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Acute Liver Failure and Artificial Liver Support

1

Regression of liver fibrosis after HBsAg loss: a prospective matched case-control evaluation using transient elastography and serum Enhanced Liver Fibrosis (ELF) test

Dr. Lung-Yi Mak[1,2], Dr. Danny Ka-Ho Wong[1,2], Dr. Rex Wan-Hin Hui[1], Dr. Ka-Shing Cheung[1,4], Dr. Fen Liu[3], Dr. James Fung[1,2], Prof. Wai-Kay Seto[1,2,4], Prof. Man-Fung Yuen[1,2]

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Background:
We assessed the effect of hepatitis B surface antigen (HBsAg) seroclearance on liver fibrosis regression in patients with chronic hepatitis B (CHB).

Methods:
CHB patients with recent spontaneous HBsAg seroclearance (cases) were age- and gender- matched with treatment-naïve HBeAg-negative CHB infection (controls). Paired transient elastography (TE) and Enhanced Liver Fibrosis (ELF) measurements were performed at baseline and 3-year. Fibrosis progression and regression were defined as increase and decrease in ≥1 fibrosis stage, respectively.

Results:
In this interim analysis, 40 cases and 142 controls were recruited [median age 55.6 (interquartile range, IQR 49.8-60.9), 53.8% male]. The median liver stiffness (LS) values were similar between the two groups at baseline (5.4 vs. 5.2 kPa, P=0.765) and at 3-years (5.9 vs. 5.5 kPa, P=0.455) respectively. The baseline controlled attenuation parameter values were significantly higher in cases vs controls (288 vs 251 dB/m, respectively, P=0.001). The median ELF at 3-year was significantly higher than baseline in the controls (8.6 vs. 8.4, P=0.033). All patients with severe steatosis had significantly higher baseline LS (5.9 vs. 4.8 kPa; P<0.001), 3-year LS (6.4 vs 5.2 kPa; P<0.001), and baseline ELF (8.8 vs. 8.3, P=0.028). The proportion of patients with fibrosis progression (25.6% vs. 15.5%, respectively, P=0.111) and regression (10.3% vs. 14.8%, P=0.604) was similar in cases vs controls.

Conclusions:
Over a period of 3 years, fibrosis regression and progression were observed at a similar rate in patients with HBsAg seroclearance compared to patients with inactive CHB. Severe hepatic steatosis was associated with higher LS and ELF.

Hepatitis C

2

Genotype and Serotype Analysis on Potential Hepatitis B Virus as a Candidate Sequence for Hepatitis B Vaccine in Web-Based Bioinformatics

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Objectives:
This study aims to determine the genotype and serotype of the hepatitis B virus that has potential as a hepatitis B vaccine candidate. One effective method at present is bioinformatics, a multidisciplinary web-based biological science that can explore various sequences and see phylogeny.

Methods:
The first stage is the collection and selection of nucleotide DNA sequences or hepatitis B virus amino acids. All data on nucleotide DNA sequences and hepatitis B virus amino acids with the target genotype and serotype are accessed and collected from GenBank. Next, a kinship tree is made. This kinship tree is designed with multiple alignments, phylogeny, and tree viewers using phylogeny.fr.

Results:
The data obtained shows that there are 43 sequences with the same subtype, Adw, but the genotype and distribution of the spread of the hepatitis B virus are different. Genotype A originates from Somalia (Africa), and the Philippines (Asia), genotype B originates from Indonesia and China. Genotype C explains that genotype C is found around South Asia and East Asia, genotype H obtained information from America and Mexico, and genotype I originates from China.

Conclusions:
Sequence data that can be candidates for hepatitis B vaccine design are hepatitis B virus genotype B with subgenotype B3, genotype C with subgenotype C6 for the scope of Indonesia, while for the scope of the world obtained the potential of the Adw serotype.

Hepatobiliary Neoplasia

3

Novel miRNA-based Dr.ug CD5-2 reduces liver tumour growth in diethylnitrosamine (DEN)-treated mice by normalising tumour vasculature and altering immune infiltrate

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Objectives:
Normalisation of leaky tumour vasculature is an emerging approach to treat hepatocellular carcinoma (HCC). Blockmir CD5-2 is an oligonucleotide-based inhibitor of the miR-27a interaction with VE-Cadherin, the endothelial specific cadherin. We studied the effect of CD5-2 combined with checkpoint inhibition in the DEN-induced liver tumour mouse model.

Materials and Methods:
DEN was given (25mg/kg intraperitoneally) to male C57BL/6 mice at postnatal day 14. CD5-2 (30mg/kg intravenously fortnightly) and/or anti-PD1 antibody (250µg intraperitoneally every 4 days) with their respective controls (4 groups) were given to the mice from age 7-months until harvest at age 9-months.

Results:
Human HCC data from The Cancer Genome Atlas showed high miR-27a and low VE-Cadherin were both associated with poorer survival (Log-Rank P=0.02 and P=0.01, respectively). In untreated mice, miR-27a expression was significantly increased in tumours compared to adjacent normal tissue. Mice treated with CD5-2 + anti-PD1 antibody had significantly smaller tumours (50% reduction) compared to mice treated with either agent alone, controls, or untreated mice. Histologically, tumours in the CD5-2 + anti-PD1 antibody group exhibited a more favourable immune infiltrate (significantly higher CD3+ and CD8+ T cells and lower Ly6G+ neutrophils) compared to tumours from other groups. Tumours in CD5-2-treated mice had less leaky vasculature (extravasation of Dextran beads) and tumour hypoxia (carbonic anhyDr.ase IX staining) compared to non-CD5-2-treated mice.

Conclusions:
In the DEN mouse model, CD5-2 normalised liver tumour vasculature and reduced tumour hypoxia. CD5-2 plus anti-PD1 antibody reduced tumour size possibly by altering the immune infiltrate to being immunosupportive.

NAFLD and NASH

4

Novel non-invasive risk prediction model for significant Coronary artery disease in Non-alcoholic fatty liver disease

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Objectives:
To devise a highly sensitive and specific non-invasive model comprising CIMT to predict risk for significant coronary artery disease in patients with NAFLD

Materials and Methods:
A nested case-control study was done on 140 NAFLD subjects identified from 250 patients who underwent coronary angiography. Logistic regression analysis was performed to find variables in risk prediction model. Receiver Operating Characteristics (ROC) curve plotted to derive best model.

Results:
Of 140 NAFLD patients, 82 had significant CAD and 58 normal coronaries. Male gender ($p<0.001$), systemic hypertension ($p=0.045$), waist to hip ratio ($p=0.045$) and mean carotid intima-media thickness (CIMT) ($p=0.042$) were independent predictors of CAD in NAFLD on multivariate analysis. A novel risk model, CIMT plus score, was developed comprising these variables with Area under ROC (AUROC) of 0.909 (95% CI, 0.849 to 0.951). Optimized cut off >11 had a sensitivity and specificity of 90.2% (95% CI, 81.7 – 95.7) and 84.5% (95% CI, 72.6 – 92.7) respectively and likelihood ratio of 5.82(3.2 – 10.6) in predicting risk for significant CAD in NAFLD. CIMT plus score performed better than CIMT (ΔAUROC= 0.234(95% CI, 0.142-0.326) ($p<0.0001$)).

Conclusions:
“CIMT plus score” is a novel non-invasive model to predict the risk for significant CAD in NAFLD. Those identified to be at high risk should be managed with aggressive preventive strategies to reduce future cardiovascular events. Prospective randomised studies are required for external validation.

Portal Hypertension and Other Complications of Cirrhosis

5

Psoas Muscle Index: A Simple and Reliable Method of Sarcopenia Assessment and Mortality Predictor on CT Scan in Patients With Chronic Liver Disease

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Objectives:
L3 SMI is the conventional method for sarcopenia assessment. Recently, psoas muscle parameters have been proposed as a simple and quick method. Aim of this study was to assess sarcopenia & predict mortality in cirrhotics by psoas muscle quantification.

Material and Methods:
One hunDr.ed and fifty patients underwent CT scan and psoas muscle index (PMI) was calculated: [PMI = Total psoas muscle area (mm) / (Height)2 (m)]. Cut off values for diagnosis of sarcopenia were derived from control group (n=75). Cases included consecutive CLD patients (n=75) who underwent CT scan. Hand Grip (HG) dynamometer was used to assess HG strength.

Results:
Sarcopenia assessed by PMI was seen in 36% (n=27) of CLD patients. Ascites, hepatic encephalopathy (HE) and gastro-intestinal bleed was seen in 48%, 18.7% and 24% respectively. Association of sarcopenia was statistically significant with ascites and HE ($P < 0.05$). Sarcopenia was significantly higher in patients with CHILD C. HG weakness was seen in 41.3% and mid-arm muscle circumference was low in 25.3% of CLD patients. 53 out of 75 patients completed the follow up period of 1 year. Out of the sarcopenia patients, 77.8% (n=7) succumbed to liver related illness, while 22.2% (n=2) without sarcopenia expired during follow-up. Association of 1 year mortality and sarcopenia was statistically significant (P value = 0.01). Kappa measure of agreement between HG and sarcopenia assessment was 0.608 (good strength).

Conclusions:
PMI sarcopenia proved to be a reliable predictor of mortality. HG dynamometer seems to be a good alternative for sarcopenia assessment.

Portal Hypertension and Other Complications of Cirrhosis

6

The Effects Of 12-Week Home-Based Exercise Training On Aerobic Capacity, Muscle Mass And Quality Of Life In Patients With Liver Cirrhosis: A Randomized Clinical Trial

Mr Pavapol Sirisunhirun[1], Ms Wimolrak Bandidniyamanon[1], Mr Yonworanut Jeerachatakorn[2], Ms Kobkun Muangsomboon[3], Mr Supot Nimanong[1], Mr Taweesak Tanwandee[1], Mr Phunchai Charatcharoenwitthaya[1], Ms Siwaporn Chainuvati[1], Mr Watcharasak Chotiyaputta[1]

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Background:
Physical inactivity and sarcopenia are predictors of mortality in cirrhotic patients. The aim of this study is to prove the benefit of home-based exercise in cirrhotic patients

Materials and Methods:
This is a randomized controlled study including cirrhotic pts with Child-Pugh A. Patients were randomized to home-based exercise training (HPET) (N=20) or control (N=20) for 12 weeks. HPET includes high intensity interval trainings (keep 60-80% of maximum HR). The primary aim was the changes in 6 minute-walk test(6MWT). Secondary aims were the changes in thigh muscle thickness(TMT), liver stiffness(LS) and splenic stiffness(SS), and Chronic Liver Disease Questionnaire(CLDQ).

Results:
Total 40 patients were enrolled. Mean age was 56.3(±7.8) years. Chronic hepatitis B and C were the major cause of cirrhosis. Mean baseline 6MWT was 475.2(±70.4) m. Mean LS and SS was 15.3(±9.3), 29.8(±21.7) kPa respectively. Mean TMT was 1.76(±0.4) cm. At the end of the study, the changes in 6MWT were not different between both groups. The LS showed significant improved in both groups; however, it did not demonstrate the difference when compared between groups. TMT was significantly increased in HPET compared with control. The CLDQ were not significantly changed between groups, but activity and emotional subscore improved in both groups. No adverse events occurred during HPET.

Conclusions:
12-week HPET is safe and effective. Although it did not show any differences in the changes in 6MWT, LS, SS of both groups, it demonstrated the increased TMT in exercise patients. The quality of life score were not significantly changed between groups

Hepatitis B and Hepatitis D

1

Establishment of an outreach, grouping health care system to achieve micro-elimination of HCV for uremic patients in hemodialysis centers (ERASE-C)

Professor Ming-Lung Yu[1]
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Objectives:
Hepatitis C virus (HCV) prevails in uremic hemodialysis patients. The current study aimed to achieve HCV micro-elimination in hemodialysis centers using a comprehensive outreach program.

Methods:
The ERASE-C Campaign is an outreach program for the screening, diagnosis and group treatment of HCV encompassing 2,323 uremic patients and 353 medical staff members from 18 hemodialysis centers. HCV-viremic subjects were linked to care for directly acting antivirals therapy or received on-site sofosbuvir/velpatasvir therapy. The objectives were HCV microelimination (> 80% reduction of the HCV-viremic rate 24 weeks after the end of the campaign in centers with ≥ 90% of the HCV-viremic patients treated) and “No-C HD” (no HCV-viremic subjects at the end-of-follow-up).

Results:
At the preinterventional screening, 178 (7.7%) uremic patients and 2 (0.6%) staff members were HCV-viremic. Among them, 146 (83.9%) uremic patients received anti-HCV therapy (41 link-to-care; 105 on-site sofosbuvir/velpatasvir). The rates of sustained virological response (SVR12, undetectable HCV RNA 12 weeks after the-end-of-treatment) in the full analysis set and per-protocol population were 89.5% (94/105) and 100% (86/86), respectively, in the on-site treatment group, which were comparable with the rates of 92.7% (38/41) and 100% (38/38), respectively, in the link-to-care group. Eventually, the HCV-viremic rate decreased to 0.9% (18/1,953), yielding an 88.3% reduction from baseline (range: 54.3% to 100% in each site). HCV microelimination and “No-C HD” was achieved in 92.3% (12/13) and 38.9% (7/18) of the hemodialysis centers, respectively.

Conclusions:
Outreach strategies with mass screenings and on-site group treatment greatly facilitated HCV microelimination in the hemodialysis population.

2

Preliminary results of a Phase 2 study of VIR-2218, an X-targeting RNAi therapeutic, in patients with chronic hepatitis B: sub-analyses of HBeAg-negative and HBeAg-positive patients

Professor Man-Fung Yuen[1], Professor Young-Suk Lim[2], Dr. Daniel Cloutier[3], Dr. Ling Shen[3], Dr. AnDr.ea Cathcart[3], Dr. Xiao Ding[3], Dr. AnDr.e Arizpe[3], Dr. Phillip Pang[3], Dr. Stephen Huang[4], Dr. Edward Gane[5]
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Objectives:
VIR-2218 is a GalNAc-conjugated short interfering ribonucleic acid in development for chronic hepatitis B virus infection (CHB). VIR-2218 is designed to silence HBV transcripts from cccDNA and integrated DNA across all 10 HBV genotypes. We present safety and antiviral data from a Phase 2 study in CHB patients, focusing on baseline virologic characteristics and post-treatment HBsAg reductions in HBeAg-negative and HBeAg-positive subgroups.

Materials and Methods:
Noncirrhotic, virologically suppressed CHB patients received 2 subcutaneous doses of VIR-2218 or placebo (Day 1 and Day 29). HBeAg-negative patients received 20, 50, 100 or 200mg and HBeAg-positive patients received 50 or 200mg. Cohorts included 4 or 8 subjects randomized 3:1 (VIR-2218:placebo). Assessments included safety for 12 weeks post-treatment and HBsAg follow-up for 48 weeks. Preliminary 24-week data are presented.

Results:
24 CHB patients received VIR-2218 (n=18 HBeAg-negative; n=6 HBeAg-positive). Most adverse events were mild in severity with no events leading to treatment discontinuation. No clinically significant changes in safety laboratory parameters were observed. At baseline, HBeAg-positive patients had higher burdens of HBsAg, HBV RNA and HBcrAg. Similar maximum post-treatment HBsAg declines were observed for both subgroups, with magnitude of reduction related to dose. For the 200mg dose, the mean HBsAg reduction was ≥1 log by week 12 and sustained through week 24 in both subgroups.

Conclusions:
VIR-2218 was tolerated across all dose levels with no safety signals observed. Similar magnitude of HBsAg reduction in HBeAg-positive and HBeAg-negative CHB patients suggests that it could silence transcripts from both cccDNA and integrated DNA.

Hepatitis C

3

Safety and Efficacty of Oral TLR8 Agonist, Selgantolimod (SLGN), in Virally-Suppressed Adult Patients with Chronic Hepatitis B: A Phase 2 Study

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Objectives:
To assess SLGN, an oral TLR8 agonist, as treatment for CHB in virally suppressed adults

Materials and Methods:
Patients were randomized to SLGN 3mg, 1.5mg, and PBO (2:2:1) once weekly for 24 weeks (W) and followed for 24W post-treatment with option to enter 48 W of treatment free follow-up (TFFU). Safety assessed adverse events (AE) and laboratory abnormalities. Primary efficacy endpoint was proportion of patients with ≥1 log10IU/mL decline from baseline in HBsAg levels at W24. Secondary endpoints include HBsAg and HBeAg loss rates and changes in pharmacodynamic markers (e.g. cytokines and immune cell subsets).

Results:
48 patients (24 HBeAg-positive and 24-negative) randomized. Baseline characteristics were similar across groups. One patient achieved the primary endpoint of ≥1 log10IU/mL decline at W24. By W48, 2(5%) patients achieved HBsAg loss, 3(16%) HBeAg loss, and 10(34%) ≥0.1 log10 HBsAg decline in SLGN-treated groups vs 0(0%) placebo group. One HBsAg loss patient entered TFFU and remains HBV DNA-negative, HBsAg-negative, and HBsAb-positive. Frequent AEs were nausea, URTI, headache, vomiting, and fatigue. Dose-proportional increases in cytokines were observed 4h post-dose without tachyphylaxis. Dose-proportional decreases in CD3+ T cells were also observed potentially reflecting distribution from peripheral circulation into liver.

Conclusions:
SLGN up to 3mg once weekly for 24 weeks is generally safe and elicited TH1 cytokine responses as well as shifts in peripheral immune cell subsets consistent with target engagement. Two patients achieved HBsAg loss and 3 patients achieved HBeAg loss with SLGN treatment. Further evaluation of SLGN in combination studies is planned.

4

A randomized, double-blind, phase 3, non-inferiority, 48 weeks trial: tenofovir amibufenamide versus tenofovir disoproxil fumarate for the treatment of chronic hepatitis B virus infection.

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Objectives:
Tenofovir amibufenamide is another novel proDr.ug of tenofovir, which was safe and well tolerated in previous trials. In this phase III study, we compared the efficacy and safety of tenofovir amibufenamide versus tenofovir disoproxil fumarate (TDF) in adults with chronic hepatitis B virus (HBV) infection.

Materials and Methods:
Patients with chronic HBV infection were randomly assigned (2:1) to receive either 25 mg tenofovir amibufenamide or 300 mg TDF with matching placebo. The primary efficacy endpoint was the proportion of subjects with HBV DNA less than 20 IU/mL at week 48. The key safety endpoints were bone and renal parameters.

Results:
This is an ongoing 144 weeks study. Totally 1,002 eligible patients from 51 centers were randomized to receive either tenofovir amibufenamide or TDF therapy (n=666, n=336, respectively). The baseline characteristics were well balanced between treatment groups. 52.8% (242/458) patients receiving tenofovir amibufenamide and 55.9% (128/229) TDF had HBV DNA less than 20 IU/mL at week 48 in HBeAg-positive patients; while 90.2% (157/174) patients receiving tenofovir amibufenamide and 92.9% (78/84) TDF had HBV DNA less than 20 IU/mL at week 48 in HBeAg-negative patients. The non-inferiority criterion was met in both populations. Patients receiving tenofovir amibufenamide had a significantly smaller decrease in bone mineral density at hip ($p<0.001$) and spine ($p<0.001$), while less increase in serum creatinine at week 48 ($p<0.05$). Other safety results were similar between treatment groups.

Conclusions:
In patients with chronic HBV infection, tenofovir amibufenamide was non-inferior to TDF, and had improved bone and renal effects.

5

Exosomes with miR-574 transfer anti-HBV activity mediated by the interferon from macrophage to HBV-infected hepatocyte

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Objectives:
Interferon alpha (IFN-α) has proven to be clinically effective in the treatment of chronic hepatitis B (CHB) due to its capability to reduce hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) covalently closed circular DNA (cccDNA). However, the underlying mechanisms are not well defined. The purpose of this study is to explore the role of exosomes in the antiviral process of IFN

Materials and Methods:
We investigated the anti-HBV activities of exosomes both from pegylated IFN-α (PegIFN-α) treated patients and the supernatants of IFN-α-treated THP-1(the human leukemia monocyte cell line) derived macrophages. Then, we identified three upregulated miRNAs in exosomes through miRNA sequencing. By luciferase reporter assay, we found hsa-miR-574-5p reduced pregenomic RNA (pgRNA) and polymerase mRNA levels by binding to the nucleotides 2750-2757 position of HBV genomic sequence.

Results:
Exosomes from patients and the supernatants exhibited anti-HBV activities including the suppression of supernatant HBsAg, HBeAg, and HBV DNA levels as well as intracellular HBV cccDNA in HBV related cell lines. MicroRNA sequencing revealed that PegIFN-α treatment upregulated exosomal hsa-miR-193a-5p, hsa-miR-25-5p, and hsa-miR-574-5p that could partially inhibit HBV replication and transcription. The luciferase reporter assay confirmed that hsa-miR-574-5p reduced pgRNA and polymerase mRNA levels by binding to the 2750-2757 position of HBV genomic sequence.

Conclusions:
Exosomes can transfer IFN-α-related miRNAs from macrophages to HBV-infected hepatocytes, thereby suppressing HBV replication and expression.

Hepatobiliary Neoplasia

6

The Novel Regimen of a Single, Priming Dose of Tremelimumab (T) + Durvalumab (D) in Patients With Unresectable Hepatocellular Carcinoma (uHCC) by Viral Etiology

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Objectives:
The novel immune checkpoint (IC) regimen T300+D provided the best benefit-risk Prof.ile vs other IC regimens in a Phase 1/2 study (Study 22, NCT02519348). Viral etiology may affect uHCC prognosis, thus we evaluated whether hepatitis B and C viral infection (HBV, HCV) impacted response and survival.

Materials and Methods:
Immunotherapy-naïve patients with uHCC progressing on, intolerant to, or refusing sorafenib were randomized to T300+D (T, 300mg [1X] +D 1500mg, then D 1500mg Q4W), T75+D (T, 75mg Q4W [4X] + D, 1500mg Q4W), D (1500mg Q4W), or T (750mg Q4W [7X] then Q12W). Active HBV required antiviral therapy. The primary endpoint was safety. Efficacy is presented by viral etiology.

Results:
As of Feb 28, 2020, 332 patients were randomized (T300+D, n=75; T75+D, 84; D, 104; T, 69). 218 were infected with hepatitis (HBV n=123, HCV n=95); 114 were uninfected. Grade 3/4 treatment-related AEs occurred in 29.4% (T300+D, 35.1%; T75+D, 24.4%; D, 19.8%; T, 43.5%). T300+D produced the highest ORR for all subgroups (overall, n=18 [24.0%]; HBV, 5 [18.5%]; HCV, 6 [28.6%]; nonviral, 7 [25.9%]) and the longest median [95% CI] OS overall (18.7 [10.8-27.3] months) and for the HCV subgroup (22.3 [10.8-not reached] months).

Conclusions:
Response and survival varied with infection status; however, the T300+D regimen consistently demonstrated the highest ORR independent of viral status and the longest median OS in the overall group. T300+D and D are being evaluated in the ongoing Phase 3 HIMALAYA study (NCT03298451) in first-line HCC vs sorafenib.
Funding: AstraZeneca

Inflammation and Immunobiology

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IMbrave150: updated overall survival (OS) data from a global, randomized, open-label Phase III study of atezolizumab + bevacizumab vs sorafenib in unresectable hepatocellular carcinoma (HCC)

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Objectives:
Atezolizumab+bevacizumab has been approved globally for pts with unresectable HCC without prior systemic therapy based on IMbrave150 (NCT03434379). Here, we report an updated OS analysis for IMbrave150.

