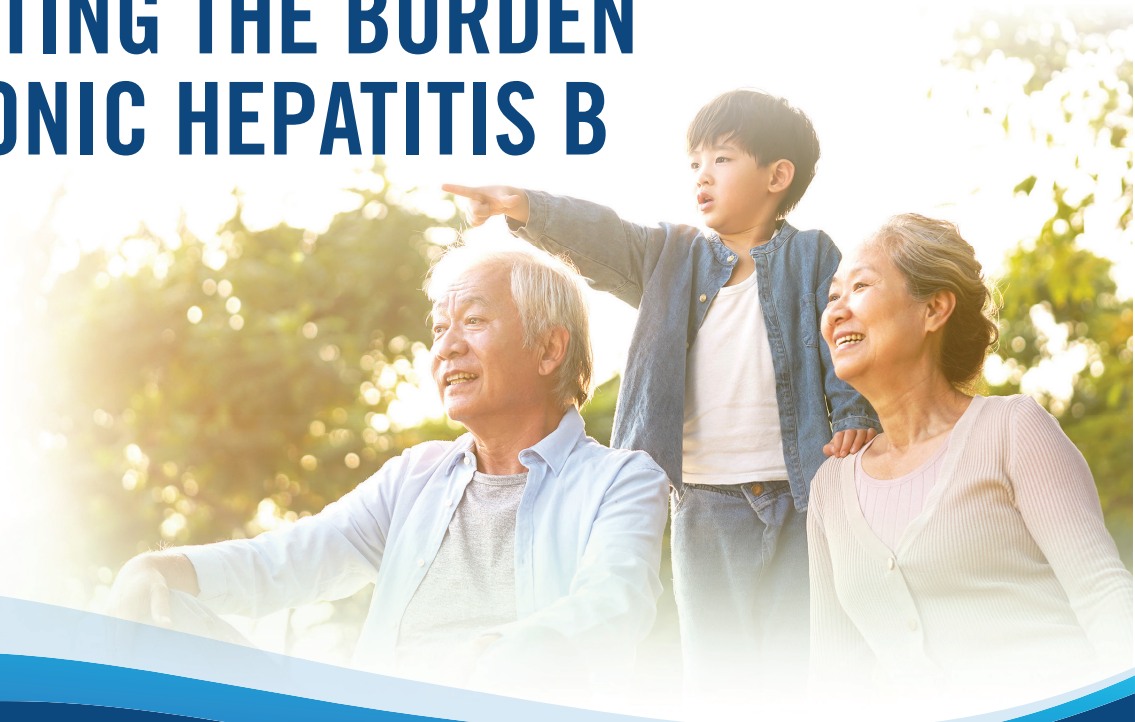
Reference

1) Unex. Pub. No. 10-2014-0028790 (Korean Intellectual Property Office) 2) Clinical Trials gov NCT02805738

HBV, Hepatitis B virus

WE INVITE YOU TO JOIN US ON A JOURNEY OF

ELIMINATING THE BURDEN OF CHRONIC HEPATITIS B



Janssen APASL 2022 Lunch Symposium:

Chronic hepatitis B path to cure: Current perspectives and novel therapeutic approaches

Room #209AB, 2nd Floor, Coex, Seoul, Korea

11:20–12:50 (China, Hong Kong & Singapore time)

12.20–13.50 (Korea time)

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PHARMACEUTICAL COMPANIES OF Johnson & Johnson