Materials and Methods:
The global, multicenter, randomized, open-label, Phase III study IMbrave150 enrolled 501 systemic treatment–naive pts with unresectable HCC, ≥1 measurable untreated lesion (RECIST 1.1), Child-Pugh class A liver function and ECOG PS 0/1. Patients were randomized 2:1 to atezolizumab 1200 mg IV q3w + bevacizumab 15 mg/kg IV q3w or sorafenib 400 mg bid until unacceptable toxicity or loss of clinical benefit per investigator. This post hoc descriptive OS analysis included 12 mo of additional follow-up from the primary analysis.

Results:
501 patients were enrolled (336 to atezolizumab+bevacizumab; 165 to sorafenib). At the clinical cut-off date of August 31, 2020, median follow-up was 15.6 mo and 280 OS events were observed. Median OS was 19.2 mo with atezolizumab+bevacizumab vs 13.4 mo with sorafenib (HR, 0.66 [95% CI, 0.52, 0.85]; P=0.0009). Updated objective response rates (RECIST 1.1) were 29.8% and 11.3% with atezolizumab+bevacizumab and sorafenib, respectively; complete response rates were 7.7% and 0.6%. Similar results were obtained per HCC mRECIST. Safety was consistent with the primary analysis, with no new signals identified.

Conclusions:
IMbrave150 showed consistent clinically meaningful treatment benefit and safety with an additional 12 mo of follow-up. The combination provides the longest survival seen in a front-line Phase III study in advanced HCC, confirming atezolizumab+bevacizumab as a standard of care for previously untreated, unresectable HCC.

Liver Fibrogenesis and Non-Parenchymal Cell Biology

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MiR-24 Regulates Hepatic stellate cells Activation by Targeting ALK4 in Liver Fibrosis

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Objectives:
MicroRNAs (miRNA, miR) are the crucial regulator of organ fibrosis. MiR-24 is reported to be involved in the process of cardiac and muscle fibrosis, the role of miR-24 in liver fibrosis remains to be known.

Materials and Methods:
EdU incorporation and flow cytometry, transwell assay were used to determine hepatic stellate cells (HSC) cell proliferation, and cell cycle, migration ability, respectively. The levels of α-SMA and collagen type I were measured using qRT-PCR. Western blot was performed to determine the level of target gene in HSCs. Fluorescence reporter assay was conducted to prove the interaction of miR-24 and target gene. MiR-24 level was measured in the plasma of liver fibrosis patients using qRT-PCR. Results: Downregulation of miR-24 was detected in the CCl4-induced fibrotic liver and activated HSC. Overexpression of miR-24 led to decreased proliferation and activation of rat HSC, simultaneously suppressed the migration of HSC. MiR-24 inhibition had the opposite function. We further found that miR-24 acts on the 3'UTR region of ALK4 and thereby affecting the phosphorylation of Smad3. In addition, we showed that Runt-related transcription factor 1 (RUNX1) was firstly induced and then subsequently caused transcription and expression of miR-24 in HSC. Moreover, miR-24 was lower in the serum of liver cirrhosis patient in contrast to healthy people and correlated to the Child-Pugh stage. In conclusion, our study suggested that miR-24 may play an important role in HSC biological function including activation and migration.

Conclusions:
MiR-24 can provide new treatment strategy and screening biomarkers for liver fibrosis.

NAFLD and NASH

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Safety and Efficacy of Combination Therapies Including Cilofexor/Firsocostat in Patients With Bridging Fibrosis and Cirrhosis Due to NASH: Results of the Phase 2b ATLAS Trial

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Objectives:
To evaluate the safety and efficacy of an ACC inhibitor, FXR agonist, and ASK1 inhibitor, alone and in combination, in NASH patients with advanced fibrosis.

Materials and Methods:
In this phase 2b trial, 392 NASH patients with advanced fibrosis (F3-F4) were randomized to placebo, selonsertib 18 mg, cilofexor 30 mg (CILO), or firsocostat 20 mg (FIR), alone or in two-Dr.ug combinations, once daily for 48 weeks (W48). Baseline (BL) and W48 biopsies were evaluated by a central reader. The primary endpoint was ≥1-stage improvement in fibrosis without worsening of NASH. Secondary endpoints included changes in NAFLD Activity Score (NAS), liver biochemistry, and noninvasive fibrosis markers.

Results:
The majority of patients had cirrhosis (56%), diabetes (72%), and NAS ≥5 (83%). For the primary endpoint, combinations led to higher response rates vs placebo, the greatest with CILO/FIR (11% vs 21%, p=0.17). Compared to placebo, CILO/FIR led to significantly increased proportions of patients with ≥2-pt reduction in NAS and ≥1-grade improvements in steatosis, lobular inflammation, and ballooning (all p<0.05). CILO/FIR led to significant improvements in ALT, AST, bilirubin, bile acids, CK18, insulin, eGFR, liver stiffness, and ELF (all p≤0.05). All regimens were well tolerated. Pruritus occurred in 28% of CILO/FIR patients (no discontinuations) vs 15% on placebo. At W48, CILO/FIR led to an increase vs placebo in triglycerides (+45 mg/dL, p<0.001); changes in LDL (+9 mg/dL, p=0.080) were not significant.

Conclusions:
In patients with F3-F4 fibrosis, CILO/FIR was well tolerated and led to improvements in fibrosis and NASH activity.

Hepatitis B and Hepatitis D

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Disappeared steatosis relates to fibrosis regression in on-treatment patients with chronic hepatitis B

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Objectives:
Despite the increasing prevalence of steatosis in patients with chronic hepatitis B (CHB), the interaction between steatosis and fibrosis in the course of anti-HBV therapy remains unclear. We aimed to identify the correlation between dynamic changes of steatosis and fibrosis based on histology in on-treatment patients with CHB.

Materials and Methods:
CHB patients with paired liver biopsies before and after 78 weeks of anti-HBV therapy were enrolled in this study. Liver fibrosis regression/progression was defined by both changes of Ishak score and post-treatment P-I-R system of Beijing Classification. Hepatic steatosis was assessed by the NAFLD activity score. Collagen percentage area (CPA) in different sites was identified by SHG/TPEF-based technology.

Results:
A total of 239 CHB patients with paired liver biopsies were included in the final analysis. They were divided into four groups according to the changes of steatosis during therapy: 162 (67.8%) persistent without steatosis, 24 (10.0%) developed new-onset steatosis, 21 (8.8%) with disappeared steatosis, and 32 (13.4%) persistent with steatosis. Fibrosis regression rate was the highest in group of disappeared steatosis, and the lowest in persistent steatosis group (76.1% vs. 43.8%, OR = 4.114, 95%CI: 1.211–13.980, P = 0.026). The most significant decline of CPA was also shown in the group of disappeared steatosis (decrease 50.8% from baseline, P = 0.216), which was mainly observed in septal and sinusoidal area.

Conclusions:
Disappeared steatosis is correlated to fibrosis regression. Changes in steatosis influence the collagen content in septal and sinusoidal areas.

Group 1 - 1

Liver Function Test Abnormalities in COVID-19 and Associations with Outcomes: ICU Experience from India

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Objectives:
Abnormalities in liver function tests have been reported with COVID-19. This study examines spectrum of LFT abnormalities and association with outcomes in COVID-19.

Materials and Methods:
Analysis of LFT parameters (bilirubin, ALT, AST) of 191 COVID-19 patients admitted to ICU was done. LFT status at baseline and subsequent testing were classified as “Normal”-all 3 parameters < ULN, “Liver injury (LI)”-any parameter between 1-3X ULN, “Severe liver injury (SLI)”- any parameter >3x ULN. LFT trend was defined as “Improvement”, “Stable” and “Worsening” after comparing LFT status at baseline and subsequent testing. Association of clinical outcomes and complications with LFT status at baseline, at subsequent testing and LFT trend was calculated.

Results:
LI and SLI were present respectively in 54.4% and 7.8% patients at baseline and 56.3% and 22.8% patients subsequently. LFT trends showed “Improvement”, “Stable” and “Worsening” in 20.3%, 57.0% and 22.8% patients respectively. SLI at baseline was significantly associated with more requirement of invasive ventilation, development of pneumothorax and longer ICU stay. SLI at subsequent testing was significantly associated with higher incidence of shock, longer duration of inotropes, cardiac arrest, bleeding, need for dialysis and death. “Worsening” LFT trend was significantly associated with higher incidence of shock, cardiac arrest, pneumonia, need for invasive ventilation and death.

Conclusions:
Severe liver injury either at admission or subsequently, as well as worsening LFT trend during hospitalization are associated with increased incidence of life-threatening complications and death, and can be used as vital clinical clues for physicians treating COVID-19 patients.

Group 1 - 2

Comparison between using Hepatocellular carcinoma (HCC) risk scores and current criteria to identify high-risk patient for HCC surveillance in chronic hepatitis B patients in Thailand.

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Background:
The current guideline for HCC surveillance is based on age/sex using ultrasound abdomen +/- AFP 6-12 monthly, and is a resource burden. From previous study, HCC surveillance program is cost-effective if HCC incidence ≥0.2% per year or ~ 1% in 5 years. Validated Asian HCC risk scores have been developed to classify HCC risk and may improve cost-effectiveness of surveillance.

Objectives:
We studied the difference in the number of HBV patients needing surveillance if HCC risk scores were used, compared to using the current national guideline for HCC surveillance.

Methods:
HBV patients age >18 years seen in the liver clinic (1st October 2019 to 30th September 2020) were included. Exclusion criteria were diagnosed HCC, post-liver transplantation, cirrhosis Child-Pugh C not on transplant list, co-existing liver disease, chronic alcoholic use. Patients were classed into two groups: Non-cirrhotic and Cirrhotic groups. Each group was then separated into subgroups; Untreated subgroup (or treated <2 years) was analyzed by CU-HCC, GAG-HCC, REACH-B and LSM-HCC scores. Treated subgroup (treated ≥2 years) was analyzed by CU-HCC, GAG-HCC,REACH-B and mPAGE-B score.

Results:
Of 713 HBV patients: 50.6% were male, with mean age 55.43 years, 10.7% cirrhosis and 10.7% HBeAg+. The 627 non-cirrhotic patients were separated into 2 subgroups: 318 patients were in untreated group and 319 patients were in treated group. The results showed that, compared to the national guideline, the number patients needing HCC surveillance decreased if HCC risk scores were used. In untreated non-cirrhotic subgroup, the reduction of patients needing HCC surveillance was -69.5%, -58.9%, -58.8% and -54.1% for GAG-HCC, LSM-HCC, CU-HCC and REACH-B, respectively. In treated non-cirrhotic subgroup, it was -80%,-75.2%,-75.2% and -2.8% for GAG-HCC, CU-HCC, REACH-B and mPAGE-B, respectively. For cirrhotic patients, HCC risk scores didn't significantly change the percentage of patients needing HCC surveillance when compared with current guideline.

Conclusions:
1. In non-cirrhotic HBV patients, HCC risk scores reduced the number of patients needing HCC surveillance significantly(most risk scores reduced by 54-80%). This would impact on the resources needed for HCC surveillance nationally.
2. For cirrhotic patients, HCC risk scores were unnecessary.

Keywords:
Hepatocellular carcinoma (HCC), HCC risk scores, HCC surveillance, chronic hepatitis B(HBV)

Group 1 - 3

Risk of Metabolic Acidosis with Metformin Use amongst Diabetic Patients with Chronic Hepatitis-B-Related Cirrhosis and Chronic Kidney Disease

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Objectives:
We examined the impact of metformin dosage on risk of metabolic acidosis in diabetic patients across different degree of chronic hepatitis B (CHB)-related cirrhosis and chronic kidney disease (CKD).

Materials and Methods:
We identified a territory-wide cohort of diabetes mellitus (DM) patients with CHB-related cirrhosis from 2000 to 2017 in Hong Kong. Metabolic acidosis was defined by blood pH ≤7.35 with lactate >5mmol/L or arterial bicarbonate ≤18mmol/L or venous bicarbonate ≤21mmol/L, and/or diagnosis codes. Child-Pugh class and CKD stage were modelled as time-dependent covariate. Age, gender, comorbidities and use of other medications were adjusted as covariates. The maximum daily dose of metformin was modelled in categories of ≤1000mg and >1000mg. Patients with estimated glomerular filtration rate <30 mL/min/1.73 m2 or renal replacement therapy at baseline were excluded.

Results:
Of 4,431 subjects with DM and CHB-related cirrhosis, 2,670 were metformin users. The risk of metabolic acidosis increased with more advanced cirrhosis and CKD. Metformin use was associated with even higher risk in patients with stage 4/5 CKD regardless of severity of cirrhosis (aHR ranged from 1.97-2.41). In stage 4/5 CKD, a daily dose of metformin ≤1000mg was still associated with higher risk of metabolic acidosis regardless of severity of cirrhosis (aHR ranged from 2.45-3.92).

Conclusions:
Patients with Child-Pugh class B cirrhosis or above were at a higher risk of metabolic acidosis. Metformin further increased the risk in patients with stage 4/5 CKD. Dose adjustment in stage 4/5 CKD may not reduce risk of metabolic acidosis regardless of Child Pugh classes.

Group 1 - 4

Oligonol and Its Beneficial Effects in Non-alcoholic Fatty Liver Disease: A Randomized, Double-blinded, Placebo-controlled Trial

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Objectives:
Oligonol, a low molecular weight oligomer of long-chain polyphenols from lychee extracts, has been shown to have insulin sensitizing, lipid lowering, and weight loss effects. The aim of this study was to evaluate the therapeutic effects of Oligonol in patients with non-alcoholic fatty liver disease (NAFLD).

Materials and Methods:
Adult patients with NAFLD defined by MRI proton density fat fraction (MRI-PDFF) ≥11% were enrolled in the study and then randomly assigned to receive either Oligonol or placebo. Basic demographic data, body weight, waist circumference, biochemical blood tests, and MRI-PDFF were obtained at baseline and at the end of treatment (week 24). Primary endpoint was ≥ 30% reduction in MRI-PDFF at 24 weeks.

Results:
Forty patients were enrolled (n=20 in each group). Demographic data, body weight, waist circumference, body mass index, MRI-PDFF, ALT, fasting blood sugar, lipid Prof.ile, HOMA-IR were similar between the two groups at baseline. Primary endpoint was achieved in 20% in Oligonol group and 15% in placebo group (p=0.68). We found a significant reduction in MRI-PDFF between week 0 and week 24 in Oligonol group (mean reduction 3.74%, p=0.002) and a non-significant reduction in placebo group (mean reduction 2.61%, p=0.06). Significant reductions in body weight, waist circumference, ALT and fasting blood sugar were observed in Oligonol group. In contrast, only body weight significantly declined at week 24 in placebo group. No serious adverse events were observed in both groups.

Conclusions:
Oligonol treatment could significantly reduce hepatic fat content, body weight, waist circumference, ALT and fasting blood sugar.

Group 1 - 5

Acute kidney injury defined by cystatin C may be superior for predicting the outcomes of liver cirrhosis with acute gastrointestinal bleeding

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Background & Aims:
Acute kidney injury (AKI) is conventionally evaluated by a dynamic change of serum creatinine (Scr). Cystatin C (CysC) seems to be a more accurate biomarker for assessing the kidney function. This retrospective multicenter study aims to investigate the role of CysC for evaluating the in-hospital outcomes of patients with liver cirrhosis and acute gastrointestinal bleeding.

Methods:
Overall, 677 cirrhotic patients with acute gastrointestinal bleeding, who had both Scr and CysC levels detected at their admissions, were screened. eGFR-Scr, eGFR-CysC, and CKD-EPI Scr-CysC were calculated. MELD score and AKI were re-evaluated by CysC instead of Scr. Odds ratios (ORs) were calculated in the logistic regression analyses. Areas under curves (AUCs) were also calculated in the receiver operating characteristic (ROC) curve analyses.

Results:
Univariate logistic regression analyses demonstrated that baseline Scr (OR=1.015, P<0.001) and CysC (OR=3.366, P<0.001) levels, eGFR-Scr (OR=0.970, P<0.001), eGFR-CysC (OR=0.978, P=0.005), CKD-EPI Scr-CysC (OR=0.973, P=0.001), conventional MELD score defined by Scr (OR=1.156, P<0.001), MELD score re-defined by CysC (OR=1.153, P<0.001), and AKI re-defined by CysC (OR=3.484, P=0.022) were significantly associated with in-hospital death, but not conventional AKI defined by Scr (OR=2.735, P=0.085). ROC analyses showed that baseline CysC level (AUC=0.673), eGFR-Scr (AUC=0.658), eGFR-CysC (AUC=0.674), CKD-EPI Scr-CysC (AUC=0.677), conventional MELD score defined by Scr (AUC=0.767), and MELD score re-defined by CysC (AUC=0.751) could significantly predict the risk of in-hospital death, but not baseline Scr level (AUC=0.637).

Conclusions:
AKI re-defined by CysC may be superior for predicting the in-hospital mortality of patients with cirrhosis and acute gastrointestinal bleeding.

Group 1 - 6

Outcomes of Patients with Advanced Stage Hepatocellular Carcinoma (HCC) Receiving Different Treatment Modalities: Real-World Data

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Introduction:
Although sorafenib is recommended for patients with Barcelona Clinic Liver Cancer (BCLC) stage C HCC, many of these patients do not receive sorafenib given its high cost. We therefore aimed to determine outcomes of advanced HCC treated with different therapies.

Methods:
Data of 255 patients with BCLC C HCC between 2013 and 2020 were retrospectively abstracted. Overall survival and factors affecting survival were determined using Kaplan-Meier method and Cox proportional hazard analysis.

Results:
The mean age was 59 years, 85.5% were male, 85.1% had portal vein invasion. Most patients (73.3%) received locoregional therapy (TACE, Y-90 SIRT, external radiation) as the first-line treatment. Other first-line treatments included surgical resection (10%), systemic therapy (targeted therapy, chemotherapy, immunotherapy) (6.3%) and palliation (16.5%). Overall survival of the entire cohort was 4.62 months. Patients receiving resection as the first-line treatment had the longest survival of 13.1 months, followed by locoregional therapy (6.1 months), systemic therapy (2.1 months) and palliation (1.5 months). By univariate analysis, ECOG, tumor number and size, bilobar involvement, tumor burden >50%, distance metastasis, Child-Pugh class, OKUDA score, treatment with resection and locoregional therapy were associated with survival. By multivariate analysis, tumor size, bilobar involvement, OKUDA score, resection and locoregional therapy remained significantly associated with survival, with adjusted hazard ratio (95%CI) of 1.04 (1.01-1.07), 1.53 (1.11-2.11), 1.26 (1.03-1.56), 0.42 (0.19-0.93) and 0.58 (0.4-0.86), respectively, P <0.05all.

Conclusions:
In real-world setting, surgical resection and locoregional therapy significantly improved outcomes of advanced HCC patients, while systemic treatment including targeted therapy did not prolong survival.

Group 2 - 1

A Study On The Role Of Lille's Score In Predicting Response To Granulocyte Colony-stimulating Factor Therapy In Patients With Severe Alcoholic Hepatitis

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Objectives:
The primary-aim- To assess the role of Lille score on day 6 in predicting response to G-CSF therapy in severe alcoholic hepatitis.
Secondary-Aims were to assess parameters like mDF,MELD,and CTPS after G-CSF. To assess survival in patients at 30 and 90 days.

Material:
Prospective, open-label, single center study between December 2018 to April 2020.

Result:
We enrolled total 67 patients, all were male. 26 were excluded as per exclusion criteria. Thus, 41 enrolled for therapy. Out of which 37 received first 5 doses and 25 patients completed 12doses. Over all mortality at 90days was 31.7%(13/41).
Lille's score on Day6 had significant correlation (p-value <0.005) with survival at 90days. AUC was 0.925(CI 95%, 0.838 to 1.000). The cut-off value of 0.195 (sensitivity-81.8% and Specificity-86.7%).Kaplan Miere plot showed that the two groups as ≤0.195 and >0.195, showed at survival at 90days was 90% and 26.7%respectively. Lille's score also independently predicted mortality with cut-off 0.195 (p-value 0.009) and Odds Ratio is 16.3. In survival group there was a significant improvement in CTPS, DF, Bilirubin and transaminases on Day6 and Day30. MELD score improved on day6 and day30, but was significant on day30. Creatinine and serum albumin showed no significant change at day6 and day30. In non-survival group, no significant improvement in liver disease clinical score and biochemical parameters. G-CSF therapy was well tolerated in patients.

Conclusions:
G-CSF is appearing as a promising agent. Lille's score may be used as prognostic marker for survival. However, larger data is needed to validate it.

Group 2 - 2

Impact Of Overweight And Obesity On Live Attenuated Hepatitis A Vaccine Response In ChilDr.en And Young Adult

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Objectives:
Our aim was to evaluate the effect of overweight and obesity on the response to live attenuated hepatitis A vaccine in chilDr.en and young adult.

Materials and Methods:
This was a prospective cohort study conducted at 3 schools, 1 university and 1 obesity clinic at hospital. The subjects aged 7 to 25 years were tested for baseline anti-HAV antibodies and administered 0.5 mL of live attenuated hepatitis A vaccine (MEVAC-A™). Participants with seronegative defined by anti-HAV antibodies (<20 mIU/mL) were divided into three groups according to obesity defined as follows WHO classification. We evaluated immunogenicity and adverse events (AE) after 8-9 weeks from vaccination.

Results:
A total of 212 subjects completing the study (female: 131, median age (IQR): 13 years (11-16). Of these, 95 subjects (46%) were in overweight/obesity group. All the AE (n=106) were non-serious and most event was myalgia (34%). The seroprotection (≥20 mIU/mL antibody titer after vaccination) rates were 100 %. Post vaccination geometric mean titers of anti-HAV (IU/L) were 451.1 [95%CI: 374.76-543.0] in underweight group, 428.38 [95%CI: 399.61-459.22] in normal weight group and 467.46 [95%CI: 425.01-514.16] in overweight/obesity group. No significant differences in immunogenicity were found between 3 groups (p=0.33).

Conclusions:
Live attenuated hepatitis A vaccine is safe and highly immunogenic because all of participants were seroprotection.

Group 2 - 3

Elevated Serum Ferritin And CRP Levels As Prognostic Markers In Decompensated Cirrhosis: A Prospective Cohort Study

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Objectives:
The aim of the study was to analyse serum ferritin and CRP levels as prognostic markers in patients with decompensated cirrhosis and compare it with MELD and CTP scores.

Materials and Methods:
220 consecutive patients with decompensated cirrhosis were included. Serum Ferritin and CRP levels at presentation and factors predicting mortality at 3 months were assessed.

Results:
Patients with decompensated cirrhosis (n=220) (M:F 168:52 ,mean age 55.7 yrs +/- 11) were followed up for a period of 3 months. At presentation, median serum ferritin level was 321.45 (7.4-750) ng/ml in survivors and 725(275-3000) ng/ml in non-survivors, and median serum CRP level was 9 (2-60) mg/L in survivors and 18.5 (6-64) mg/L in non-survivors. Serum ferritin levels were significantly different between survivors and non-survivors [p <0.05] and showed significant correlation with CRP levels (p <0.01). Serum ferritin, CRP, total leucocyte count, MELD score, CTP score, presence of hepatorenal synDr.ome, spontaneous bacterial peritonitis, hepatic encephalopathy and ACLF were significant predictors of mortality on univariate analysis. Ferritin, MELD and presence of hepatorenal synDr.ome were significant predictors of mortality on multivariate analysis. Serum ferritin [AUROC 0.91, 95% CI 0.87-0.95] was comparable to MELD score [AUROC 0.92, 95% CI 0.891-0.961] and better than CRP [AUROC 0.74, 95% CI 0.67-0.80] and CTP score [AUROC 0.847, 95% CI 0.79-0.89], in predicting death at 3 months.

Conclusions:
Elevated serum ferritin level is an independent prognostic marker in decompensated cirrhosis. Elevated serum CRP levels did not show association with mortality at three months in decompensated cirrhosis.

Group 2 - 4

Aetiology And Staging Of Chronic Liver Disease In A Cohort Of Patients In A Tertiary Care Hospital In Sri Lanka

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Objectives:
The aim of this study was to share our experience with Chronic Liver-cell Disease (CLD) patients with regard to the aetiology, severity and complications.

Material and Methods:
A descriptive cross-sectional study was carried out at National Hospital Kandy (NHK), Sri Lanka form June 2019 to December 2019. Data of patients diagnosed with CLD were obtained from patient records after obtaining ethical clearance. These included the patient demographics, details on aetiology, severity and associated complications through clinical records and questionnaires.

Results:
The study included 106 patients with a mean age of 57.4(±10.6), 69(65%) were males. Most (70.8%.) were from Central Province of Sri-Lanka.
Non-alcoholic steatohepatitis (NASH) and Cryptogenic cirrhosis combined was the most common cause of CLD (39.6%) followed by Alcohol related (AR) CLD (25.5%), Autoimmune hepatitis (14.2%) and Dr.ug induced CLD (7.5%). In 6.6% the aetiology was inconclusive. Chronic viral hepatitis, Metabolic disease (Wilson's and Haemochromatosis) were seen in 0.9% each respectively.
More than two thirds had decompensated cirrhosis with Child-Pugh scores of 28%, 42% and 30% for Child-Pugh grade A, B, C respectively. Average MELD score was 14.82(±5). Diabetes and hyperlipidaemia were seen in 44.3% and 13.2% respectively.

Conclusions:
NASH combined with Cryptogenic CLD was the most common aetiology. Most were diagnosed of CLD at an advanced stage.

Group 2 - 5

Immunoprophylactic Failure Against Hepatitis B Virus Mother-to-infant Transmission

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Objectives:
Since 1992, the prevalence of hepatitis B virus (HBV) in Thailand has been declining due to the expanded program of immunization (EPI) for the hepatitis B vaccine. Vertical transmission is the major route of HBV infection and contributes to chronic liver disease. Although adequate hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) coverage has been shown, immunoprophylactic failure also occurs. This study evaluated the prevalence and factors associated with the failure of immunoprophylactic vaccines.

Materials and Methods:
A prospective study was conducted from March 2018 to March 2020. A total of 67 chilDr.en of hepatitis B surface antigen (HBsAg)-seropositive mothers with known HBeAg status were enrolled. Twenty-three (34.3%) and 44 (65.7%) chilDr.en were born to HBeAg-seropositive and HBeAg-seronegative mothers, respectively. Neonates received both the HB vaccine and HBIG within two hours post-birth followed by four subsequent HB vaccinations at ages 1, 2, 4, and 6 months according to Thailand's policy. HBsAg and Anti-HBs were evaluated at ages 9–12 months.

Results:
Four chilDr.en (6%) with HBeAg-seropositive mothers and HBV DNA levels >108 IU/mL (17.4 %) were defined as immunoprophylactic failures based on HBsAg-seropositivity. One developed acute liver failure. Two HBeAg-seropositive mothers with high viral load had histories of irregular medical (Tenofovir) intake.

Conclusions:
Immunoprophylactic failure in chilDr.en also occurred even with effective immunoprophylactic protocols, especially those with HBeAg-seropositive mothers and high HBV DNA levels. Inadequate treatment may be one of the reasons for this failure. Novel strategies and large number of cases for further vertical transmission prevention should be considered.

Group 3 - 1

Real-world efficacy of sofosbuvir and velpatasvir treatment for patients with hepatitis C virus-related decompensated cirrhosis

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Objectives:
Real-world reports of efficacy of sofosbuvir and velpatasvir (SOF/VEL) treatment for patients with hepatitis C virus (HCV)-related decompensated cirrhosis are limited from Asia.

Materials and Methods:
A total of 94 patients with decompensated cirrhosis who started SOF/VEL treatment between February 2019 and October 2019 at 26 Japanese institutions were included. We defined sustained virologic response (SVR) as undetectable serum HCV-RNA at 12 weeks after the end of treatment (EOT). This research has been approved by an ethical committee.

Results:
The mean age was 67 years. For the Child-Pugh class, 7% were class A, 74% were class B and 18% were class C. The SVR12 rate was 88.3% (83/94) and 6 patients were relapsed after the EOT, 3 patients died before judging SVR12 and 2 patients were missing data. The treatment completion rate was 95.7% (90/94) and 3 of 4 patients discontinued treatment because of liver-related events. Among patients with SVR12, improvement rates of Child-Pugh class B to A were 35% at the EOT and 48% at SVR12, and improvement rates of Child-Pugh class C to B or A were 36% at the EOT and 43% at SVR12. On the other hand, the deterioration rates of Child-Pugh class B to C were 5% at SVR12. Among 6 patients with relapsed, Child-Pugh class were not improved between baseline and 12 weeks after the EOT.

Conclusions:
Real-world efficacy of SOF/VEL treatment for patients with decompensated cirrhosis was preferable. Achieving SVR is expected to improve liver function even in patients with decompensated cirrhosis.

Group 3 - 2

Tenofovir Alafenamide Attenuates Effects of Diabetes and Body Mass on Serum Alanine Aminotransferase Activities in Patients with Chronic Hepatitis B

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Objectives:
Tenofovir alafenamide (TAF) associates with a higher proportion for alanine aminotransferase (ALT) normalization in chronic hepatitis B (CHB) patients compared with tenofovir disoproxil fumarate (TDF). The underlying mechanism is to yet be defined. We investigated ALT determinants in CHB patients who were switched to TAF.

Methods:
From an institutional electronic registry, we identified 97 CHB patients who received a prior antiviral for ≥48 weeks before transitioning to TAF for ≥48 weeks. Multivariable linear regression analyses were performed to model ALT based on demographic and clinical variables, separately before and after switching to TAF.

Results:
At switch, 83.5% of patients were receiving TDF monotherapy, the median ALT was 33 U/L with 42% being within normal limits (WNL). At 48 weeks post-switch, the median ALT decreased to 28 U/L ($p<0.01$) with the proportion WNL increasing to 63% ($p<0.01$). Changes in ALT occurred despite median BMI increasing by +0.44 kg/m2 ($p<0.01$). In multivariable regression analyses, higher BMI and diabetes significantly increased ALT ($p=0.03$, $p<0.01$, respectively) while patients were receiving non-TAF regimen. In contrast, after 48 weeks of TAF, neither BMI nor diabetes had a significant association with ALT, with regression coefficients diminishing by >50% compared to the model before switch.

Conclusions:
In CHB patients receiving non-TAF antiviral, persistently abnormal ALT may be attributed to non-alcoholic fatty liver disease (NAFLD). Under TAF, the relation between ALT and obesity or diabetes is disrupted. Focused studies for the mechanism by which TAF may decouple metabolic risk factors from ALT, and NAFLD, in CHB are warranted.

Group 3 - 3

Hepatic Sarcoidosis In Malaysia: A Monocentric 10-Year Old Retrospective Review

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Objectives:
Sarcoidosis is a multisystem granulomatous disorder that commonly affects the lungs and rarely involves the liver. We aimed to describe the cases of hepatic sarcoidosis which were treated in University Malaya Medical Centre (UMMC) over the past 10 years.

Materials and Methods:
The electronic database of patients attending the Gastroentrology clinic in UMMC from 2010 till 2020 was reviewed. Patients with biopsy proven hepatic sarcoidosis were identified; their medical records were examined, and the relevant information was extracted for statistical analysis.

Results:
There were seven patients with hepatic sarcoidosis identified. All patients were females and of Indian ethnicity. The median (IQR) age was 50 (41-58) years and the median (IQR) duration of follow up was 6 (3-8) years. All patients presented with weight loss and had cholestatic liver injury on the serum biochemistry; liver biopsy showed presence of granulomatous inflammation in all. All but one patient was found to have lung involvement. All patients were given high dose steroids post-diagnosis; four patients were treated with azathioprine; two patients with methotrexate; and two more with infliximab. All patients did not have liver cirrhosis during diagnosis; however, 57% went on to develop liver cirrhosis despite treatment. One patient died from non-liver related cause three years after diagnosis, while the rest are still alive.

Conclusions:
Hepatic sarcoidosis has a predilection for female gender and Indian ethnicity in Malaysia with a high rate of progression to cirrhosis despite treatment.

Group 3 - 4

Downstaging Hepatocellular Carcinoma To Milan Criteria Yields Similar Post-liver Transplant Outcomes To Tumors Within Milan Criteria: A Systematic Review And Meta-analysis

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Objectives:
Patients with hepatocellular carcinoma(HCC) beyond the Milan criteria(MC) are recommended for liver transplantation(LT) if they have successfully undergone downstaging (DS) to meet the criteria, despite a lack of high-level evidence supporting this approach. This systematic review and meta-analysis study was performed to compare the survival and recurrence outcomes between the DS and those within the MC to provide further evidence in support of this aspect of the current guideline.

Materials and Methods:
Studies were identified from MEDLINE and SCOPUS since inception to August, 2019. Two independent screened titles and full articles to ensure eligibility. Relevant data was extracted and converted to individual patient data and a Kaplan-Meier(KM) curve was constructed. A log-rank test and cox regression were applied to compare between both groups.

Results:
From 1201 studies, nine cohorts were eligible (DS vs. within the MC = 449 vs. 2039). Among these, eight and six studies reported post-transplant OS and DFS, respectively. The 1-, 3-, and 5-year overall survival rates were 86.3%, 73.9%, and 62.7% for those in the DS group, and 81.6%, 72.5%, and 66.4% for those within the MC. The 1-, 3-, and 5-year disease-free survival rates were 85.4%, 73.0%, and 64.0% for those in the DS group and 87.8%, 77.9%, and 69.6% for those within the MC group. The OS (HR 1.08;0.89–1.33;P=0.40) and DFS (HR 1.21;0.79–1.85;P=0.37) were not significantly different between both groups.

Conclusions:
Applying the DS protocol into the LT program in intermediate-stage HCC is proven to be of benefit, without compromising post-transplant survival outcomes.

Group 3 - 5

Granulocyte-Colony Stimulating Factor (G-CSF) For Pediatric Decompensated Liver Cirrhosis: A Preliminary Study

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Objectives:
Decompensated cirrhosis (DC) in chilDr.en is a leading indication of liver transplantation (LT). Optimizing therapy is needed to reduce mortality of chilDr.en on the LT waiting list. Organ allocation is based on pediatric end-stage liver disease (PELD) score. Granulocyte-colony stimulating factor (G-CSF) therapy has shown promising results in adult DC, known for its role in the mobilization of hematopoetic stem cells. Our study aimed to investigate the effect of G-CSF on nutritional status, PELD score, liver function and short-term side effects of G-CSF in chilDr.en indicated for LT.

Materials and Methods:
ChilDr.en aged between 3 months – 12 years old with DC were randomly divided into control and intervention group. Intervention received subcutaneous injection of G-CSF (5 µg/kg/day) for twelve courses. Both groups received standard medical treatment for DC. Primary outcomes were nutritional status and PELD score at 90 days, while secondary outcomes was liver function within 90 days. Short-term effects were also observed.

Results:
Twenty-six chilDr.en (mean age ±23 months) were eligible in the open-label study. Weight, height, mid-arm circumference and PELD score did not show significant change at 90 days. AST and ALT levels decreased on day-60 and remained stable on day-90. Albumin rose on day-30 and showed further increase on day-90. Low grade fever was the most common side effect reported in 54% of intervention.

Conclusions:
Multiple doses of G-CSF did not improve nutritional status and PELD score after three months, however, the treatment showed clinical improvement of liver enzymes and albumin.

Group 4 - 1

Improvement of liver stiffness assessed by imaging-based techniques and non-invasive fibrosis scores in chronic hepatitis C patients with sustained virological response after direct-acting antiviral therapy

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Objectives:
To demonstrate sequential changes in liver stiffness using imaging-based techniques and simple biomarkers in patients with chronic hepatitis C virus (HCV) who received direct-acting antiviral (DAA) and achieved sustained virological response at 12 weeks (SVR12).

Methods:
A total of 81 HCV patients with SVR12 after DAA treatment were prospectively analyzed. Liver stiffness evaluated by transient elastography (TE), ultrasound elastography (USE), magnetic resonance elastography (MRE) and fibrosis scores using APRI and FIB-4 were assessed before treatment and 1-year after starting DAA.

Results:
The values of TE (17.7±14.2 vs 12.9±11.1 kPa,p<0.001), USE (10.5±3.5 vs 8.9±3.5 kPa,p<0.001), MRE (4.3±1.9 vs 3.7±2.0 kPa,p<0.001), APRI (1.6±1.7 vs 0.7±0.6,p<0.001) and FIB-4 (3.8±3.2 vs 3.0±3.2,p<0.001) significantly decreased from the baseline to follow-up measurements. Advanced fibrosis (F3) by elastography tests was found in 50-65.4% of patients but reduced to 37.1-43.1% after SVR12. While liver steatosis assessed by TE-based controlled attenuation parameter and MRI-determined proton density fat fraction values were not different. Aspartate (AST) and alanine (ALT) aminotransferase, total bilirubin and albumin were significantly improved whereas platelet count and body mass index did not change over time. A significant positive correlation could be found between all studied tests before and after therapy. Strong correlation was found among three imaging-based techniques before (r=0.65-0.77,p<0.001) and after (r=0.69-0.79,p<0.001) therapy. The strength of correlation between elastography and biomarker was moderate before therapy (r=0.38-0.50,p<0.001) but increased at post SVR12 (r=0.42-0.69,p=0.001).

Conclusions:
Viral eradication after DAA therapy in HCV patients resulted in the improvement of APRI and FIB-4, and liver stiffness as assessed by TE, USE and MRE.

Group 4 - 2

Recurrence Predictive Models for Patients with Hepatocellular Carcinoma after Radiofrequency Ablation based on Machine Learning Algorithms

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Objectives:
Hepatocellular carcinoma (HCC) has been one of the leading causes of cancer death. Despite accurate diagnosis and effective treatments, the recurrence rate of HCC is still high. To build a recursive model by analyzing preoperative reports is helpful for follow-up and observing recurrence of tumor.

Materials and Methods:
Newly diagnosed HCC patients in National Taiwan University Hospital (NTUH) who received radiofrequency ablation (RFA) as the first treatment, were enrolled. Among 334 enrolled patients, 256 patients did not have recurrent HCC one year after RFA treatment and the other 78 patients had HCC recurrences. Data was processed with workflow of feature extraction and data imputation to acquire 16 features. We use different machine-learning methods to build the recurrence prediction model of HCC. The model performance among linear regression (LR), support vector machine (SVM), random forest (RF), and deep neural network (DNN) under a variety of experimental environment, including different parameters of models, data normalizations, and methods of data up-sampling were compared.

Results:
DNN model has the relatively best result that is the highest accuracy (82.65%) and second balanced accuracy (BAC=66.03%) among all models. SVM with feature selection according to importance in RF has the best BAC result (66.48%) with 10% lower accuracy (72.51%). RF has the worst accuracy (56.32%). SVM has the worst BAC (61.66%).

Conclusions:
Among the different prediction models, DNN achieved the best results by considering both accuracy and balanced accuracy. Establishment of prediction model could identify the risk patients with close monitoring of tumor recurrence.

Group 4 - 3

Performance of Non-invasive Liver Fibrosis Tests in Predicting Variceal Bleeding among Patients with Upper Gastrointestinal Hemorrhage

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Background and Aims:
Various non-invasive liver fibrosis tests (NIFTs) have been studied aiming to predict the degree of liver fibrosis and the presence of esophageal varices in patients with cirrhosis. However, the use of NIFTs to predict variceal bleeding (VB) in the setting of upper gastrointestinal bleeding (UGIB) remains unexplored. This study aimed to evaluate the performance of NIFTs in predicting VB as a cause of bleeding in patients with UGIB.

Methods:
Consecutive patients presented with UGIB who underwent esophagogastroduodenoscopy (EGD), between June 2018 and August 2019 at Rajavithi Hospital, Bangkok, were prospectively enrolled. Baseline clinical/lab characteristics and NIFTs-scoring systems, including APRI, ARR, FIB-4, Fibrosis Index, Lok Index, GUCI, and King's score, were evaluated.

Results:
A total of 215 patients with UGIB were included: mean age was 56.4 years, mean Glasgow-Blatchford score was 9.8 and 39.5% were VB. In the overall analysis, the AUCs of NIFTs for predicting VB ranged between 0.686 and 0.867. GUCI and APRI (both at the cut-off of 0.5) showed best performance in predicting VB with sensitivity of 95.3% and 90.6%, and specificity of 73.1% and 75.4%, respectively. In patients without known cirrhosis status (n=132), the AUCs of GUCI and APRI in predicting VB were 0.860 and 0.895, respectively.

Conclusions:
GUCI and APRI scores have good performance in predicting VB in patients presenting with UGIB regardless of known cirrhosis status. They may be helpful to select patients for prompt administration of vasoactive agents, antibiotics and urgent EGD.

Group 4 - 4

Acute Liver Failure: Outcome and Prognostic Predictors

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Objectives:
Acute liver failure (ALF) is defined as a rapid hepatic dysfunction and encephalopathy in the absence of pre-existing liver disease. It is relatively uncommon, however, it progresses rapidly with high mortality. Globally, viral hepatitis is responsible for the majority of cases of ALF. This study aimed to determine the etiology, outcome and predictive factors for in-hospital mortality in Acute Live Failure (ALF) patients.

Materials and Methods:
A descriptive study was conducted with ALF patients hospitalized at the Gastro-hepatology Department of Asian Institute of Medical Sciences, Hyderabad from May 2018 to September 2019. A total of 31 patients having clinical and biochemical markers suggestive of ALF were included in the study and evaluated for etiology and outcome during the hospital stay and prognostic scores {King College Criteria (KCC) and Model End-Stage Liver Disease (MELD)} were compared.

Results:
Thirty-one patients with a mean age of 22 years, 21 (67.7%) were males. Most common etiology was indeterminate 21 (67.7%) while 5 (16.15%) were Hepatitis B and 5 (16.15%) were Hepatitis E. The in-hospital mortality was 19 (61.3%), out of which 14 (73.3%) were males, and 12 (38.7%) were spontaneously recovered. High International Normalized Ratio (INR) > 5.00 (p=0.02), MELD score >32 (p=0.049), KCC 2 or more out of 5 and sepsis (p= 0.008) were independently associated with in-hospital mortality.

Conclusions:
The in-hospital mortality of ALF was significantly high with raised INR, MELD (>32), KCC (2/5) and sepsis being the poor prognostic factors.

Group 4 - 5

Significant Liver Fibrosis is Associated with Increased Risk of Advanced Adenoma in Average-Risk Population with Metabolic Associated Fatty Liver Disease

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Background:
Metabolic associated fatty liver disease (MAFLD) shares several risk factors for colorectal neoplasia. This prospective study was conducted to evaluate the relationship between MAFLD and colorectal neoplasia.

Methods:
We invited patients aged ≥50 years who underwent colonoscopy for colorectal cancer screening during 2018-2020 to determine the presence of steatosis and fibrosis with transient elastography. Logistic regression models were used to calculate odds ratio (OD) for the effect of steatosis and fibrosis on colorectal neoplasia after adjusting for confounders, including age, gender, smoking, and metabolic parameters.

Results:
956 participants (mean age 62.0±7.1 years, 33.3% male) were enrolled. Adenomatous polyps were observed in 412 (43%), 66 of them had advanced adenoma, and 3 were diagnosed with colorectal cancers. 480 (50.2%) participants had steatosis (controlled attenuation parameter ≥248 dB/m), with 279 (29.5%) presenting with severe steatosis (≥280 dB/m) and 45 (4.7%) having significant fibrosis (liver stiffness ≥7.9 kPa). The presence of steatosis was not associated with the detection of adenomatous polyps (OD=1.26, 95% CI, 0.94-1.70) and advanced adenoma (OD=1.26, 95% CI, 0.72-2.20). MAFLD patients with significant fibrosis did not have a higher detection rate of adenomatous polyps (OD=1.61, 95% CI, 0.85-3.04) but had an increased incidence of advanced adenoma (OD=2.61, 95% CI, 1.11-6.12) after adjusting for all confounders.

Conclusions:
Among the average-risk population, steatosis was not associated with the risk of adenomatous neoplasia. However, the risk of advanced adenoma appears to be higher in MAFLD patients with significant fibrosis. Liver steatosis and fibrosis assessment could help stratify individuals for colorectal cancer screening.

Group 5 - 1

Improvement of Gut Diversity and Composition after Direct-Acting Antivirals in HCV-Infected Patients with or without HIV Coinfection

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Background:
The influence of direct-acting antivirals (DAAs) on the composition of gut microbiota in hepatitis C virus (HCV)-infected patients with or without human immunodeficiency virus (HIV) is unclear.

Methods:
We enrolled 62 patients with HCV monoinfection and 24 patients with HCV/HIV coinfection receiving elbasvir/grazoprevir from a clinical trial. Fecal specimens collected at pre-treatment and 12 weeks post-treatment were analyzed using amplicon-based 16S rRNA sequencing.

Results:
Sustained virological response (SVR12) rates in the mono- and co-infection groups were similar (98.4%vs.95.8%). Pre-treatment bacterial communities in the patient groups were less diverse and distinct from those of healthy controls. Compared with HCV-monoinfected patients, HCV/HIV-coinfected individuals showed comparable microbial alpha-diversity but displayed declined Firmicutes/Bacteroidetes ratio. The improvement of microbial dysbiosis was observed in responders achieving SVR12 across fibrosis stages but was not found in non-responders. Responders with low degree of fibrosis exhibited a recovery in alpha-diversity to level comparable with healthy controls. Reciprocal alterations of increased beneficial bacteria and reduced pathogenic bacteria were also observed in responders.

Conclusions:
This study indicates short-term effect of DAAs in restoration of microbial dysbiosis. The favorable changes in gut microbiota Prof.iles after viral eradication might potentially contribute towards the reduction of HCV-related complications among infected individuals.

Group 5 - 2

A Survey On Approaches Towards Patients With Elevated Liver Enzymes Before Surgery In Vietnamese Hospitals

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Background:
Approaching to patients with liver enzymes elevation before surgery is a debating topic globally and in Vietnam.

Objectives:
To explore the clinical practice situation of Vietnamese physicians on elevated-liver-enzymes patients before elective surgery.

Materials and Methods:
An online survey was implemented between 01-31/07/2020, to obtain doctors' characteristics and their approaches to patients with elevated liver enzymes before elective surgery in different levels of Vietnamese hospitals.

Results:
114 doctors (53.5% males) with the mean age of 32.8 ± 6.9 years completed our survey. Their employment mainly are provincial-level or university hospitals (35.1% and 30.7% respectively). Most of the participants had 1 to 5 years (40.4%) or 5 to 10 years (36.0%) in experience. 42.1%, 22.8%, and 13.2% of participants were anesthesiologists, internal gastroenterologists, hepatologists, and surgeons, respectively. The clinician's decisions were categorized into 3 main groups, including assessing severity and etiologies (hepatitis virus tests, liver functions tests and imaging tests were prevalent at 71.9%, 70.2% and 58.8%, respectively), using liver-enzymes-reducing medicines (44.7%), and consulting with hepatologists (73.7%). In terms of comparing opinions between groups of doctors by experience, only the differences in the proportions of "imaging indications" are statistically significant. In terms of surgery decision, 56.1% decided to delay when liver enzymes level is above 5ULN while others 13.1% would not delay if the liver functions remain stable.