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Diagnosis Advanced Fibrosis in NAFLD
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Early diagnosis liver fibrosis in Health check up
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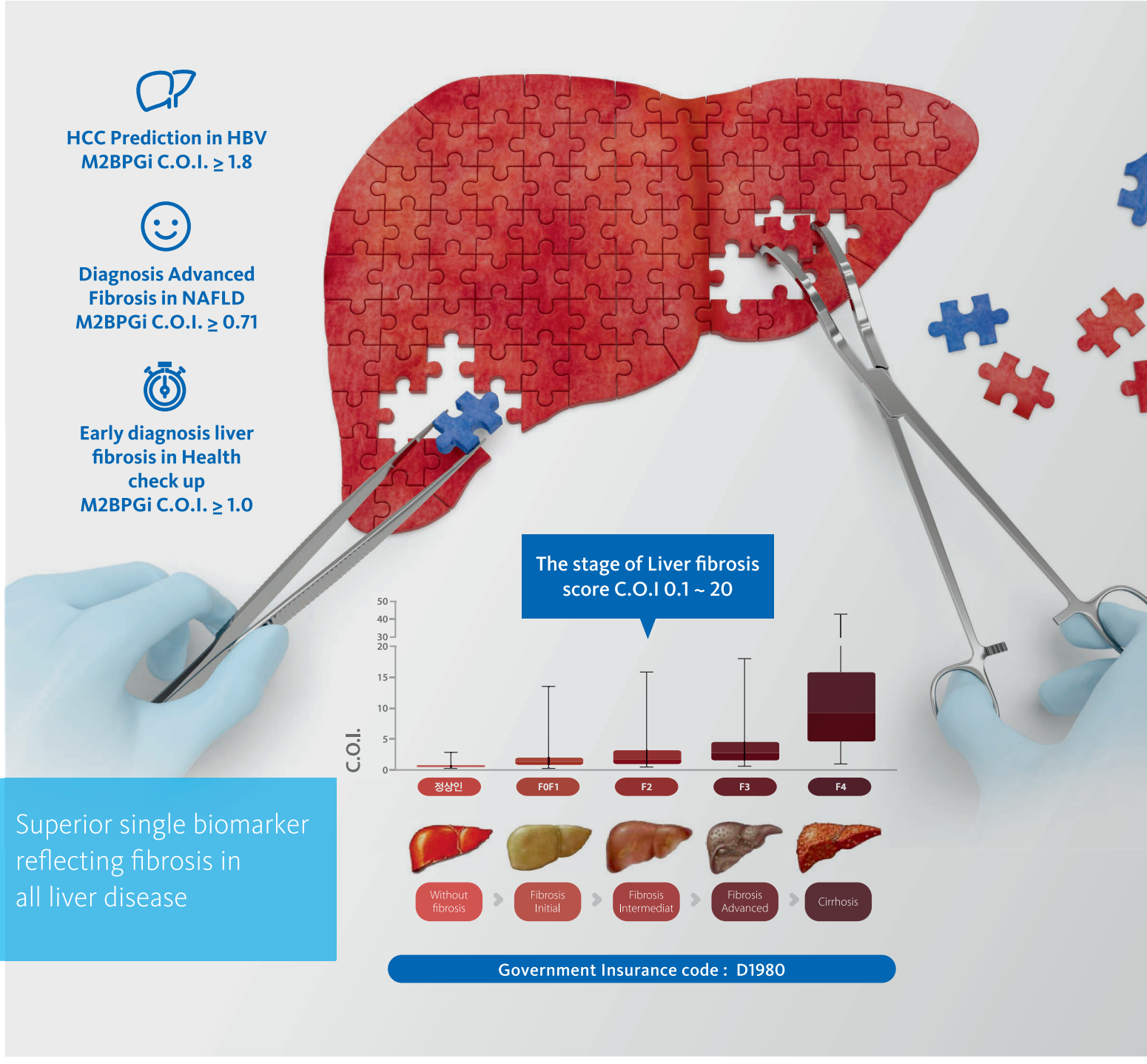

Superior single biomarker reflecting fibrosis in all liver disease

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Obtained 'Exclusive Marketing Rights'! First Generic of Sorafenib

Soranib was officially approved by MFDS on October 29th, 2020.

Treatment of hepatocellular carcinoma, thyroid carcinoma and renal cell carcinoma

Soranib Tab. 200mg on Market!

(Sorafenib tosylate(Micronized))

1. **Obtained 'exclusive marketing rights'** by demonstrating bioequivalence to the original product
2. **Accumulated more than 10 years of experience** in prescribing Sorafenib[1-4]
3. **The First-generic to ease the burden of medication cost**
4. **Improved patient convenience** by redesigning the package

HM-Design 2012_01

Hanmi Pharm.