Conclusions:
There is a lack of conformity in Vietnamese doctors' approaches towards patients with elevated liver enzymes before elective surgery, which raise the requirement of a standardized protocol in clinical practice.

Group 5 - 3

The effects on HBsAg clearance, relapse and safety after tenofovir and entecavir cessation in non-cirrhotic chronic hepatitis B, HBeAg negative patients

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Objectives:
To evaluate the incidence and predictors of HBsAg loss, virological relapse (VR), clinical relapse (CR) and safety after cessation of tenofovir (TDF) or entecavir (ETV).

Methods:
A total of 98 non-cirrhotic chronic hepatitis B, HBeAg negative patients (CHB), treated with either TDF or ETV for at least 3 years with suppressed HBV DNA for at least 2 years, were enrolled into either TDF discontinued (TDF-D, n=39) or ETV discontinued (ETV-D, n=27) groups compared to nucleoside analogue (NA) continued group (NA-C, n=32). All patients were followed for at least 48 weeks.

Results:
Seven patients (10.6%) achieved HBsAg clearance 48 weeks in NA discontinued groups which was not significant compared to NA-C group(P=0.092). HBsAg level was the only significant predictor for HBsAg clearance (Hazard ratio(HR), 0.21 95% confidence interval(CI), 0.007-0.61, P=0.004). Cumulative incidences of VR were 66.7% and 40.7% (P=0.037), cumulative incidences of CR were 43.6% and 22.2% (P=0.073) in TDF-D and ETV-D at week 48, respectively. Six patients (15.4%) in TDF-D group had severe ALT flares, 2 required admission and one death. TDF treatment before cessation and HBsAg level less than 100 IU/ml were predictive factors of VR.

Conclusions:
NA cessation can induce HBsAg clearance more than NA continuation. However, NA cessation increased the risk of VR and CR, especially TDF discontinuation which occurred earlier that ETV discontinuation. Some may result in severe CR leads to hepatic decompensation and death even in the patients without cirrhosis. NA cessation could be done carefully with under NA-specific monitoring.

Group 5 - 4

Prevalence of Cholelithiasis and Fatty Liver Disease with Ultrasonographic Confirmation among Patients with Diabetes Mellitus in a Tertiary Hospital – A Cross Sectional Study

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Objectives:
To determine the association of Duration of DM, BMI, and HbA1c levels with the prevalence of GD and NAFLD among patients with DM.

Materials and Methods:
- Design: Observational, Prospective Cross-Sectional study
- Study Population: Inclusion Criteria: a.)T2DM, b.)Recent HbA1c result, c.)Aged 20-79. Every 3rd patient by systematic random sampling. Exclusion Criteria were: a.)T1DM, b.)s/p Cholecystectomy, c.)Liver pathologies, d.) Significant alcohol intake
- Intervention: Hepatobiliary Tract Ultrasound(HBT) evaluated the presence of Cholelithiasis and/or NAFLD
- Statistical Analysis:
  - DM prevalence of 6.2% was used in OpenEpi revealing a sample size of 90
  - Descriptive statistics, Z-test, Cramer's V and Chi-square test

Results:
90 patients included with no Dr.op-outs, 11 had Cholelithiasis alone(12.2%), 26 had NAFLD alone(28.9%), 15 had both(16.7%). Among 26 patients with Cholelithiasis, 9 male, 17 female(p=0.23), most being 40-49(p=0.35) with majority married(p=0.15). Highest prevalence of GD seen in: a.)Duration of DM: 6-10 years(p=0.006), b.)BMI: 23-24.9(p=0.636), c.)HbA1c:8.1-9%(p=0.007). Among 41 patients with NAFLD, 16 male, 25 female(p=0.26), with most aged 70-79(p=0.01), majority married(p=<0.001); Highest prevalence of NAFLD:a.)Duration of DM: 6-10 years(p=0.014), b.)BMI: 25-29.9(p=0.113), c.)HbA1c: <7(p=0.038).

Conclusions:
Duration of DM and HbA1c levels have a significant association with Cholelithiasis. Age, Gender, Marital Status, and BMI showed no significant association with the development of Cholelithiasis. Age, Marital Status, Duration of DM, and HbA1c levels showed a significant association with the prevalence of NAFLD; BMI and Gender showed no significant difference. This study highlights the need to formulate preventive strategies and to possibly include HBT ultrasound as a screening tool among diabetic patients.

Group 5 - 5

Validation of the "six-and-twelve" prognostic score in transarterial chemoembolization-treated hepatocellular carcinoma patients.

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Objectives:
The "six-and-twelve" prognostic score was proposed recently to predict survival rate in patients with unresectable hepatocellular carcinoma (HCC) treated with transarterial chemoembolization (TACE). However, it has not been validated externally. We validated this score and prior prognostic scores in Thai HCC patients treated with TACE.

Material and Methods:
We identified all HCC patients who underwent TACE between January 2007 and December 2018 at our hospital. The inclusion criteria were treatment-naive, unresectable HCC BCLC-A and BCLC-B; if cirrhosis was present, Child-Pugh score <7; and baseline performance status 0–1.

Results:
Of 716 HCC patients undergoing TACE, 281 (mean age, 61.1 years; 73.0% males, 92.2% with cirrhosis) were eligible. Approximately half of the patients had hepatitis B virus. Median overall survival (OS) was 20.3 (95% confidence limits [CI] 16.4–26.3) months. By stratifying with the "six-and-twelve" score (<6, >6–2, >12), median (95% CI) OS was 35.1 (26.4–53.0), 16.0 (11.6–22.6), and 7.6 (5.4–14.9) months, respectively. AUROCs predicting death at 1, 2, and 3 years for the "six-and-twelve" score were 0.714, 0.700, and 0.688, respectively. Compared with the other currently available scores, the AUROC predicting death at 1 year for the "six-and-twelve" score was the most predictive and better than other models except the up-to-seven model.

Conclusions:
Our study confirms the value of the "six-and-twelve" score to predict survival rate of unresectable HCC treated with TACE. However, in our validation cohort, AUROC of the "six-and-twelve" score was slightly lower than that of the original Chinese cohort (0.73).

Group 6 - 1

Clinician Experience and Attitudes to Palliative Care in Patients with HCC – An Australia-wide survey

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Objectives:
Palliative care (PC) service involvement in HCC patients is suboptimal. Little is known about clinician experience and attitudes towards PC in HCC.

Materials and Methods:
A nationwide survey of consultants/trainees was conducted. Clinician demographics, experience and attitudes towards PC use in HCC patients were collected.

Results:
161 respondents participated (61% male, 94% gastroenterologist/hepatologist). 59% attended weekly multidisciplinary tumour board meetings (MDTBM) and 71% had no formal PC training. MDTBM with PC attendance was reported by 11%. Rates of PC referral and perceived usefulness of PC increased incrementally from BCLC-0/A to BCLC-D patients but were not universal even in advanced (46%)/terminal(87%) stages. Those with prior PC training were more likely to refer BCLC-0/A patients for early PC (P=0.01). Referral rates for outpatient PC were higher in respondents who attended MDTBM with PC present (P<0.05 for all stages). Common reasons for referral: end-of-life care(93%), pain(63%) and psychological symptoms(21%). 61% acknowledged PC patient discussions occurred too late and the best time was thought to be at diagnosis of incurable disease. PC service was rated good/very good by 70%/81% for outpatients/inpatients. Barriers identified to PC referral: negative associations with PC(83%), patient/family lack of acceptance(82%/77%), and insufficient time(70%). 78% thought patients would be more accepting of PC if the name was changed to “supportive care”.

Conclusions:
PC referral for HCC patients occurs late and is not universal even in late-stage disease. Barriers to PC referral were not related to quality of PC services but rather to clinician perception of lack of acceptance by patients/families.

Group 6 - 2

Role of Liver Stiffness Value in Predicting of Hepatocellular Carcinoma and Liver Related Complications among Advanced Fibrosis Nafld Patients

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Objectives:
Nonalcoholic fatty liver disease (NAFLD) becomes the prevalent chronic liver diseases worldwide. The incidence of NAFLD-HCC and liver related complications (LRC) were 0.44 and 0.77 per 1,000 person-years respectively.Transient elastography (TE) showed significant correlation with fibrosis staging and portal hypertension in previous studies. We aim to identify the predictors for HCC and LRC in NAFLD patients with advanced fibrosis.

Materials and Methods:
Patients diagnosed NAFLD who underwent TE (10 successful acquisitions and IQR: median ratio <30) at King Chulalongkorn Memorial hospital during January 2015 to December 2019 were included. According to Wong VW, et al., advanced fibrosis were LS values >15 kilopascal (kPa). The diagnosis of HCC was established based on the AASLD guideline 2018. The definition of LRC included variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy or hepatorenal synDr.ome.

Results:
From NAFLD cohort of 2,850 cases, a total of 136 NAFLD patients with advanced fibrosis (4.8%) were enrolled. The median TE was 21.4 (IQR 17.3 -29.9) kPa. A median follow-up period was 29 months (IQR 18.0 – 44.0), three patients (2.2%) developed HCC. Additionally, 6 patients (4.4%) experienced LRC development [2 patients with SBP (2.3%) and 4 patients with ascites (2.9%)].
By multivariate analysis, only low albumin showed significant association with LRE (OR 0.11 ;95%CI 0.02 – 0.79, p=0.029). None of the factors including LS value showed significant association with HCC development.

Conclusions:
In NAFLD patients with advanced fibrosis, only low albumin is independent factor for LRC. None of the factors including LS value can predict HCC.

Group 6 - 3

Genetic Variation in Patatin-like phospholipase domain containing 3 and the Risk of Nonalcoholic Fatty Liver Disease and Cardiac Arrhythmia: Mendelian Randomization Analysis.

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Objectives:
The causal relationship between nonalcoholic fatty liver disease (NAFLD) and cardiac arrhythmia, a risk factor for sudden cardiac death, is currently unknown. Mendelian randomization uses genetic variants in nonexperimental data to make causal inferences regarding the effect of an exposure on an outcome. We therefore used mendelian randomization analysis to explore the causal relationship between NAFLD and cardiac arrhythmia in patients with metabolic synDr.ome.

Materials & Methods:
Six-hunDr.ed and one patients with metabolic synDr.ome according to NCEP ATP III criteria were prospectively enrolled during 2019-2020. Computerized electrocardiograms were performed for analysis and quantification of intervals and amplitude parameters. NAFLD was diagnosed by transient elastography using the controlled attenuation parameter >248 dB/m in the absence of other liver diseases. PNPLA3 rs738409 was genotyped using real-time PCR protocol based on PCR-RFLP method.

Results:
Overall, 66.1% and 5.5% of recruited individuals presented with NAFLD and cardiac arrhythmia, respectively. The PNPLA3 G allele was present in 51.7% of individuals. The PNPLA3 variant was significantly associated with NAFLD (OR 1.98,95%CI 1.34-2.93) but not with cardiac arrhythmia (OR 1.13,95%CI 0.56-2.28). Cardiac arrhythmia was not statistically associated with NAFLD (OR 1.19,95%CI 0.56-2.56). Atrial fibrillation and QTc prolongation were not significantly associated with NAFLD (OR 0.51,95%CI 0.13-2.06 and OR 1.75,95%CI 0.69-4.43, respectively) and PNPLA3 variant (OR 1.56,95%CI 0.37-6.60 and OR 0.93,95%CI 0.43-2.04, respectively). Significant fibrosis was significantly associated with cardiac arrhythmia (OR 2.92,95%CI 1.19 – 7.718).

Conclusions:
Our results indicate no causal association between NAFLD and cardiac arrhythmia using Mendelian randomization approach in a population of metabolic synDr.ome.

Group 6 - 4

Rate Of Hepatic Steatosis Occurrence Among HCV And HBV Patients In Uzbekistan (Scientific)

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Objectives:
The frequency of hepatic steatosis presence determined in HCV and HBV patients by this study that have come for doctor's visit in Uzbekistan.

Materials and Methods:
There were involved 61 and 60 patients with chronic hepatitis C and B, respectively to this study. They were observed on the basis of Hepatology Center of the Research Institute of Virology MOH of Uzbekistan for 4 months in 2020 year. The results of hepatitis C virus genotyping studies by using real-time PCR in a thermocycler Rotor-Gene ™ 6000 (Corbett Research, Australia) and the diagnosis of liver steatosis by indirect (non-invasive) elastometry on instrument «FibroScan-502» (Echosens, France).

Results:
In 1st group with HCV, women exceeded with – 52.46%, and in 2nd group – men with 58.33%. The presence of hepatic steatosis was in the follow's manner: S0 in 29 and 41 cases, and S1 in 18 and 16 cases in HCV and HBV patients, respectively. The existence of S2 and S3 in HCV and HBV patients were 9 and 2 cases, along with 5 and 1 cases, consistently.

Conclusions:
The foresaid shows that the rate of the moderate and severe liver steatosis grades was determined often at the HCV patients in comparison with HBV patients. Also, rate of occurrence of liver steatosis was almost two times higher in patients with HCV infection in comparison with patients HBV infection.

Group 6 - 5

Liver and Spleen Stiffness by 2-dimensional shear wave elastography to Predict Esophageal Varices in patients with Hepatitis C virus-related cirrhosis

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Objectives:
To evaluate the diagnostic performance of liver stiffness and spleen stiffness measured by two-dimensional shear wave elastography (2D-SWE) to predict esophageal varices (EV) in patients with hepatitis C virus (HCV)-related cirrhosis.

Materials and Methods:
HCV-related compensated cirrhosis patients underwent liver and spleen stiffness measurement by 2D-SWE and esophagogastroduodenoscopy within 1 month apart. Other noninvasive markers (Aspartate aminotransferase-to-platelet ratio index, platelet count-to-spleen diameter ratio, FIB-4 score, fibrosis index, King's score, and liver stiffness-spleen size-to-platelet ratio score) were also collected. Receiver operating characteristic curve was used to identify the diagnostic abilities of liver stiffness, spleen stiffness, and other noninvasive markers to predict EV.

Results:
A total of 52 patients were included. Twenty-one patients (40.4 %) had EV. Liver stiffness was superior to spleen stiffness and other noninvasive markers to detect EV. The optimal cutoff values of liver stiffness for detect EV was 13.49 kPa, at which area under the curve (AUC) and negative predictive value were 0.92 and 93.10 %, respectively. The optimal cutoff values of spleen stiffness for detect EV was 21.92 kPa, at which AUC and negative predictive value were 0.79 and 85.19 %, respectively.

Conclusions:
Liver stiffness by 2D-SWE can predict EV with high diagnostic performance in patients with HCV-related cirrhosis, while spleen stiffness had lower diagnostic performance to predict EV.

Acute Liver Failure and Artificial Liver

A-02

Chemokine receptor CCR5 and its corresponding chemokine contributes to virus-induced liver injury via conventional NK cells recruitment

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Objectives:
This study aimed to investigate the role of chemokine receptors and their corresponding chemokines in the migration of conventional NK cells (cNK) in virus-induced liver injury.

Materials and Methods:
Mice were injected intraperitoneally with MHV-3 to imitate virus-induced fulminant hepatic failure (FHF) model.

Results:
Gene expression analysis indicated that chemokine receptor CCR5 in cNK cells own the highest expression comparing with other receptors including CCR1, CXCR3 and CXCR4 after MHV-3 infection in BALB/cJ mice. The number of hepatic CCR5+ cNK cells increased and reached peak at 48 hours post MHV-3 infection, and its corresponding MIP-1α, MIP-1β and RANTES multiplied throughout the whole course of infection. In vitro, the transwell migration assay displayed a decreased migration of splenic cNK cells towards infectious hepatocyte after blocking CCR5 on cNK cells, and individual neutralization of CCR5 ligands MIP-1β and RANTES but not MIP-1α decreased cNK cells migration. In vivo, pharmacological inhibition of CCR5 (maraviroc) reduced hepatic cNK cells infiltration and liver damage after MHV-3 infection. Meanwhile, CCR5 knockout (KO) mice displayed reduced infiltration of cNK cells in liver post MHV-3 infection, this was accompanied with attenuated liver injury and improvement of survival time.

Conclusions:
These results indicated that CCR5 and its ligands MIP-1β, RANTES play a critical role in the hepatic recruitment of cNK cells in MHV-3-induced liver injury, and the CCR5 inhibitor might bear therapeutic potential to ameliorate liver damage during virus-induced FHF.

A-03

Factors associated with death and respiratory failure among patients with acute liver injury. Somdejprachaotaksin Maharaj Hospital, 2020

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Objectives:
The objective of this study is to find the correlation between mortality and respiratory failure, and risk factors in acute liver injury in the internal medicine department of Somdejphrajaotaksin Maharaj Hospital.

Materials and Methods:
The research method uses cross-sectional study. The participants were acute hepatitis patients in the inpatient department between 1 January 2019- 31 March 2020. The data collected were symptoms, signs and results of laboratory examination. The analysis used is descriptive statistics and inferential statistics such as chi-square and multiple-logistic regression.

Results:
The results of the study shows that there were 729 patients with acute hepatitis,129 with respiratory failure and 120 deaths. The analysis shows that patients who were older than 60 years had acute liver failure and the patients who had the duration of the hospital stay of 5 days or more had a statistically significant association with respiratory failure. In addition, it was found that patients who were older than 60 years old and patients with acute liver failure had a statistically significantly higher association with death. This acute liver failure was the highest in association with death, both respiratory failure (adjusted OR= 9.2; 95% CI= 2.7-30.9) and mortality (adjusted OR= 3.9; 95% CI= 1.3-12.1).

Conclusions:
Therefore, the treatment of acute liver injury should be taken seriously with those who have high risk over other group. This includes the elderly, patients who are in the hospital for a long duration and patients with acute liver failure during the treatment to prevent respiratory failure and deaths.

A-04

Fulminant Hepatic Failure Etiology, Clinical Manifestations, and Outcome: An Experience of Tertiary Care Hospital of Karachi, Pakistan.

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[1]*Jinnah Postgraduate Medical Center, KARACHI, Pakistan*

Objectives:
The study was aimed to determine the etiology, clinical manifestations, and outcome associated with Fulminant hepatic failure (FHF)

Materials and Methodology:
A cross-sectional study was conducted at the Department of Gastroenterology, Jinnah Postgraduate Medical Center, Karachi, Pakistan from January 2018 till to date. All patients of both gender ≥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 71 patients were enrolled, out of which 46 (65%) were males and 25 (35%) were females with a mean age of 28.03 ± 7.85 years. Hepatitis E was found to be the most common cause of FHF 39 (55%). Sixty two (87%) of patients died and 9 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 56 patients (out of 71) of which 51 patients died.

Conclusions:
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.

A-05

Risk factor and severity of acute liver injury between non-chronic liver disease and chronic liver disease

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Objectives:
To study the factors of acute liver injury and compare the severity and risk factors of acute liver injury between patients with and without chronic liver disease.

Materials and Methods:
The study design was cross-sectional study in patients who admitted to Somdejphrajaotaksinmaharaj Hospital during January-September 2019.Data was collected on clinical background,signs and symptoms and laboratory results.

Results:
Out of 323 patients,188 were without chronic liver disease patients (58.2%)and 135 were with chronic liver disease (41.8%). Associated risk factors for acute liver injury in the population without chronic liver disease include dengue infection and alcohol consumption.For the chronic liver disease population,those factors include bacterial infection,sepsis and spontaneous bacterial peritonitis.It was found that bacterial infection,sepsis and spontaneous bacterial peritonitis in the chronic liver disease population with high severity cause severe complications with organ failures resulting in high mortality rate,especially in cirrhosis Child-Pugh class C.

Conclusions:
The most common risk factors for acute liver injury in patients without chronic liver disease and with chronic liver disease in this study were bacterial infections,alcohol Dr.inking,sepsis,upper gastrointestinal bleeding and dengue infection respectively.Unlike any previous study,it was found that dengue infection was an important risk factor since Tak Province was an endemic tropical area.The results of the study found that chronic liver disease patients have organ failure more than without chronic liver disease patients resulting in complications with high mortality rate.Careful monitoring and treatment for chronic liver disease patients will prevent for organ failure complication and decrease mortality rate.

A-06

Risk of the Development of Acute-on-Chronic Liver Failure and Overall Mortality among Nonalcoholic Steatohepatitis-related Cirrhosis Patients with Acute Decompensation

Asst Prof. Siwaporn Chainuvati[1], Dr. Sombat Teeprasertsuk[2], Dr. Tongluk Teerasarntipan[2], Dr. Sakkarin Chirapongsathorn[3], Tanita Suttichaimongkol[4], Dr. Naichaya Chamroonkul[5], Dr. Chalermrat Bunchorntavakul[6], Dr. Sith Siramolpiwat[7], Dr. Abhasnee Sobhonslidsuk[8], Dr. Apinya Leerapun[9], Dr. Tawesak Tanwandee[1], Dr. Teerha Piratvisuth[5], Dr. Wattana Sukeepaisarnjaroen[4], Dr. Phunchai Charatcharoenwitthaya[1]

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Objectives:
Nonalcoholic steatohepatitis (NASH)-related cirrhosis has become the important underlying liver disease of acute-on-chronic liver failure (ACLF). This study aimed to scrutinize the outcome of hospitalized patients with NASH-related cirrhosis compared to other etiologies.

Methods:
We retrospectively collected data from 638 cirrhotic patients hospitalized with acute decompensation (AD) during 2006-2020 seen at 9 centers in Thailand. Outcomes analyzed were the development of ACLF and overall mortality within 90 days.

Results:
The etiologies of cirrhosis were mainly alcoholism (48.3%), followed by hepatitis C (21%) or hepatitis B (19.1%), NASH (8.5%), and cryptogenic (6.9%). Patients with NASH-related cirrhosis were older and female predominance and had less severe underlying liver disease as defined by lower CTP and MELD scores compared to those with other etiologies. 321 patients developed ACLF during their hospitalization according to the EASL-CLIF Consortium definition. Concerning organ failures, patients with NASH-related cirrhosis developed lower frequency of liver (11.0% vs. 29.6%, p<0.001) and coagulation failures (8.9% vs. 17.6%, p=0.04) than those with other etiologies. The risk of developing ACLF was not different between patients with NASH-related cirrhosis and other etiologies (odds ratio (OD)=0.51; 95%CI, 0.29-0.90). All-cause mortalities were not different between NASH-related cirrhosis and other etiologies at 28 days (OD=1.19; 95%CI, 0.76-1.86) and 90 days (OD=1.49; 95%CI, 0.91-2.44). In the multivariate analysis, age (OD=1.04; 95%CI, 1.01-1.08) and MELD score (OD=1.14, 95%CI, 1.06-1.22) had independent prognostic significance for predicting overall mortality.

Conclusions:
Patients with NASH-related cirrhosis have similar risks of developing ACLF and death compared to those with other etiologies.

A-07

Validation of Prognostic Scores to Predict Short-term Mortality in Acute-on-Chronic Liver Failure Among Patients with Hepatitis B infection: A Multicenter Study

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Objectives:
Hepatitis B virus (HBV) infection is common etiology in patients with cirrhosis who developed acute-on-chronic liver failure (ACLF) which has high short-term mortality rate. The good prognostic scores may guide management intervention and improve outcome. We aimed to investigate characteristics, mortality and validate the performance of CLIF Consortium ACLF score (CLIF-C ACLF), CLIF Consortium Organ Failure score (CLIF-C OF), model for end-stage liver disease score (MELD), and Child-Pugh score (CTP) in predicting the short-term mortality in this population.