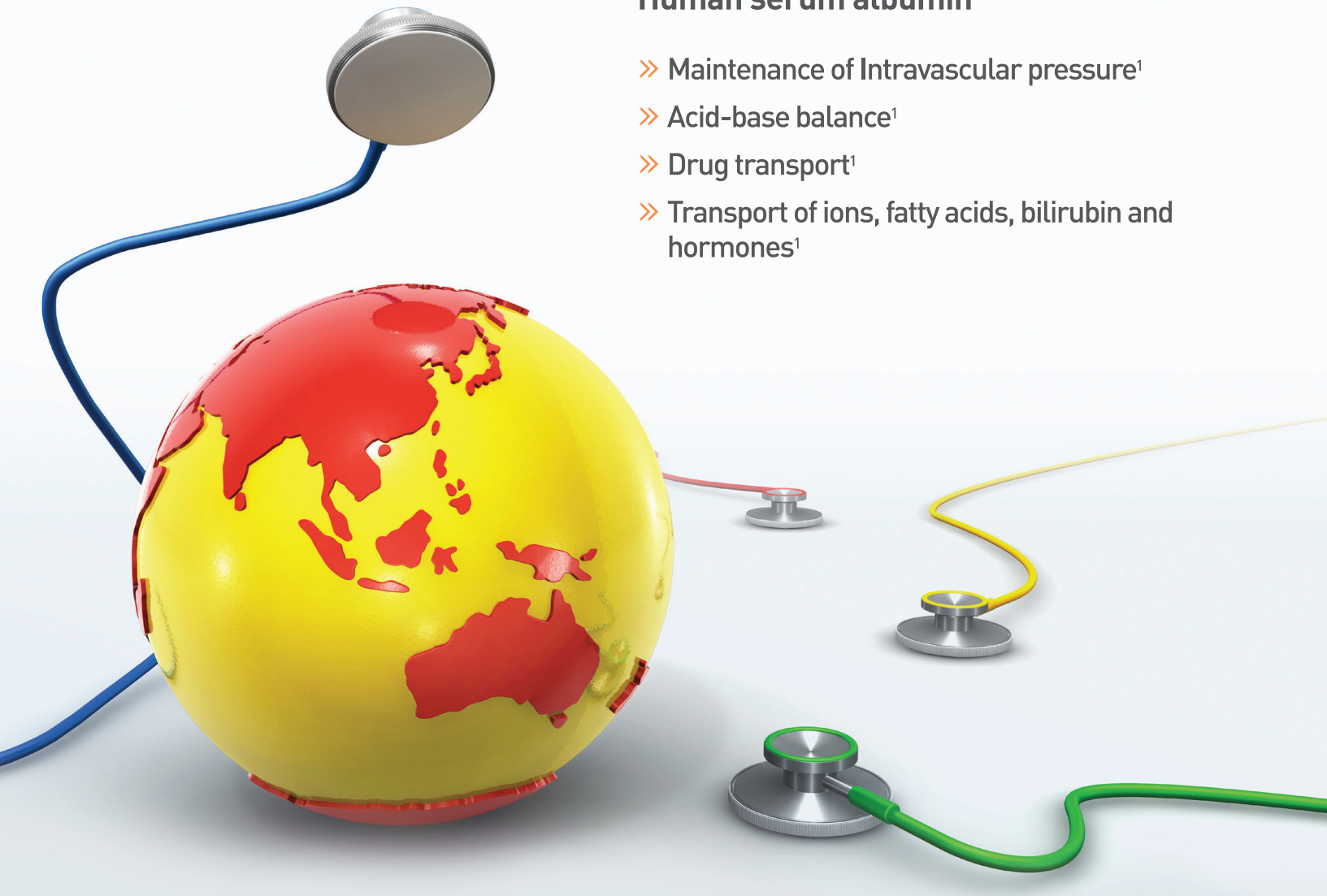
Ref. 1) Llovet JM,*et al. N Engl J Med*,2008;359(4):378-390. 2) Bernard E, *et al. N Engl J Med*, 2007;356:125-34. 3) Robert CK, *et al. Clin Cancer Res*, 2006 Dec;12(24):7271-7278. 4) BroseMS,*et al. The lancet*, 2014 Apr;384(9940):319-328.

SOR-II-2012-01

SK Albumin Inj. 5%/20%

Human serum albumin

- Maintenance of Intravascular pressure[1]
- Acid-base balance[1]
- Drug transport[1]
- Transport of ions, fatty acids, bilirubin and hormones[1]



SK plasma

ECO Lab, 310 Pangyo-ro, Bundang-gu, Seongnam-si, Gyenggi-do, Republic of Korea
Tel +82-2-2008-2008 www. skplasma.com

Prescription drug

Summary of Prescribing information[2]

【PRODUCT NAME】 SK Albumin 5%/20% Inj. 【CONTENTS】 Each 100 mL contains 5 g and 20 g of Human Serum Albumin as active ingredient, for 5% Inj. and 20% Inj. respectively 【INDICATION AND USAGE】 Hypoalbuminemia caused by albumin loss (burn, nephrotic syndrome, etc.) and dysfunction of albumin synthesis (liver cirrhosis, etc.), hemorrhagic shock 【DOSAGE AND ADMINISTRATION】 1. 5% Inj.: 500 mL, equivalent to human serum albumin 25 g should be administered by intravenous drip infusion or by slow direct intravenous injection. The recommended infusion rate is 2–4 mL/min. The dosage may be adjusted according to body weight, age and symptoms. 2. 20% Inj.: 125–375 mL, equivalent to human serum albumin 25–75 g should be administered by intravenous drip infusion or by slow direct intravenous injection. The recommended infusion rate is 2–4 mL/min. It may be diluted with 5 % glucose when necessary. The dosage may be adjusted according to body weight, age and symptoms. 【CONTRAINDICATION】 Patients with a history of hypersensitivity reactions to this drug and its components 【MANUFACTURER】 SK Plasma Co., Ltd. (36618) 157 Saneopdanjigil, Pungsan-eup, Andong-si, Gyeongsangbuk-do, Republic of Korea 【MA HOLDER】 SK Plasma Co., Ltd. (13494) 310 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, Republic of Korea

* For the details, you are recommended to check on prescribing information. The latest approved label is available on the website following. http://drug.mfds.go.kr