Materials and Methods:
We prospectively collected data from ACLF: multicenter study group (ACLF-TM), enrolled by 9 tertiary hospitals in Thailand during January 2014 to August 2020. The patients with ACLF were diagnosed according to EASL-CLIF or APASL-AARC 2019 criteria. We analyzed all patients with HBsAg positive.

Results:
Of 638 patients, 123 (20%) were HBV infected patients, from that 75 were ACLF. 70.7% were male with mean age 60.4+3.6 years. The mean CLIF-C ACLF, CLIF-C OF, MELD, and CTP score was 55.3+10.1, 10.4+2.6, 27.8+8.5, and 11.7+2.1, respectively. The 1-month and 3-month mortality rates were 47 (63.5%) and 51 (70.8%), respectively. The AUROC of CLIF-C ACLF, CLIF-C OF, MELD, and CTP for predicting 3-month mortality were 0.783 (95%CI 0.628-0.939, p=0.01), 0.629, 0.523, and 0.635, respectively. The cut-point for baseline CLIF-C ACLF in predicting 3-month mortality was 52.2 showed sensitivity of 79.2% and specificity of 80.0%.

Conclusions:
We demonstrated that CLIF-C ACLF score had better performance for predicting 3-month mortality compared to CLIF-C OF, MELD, and CTP score in HBV infected patients with ACLF.

A-09

Acute-on-Chronic Liver Failure: Epidemiology, Prognosis and Outcome in Thai population, multicenter study (ACLF-TM)

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Objectives:
ACLF made multi-organs failure that relate to high mortality rate.
This study aimed to understand natural history of ACLF in Thai populations

Methods :
This study design is retrospective and prospective cohort study that collect data from multi-center tertiary care hospitals in Thailand (9 hospitals) from January 2010 to June 2020.

Results :
The incidence of ACLF patients was 54%. Main cause of chronic liver disease was alcoholic consumption. Sepsis was the most precipitating factor in this study. ACLF patient with coagulopathy, metabolic acidosis, high AST was associated high 30th days mortality rate. The 30th days mortality rate of AD patients and ACLF patients was 40.4% and 54.9%, respectively. The 90th days mortality rate of AD patients and ACLF patients was 46.2% and 64.5% respectively. Respiratory system was the main organ failure in CLIF-SOFA score that was significant to predict mortality rate. CLIF SOFA scores that category grades of ACLF with 30th day mortalities are 10%, 23.2%, 32.6%, 32.6% respectively. MELD-Na score ≥30 and CLIF-SOFA score ≥12 were associated with high mortality rate. The AUROC of total CLIF-SOFA score is superior to other predicted score (0.644, 95% CI 0.585-0.704)

Conclusions :
ACLF patients with more organs failure, high MELD-Na score and high CLIF-SOFA score are associated with high mortality rate.

A-10

Comparing Four Prognostic Scores in Predicting Short-term Mortality of Patients with Acute-On-Chronic Liver Failure: a multi-center study

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Objectives:
This study aimed to evaluate the prognostic value of MELD, MELD-Na, CLIF-C OF, CLIF-C ACLF in predicting 30-day mortality in patients with acute-on-chronic liver failure (ACLF).

Materials and Methods:
Data of hospitalized cirrhotic patients included from 9 tertiary care hospitals in the Thai Association for the Study of Liver (THASL) from January 2014 to August 2020 were used. ACLF was defined according to EASL-CLIF or APASL-AARC 2019 criteria.

Results:
Three hunDr.ed and fourteen patients (52.7%) out of 596 hospitalized cirrhosis patients developed ACLF during admission. Bacterial infection (54.5%), gastrointestinal bleeding (22.6%) and alcohol Dr.inking (11.8%) were the frequent precipitating causes of ACLF. The 30-day and 90-day transplant-free mortality in patients with ACLF grade-1, -2, and -3 were 49.3%, 58.1%, 68.8%, and 55.1%, 65.1%, 68.8%, respectively. MELD, MELD-Na, CLIF-C OF and CLIF-C ACLF were significantly higher in patients who died within 30-day than those who survived. Accuracy of MELD, MELD-Na, CLIF-C OF, and CLIF-C ACLF score for predicting 30-day mortality were comparable with an area under the receiver operator characteristic (AUC) of 0.62, 0.65, 0.64, and 0.61, respectively. ACLF grade 2 or 3 on the first day of admission increased risk of 30-day mortality (OR 1.74, 95%CI 1.04-2.91, p=0.03).

Conclusions:
In patients with cirrhotic who are hospitalized due to acute decompensation, MELD, MELD-Na, CLIF-C OF, and CLIF-C ACLF scores are able to use for predicting 30-day mortality in patients who develop ACLF during admission.

Alcoholic Liver Diseases: Clinical and Experimental

B-01

Clinical outcomes of acute decompensation and acute-on-chronic liver failure in patients with alcohol-related liver disease: a multi-center study

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Background:
Alcohol-related liver disease (ALD) frequently develops acute decompensation (AD) or acute-on-chronic liver failure (ACLF). We aimed to compare clinical outcomes between ALD and non-ALD patients who had AD and ACLF.

Methods:
We analyzed information from ACLF:multicenter study group (ACLF-TM), enrolled by 9 tertiary hospitals in Thailand. ACLF were diagnosed following EASL-CLIF or APASL-AARC 2019 criteria.

Result:
Of 638 patients, ALD was the most prevalent (n=248) cause of underlying liver disease. Active alcoholism and bacterial infection tended to precipitate ACLF than AD (OR=3.81, 95%CI=1.74-8.37, p=0.001 and OR=3.44, 95%CI=2.04-5.79, p<0.001, respectively) whereas gastrointestinal bleeding (GIB) tended to precipitate AD than ACLF (OR=3.04, 95%CI=1.75-5.28, p<0.001). Mortality rates (MR) were higher in ALD patients who develop ACLF (n=134) than AD (n=114) with 30-day MR of 48.1%vs.32.1%, p=0.017, OR=1.96 and 90-day MR of 60.5%vs.40.8%, p=0.004, OR=2.22. From 347 ACLF patients, clinical outcomes between ALD (n=134) and non-ALD patients (n=213) were compared and showed no difference between two groups in terms of presenting clinical features, including rates of major acute insults (bacterial infection, GIB), most biochemical Prof.iles, prognostic scores, and organ dysfunction (ACLF grading, type and number of organ failure). However, ACLF outcomes showed that ALD patients had lower 30-day and 90-day mortality rate than non-ALD patients (48.1%vs.61.2%, p=0.018 and 60.5%vs.70.6%, p=0.063, respectively). Intriguingly, conventional scoring systems (MELD, CLIF-OF, CLIF-c-ACLF scores) could predict 30-day and 90-day mortality with higher AUROCs in ALD than non-ALD patients.

Conclusions:
ALD accounted for a large proportion of ACLF patients and associated with distinctive lower short-term mortality than non-ALD patients.

B-03

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 (MadDr.ey's discriminant function≥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).

Conclusions:
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.

B-05

Up-regulation of Fgl2 induced by chronic ethanol consumption combined with HBV promotes hepatic macrophage M1-polarization and lipid metabolism disorder

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Introduction:
As an important immuno-inflammatory regulator, fibrinogen-like protein 2 (FGL2) play a key role in HBV-related liver diseases. However, its role in alcoholic liver disease combined with HBV persistence (ALD-HP) remains unclear.

Objectives:
To investigate the mechanism of Fgl2 in ALD-HP using a new mouse model.

Methods:
Six-week-old male C57BL/6 mice with Fgl2 status (+/+ or -/-) were hyDr.odynamically injected with a pAAV-1.2HBV vector and then fed an ethanol diet for 6 weeks. Serum biomarkers and liver histology, liver fat levels, macrophages polarization and lipid metabolism related molecules were measured. In vitro assays primary bone marrow cells were stimulated to be M1 or M2 macrophages and then co-cultured with Hepa1-6 cells cells to examine the difference of lipid metabolism-related genes between Fgl2+/+ and -/- groups.

Results:
Compared with Fgl2-/- mice, Fgl2+/+ mice showed significant hepatic steatosis and increasing TG and TC contents in ALD-HP group. Both alcohol and HBV persistence led to increased hepatic Fgl2 expression, increased M1 and reduced M2 proportions, respectively. The trend was more significant in ALD-HP group and blunted after gene knockout of Fgl2. In vitro assay also demonstrated that Fgl2 promoted macrophage differentiation to M1, thus up-regulating crucial lipid metabolism-related genes in Hepa1-6 cells, including Srebp-1, NF-κB, Srebp-2 and HMGCR.

Conclusions:
Alcohol and HBV infection could up-regulate hepatic Fgl2 expression, promote macrophage towards M1, and thus result in an abnormal hepatic lipid metabolism. The condition was significantly improved by knock-out of Fgl2.

B-06

Utility of point shear wave elastography done at Day 28 and Day 90 in prognosticating patients with alcohol related patients with Acute-on-chronic liver failure

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Objectives:
Various baseline scores are available for prognosticating patients with ACLF. Objective was to evaluate the utility of point shear wave elastography (pSWE) done at day 28 and 90 in prognostication patients with alcohol related ACLF.

Methods:
In a prospective study (January 2019 to February 2020), pSWE was done in the surviving patients at day 28 and day 90 with alcohol related ACLF as per APASL and combined (APASL+CANONIC) definitions to predict their severity, organ failure and 28-day and 90-day mortality.

Results:
In APASL ACLF group (male/female=32/1, mean age= 42.54±8.60), pSWE done in 33 survivors at day 28 correlated with CTP (r=0.404, n=33, p=0.020) and simple organ failure count [SOFC, (r=0.366, n=33, p=0.036)]. In combined ACLF group (male=26, mean age=40.23±7.90), pSWE done in 26 survivors at day-28 correlated with CLIF-C-OF score (r=0.424, n=26, p=0.031). In addition, pSWE at day-28 in the APASL and combined group predicted the 90-day mortality [(cut off 29.25 kPa, AUROC-0.978, p<0.001, diagnostic accuracy 96.97%) and (cut off of 32.2 kPa, AUROC-0.858, p<0.001, diagnostic accuracy of 76.92%)] respectively. In APASL ACLF group, pSWE in 22 survivor patients at day 90 correlated with MELD, MELD-Na, AARC, SOFC scores [(r=0.665, p=0.001), (r=0.662, p=0.001), (r=0.634, p=0.002) and (r=0.654, p=0.001)] respectively. In combined ACLF, pSWE at day-90 correlated with MELD, MELD-Na, AARC, CLIF-C-OF score and SOFC [(r=0.661, p=0.001), (r=0.541, p=0.009), (r=0.449, p=0.036), (r=0.649, p=0.001) and (r=0.698, p<0.001)] respectively.

Conclusions:
Point shear wave elastography done at Day 28 and Day 90 is helpful in prognosticating patients with alcohol related patients with ACLF

B-07

WPSU (wellness programme for substance user) - for alcohol relapse prevention: A Ray of Hope in dark

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Objectives:
A large unmet need for a robust system for relapse prevention in alcohol dependent. Meditation is an emerging non pharmacologic treatment for alcohol relapse prevention. This 16-week prospective study was done to evaluate efficacy of WPSU (a combination of meditation ,motivation, coping strategies and group support) for relapse prevention .

Materials and Methods:
72 adult alcohol-dependent patient were enrolled for online WPSU . 68 patients completed the 7 day online WPSU meditation course supplemented by at-home meditation and "standard of care" therapy. Outcome measures included relevant surveys.

Results:
59 patients (86.76 %) were abstinent for 30.9 (SD = 22.2) days at enrollment. Completers (N = 59) attended 85% of meditation course sessions and meditated on average 4.6 (SD = 1.1) days per week; they were abstinent on 94.5% (SD = 7.4) of study days, with 49% reporting complete abstinence and 51% reporting 1 or more heavy Dr.inking days. Their severity of depression, anxiety, stress ($P < 0.05$), and craving ($P < 0.08$), documented relapse triggers, decreased, and the degree of mindfulness increased ($P < 0.05$). "Gaining skills to reduce stress," "coping with craving," and "good group support" were the most common qualitative comments about the course value. There were no adverse events or side effects.

Conclusions:
Meditation may be an effective adjunctive therapy for relapse prevention in alcohol dependence. Needs revalidation in larger RCT.
Keywords WPSU (wellness programme for substance user).alcohol dependence ,meditation; relapse prevention addiction;; substance use disorders.

Biliary Physiology, Transport, Cholangiocyte Biology, and Experimental Cholestasis

C-02

Proteomic Prof.iling of Liver Tissue Specimens identify Novel Phosphoproteins in Patients with Intrahepatic Cholangiocarcinoma

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Background and Aims:
Intrahepatic cholangiocarcinoma (iCCA) is a common primary liver cancer in Southeast Asia and highly prevalent in northeastern Thailand. The most common of posttranslational modifications is phosphorylation process, which is involved in regulating several cellular processes. The aim of this study was to comparatively analyze tissue phosphoprotein Prof.iles in tumor vs. non-tumorous liver tissue specimens of patients with iCCA undergoing surgical resection.

Methods:
Quantitative phospho-proteomics background were assessed by using LTQ-Orbitrap-XL mass spectrometer in 12 pairs of liver tissues tumor and adjacent non-tumorous in patients with iCCA. The protein-protein interaction and gene ontology were performed by STRING tool.

Results:
In this study, 21 down-regulated, 35 absent, 14 up-regulated and 7 newly present phosphoproteins were identified in tumor vs. adjacent non-tumorous tissues. Assessment of protein-protein interactions were predicted using STRING database. The most common functions of the down-regulated, absent phosphoproteins involved in biological process, molecular function, and cellular components while up-regulated phosphoproteins involved only in biological process and molecular function. However, 7 newly phosphoproteins exhibited no significant functional enrichment.

Conclusions:
We first report phospho-proteome dataset of iCCA, which demonstrates a number of novel phosphoproteins that might be linked to carcinogenesis and could lead to the discovery of new biomarkers or therapeutic targets for iCCA.

Cell and Molecular Biology

D-02

Could Cell-Free DNA And Methylations In RASSF1 And CDKN2AIP Genes Be New Biomarkers In The Diagnosis Of HCC? (Scientific)

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Objectives:
We aimed to determine the importance of methylation of circulating cell-free DNA(cfDNA) for RASSF1 and CDKN2AIP genes in the diagnosis of HCC.

Materials and Methods:
A total of 47 HBsAg-positive patients included in the study. Patients were divided into two groups including those with HBV cirrhosis with HCC(group 1,n=22) and those with HBV cirrhosis without HCC(group 2,n=25). Nuclear DNA and cfDNA were isolated from plasma samples(QIAamp Circulating Nucleic Acid Kit Cat No./ID:55114,Qiagen,UK). Methylation analysis for the RASSF1 and CDKN2AIP genes(Qiagen-EpiTectMethyl II PCR Assay form 2 Genes Using 1 DNA Sample,Cat No./ID:335002, Qiagen,UK) were performed by using real-time PCR(Agilent Technologies,CA,USA).

Results:
cfDNA levels were similar in both groups($p>0.05$). The mean methylation percentage of the CDKN2AIP gene was 0.001±0.004% in group 1 and 0.008± 0.004% in group 2. No methylation was detected in the CDKN2AIP gene in 80% of patients in group 2 and 95% of patients in group 1. The mean methylation percentage of the RASSF1 gene was 9.7±25.9% in group 2 and 5.1±16.1 in group 1. No methylation was detected for the RASSF1 gene in 64% of patients in group 2 and 72.7% of patients in group 1. The methylation rate of CDKN2AIP gene was significantly lower in the HCC group($p=0.027$). Unmethylation of the CDKN2AIP gene was positively correlated with the HCC($R=0.667$, $p=0.018$).

Conclusions:
cfDNA levels were similar in patients with HBV cirrhosis with and without HCC. The frequency of methylation in the CDKN2AIP gene was higher in cirrhotic patients without HCC.

D-03

Fried Mung Bean (Vigna Radiata) and Roasted Black Sesame (Sesamum Indicum) Supplement to Slow Down Diabetic Kidney and Fatty Liver

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Background:
Diabetes mellitus (DM) is a chronic disease. Patients with type 2 diabetes (T2D) are at increased risk for developing complications such as fatty liver and diabetic nephropathy. For control blood sugar level, a patient has been advised to limit calories intake/meal, and add low glycemic snacks between meals. Several studies reported that mung bean and sesame can prevent hyperlipidemia and diabetes. However, the effect of mung bean and black sesame on the improvement of diabetes complications have not been reported. Therefore, this study aimed to investigate the benefit of fried mung bean and roasted black sesame in T2D rat.

Methods:
Wistar rats were divided into four groups: Normal control group (NC), Diabetes mellitus control group (DMC), Fried mung bean group (FMB), and Roasted black sesame group (RBS). For DMC, FMB, and RBS groups, STZ (30 mg/kg) was intraperitoneal injected at week 0 of experiment. Blood, urine, and tissue samples were collected at week 12.

Results:
The results showed that fat accumulation in liver, glomerular basement membrane thickening, and podocyte foot process effacement were detected in kidney in diabetes mellitus control group, which were significantly higher than normal control group, while no abnormal morphology of liver and kidney were observed in rat fed with Fried mung bean and Roasted black sesame group. These abnormalities were early pathologic change of liver and kidney complication in diabetes.

Conclusions:
Fried mung bean and roasted black sesame consumption can reduce fat accumulation in liver and glomerular basement membrane thickening in type 2 diabetic rats.

D-06

Hematopoietic Stem Cells Therapy In Patients With End Stage Liver Disease: A Systematic Review Of Randomized Controlled Trial

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Objectives:
Liver transplant is known as the best method of therapy for End-stage liver disease (ESLD). However, there are still limitations namely the high cost and lack of donors. Several studies have shown hematopoietic stem cells (HSCs) can regenerate liver cells in ESLD patients. This study aims to review the effectiveness of HSCs therapy for patients with ESLD.

Materials and Methods:
Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines were used for literature research. PubMed, EBSCOhost, Proquest search database were used, with studies dating up to November 2020. Cochrane Risk of Bias Tool 2.0 was used to access risk of bias.

Results:
Total of 184 studies were identified, with 7 relevant studies. Six studies have unclear and high risk in selection, performance and detection bias. All studies showed low risk in attrition and reporting bias. Comparisons are made between HCSs therapy such as granulocyte colony-stimulating factor (G-CSF), CD133+, and mononuclear cell (MNC) to the standard medical therapy (SMT). Three studies showed greater reduction of model end-stage liver disease (MELD) score ($p<0.05$) and two studies showed greater reduction of Child-Turcotte-Pugh (CTP) score, both with G-CSF ($p<0,05$). One study showed MNC and CD133+ were associated with greater reduction of MELD score. Two studies showed no significant improvement of MELD and CTP score.

Conclusions:
HSCs are associated with reduction of MELD and CTP score in ESLD, and can be considered as treatment options for ESLD. Further studies with higher population samples are needed for better understanding of ESLD management.

D-07

Role of lumican in the metastasis of hepatocellular carcinoma

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Objectives:
Hepatocellular carcinoma (HCC) is a leading cause of cancer death worldwide with a high rate of local recurrence and distant metastasis. Lumican (LUM) is an extracellular matrix (ECM) protein. Its role in human cancers is divergent depending on the tissue origin. The function of LUM in HCC remains to be elucidated. In this study, we aimed at investigating the clinical and functional significance of LUM in metastasis of HCC.

Materials and Methods:
ELISA was used to detect the level of secreted LUM in patient serum samples. Serum lumican level in patients was statistically analyzed against clinicopathological parameters including survival outcome. Human recombinant LUM (rhLUM) and anti-LUM antibody were adopted in the in vitro assays. Migratory and invasive effects of LUM were measured by transwell assays. Tube formation assay with HUVEC cells was performed to examine the angiogenic property of LUM.

Results:
In clinical serum samples, a higher LUM level was correlated with poorer tumor cell differentiation and worse overall survival of HCC patients. Results from the in vitro functional assays demonstrated that administration of rhLUM enhanced migratory, invasive and angiogenic abilities of HCC cells; and anti-LUM antibody antagonized these pro-metastatic effects exerted by rhLUM.

Conclusions:
To conclude, our results have shown that secreted lumican promotes the metastatic potential of HCC cells. It is a potential prognostic biomarker for HCC patients.

D-09

A comparison of propofol and desflurane anesthesia on miRNA Prof.iles after major hepatic resection in patients with hepatocellular carcinoma

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Objectives:
This study aims to compare miRNA Prof.ile in patients with hepatocellular carcinoma after major hepatic resection under propofol and desflurane anesthesia

Materials and Methods:
Serum samples were collected at baseline and 24-hour after surgery from 6 patients with HCC (3 each received propofol or desflurane). Screening of 800 human miRNAs in the serum samples was performed by NanoString nCounter® Human v2 miRNA Expression Assay.

Results:
Overall, the expression of miRNA Prof.ile after surgery were significantly different from baseline. Of these, 3 miRNAs including miR-664b-3p, miR-103a-3p and miR-2682-5p were significantly upregulated, whereas the expression levels of 4 miRNAs including miR-337-3p, miR-450b-3p, miR-443-5p and miR-1277-3p, were significantly downregulated. After surgery, the expression patterns of 3 miRNAs including miR-1307-5p, miR-887-5p and miR-370-3p were found to be significantly increased in the desflurane group. All these up-regulated miRNAs were reported to be associated with the aggressiveness and poor prognosis in other several cancers. In contrast, there was no significant change of miRNA expression after surgery in the propofol group.

Conclusions:
This study demonstrates for the first time that propofol and desflurane exhibit different miRNA Prof.iles after major hepatic resection in patients with HCC. In the desflurane group, up-regulated miRNAs with unfavorable prognosis in other cancers were found. Whether the alteration of these miRNAs plays an important role in patients with HCC needs further investigation.

D-10

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

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Objectives:
We aim to investigate the role of fgl2 in regulating neutrophil and neutrophil extracellular traps(NETs) in fulminant hepatitis(FH).

Materials and Methods:
Neutrophil amount and NETsformation were detected inserum and liver of C57BL/6 wild type andfgl2-/-C57BL/6 mice followingmurine 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 lesionsand increased ALT and AST, abundant neutrophil accumulation and NETs formation were observed in mice following MHV-3 infection. NETs depletion significantlyimproved 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 offgl2 on neutrophils was upregulatedpost MHV-3 infection. Fgl2 destruction reduced neutrophil accumulation in liver of the infected mice, and downregulatedexpression of hepatic ICAM-1, CXCL1, CXCL2 and CXCR2. Both in vivo and in vitro studies revealed that fgl2 promoted NETsgeneration through the ROS-dependent PAD4 pathway. Moreover, fgl2 directed fibrin deposition in NETs area, aggravating the following coagulation cascade and tissue lesions.

Conclusions:
Fgl2 promotesFH progression partiallyvia 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.

Genomics and Precision Medicine

E-02

Influence Of TLR7 Polymorphism And Sex On Pharmacodynamic Response To TLR7 Agonist (RO7020531)

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Objectives:
RO7020531 is an oral proDr.ug of a toll-like receptor 7 (TLR7) agonist, currently under clinical development against chronic hepatitis B. TLR7 SNP rs3853839 (G vs. C) is associated with autoimmune disease susceptibility and higher TLR7 transcripts levels. Here, we explored the influence of TLR7 SNP rs3853839 and sex on pharmacodynamic (PD) response to RO7020531.

Materials and Methods:
The study population included 32 healthy volunteers and 22 virally suppressed chronic hepatitis B patients dosed with 140, 150 or 170 mg RO7020531 every other day (QOD) from Phase 1 studies YP39553 and NP39305. Blood PD and clinical genotyping analysis were performed. The on-treatment maximum fold change from baseline in CXCL10 and ISG15 transcripts as well as the highest interferon alpha (IFN-α) induction value were determined for each subject and categorized by TLR7 rs3853839 G/C SNP and sex for correlation analysis.

Results:
We observed higher baseline of TLR7 transcripts in females containing G vs. C only, consistent with previous reports. In contrast, no obvious difference was observed for the baseline of CXCL10 and ISG15 transcripts between different genotypes. Interestingly, subjects with the G allele tended to have higher PD response (CXCL10, IFN-α, ISG15 transcripts) compared to those with only the C allele. In addition, PD response appeared higher in homozygous females (G/G or C/C) vs. males with a single copy of the respective allele.

Conclusions:
Polymorphism of TLR7 rs3853839 and sex influence PD response to RO7020531. This may help explain the individual response variability.

E-03

Liver Cancer and Atherosclerosis are Interconnected through the MicroRNA

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Introduction:
Atherosclerosis and cancer being two common diseases share not only risk factors but molecular signaling pathways too. MiRNAs molecules, playing role in different signaling pathway regulation, may serve as a marker for signaling regulation changes that happen during carcinogenesis and chronic inflammation processes. However, these changes become evident before clinical manifestation that make miRNA a promising prognostic biomarker to identify patients from risk group for cancer development and progression.

Material and Methods:
Blood plasma was collected from healthy volunteers (n=10), patients with atherosclerosis (n=20) and liver cancer (n=10). Exosomal and free miRNA expression level was identified with PCR-RT.

Results:
Exosomal expression levels of 3 miRNAs – miRNA-21-5p; -126-3p; -182-5p – were increased in samples from patients with atherosclerosis and liver cancer in comparison with samples from healthy volunteers. Exosomal expression level of miRNA-24-3p was decreased in both study groups in comparison with control group. Expression levels of free plasma miRNAs were different from expression levels of exosomal miRNAs.

Conclusions:
All three miRNAs - miRNA-21-5p; -126-3p; -182-5p – with increased expression levels involved in regulation of the p38 mitogen-activated protein kinase (MAPK) signaling pathway activated in response to oxidative stress, growth factors and cytokines and its regulation changes during carcinogenesis and atherogenesis. These gives reason to assume that miRNA-21-5p; -126-3p; -182-5p may simultaneously serve as a prognostic biomarker for patients with liver cancer and atherosclerosis indicating diseases progression and identifying patients of risk group for more severe course of the disease.

E-04

Prof.iling of cell-free DNA using Whole-exome sequencing in patients with Hepatocellular carcinoma in Thailand

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Objectives:
Hepatocellular carcinoma (HCC) was highly observed in Thailand with a high mortality rate globally. Cell-free DNA (cfDNA) is a liquid biopsy with minimally invasive and providing of tumor genetic Prof.ile. We evaluate the potential of cfDNA as a biomarker in Thai HCC patients.

Methods:
Paired of cfDNA and germline DNA were isolated from patients with HCC (n = 60) and chronic hepatitis (CH) (n = 17). Levels of cfDNA were quantified using Qubit fluorometry. Whole-exome sequencing (WES) was performed to investigate mutation Prof.ile of cfDNA. The mutation Prof.ile of cfDNA was compared with Thai HCC tissues and TCGA data.

Results:
The level of cfDNA was significantly higher in HCC group compared with CH group. The combined of serum alpha-fetoprotein and cfDNA present high sensitivity (88.46%) and specificity (100%). All patients had identified 2,732 altered genes with a median of 49.5 variants per sample (3 - 818). The altered genes in cfDNA present a concordance with Thai HCC tissues (31%). The high mutated genes in cfDNA (ZNF814, ZNF492, HRNR, TP53, OBSCN, TTN, ADAMTS12, FLG) were covered 62% in TCGA. Additionally, co-occurrence of HRNR and TTN in cfDNA was found that HCC patients with these mutations in TCGA data were associated with shorter survival time compared with non-mutation.

Conclusions:
Our study represents the first analysis of cfDNA from HCC in Thailand. The mutations of cfDNA were detected in all patients using WES. In addition, a high mutation gene could be diagnosis and prognosis in cfDNA of patients with HCC in Thailand.

E-05

The significance of quantified extracellular matrix features in patients with hepatocellular carcinoma after curative liver resection

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Objectives:
Survival of patients with hepatocellular carcinoma (HCC) had gradually improved because of a rapid growth in treatment options in recent years. In the era of precision medicine, there is a need of systematic approach for more personalized treatment based on efficacy and costs. Utilizing digital pathological system to examine dynamics of extracellular matrix (ECM), i.e. qFibrosis, has recently been validated in Dr.ug development for Nonalcoholic steatohepatitis. Therefore, we aim to demonstrate a histopathological evidence-based approach to fulfil this need.

Materials and Methods:
Normal liver tissue and liver tumor from 203 patients with HCC who underwent curative tumor resection were imaged and assessed using qFibrosis system, which later generated a total of 33 and 156 collagen parameters from normal liver tissue and tumor part, respectively. We used these collagen parameters to build two models, (RFS-index and OS-index) for prediction of patient's recurrence-free survival (RFS) and overall survival (OS) years. The models were validated using leave-one-out method.

Results:
The RFS-index can differentiate the patients with RFS>2 years (n=131) and RFS≤2 years ($p<0.001$) with a cut-off value RFS-index=0.65. The OS-index can also differentiate the patients with OS>3 years (n=152) and OS≤3 years ($p=0.013$) with a cut-off value RFS-index=0.8.

Conclusions:
We demonstrate the capability of a histopathological evidence-based evaluation on HCC patient outcome. The quantified ECM features of HCC patients appear to be an important parameter along with other clinical and biochemical data such as tumor staging, alpha-fetoprotein, etc., which could help to build a system of a cost-effective and personalized treatment platform.

E-06

Transcriptomic analyses reveal cancer-induce genes in PBMCs of Hepatocellular carcinoma for early diagnosis and prognosis

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Objectives:
Hepatocellular carcinoma (HCC) is the most common cause of cancer related-death. Thus, novel and sensitive biomarker is still required for predicting early HCC.

Methods:
We performed RNA sequencing to investigate the transcriptome Prof.ile of peripheral blood mononuclear cells (PBMCs) from patients with HCC and healthy controls (HC) and also in PBMCs co-cultured with HCC cell lines. The raw data of GSE 58208 and 49519 were downloaded from the Gene Expression Omnibus (GEO) database and the differentially expressed genes (DEGs) were identified by CU-Dr.EAM

Results:
A total of 24 DEGs were identified in PBMCs from patients with HCC compared with healthy controls and co-cultured model, including 18 upregulated and 6 downregulated DEGs. The KEGG pathway results showed that these enriched genes were mainly associated with immune response pathways. Five candidate genes (BHLHE40, AREG, SOCS1, CCL5, and DDIT4) were selected and validated in PBMCs from 100 patients with HCC, 100 patients with chronic hepatitis B and 100 HC. These genes were significantly higher in HCC group compared with other groups. BHLHE40 and DDIT4 expression had a higher sensitivity than alpha-fetoprotein (AFP) for detecting early HCC (71% and 77% vs. 31%, respectively). In addition, BHLHE40 was identified as an independent prognostic factor of overall survival in patients with HCC.

Conclusions:
Our study suggested that these two DEGs might be promising diagnostic and prognostic biomarkers for early-stage of HCC.

E-07

Transcriptomic Characterization Reveals Prognostic Molecular Signatures of Sorafenib Resistance in Hepatocellular Carcinoma

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Objectives:
Sorafenib is the first-line treatment for patients with advanced unresectable hepatocellular carcinoma (HCC); however, only a small number of patients benefit from sorafenib, and many develop sorafenib resistance (SR) and severe side effects. This highlights the need for continued development of biomarkers for SR and a better understanding of the molecular mechanisms involved.

Material and Methods:
Two microarray datasets from the Gene Expression Omnibus and The Cancer Genome Atlas were analyzed using a series of bioinformatics tools. LO2 and Huh7 cell lines were applied to the in vitro experimental verification.

Results:
Four genes (C2orf27a, insulin-like growth factor 2 receptor, complement factor B, and paraoxonase 1) were identified as key genes related to SR in HCC and as independent prognostic factors significantly associated with clinical cancer stages and pathological tumor grades of liver cancer. These genes can affect the cytotoxicity of sorafenib to regulate the proliferation and invasion of Huh7 cells in vitro. Additionally, immune-cell infiltration according to tumor immune dysfunction and exclusion (TIDE), a biomarker integrating the dysfunction and exclusion of T cells used to evaluate tumor immune evasion, showed good predictive power for SR, with an AUC of 0.869.

Conclusions:
These findings suggested that the four selected genes are key genes and prognostic biomarkers for SR in HCC patients, and immunotherapy maybe a potential strategy for treating sorafenib-resistant HCC. Furthermore, the results enhance the understanding of the underlying molecular mechanisms of SR in HCC and will facilitate the development of precision therapy for patients with liver cancer.

E-09

Circulating Mir-122 Levels At Baseline Predict Overall Survival Of Patients With Hepatocellular Carcinoma Treated With Transarterial Chemoembolization

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Background and Aims:
MicroRNA (miR)-122 plays an important role in liver biology and diseases, including the hepatocellular carcinoma (HCC). In this study, we investigated the clinical correlation and prognostic role of circulating miR-122 levels in patients with hepatitis B virus (HBV)-related HCC treated with transarterial chemoembolization (TACE).

Methods:
Stored serum samples for measuring miR-122 levels before receiving TACE were assessed by Taqman probe using quantitative real time PCR assay. Relative miR-122 expression (fold change) was determined by absolute quantification method.

Results:
A total of 100 patients with HBV-related HCC (84% male, mean age 60 years) receiving TACE were included. The patients were divided into 2 groups based on miR-122 expression at baseline with the median cut-off point of 4.3 log10 copies. Low miR-122 expression was significantly correlated with more advanced tumor stage. Multivariate analysis demonstrated that high AFP level, advanced BCLC stages and low miR-122 expression were independently associated with poor survival. The median overall survival of patients with low and high miR-122 expression were 12 and 21 months, respectively (P=0.024 by log-rank test).

Conclusions:
These data suggested that low circulating miR-122 expression was associated with advanced tumor stage and poor overall survival in patients with HBV-related HCC who were treated with TACE.

Gut Liver Axis and Microbiome

F-02

Observation of the clinical features of bacterial liver abscess with endogenous endophthalmitis

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Introduction and Objectives:
To summarize and analyze the clinical features, pathogenetic factors, treatment and prognosis of of bacterial liver abscess with endogenous endophthalmitis.

Methods:
The clinical information, treatment and outcome of 15 cases (17 eyes) of bacterial liver abscess and endogenous endophthalmitis patients admitted to the First Affiliated Hospital of Nanjing Medical University from January 2009 to December 2020 were retrospectively analyzed.

Results:
The patients selected were dominated by middle aged and old people with no typical clinical manifestations. The initial symptoms of most of them are fever or eye pain, 11 cases□73%□ were determined diabetes, 5 patients□33%□with liver abscess puncture fluid or eye puncture fluid germiculture positive,and 6 patients□40%□who underwent blood culture were positive, are all with klebsiella pneumoniae.

Conclusions:
Bacterial liver abscess with endogenous ophthalmitis is not typical clinically, progresses rapidly and has a poor prognosis. Invading synDr.ome caused by Klebsiella pneumoniae liver abscess (invasive Klebsiella pneumoniae liver abscess synDr. ome, IKLAS) can quickly cause infection in the lungs, brain, eyes, etc. through the circulatory system, among which endophthalmitis is the most serious complication Diabetes is the risk factor in the development of disease. Prompt anti - infection treatment is beneficial to control the condition, preserve the patient's useful vision and improve the prognosis.

F-03

Prevalence And Predictive Factors Of Small Intestinal Bacterial Overgrowth (SIBO) In Patients With Cirrhosis Of Liver

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Objectives:
1. Prevalence of SIBO in patients with cirrhosis of liver and healthy controls
2. Predisposing factors of SIBO in patients with cirrhosis of liver
3. Risk of SIBO predisposing to sepsis in patients with cirrhosis of liver
4. Association of various clinical and laboratory parameters in the presence of SIBO

Materials and Methods:
SIBO was diagnosed by glucose hyDr.ogen breath test (GHBT) and basal breath hyDr.ogen value >20 ppm or rise by ≥12 ppm above baseline following glucose ingestion was considered as positive result. A total of 54 cirrhotic cases and 18 healthy controls were studied prospectively over a period of 18 months.

Results:
SIBO was more prevalent in cirrhotic patients than healthy controls (p=0.039). The frequency of SBP (p=0.001), other infections (p=0.015), ascites (p=0.029) and large varices (p=0.043) were more in SIBO group as compared to non SIBO group. CTP (p=0.035), MELD (0.073) and MELD-Na (p=0.064) scores were also higher amongst cirrhotic patients with SIBO. On univariate analysis of different biochemical parameters, statistically significant difference was seen between the SIBO and non SIBO group for serum albumin ≤2.8 (p=0.016).

Conclusions:
SIBO was prevalent in one third of cirrhotic patients. It's frequency increased with increase in severity of cirrhosis. SBP, past history of any infections, clinically significant ascites (grade 2 or 3), large esophageal varices, low serum albumin and high CTP score predicted SIBO.

F-04

The alteration of gut microbiota composition in patients with hepatitis C virus (HCV) monoinfection and human immunodeficiency virus (HIV) coinfection.

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Background:
Gut microbiota composition changed has been described in hepatitis C virus (HCV) infection. Beside HCV mono-infection, co-infection with HCV and human immunodeficiency virus (HIV) is also common. However, the effect of HCV/HIV co-infection and gut dysbiosis are not well characterized in patients.

Objectives:
The purpose of this study was to examine the alteration of gut microbiome compare in chronic HCV mono- and HCV/HIV co-infection.
Methods: Fecal specimens from Thai patients with HCV mono- and co-infection were collected and extracted for DNA. Gut microbial compositions were analyzed using 16S ribosomal RNA sequencing by Illumina MiSeq sequencing platform.

Results:
This study included 58 patients with mono-infection and 28 patients with co-infection, who were age and gender-matched. Compared with the mono-infected group, patients with co-infection exhibited lower alpha and Shannon diversity of gut microbiota. Co-infected individuals also showed significantly lower in the relative abundance of genus Faecalibacteria (6.34±5.96 vs. 8.57±6.24, P=0.043) and Blautia (1.66±1.19 vs. 2.71±2.29, P=0.044), but higher in Agathobacteria (4.31±8.23 vs. 1.87±1.72, P=0.032). Among patients with cirrhosis, Prevotella was significantly higher in co-infection compared with mono-infection (7.5±8.5 vs. 1.08±2.66, P=0.007). Of note, Faecalibacteria and Agathobacteria were weakly correlated with patients' body mass index (r=0.214, P=0.049 and r=0.241, P=0.026, respectively), but did not correlate with severity of liver disease.

Conclusions:
This is the first study that reported the comparison of gut microbiome Prof.iles in patients with HCV mono- and HCV/HIV co-infection. The difference of microbe community in HIV occurrence might be related to increase of disease progression in co-infected patients.

Health Services Research

G-02

Application of Artificial Intelligence in Chronic Liver Diseases: A Systematic Review and Meta-analysis

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Objectives:
The gold standard for the diagnosis of liver fibrosis and nonalcoholic fatty liver disease (NAFLD) is liver biopsy. Various noninvasive modalities, e.g., ultrasonography, elastography and clinical predictive scores, have been used as alternatives to liver biopsy, with limited performance. Recently, artificial intelligence (AI) models have been developed and integrated into noninvasive diagnostic tools to improve their performance.

Materials and Methods:
We systematically searched for studies on AI-assisted diagnosis of liver fibrosis and NAFLD on MEDLINE, Scopus, Web of Science and Google Scholar. The pooled sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic odds ratio (DOR) were calculated using a random effects model. A summary receiver operating characteristic curve and the area under the curve was generated. Subgroup analyses by diagnostic modalities were performed.

Results:
We included 17 studies reporting the performances of AI-assisted ultrasonography, elastrography, computed tomography (CT), magnetic resonance imaging (MRI) and clinical parameters for the diagnosis of liver fibrosis and steatosis. For the diagnosis of liver fibrosis, the pooled sensitivity, specificity, PPV, NPV and DOR were 0.78, 0.88, 0.73, 0.91 and 29.57, respectively, for cirrhosis; 0.86, 0.87, 0.85, 0.88 and 37.95, respectively; for advanced fibrosis; and 0.86, 0.81, 0.88, 0.77 and 26.79, respectively, for significant fibrosis. Subgroup analyses showed significant differences in performance for the diagnosis of fibrosis among different modalities.

Conclusions:
AI-assisted systems have promising potential for the diagnosis of liver fibrosis and NAFLD. Validations of their performances are warranted before implementing these AI-assisted systems in clinical practice.

G-03

Assessment of the Quality of Life of Chronic Liver Disease Patients using the Filipino Versions of CLDQ and HADS

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Objectives:
Health related quality of life (HRQoL) among Chronic Liver Disease (CLD) patients worsens as the severity increases. Although anxiety and depression has a growing prevalence, it remains underdiagnosed among CLD patients. This study aims to assess the severity of the quality of life of CLD patients using the Filipino Versions of CLDQ and HADS and to correlate the prevalence of anxiety and depression in relation to the quality of life of patients with CLD.

Materials and Methods:
This is an Observational, Cross-Sectional prospective study, using the Simple Random Sampling Technique that involved CLD patients who sought consult at the OPD of BGHMC last October 2019. Filipino versions of CLDQ and HADS were used in measuring the HRQoL among CLD patients and the prevalence of anxiety and depression respectively. Collated data via Microsoft Excel was analyzed using IBM SPSS Statistics.

Results:
Out of 58 patients (CI 80%), majority were 47-60 years old (34.5%, mean=50.78), males (58.6%), married (67.2%), and finished tertiary level (60.3%). Abdominal Symptoms had no significant difference among each stage of CLD, (p value = 0.87), while the remaining 5 domains had p values <0.05. Anxiety and depression among CLD patients was at 6.9%. CLDQ scores were decreasing, being lowest among patients noted to have anxiety. P values of the 6 domains were all significantly different (p <0.05).

Conclusions:
As the severity of CLD increases, the quality of life is more impaired. Anxiety and Depression among CLD patients poses an increasing HRQoL impairment as the CTP Score increases.

G-05

Crowdsourcing to Promote Hepatitis C Testing and Linkage-to-care in China: Randomized Controlled Trial Interim report

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Objectives:
Many people living with HCV in China are unaware of their HCV status, despite a large burden of disease and increasing treatment access. Crowdsourcing has a group of individuals solve a problem (e.g., messaging to promote HCV testing and linkage) and then implement solutions.

Materials and Methods:
A two-armed randomized controlled trial is being conducted at primary care sectors of Shenzhen among local residents ≥30 years old not known to have HCV. The intervention group would receive crowdsourcing materials to promote HCV testing twice a week for two weeks, while the control group received standard promotional materials. Those identified HCV antibody-positive would be referred to specialists for confirmation and treatment.

Results:
As of 4th November 2020, 614 persons were recruited into the study (311 in the intervention group and 303 in the control). 47.1% were male; majority married (81.6%) with an average age of 43.2 years. 490 (79.8%; 249 in the intervention vs 241 in the control) had been tested and 12 (8 in the intervention and 4 in the control) were found to be positive for HCV. Significantly more were tested at HKUSZH in the intervention group (129/179 in the intervention vs 105/197 in the control; $p<0.001$). In those detected HCV. there were significantly more who did not think HCV was a serious problem before ($p=0.048$).

Discussion:
This interim analysis demonstrates the feasibility and acceptability of this approach. This community-based hospital approach could be used to scale up HCV testing in many settings.
(Chinese Clinical Trial Registry ChiCTR19000025771)

G-06

Lower GI Endoscopy-Indications and findings in a Tertiary Care Hospital

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Objectives:
Colonoscopy is one of the most important diagnostic tools to assess the structural abnormalities of the large intestine and distal ileum. To date, there is a paucity of data in Pakistan on indications and findings of colonoscopy. Therefore, our study aimed to evaluate the indications and endoscopic findings of patients who underwent colonoscopy at a tertiary care hospital in interior Sindh, Pakistan.

Materials and Methods:
This prospective cross-sectional study of 125 patients who underwent lower GI endoscopy was conducted in the Endoscopy Unit of LUMHS Civil Hospital Hyderabad / Jamshoro from April 2020 to September 2020. To be eligible participants had to be 14 years or older, of either gender and giving informed consent. Data regarding demographic characteristics, indications, and endoscopic findings were gathered on a pre-designed Prof.orma.

Results:
A total of 125 participants were recruited with a mean age of 39 ± 20, out of which 60% were males. Rectal bleeding was the most common indication (70.4%) followed by abdominal pain (9.6%), chronic diarrhea (8%), altered bowel habits (6.4%), constipation (2.4%), post-cancer surveillance (1.6%), weight loss, and anemia (0.8%) each. The most common colonoscopy findings were hemorrhoids (29.6%), normal (22.4%), and suspected tumor/growth (14.4%).

Conclusions:
The most common indication in our study was per rectal bleeding with hemorrhoids as the most common endoscopic finding on colonoscopy.

G-07

Public Awareness and Knowledge on Liver Disease and Liver Health in Singapore

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Objectives:
Despite efforts to control and manage liver diseases, significant health issues remain. Our aim is to study the degree of public awareness and knowledge regarding liver diseases and liver health in Singapore.

Materials and Methods:
A cross-sectional, self-reported, web-based questionnaire was administered to 500 adult individuals. Questionnaire items pertained to knowledge and awareness of overall liver health, liver diseases and their associated risk factors.

Results:
Sixty-four percent of respondents were ≥35 years old and 54.0% were males. Majority (85.8%) were aware of the liver's detoxification function. More have heard about hepatitis B (HBV, 85.0%) than hepatitis C (HCV, 50.6%). Approximately 7 in 10 were knowledgeable that consequences of viral hepatitis included liver cirrhosis, liver failure and/or cancer. However, only 15% were aware there is no vaccine available for HCV and more than half mistaken that HBV and HCV are transmissible via contaminated food or raw seafood. Although 75% of respondents had heard of non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, more than 50% were not aware of the related risk factors and complications. Awareness of specific tests for liver health screening and diagnosis was poor. Only 40% understood the implications of blood transaminase levels and only one-fifth correctly identified the diagnostic tests for viral hepatitis.

Conclusions:
While the public had some degree of general awareness about liver diseases, the level of understanding of liver diseases, risk factors and potential complications was superficial. There should be more public education efforts to adDr.ess misperceptions and increase the knowledge about liver diseases.

G-09

Specificity and Positive Predictive Value of International Classification of Diseases - 10 Diagnosis Codes for Cirrhosis

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Objectives:
A number of International Classification of Diseases (ICD)-10 codes may correspond to a cirrhosis diagnosis. However, these codes have not been as well-studied as ICD-9 codes. We aimed to identify which ICD-10 codes have the highest specificity and positive predictive value (PPV) for cirrhosis.