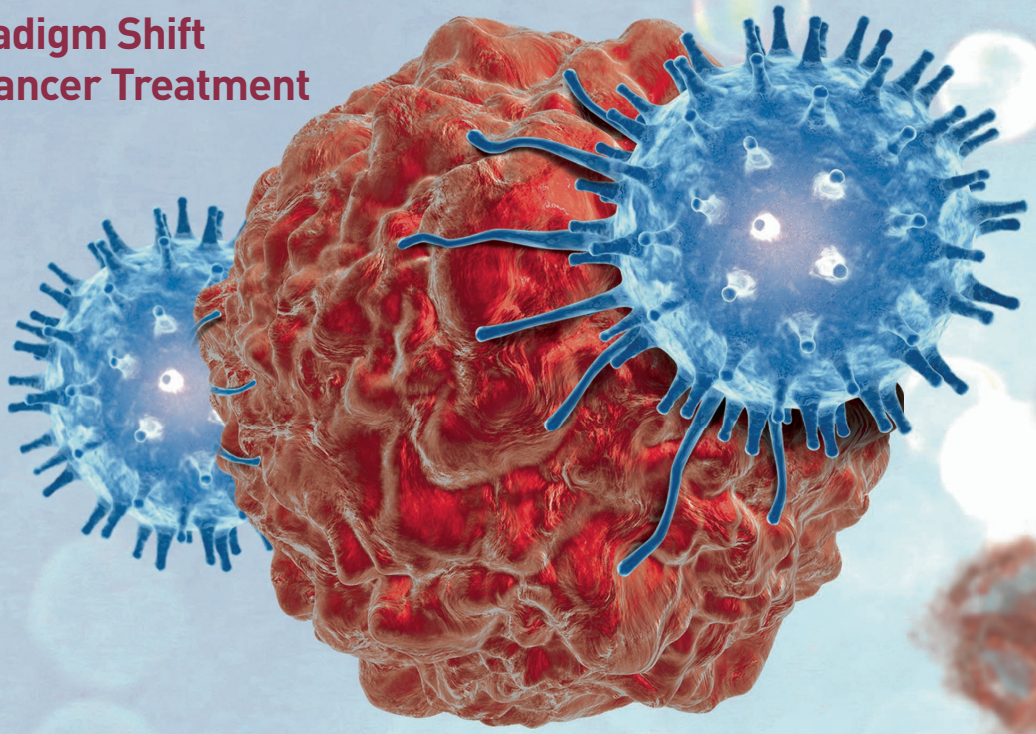
References 1. Haroldo Falcao et al. Albumin in critically ill patients: controversies and recommendations. Rev Bras Ter Intensiva. 2011; 23(1) **2.** SK Albumin 5%/20% Inj. Approval information, MFDS [Cited 2021.11.17] Available from: https://nedrug.mfds.go.kr

ABM-HA04-202112-01

GC Cell

RECOGNIZE & KILL CANCER CELLS

Paradigm Shift in Cancer Treatment



Recognize & Kill the cancer cells[1]

이뮨셀엘씨주

Immuncell-LC Anticancer cellular Immunotherapeutics

ANTI-CANCER ↑ **SAFETY** ↑ (No related serious AE[1]) **QUALITY of LIFE**[2] ↑

이뮨셀-엘씨는 암환자 본인의 몸 속에 있는 면역세포를 이용하여 암세포를 제거하는 치료제로, 2007년 식품의약품안전처의 승인을 받은 항암제입니다.

Ref. 1. Gastroenterology 2015;148:1383–1391 I 2. Cancer Immunol Immunother (2014) 63:939–946

제 품 명 : 이뮨셀엘씨주(엘씨자가혈액유래티림프구)
의약품분류 : 항악성종양제(421) / 전문의약품
효 능 효 과 : 간세포암 제거술(수술, 고주파절제술, 경피적에탄올 주입술) 후 종양제거가 확인된 환자에서 보조요법
용 법 용 량 : 투여 전 백을 부드럽게 3~4회 정도 잘 흔들어 세포가 용제에 완전히 부유될 수 있게 한다. 투여 시 22G 이하의 주사침으로 정맥점적 주사하며 1시간 이내에 투여될 수 있도록 한다. 1회 투여용량은 $1x10^{9}$~$2x10^{10}$ 세포가 포함된 200㎖이며, 투여주기 및 횟수는 1주 간격 4회, 2주 간격 4회, 4주 간격 4회, 8주 간격 4회로 총 16회 투여한다.

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PP-0601
GLIMMER: A randomized double-blind placebo-controlled study of linerixibat, an ileal bile acid transporter inhibitor, in the treatment of cholestatic pruritus in primary biliary cholangitis (PBC)

NX-GBL-836-ADVT-220001 Date of Preparation: March 2022