Methods:
We conducted a single-center retrospective study of participants in Michigan Genomics Initiative, a genetic cohort based in Ann Arbor, MI, USA. We evaluated 2778 patients with at least one of 26 ICD-10 codes to suggest cirrhosis. We manually reviewed these patients' charts to determine whether cirrhosis was present based on imaging findings, transient elastography, or liver biopsy. Codes which <10 patients had were excluded.

Results:
Of the 2778 patients studied, 787 had cirrhosis identified via chart review. After excluding six codes found in <10 patients, we studied 20 ICD codes suggestive of cirrhosis. The most common code, R18.8 (other ascites) demonstrated poor specificity and PPV (0.47 and 0.26, respectively). Codes for encephalopathy such as G93.40 (encephalopathy, unspecified) and G93.41 (metabolic encephalopathy) also demonstrated low PPV of 0.13 and 0.27, respectively. However, codes explicitly related to cirrhosis (K74.60, K74.69, K74.5, K70.30, K70.31) had much higher specificity (>=0.90) and PPV (0.78-0.92). Codes for varices (I85.1X, I85.0X, I86.4), hepatorenal synDr.ome (K76.7), or spontaneous bacterial peritonitis (K65.2) also had high specificity (>0.95). ICD-10 codes specifying alcohol-related liver disease (K70.40, K70.31, K70.30) had high PPVs (0.92-1.00).

Conclusions:
While ICD-10 codes for cirrhosis and varices had high specificity and PPV, codes for ascites and encephalopathy had much lower PPV.

G-11

Understanding the Knowledge, Attitudes and Practices of the Public towards Liver Disease in Malaysia

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Objectives:
Viral hepatitis B and C (HBV, HCV) and fatty liver disease (FLD) are the commonest etiologies of deaths by liver cirrhosis and/or liver cancer in Malaysia. The aim of this study is to explore and understand the gaps in knowledge, attitudes and practices of the public towards liver-related diseases in Malaysia.

Materials and Methods:
A cross-sectional, self-reported, web-based questionnaire was administered to 500 adult individuals between Feb–Mar 2020. Questionnaire items were pertained to the knowledge, attitudes and practices towards liver health and liver-related diseases.

Results:
Half of the respondents were ≥35 years old and 52.0% were males. The knowledge areas lacking among the respondents included awareness of different types of hepatitis, knowledge of viral hepatitis, and potential risks and complications of liver diseases. A higher proportion rightly recognized the diagnostic test for HCV (40.8%) than HBV (30.0%). More respondents associated FLD (63.0%) with liver diseases than hepatitis (47.2%). Less than one-third had the knowledge regarding risk factors, screening tests and complications of non-alcoholic FLD (NAFLD). While majority (92.8%) agreed regular screening was important to liver health, only 67% recently attended health screening. Approximately one-fifth indicated their likelihood to attend screening if exposed to viral hepatitis risk factors. Some reasons for this low urgency included the perception of being healthy, screening and treatment costs and societal discrimination.

Conclusions:
There is an unmet need for robust education efforts to boost awareness and empower individuals within the community with knowledge on liver-related diseases, particularly for viral hepatitis and NAFLD, in Malaysia.

G-12

Upper GI Endoscopy-Indications and findings in a Tertiary Care Hospital

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Objectives:
To document different indications and findings of upper GI Endoscopy in our endoscopy suite.

Materials and Methods:
A descriptive study of 500 patients who underwent UGI endoscopy was conducted in the Endoscopy unit from April to September 2020. We analyzed demographic characteristics, indications, and endoscopic findings in patients.

Results:
We studied five hunDr.ed patients with a mean age of 42.4 ± 16.8, out of which 52.8% were males. Upper gastrointestinal bleed (UGIB) was the commonest indication (33.2%) followed by dysphagia (21.6%), epigastric pain (10%), surveillance and screening of varices (9% and 8.2% respectively). The most common endoscopic findings were esophageal varices (32.2 %), gastritis (18.8%), and normal (11.4%). In patients with esophageal varices, 77.4% had chronic liver disease with positive serology for HCV and HBV in 63.4% and 23% respectively.

Conclusions:
The most common indication was upper GI bleed with esophageal varices on endoscopy as the commonest finding. The underlying etiology of varices reflects the high burden of chronic liver disease due to viral hepatitis.

G-13

Diagnosis of Liver Disease based on Artificial Intelligence Systems using the Decision Tree Algorithm Implementation

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Objectives:
This study will discuss the classification of liver disease using the Decision Tree C4.5 Algorithm using the Indonesian Liver Patient Dataset. This study will also prove the most influential variable of the 11 variables that determine the liver disease.

Material and Methods:
The research conducted includes processing the dataset using the help of the Rapidminer data mining application. The dataset used in this study was taken from The Ministry of Health of the Republic of Indonesia Database. Indonesian Liver Patient Dataset contains 583 clinical data with 10 attributes with 416 positive liver output targets and 167 negatives. Based on 583 processed data, 433 data are used as training data and 150 data are used as test data.

Results:
This study shows that only two variables (Almine Alminotransferase and Age) among the 11 variables in the dataset are the most influential in determining the classification of liver disease. This study also showed an accuracy of 72.7% in determining the classification of liver disease using the Dataset of the Ministry of Health of the Republic of Indonesia.

Conclusions:
Detection or classification results can be said to be quite good based on an accuracy value of more than 70%.

G-14

Deep learning of CT images in patients with chronic viral hepatitis – a territory-wide study with data from HADCL from year 2000 to 2017

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Objectives:
We aimed to develop novel machine-learning computer-aided diagnosis (CAD) for liver nodules in CVH patients with data retrieved from the Hospital Authority Data Collaboration Lab (HADCL).

Materials and Methods:
This was a territory-wide retrospective observational cohort study in Hong Kong. We identified CVH patients through HADCL based on laboratory, diagnosis and Dr.ug data. We designed a dedicated model to analyze the CT images. With the weak information, we adopt a weakly supervised approach to refine the detector dedicated for detecting liver nodules.

Results:
3360 CT volumes of CVH patients were included. We first validated the performance of the pretrained detector using the testing set of DeepLesion. Our novel machine learning model has the best sensitivity at various false positives/image compared to the existing approaches (3DCE, MVP and MULAN) (Table). Then we fine-tuned the detector using HA data. We comprehended the radiology reports with natural language processing, and tokenized all the words in the radiology reports and keep tokens with 3 or more occurrences. With the weak information extracted from the reports, we are in the process of refining the detector using weakly-supervised leaning.

Conclusions:
Novel machine learning model has the best sensitivity to detect lesions of different types. After fine-tuning, the detector will perform better for detecting liver nodules in the CT images of patients with chronic hepatitis B and C.

Acknowledgement:
HADCL provided data, tools, platforms, heath informatics and Prof.essional support. DeepLesion provided annotated lesion CT images. All data were anonymized and not identifiable data were retrieved.

G-15

Impact of Expanding Antiviral Treatment Criteria at a Population Level in the Republic of Korea: A modeling analysis

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Objectives:
HBV is a major disease burden in the Republic of Korea. Current antiviral treatment for HBV decreases disease progression, however, cannot eradicate the virus. Hence, antiviral treatment is offered for a subset of chronic HBV infected individuals. This study examined the impact of expanding treatment criteria on the future disease burden at the population level.

Methods:
A dynamic country-level transmission and disease burden model was calibrated to Korean data and estimated the HBV disease progression and mortality. Three scenarios were developed and compared to the Base case which maintained the current eligibility requirements and treatment levels. An economic analysis was also conducted.

Results:
Through 2035, expanding the current guidelines to include all cirrhotic individuals and treating 70% of everyone eligible would result in averting 4,300 cases of decompensated cirrhosis, 13,000 cases of HCC, and would save 11,800 lives. Reducing the ALT restriction to the ULN and treating 70% of those eligible would result in averting 7,200 cases of decompensated cirrhosis, 26,700 cases of HCC, and would save 23,300 lives. Treating 70% of individuals a viral load ≥2,000 IU/mL would result in averting 9,800 cases of decompensated cirrhosis, 43,300 cases of HCC, and would save 37,000 lives. All scenarios were highly cost-effective through 2035.

Conclusions:
Expanding treatment criteria in Korea would result in almost 12,000 lives saved, but by fundamentally shifting the guidelines this number can be doubled or tripled. As many of these individuals are of working-age the ICER for all scenarios were below the GNI per capita.

G-16

Crush Smear Cytology - An Adjunct To Biopsy In Gastrointestinal Malignancies

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Objectives:
Diagnostic yield following crush cytology and biopsy as adjunctive tool.

Materials and Methods:
Crush cytology and biopsy of esophagus , gastric and colonic malignancy taken by upper GI and Ileo-colonoscopes with total sample size of 70.

Results:
The diagnostic outcomes were examined by correlating with clinical and histological data. Out of 20 cases of suspected oesophageal malignancies 19 were diagnosed as carcinoma by histopathology with one being repeat and 17 cases by crush smear . Out of 20 cases of gastric lesion 14 and 11cases were proved to be malignant by histopathology and crush smear cytology respectively. 24 of the 30 cases of colonic mass were proved to be malignant by histopathology with 6 being benign and 18 were malignant by crush cytology.

Conclusions:
Thus with this data we can say crush cytology can be a useful adjunct to conventional histopathology. Though it has limitations as benign, reactive, in situ and invasion cannot be commented but its high sensitivity can be of help in providing quick information and an adjunct to biopsy.

G-17

Point-of-Care Interactive Decision Support Tool Demonstrates Discordance Between Healthcare Practitioner Approaches and APASL Guideline Recommendations in the Management of HBV Infection

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Objectives:
Patient variables that inform HBV treatment candidacy and treatment selection are complex and interconnected. To aid healthcare practitioners (HCPs) in aligning management decisions with practice guidance, we developed a decision support tool.

Materials and Methods:
The tool enables users to specify a guideline (AASLD, EASL, or APASL) and enter patient variables: HBV DNA/ALT levels, liver fibrosis, etc. Users select their intended approach, after which the tool displays guideline recommendations specific to the case. Cases specifying APASL guidance entered from January 2019-August 2020 were assessed (N=3254).

Results:
For 31.4% of cases, the user selected “unknown” for a variable necessary to reach a guideline recommendation. HBeAg status/HBV DNA level was most often missing (13.6% of cases). HCPs’ intended approach matched guidelines in 60.3% of cases for which a recommendation was possible (n=1106). Cases in which the HCP chose to treat when monitoring was indicated (17.4%) and those in which the HCP was unsure (9.4%) represented the largest discrepancies. Certain types of cases demonstrated higher discordance. Intended approach did not match guidelines for 55.7% of immune-tolerant cases (n=95) and 43.4% of cases with ALT 1-2x the upper limit of normal (n=339). Many HCPs also intended to treat patients with minimal inflammation/fibrosis when treatment was not indicated (31.8%;n=603) or to monitor patients with moderate to severe inflammation/significant fibrosis (20.5%,n=122) or compensated cirrhosis (16.4%;n=55) rather than treat as indicated.

Conclusions:
This tool highlights knowledge gaps in patient information needed to make appropriate HBV management decisions and demonstrates differences between HCPs’ approaches and recommendations.

Hepatitis B and Hepatitis D

H-01

96-week Efficacy and Safety of Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide Switch vs. Continued TDF Treatment among Virologically-suppressed Hepatitis B patients of Asian Ethnicity (AE)

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Objectives:
Study 4018, an international Phase 3 study, previously demonstrated switching to tenofovir alafenamide (TAF) vs continued tenofovir disoproxil fumarate (TDF) in suppressed chronic hepatitis B (CHB) patients has noninferior efficacy (TAF vs TDF) with superior bone/renal safety. We analyzed the efficacy and safety of switching in AE patients in Study 4018.

Methods:
CHB patients on TDF for ≥48 weeks with HBV DNA less than LLOQ for ≥12 weeks and <20 IU/mL at screening were randomized to TAF 25mg QD or TDF 300mg QD, each with matching placebo, and treated for 48 weeks in a double-blind (DB) fashion followed by all patients receiving open-label (OL) TAF 25 mg QD for an additional 48 weeks.

Results:
400/488 (82%) were AE patients who received at least 1 dose of study Dr.ug, with 195 in the TAF-TAF arm and 205 in the TDF-TAF arm. Virologic suppression was similarly maintained at 96-wks in both groups (95%: TAF and 94%: TDF). Higher percent changes in BMD from baseline (both hip and spine) were seen among the TAF-TAF group [1.2 (3.0 SD) for hip and 2.5 (4.0 SD) for spine] vs TDF-TAF group (0.12 (2.8 SD) for hip and 1.5 (3.8) for spine]. eGFRCG increased over 2 years in the TAF-TAF group and from Week 48 to 96 in the TDF-TAF group. There were no study Dr.ug-related treatment-emergent grade 3 or 4 AEs or SAEs.

Conclusions:
Following TDF-TAF switch, viral suppression was maintained, with improved bone and renal safety parameters through 96 weeks in AE patients.

H-02

A real-world clinical study of lipid changes on TAF treatment in Chinese chronic hepatitis B patients with diabetes

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Objectives:
To evaluate changes of blood lipids when treated with Tenofovir Alafenamide (TAF) in CHB with diabetes.

Materials and methods:
In this study, 34 CHB patients with diabetes were included for TAF treatment. Blood lipids were tested at 12 and 24 weeks of follow-up, as well as eGFR and urine β2-microglobulin.

Results:
Patients' median age was 49.4 ± 9.0, of which HbA1c% was 6.9 ± 1.1%. There were no significant changes in blood lipids ($P > 0.05$) in all patients, TC was 4.44 ± 1.02, 4.56 ± 0.93, 4.57 ± 0.83mmol/L ($P = 0.840$), TG was 1.54 ± 0.61, 1.61 ± 0.87, 1.71 ± 1.03mmol/L ($P = 0.743$), LDL was 2.80 ± 1.01, 2.94 ± 0.98, 3.04 ± 1.03mmol/L ($P = 0.670$), TC:HDL was 4.55 ± 1.06, 4.37 ± 1.03, 4.60 ± 0.93 ($P = 0.685$), respectively at baseline, weeks 12 and 24. When sub-analyzed for 13 patients switching from TDF to TAF, LDL was 2.79 ± 1.08, 2.79 ± 1.16, 3.17 ± 1.39mmol/L ($P = 0.721$); for 7 patients switching from ETV to TAF, LDL was 3.05 ± 1.24, 2.76 ± 1.19, 3.16 ± 0.56mmol/L ($P = 0.828$). 16 patients (47%) had complication of renal injury, and 9 patients were TDF-related, eGFR showed an increasing trend ($P = 0.494$), and urine β2-microglobulin decreased gradually ($P = 0.005$) , after switching to TAF.

Conclusions:
TAF can be selected as an optimal regimen for CHB with diabetes at high risk for kidney injury without significant impact on lipid Prof.iles.

H-03

Novel Case of Chronic Hepatitis B Reactivation in a COVID-Confirmed 78-year-old Male: A Case Report

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Objectives:
The novel coronavirus (COVID-19) pandemic paved the indirect resurgence of other life-threatening conditions. Transaminitis in COVID has reported incidence of 6-22.2%. However, Chronic Hepatitis B reactivation among these patients is underreported. Several inciting agents are implicated such as investigational Dr.ugs: antivirals and Tocilizumab therapy along with disease progression.

Clinical Presentation:
A 78 year-old male presented with 1 week fever and dyspnea and was managed as RT-PCR positive COVID pneumonia. Hepatitis panel revealed recovered Hepatitis B infection with documented Anti-HBsAg and Anti-HbcAg and mildly elevated admitting SGPT (78 U/L). Upon initiation of COVID treatment, he was given Lopinavir-Ritonavir and two doses of Tocilizumab infusion. Transaminitis was then progressively recorded which reached 2400 U/L with mild elevation of bilirubin (1.7), and SGOT (310 U/L). CT Scan of the Liver was unremarkable. Other possible causes of Transminitis were ruled out. Nucleic Antibody Testing- HBV DNA was reactive thus confirming Hepatitis B reactivation. The patient had persistent desaturations thus given Lopinavir-Ritonavir and Tocilizumab infusion. With recorded HBV reactivation after immunosuppressive therapy, the implicated medications were discontinued. Patient was started on standard dose of nucleotide analogue, Tenofovir. Transaminitis resolved with normalization of SGPT (29 U/L). Patient recovered from COVID infection however succumbed to post-COVID complications.

Conclusions:
Among COVID infected patients with plans to initiate immunosuppressive therapy, antiviral prophylaxis should be promptly initiated to prevent Hepatitis B reactivation. A high degree of suspicion for a multifactorial cause of transaminitis such as disease progression, and Dr.ug-induced liver injury is of paramount importance for timely management.

H-04

Association of Aspirin with Hepatocellular Carcinoma in Patients with Chronic Hepatitis B with or without Cirrhosis

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Background/Aim:
Aspirin therapy has been reported to reduce the risk of developing hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients. We aimed to investigate the association between aspirin use and HCC risk in CHB patients with or without cirrhosis.

Methods:
We identified 329,635 CHB patients who underwent health examinations from 2007 through 2017, using the Korean National Health Insurance Database. We generated a propensity score-matched cohort to balance baseline characteristics between aspirin users (n=20,200) and non-users (n=309,435). The risk of HCC development was estimated, accounting for death as a competing event.

Results:
Propensity score matching generated 19,003 pairs with a median follow-up period of 8.5 years. The cumulative HCC incidence among aspirin users was significantly lower than that among non-users (P<0.0001). Aspirin use showed a significant association with lower risk of HCC (adjusted hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.78–0.92; P<0.0001). Among patients without cirrhosis (16,507 pairs), aspirin users had significantly lower cumulative HCC incidence (P<0.0001) and HCC risk (adjusted HR, 0.87; 95% CI, 0.79–0.95; P=0.002) compared to non-users. However, among patients with cirrhosis (2,479 pairs), the cumulative HCC incidence (P=0.51) and HCC risk (adjusted HR, 1.0; 95% CI, 0.85–1.18; P=0.99) did not differ significantly between aspirin users and non-users. Cirrhosis had a significant effect on the association between aspirin use and HCC risk (P<0.0001 for interaction).

Conclusions:
In this Korean nationwide cohort study of CHB patients, aspirin therapy was associated with a reduced risk of HCC. Cirrhosis had a substantial effect on this association.

H-05

A Literature Review of the Epidemiological and Long-term Clinical Burden of Chronic Hepatitis B (CHB) Infection in Asia-Pacific

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Objectives:
To describe the epidemiological and clinical burden of CHB in Australia, China, Japan, South Korea and Taiwan.

Methods:
EMBASE, CNKI, Wanfang, KoreaMed, ICHUSHI and Airiti databases were searched (October-2019) in English and local languages. Websites of national governments and institutions were also searched, and data were analysed descriptively.

Results:
CHB epidemiology was reported in 51 studies and government/institutional reports; 23 studies reported long-term progression to cirrhosis or hepatocellular carcinoma (HCC) in nucleos(t)ide analogue (NA)-treated patients. The most recent data from these studies (2013–2018) indicate that ~100,000,000 people in these countries have CHB (~84% in China); 30-60% of cases remaining undiagnosed. Data indicate that prevalence has decreased >10-fold among <20-year-olds in China, Taiwan and Korea due to prophylactic vaccinations, but remains particularly high among older populations (>15% prevalence among >30-year-olds in Taiwan; >7% among >20-year-olds in China). Progression to cirrhosis neared 10% within 10 years from NA initiation (n=3; N=49,782 patients), while 60% of patients with cirrhosis at NA initiation had further liver complications at five years (n=1;N=2,682). The median five-year-incidence of HCC in patients starting treatment was 4.1%(range=1-7%), and 19.1%(range=8-47%) in patients with cirrhosis at treatment initiation (n=9;N=34,480). Five-year liver-related mortality approached 3% among NA-treated CHB (n=1;N=2,897); >30% in those with cirrhosis at treatment initiation (n=2;N=5,579).

Conclusions:
Despite the wide availability of preventative vaccine programs, CHB remains highly prevalent in Asia-Pacific, with many patients progressing to liver-related morbidity and mortality even when treated with standard of care. More effective treatments are needed to improve functional cure and long-term outcomes.

H-07

Characteristics of hepatitis D in young adults

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Objectives:
Current literature on the prevalence and characteristics of hepatitis D virus (HDV) infection in young adults is limited. This study aims to determine the disease characteristics and severity in young adults.

Methods:
The case records of HDV RNA positive patients of age18-25 years were analyzed.

Results:
Out of 119 patients,105 (88%)patients were male. HBV-DNA was detectable in 83 (70%). HBeAg was non-reactive in 99 (83%). Cirrhosis was identified in 45 (37.8%) individuals; 9 (7.5%) were classified as Child class B or Child class C. Twenty four (20.2%) had a MELD score of ≥ 10, out of these 16 had a score of 15 or more. The risk of decompensation was calculated according to the Baseline-event-anticipation (BEA) score;8 (6.7%) patients were at BEA-A (mild risk), 105 (88.2%) were at BEA-B (moderate risk), and 6 (5.0%)were at BEA-C (severe risk). Notable findings in patients with cirrhosis included splenomegaly, low total leucocyte counts, low platelets, high bilirubin, elevated aspartate aminotransferase, gamma-glutamyl transferase and international normalization ratio, low albumin, high APRI, and high BEA score. The splenic size, platelet count, and albumin levels were independently associated with cirrhosis ($p<0.001$, <0.001, and 0.003). A model using a combination of platelet count, albumin, and spleen size was developed to accurately predict cirrhosis in this cohort. It had an AUROC of 0.935.

Conclusions:
HDV infected young adult patients were at a moderate to severe risk of clinical disease progression and about one-third of patients had already developed cirrhosis indicating the aggressive nature of the disease.

H-08

Chronic hepatitis B does not increase the risk of adverse clinical outcomes in patients with COVID-19: a territory-wide cohort of 2,256 patients

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Objectives:
We aimed to examine serial liver biochemistries and compare clinical outcomes in Coronavirus disease 2019 (COVID-19) patients with and without chronic hepatitis B (CHB).

Materials and Methods:
We performed a retrospective cohort study using data from a territory-wide database in Hong Kong. COVID-19 patients between 23 January and 31 July 2020 were identified by virological results and/or diagnosis codes. Patients without hepatitis B surface antigen (HBsAg) test, or with hepatits C or occult hepatitis B were excluded. Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) elevation was defined as ALT/AST ≥2x upper limit of normal (i.e. 80U/L). The primary endpoint was a composite of intensive care unit (ICU) admission, need of invasive mechanical ventilation (IMV), and/or death.

Results:
We identified 2,256 COVID-19 patients (mean age 48 years, 50% male) with HBsAg status; 111 (4.9%) had CHB. At baseline, CHB patients were older, more likely to have diabetes and hypertension, higher ALT, C-reactive protein, lactate dehyDr.ogenase, and lower albumin, platelets and lymphocytes than non-CHB patients. Among 1,814 patients with serial liver biochemistries, ALT/AST elevation occurred in 28/99 (28.3%) and 475/1715 (27.7%) of patients with and without CHB, respectively (P=0.899). Of 1,814 patients, 149 (8.2%) were admitted to ICU, 70 (3.9%) received IMV, and 53 (2.9%) died. After adjusting for demographics, relevant comorbidities and laboratory parameters, CHB was not associated with development of primary endpoint (adjusted odds ratio 1.42, 95% CI 0.71-2.85, P=0.329).

Conclusions:
ALT/AST elevation was common in both CHB and non-CHB patients. CHB was not associated with adverse clinical outcomes of COVID-19.

H-09

Comparison of HBV DNA Supression and Renal Safety Prof.ile in Chronic Hepatitis B Patients at Saiful Anwar Hospital Malang

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Objectives:
HBV DNA level is the strongest indicator of mortality and morbidity, especially in cirrhosis and Hepatocellular carcinoma. Tenofovir was proven had 78-80% conversion of HBV DNA become undetected after 1 year treatment, although the nephrotoxic effect still become problems. Telbivudine is the second line recommendation in chronic hepatitis B treatment which known had renal protection effects. This study aimed to know the comparison between HBV DNA supression and renal safety Prof.ile in chronic hepatitis B patients treated with Tenofovir or Telbivudine at Saiful Anwar Hospital Malang.

Materials and Methods:
A retrospective cohort study design conducted in chronic hepatitis B patients treated with tenofovir or telbivudine since January 2015 to December 2018. HBV DNA, ureum, creatinine level, and eGFR was measured at 0, 6th, and 12th month. Analize with Mann-Whitney test ($p < 0.05$)

Results:
78 and 39 chronic hepatitis B patients treated with tenofovir or telbivudine, respectively, in this study. By Mann-Whitney test on HBV DNA level , found did not differ significantly at 6th and 12th month evaluation in both group (p-value >0.050). The eGFR values of tenofovir decreased significantly at 6th and 12th month evaluation compared to telbivudine group (p-value <0.05).

Conclusions:
Tenofovir and Telbivudine were significantly reduced HBV DNA level. Telbivudine could become Dr.ug of choice in chronic hepatitis B patients, especially in renal impairment risk patients.

H-12

Duration of Denial-Acceptance of The Kübler-Ross Cycle in Patients After Diagnosed Hepatitis B

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Objectives:
Patients who have been diagnosed with Hepatitis B often experience sadness and grief, which usually affect the adherence to Hepatitis B treatment. Stigma, depression, social exclusion and financial problems are some of the challenges of patients that occur because of complications of illness and fear of patients and their families. The aim of the study was to examined the duration of denial-acceptance of the Kübler-Ross cycle in patients after diagnosed Hepatitis B.

Materials and Methods:
The survey was conducted cross-sectionally on 24 adult Hepatitis B patients (age:17-65 years) who had routine treatment at hepatology outpatient department of Saiful Anwar Hospital. Subject were interviewed with Acceptance of Disease and Impairments Questionnaire (ADIQ) and duration of denial to acceptance is calculated. Normality test for duration of denial-acceptance were analyzed and statistically significant if $p < 0.05$.
Results. By analyzing the data, the median duration of denial-acceptance of the Kübler-Ross cycle after diagnosed Hepatitis B were 20 weeks with the shortest duration 4 week and longest 216 weeks.

Conclusions:
We conclude that duration of denial-acceptance of the Kübler-Ross cycle after diagnosed as having Hepatitis B were 20 weeks. It is necessary to provide a longer educational time for patients newly diagnosed with hepatitis B so that information related to hepatitis B can be understood by patients. Education can also be done with a spiritual approach so that the patient can reach a phase of acceptance more quickly.

H-13

Characteristics of the Oral Mucosa in Patients with ChronicViral Hepatitis B

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Oral mucosa, HBV, Inflamatory-Dystrophic changes

Introduction:
Signs of chronic viral hepatitis in the oral cavity are various changes in the mucous membrane of the inflammatory-dystrophic nature: hyperemia, Dr.yness, edema and desquamation of the epithelium.
The aim of the study is to study the injury of oral mucosa in HBV patients.

Methods:
The paper presents the results of studies of 43 patients with chronic HBV. The mean age of patients with HBV is 37.19±10.32. Men 32, women -11

Results:
Among the 43patients with the CHBV t he oaral mucos changes were follwings:
Cracks in the corners of the mouth were observed in 20 (46.5%), p<0.001. the oral Mucosa was pale pink in 25.6% of the examined patients-11, pink -48.8% of cases - 21, p<0.001. Violation of the relief of OM was observed in 38 patients 88.4%, p<0.001. hemorrhages on the cheek mucosa were detected in 90.7% of cases – 39 patients, p<0.001, and telangiectasia-in 9 patients, i.e. 20.9% of cases. The presence of plaque on the surface of the tongue is observed in 79% of cases – 34 patients, p<0.001. Foci of epithelial desquamation on the tongue were observed in 11 patients (25.6%) p=0.0245

Conclusions:
- Patients with HBV develop inflammatory changes in the oral mucosa: stomatitis, glossitis, cheilitis.
- Lesions of the oral mucosa aggravate the course of the disease and serve as an important addition to the characteristic of the overall clinical picture of HBV.

H-14

Comparable Maternal Viral Load Reduction in TAF or TDF-treated Pregnant Women for Preventing Maternal HBV Transmission

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Objectives:
This study aims to evaluate the effect of tenofovir alafenamide fumarate (TAF) treatment in pregnant women for preventing maternal transmission of HBV.

Materials and Methods:
This is a prospective, multicenter clinical trial recruited HBV-infected pregnant women 20-45 years of age, seropositive for HBsAg and HBeAg. Pregnant women with HBV DNA level ≥6.0 log10 IU/mL received TAF 25 mg daily from gestational week 26-32 until 2 weeks postpartum in 2019-2020. The maternal viral load changes were compared with data of 53 pregnant women received TDF 300 mg daily during 2016-2018.

Results:
A total of 40 pregnant women received TAF treatment. The HBV DNA levels decreased from 7.80 ± 0.57 Log10IU/mL at baseline, to 3.99 ± 1.18 Log10IU/mL at delivery. In the 53 pregnant women receiving TDF, the HBV DNA decreased from 8.30 ± 0.36 Log10IU/mL to 4.47 ± 0.86 Log10IU/mL. The mean reduction of HBV DNA levels was comparable between the TAF group (3.83 ± 0.97 Log10IU/mL) and TDF group (3.83 ± 0.83 Log10IU/mL, P=0.98). The rate of the mothers achieved HBV DNA level ≤6.0 log10 IU/ mL at delivery were 92.5% (37/40) in the TAF group versus 98.1% (52/53) in the TDF group (P=0.31). Of the 42 newborns delivered by TAF group mothers, the average gestation age was 38.2 ± 2.0 weeks. Seven infants were followed up to 12 months and none were HBsAg positive (0/7).

Conclusions:
TAF treatment for highly viremic HBV-infected pregnant women resulted in successful HBV DNA viral reduction that were comparable with TDF-treated mothers.

H-15

Content Development of a New Self-stigma Patient-reported Outcome Instrument for Chronic Hepatitis B: A Qualitative Study In China

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Objectives:
In China ~84 million people have chronic hepatitis B (CHB). CHB stigma is common but research sparse. A qualitative study in China explored the validity of a new CHB self-stigma patient-reported outcome (PRO) instrument.

Materials and Methods:
CHB patients were interviewed on 1) CHB stigma/self-stigma experience (PRO concept elicitation [CE]), 2) if 'curative' treatment would change self-stigma, and 3) explored the validity of the content (cognitive debriefing [CD]) (instructions, item relevance, response options, recall period). Thematic and framework analyses were conducted. US FDA PRO Industry Guidance was followed. The Shanghai Ethics Committee for Clinical Research provided approval.

Results:
Twelve CHB patients (25–57 years; 7 females; 12 treatment-experienced) participated. Eight had experienced stigma: lack of awareness/understanding from others; relationship problems; others not sharing utensils/food; denied career/work-related opportunities; judgment/prejudice. Eleven participants could define self-stigma; 11 agreed CHB treatment with cure/functional cure would change self-stigma. CE identified relevant self-stigma domains (≥5 responses) as secrecy/concealment; devaluation/inferiority/worthlessness; withDr.awal/social isolation; marginalization/alienation. CD did not report misunderstanding of the questions. All 17 PRO items were considered relevant (4–12 participants noted 'relevant now'). Participants generally agreed that the 5-point response options (never/rarely/sometimes/often/always) were appropriate. Ten participants found the 4-week recall period appropriate.

Conclusions:
Stigma/self-stigma is widely experienced by CHB patients in China. This qualitative research provided evidence to support the content validity of the PRO instrument in China. Some changes to the instrument were suggested. Additional research should explore cross-cultural differences and the impact of a functional cure on self-stigma.

H-16

Early antiviral efficacy of tenofovir alafenamide in initial treatment of patients with chronic hepatitis B

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Objectives:
To investigate the early efficacy of tenofovir alafenamide (TAF) in initial treatment of chronic hepatitis B (CHB).

Methods:
The clinical data of 32 CHB patients who received TAF as initial antiviral therapy in our Hospital from June 2019 to January 2020 were retrospectively collected. The changes of ALT, HBV DNA and HBeAg/HBsAg in 4 weeks, 12 weeks and 24 weeks after antiviral treatment were analyzed.

Results:
After 24 weeks of TAF antiviral treatment, the normalization rate of ALT of all 32 patients was 87.5% (28/32). HBV DNA level was significantly lower than those at 12 weeks and baseline ($F = 415.238$, $P < 0.001$), the complete virological response (HBV DNA < 10 IU/ml) rate was 25.0% (8/32). Further analysis showed that HBV DNA at 4 weeks decreased the most compared with the baseline [(3.8 ± 0.98) lgIU/ml vs (7.5 ± 0.71) lgIU/ml] with an average decrease of 3.68 lg IU/ml. HBeAg and HBsAg at 12 weeks decreased significantly compared with the baseline ($t = 3.912$, $P = 0.001$; $t = 2.403$, $P = 0.027$), and the HBeAg clearance rate was 26.3% (5/19). Compared with baseline, serum Cr and eGFR had no significant change, TC and LDL-C showed an increasing trend and TG showed a descending trend at 24 weeks after treatment, however, the differences were not statistically significant ($P > 0.05$).

Conclusions:
TAF is effective and safe in the initial treatment of CHB.

H-17

Cost savings of the PAGE-B score in reducing hepatocellular carcinoma (HCC) surveillance in Chinese with chronic hepatitis B (CHB)-related cirrhosis

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Background and Aim:
PAGE-B score was reported to be a simple and reliable score for prediction of the 5-year hepatocellular carcinoma (HCC) risk in Caucasian chronic hepatitis B patients (CHB) receiving entecavir/tenofovir treatment. We performed an analysis of Chinese CHB patients on entecavir/tenofovir to determine the proportion subjects with PAGE-B score of 8 or 9 who would advance to the immediate(10-17) risk group within 3 years because age factor and therefore should resume HCC surveillance.

Methods:
1071 Chinese CHB patients who had received entecavir/tenofovir treatment for 5 or more years from Jan 2010 were included in analysis. PAGE-B score at the time of treatment was calculated and proportion of subjects advancing from low risk to immediate group because of age factor within 3 years determined and the potential cost savings calculated.

Results:
Totally, 166(16%) subjects had Page-B score <10, 100 subjects had risk score of 8 or 9. Among them 21(12.6%), would advance to immediate risk group in one year, 18% in 2 years, and 28% in 3 years. Assuming regular HCC surveillance is U/S every 6 month, excluding the low-risk subjects from surveillance would result in a reduction of surveillance U/S by 15.9%, 13.5%, 12.8% and 11% in the first, second, third and fourth year respectively.

Conclusions:
The PAGE-B risk score may result in an annual saving of around 13% during the first four years, but this may be an overestimate as more subjects may advance to the immediate risk group because of changes in platelets and albumin status.

H-18

Efficacy and safety of Tenofovir Alafenamide (TAF) vs Tenofovir Disoproxil Fumarate (TDF) in Chronic Hepatitis B patients of Asian Ethnicity following 5-years of treatment

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Background/objectives:
Pivotal studies GS-US-320-0108 (HBeAg-negative) and GS-US-320-0110 (HBeAg-positive), demonstrated non-inferior antiviral efficacy of TAF vs. TDF with superior renal/bone safety through 5-yrs; after up to 3-yrs of double-blind (DB) treatment, open-label (OL) TAF was available through Year 8. We analyzed TAF efficacy and safety among patients of Asian Ethnicity in Studies 108/110.

Methods:
Efficacy was assessed by individual study and included virologic, biochemical, and serologic assessments. Safety data were pooled including estimated GFR (by Cockcroft-Gault method; eGFRCG) and hip and spine bone mineral density (BMD) changes.

Results:
Among 1298 patients randomized and treated, 591 (45.5%) were Asian (TAF n=401, while n=84 and n=106 received TDF-OL-TAF-3 years and TDF-OL-TAF-2 years, respectively. Virologic control was achieved and maintained in patients receiving TAF (95%) and for TDF-OL-TAF-3 years (100%) and TDF-OL-TAF-2 years (98%). ALT normalization rates were comparable among groups (TAF: 79%, TDF-OL-TAF-3 years: 80%; TDF-OL-TAF-2-years: 79%). HBeAg loss/seroconversion was similar (TAF: 38.6%/27.4%, TDF-OL-TAF-3 years: 46.9%/37.5%; TDF-OL-TAF-2-years: 47.1/29.4%). Rates of HBsAg loss/seroconversion were similar in all groups (≤1%).
Rates of Grade 3/4 adverse events (AEs) and AEs leading to discontinuation were low (<1.5%) among all 3 groups. After experiencing declines in eGFRCG and in hip/spine BMD over 2 or 3 years of TDF treatment, renal and bone outcomes were improved following the switch to OL TAF.

Conclusions:
After 5 years of treatment, virologic suppression remained high, and TAF was safe and well tolerated with improved renal and bone safety among patients of Asian Ethnicity switching from TDF.

H-19

Efficacy of Pegylated Interferon-Alpha-2a in Chronic Hepatitis D Infected Patients. Experience from the Tertiary Care Hospital in Karachi.

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Background and Aims:
Hepatitis Delta Virus (HDV) is a unique virus because it needs Hepatitis B Virus (HBV) for its replication hence, survival. Pegylated Interferon-Alpha-2a (PEG-alfa-2a) is the only option available for the treatment of HDV. In the present study, we aimed to assess the efficacy of PEG-alfa-2a in patients with HDV infection.

Methods:
We enrolled all 65 patients with chronic HDV at department of Gastroenterology, Jinnah Postgraduate Medical Centre Karachi .On presentation, all patients were positive for both Anti-HDV and HBsAg, who were treated for 48 weeks with PEG-alfa-2a. Evaluation HDV infection through Polymerase chain reaction (PCR) was done at 6-month, and 12-month intervals.

Results:
From total 165 patients, Eighteen patients lost to follow up, 20 patients stopped treatment due to side effects of Interferon and 20 patients were excluded from the study due to liver cirrhosis, rest of 107 patients, 76 (71%) were male while 31 (29%) were female with a mean age of 27.84±10.52 years. Baseline investigations showed: Hemoglobin, 13.12+2.04 g/dL; platelets, 200.73±91.31 x109/L; and On PCR, HDV DNA was confirmed in every collected sample, with a mean value of 10786066.28±31826055.19iu/ml. Duration of treatment was 12 months, 25 (23%) patients achieved the 48-weeks End Treatment Response (ETR), 27 (25%) patients showed partial response to Peg-INF, while 54 (50%) had treatment failure (or Non-responders).

Conclusions:
Interferon therapy in patients with CHD shows a sub-optimal outcome. Only 23% achieved ETR. Patients with treatment failure or null response should urgently be given an effective alternative option.

H-20

Excellent preclinical characteristics of ALG-000184, a proDr.ug of the HBV capsid assembly modulator ALG-001075

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Objectives:
Capsid assembly modulators (CAMs) represent a clinically validated strategy for the treatment of chronic hepatitis B. Here, we describe the preclinical Prof.ile of ALG-000184, a proDr.ug of the class II CAM, ALG-001075, which is currently being tested in a phase I clinical trial.

Materials and Methods:
Cell-based antiviral activity was measured via qPCR. The in vivo activity was determined in the AAV-HBV mouse infection model. ALG-000184 and ALG-001075 were evaluated in vitro for their Dr.ug-Dr.ug interaction potential related to cytochrome P450 (CYP) and transporters.

Results:
ALG-001075 reduced encapsidated DNA by more than 4 log10 copies/ml and with an EC99.9 of 11 nM in cell-based assays. In the AAV-HBV mouse model, 15 mg/kg ALG-001075 dosed twice-daily for 8 weeks demonstrated strong antiviral activity with a reduction of serum HBV-DNA of > 5 log10 IU/mL.
Neither ALG-000184 nor ALG 001075 inhibited CYP isozymes CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4. ALG-001075 is unlikely to cause time dependent inhibition of human CYP2C8, CYP2C9, or CYP3A4. ALG-001075 had low induction potential for CYP1A2, CYP2B6, and CYP3A4. Out of 10 transporters tested, ALG-000184 was a substrate for OATP1B1/3 and ALG-001075 was a substrate for P-gp. ALG-000184 inhibited OATP1B1/3 and OAT1 while ALG 001075 inhibited OAT3 with IC50 values greater than 10 µM.

Conclusions:
Based on the potent antiviral activity of ALG-001075 in vitro and in vivo, the high projected human Ctrough levels of ALG-000184 and the low potential for Dr.ug-Dr.ug-interactions, ALG-000184 is currently advancing through Phase I clinical testing.

H-21

HBx-mediated ETV4 facilitates hepatocellular carcinoma invasion and metastasis via up-regulating the Dishevelled-2

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Objectives:
Chronic hepatitis B virus (HBV) infection is a critical risk factor for the hepatocellular carcinoma (HCC). Increasing evidence indicates that the X protein produced by the virus has been playing an important role in the tumorigenesis while the related mechanism is still not fully understood.

Materials and Methods:
The RNA-seq were conducted to find the target genes of the X protein. The ETV4 expression levels were detected in HCC tissue by quantitative real-time PCR (qPCR) and Western Blot (WB). R software was used to analyze the original information in The Cancer Genome Atlas (TCGA) database. The function of ETV4 was examined by cell invasion, cell migration, wound healing assays and tail vein injection experiments. The related mechanisms of ETV4 on its target genes were explored by ChIP, dual-luciferase reporter, electrophoretic mobility shift assay (EMSA) and WB assays.

Results:
Here, we firstly confirmed that ETV4 protein expression was significantly up-regulated in HCC tissue and could be an independent predictor of poor prognosis for patients with HCC. Evidence in vivo and vitro was provided that ETV4 can facilitate HCC cell invasion and metastasis. Further studies have found that the up-regulated ETV4 expression was related to the expression of Dishevelled-2 (Dvl2), which plays an important role in Wnt/β-catenin signaling pathway.

Conclusions:
Our study demonstrated that overexpression of HBx results in ETV4 overexpression, thereby promoting HCC invasion and metastasis by up-regulating Dvl2 expression.

This research has been approved by an ethical committee.

H-22

High Viral Suppression and Improved Safety Prof.ile of Tenofovir Alafenamide Relative to Tenofovir Disoproxil Fumarate in Chronic Hepatitis B Patients Treated for 5 Years

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Objectives:
In 2 identically-designed double-blind (DB), randomized (2:1), Phase 3 studies (HBeAg-negative patients [N=425] and HBeAg-positive patients [N=873]), TAF demonstrated antiviral efficacy non-inferior to that of TDF with superior renal and bone safety. After completing 3 years of DB treatment, all patients were eligible to receive open-label (OL) TAF through Year 8. Here we present study results at Year 5.

Materials and Methods:
Efficacy was assessed by serial virologic, biochemical, and serologic assessments, while safety data included changes in renal function and changes in hip and spine bone mineral density. Resistance testing and phenotyping was performed annually through Year 5.

Results:
Of 1298 randomized and treated patients, 1157 (89%; 775 TAF; 382 TDF) entered OL, At Year 5, 999 (77%; 675 TAF, 136 TDF-TAF OL 3y, 188 TDF-TAF OL 2y) patients remained on treatment. High rates of virologic control were achieved and maintained in patients receiving TAF throughout and for TDF patients who switched to TAF at Weeks 96 or 144. Rates of ALT normalization and serologic responses were also comparable among groups. 8 patients are undergoing phenotypic testing to assess resistance. Adverse events (AEs) leading to discontinuation were low and similar among groups. Renal and bone outcomes were improved following the switch to OL TAF from TDF.

Conclusions:
After 5 years of treatment virologic suppression rates remained high, and TAF was safe and well tolerated with improved renal and bone safety in patients switching from TDF.

H-23

In Vitro and In Vivo Antiviral Properties of GST-HG141, a Novel Hepatitis B Virus Capsid Assembly Modulator in Clinical Development

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Objectives:
Recently, the hepatitis B virus (HBV) capsid assembly modulators (CAMs) had emerged as a promising, clinically-validated agents for the chronic HBV Dr.ug development, with a potential for HBV cure. Here we report preclinical characterization of GST-HG141, a novel HBV CAM, currently under phase I clinical evaluation.

Materials and Methods:
Effects on HBV DNA were determined in cell-based HBV models, using qPCR. A biochemical quenching assay was used to determine effects on HBV core assembly. In vivo antiviral efficacy was assessed in the AAV-HBV mouse model.

Results:
GST-HG141 potently inhibited HBV DNA secretion in HepG2 2.15 cells (EC50= 8.16±3.65 nM), and was additive with Tenofovir. In the transient transfection assays, GST-HG141 retained potent antiviral activity against HBV genotypes A-D (EC50 26-228 nM), and against nucleos(t)ide-resistant mutants. No significant cytotoxicity was observed in eleven mammalian cell lines and primary cells (CC50>50 µM). No other tested DNA and plus-/minus-strand RNA viruses were inhibited by GST-HG141. In the biochemical quenching assay, GST-HG141 induced HBV core protein assembly (EC50=0.93±0.11 µM, n=3). In the AAV/HBV model, GST-HG141 demonstrated a robust dose-dependent reduction in serum (3.0 log10) and liver (0.9 log10) HBV DNA, following 28 days of dosing. Combination with Tenofovir resulted in additivity. GST-HG141 was well-tolerated, no significant effect on animal body weight was observed.

Conclusions:
GST-HG141 is a novel, orally-bioavailable HBV CAM. It has an excellent antiviral potency in vitro, efficacy in vivo, and is well-tolerated in rodents. Further development of GST-HG141 for chronic HBV infections is warranted.

H-24

Effectiveness and Safety of Tenofovir Alafenamide (Taf) in Nucleoside Analogue (Na) Treatment Naïve Patients with Chronic Hepatitis B (Chb) in China

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Objectives:
To evaluate the efficacy and renal safety of TAF in NA treatment naive CHB patients.

Methods:
This cohort study included CHB patients without NA experience who initiated TAF from June 2019 to Mar 2020. The changes of ALT, HBV DNA, HBeAg/HBsAg in 4 weeks, 12 weeks, 24 weeks and 48 weeks were analyzed, along with liver stiffness measurement (LSM) and estimated glomerular filtration rate (eGFR) at baseline and 24, 48 weeks.

Results:
61 patients were followed up to 24 weeks, 42 of which were followed up to 48 weeks of TAF treatment. All the patients were HBeAg positive. After 48 weeks, ALT normalization rate was 95.24% (40/42), complete virological response (HBV DNA < 20 IU/ml) rate was 69.05% (29/42), HBeAg seroconversion rate was 7.14% (3/42). HBV DNA and HBsAg significantly declined separately from baseline 5.22±1.91logIU/ml to 1.26±0.66logIU/ml; and from 3.59±0.81logIU/ml to 3.32±0.55logIU/ml, both P<0.05. Comparing with baseline, LSM at 48 weeks significantly decreased (13.00±8.15kpa vs 8.66±4.45kpa, P<0.05). There was no significant difference in eGFR (P>0.05). When categoried by baseline ALT level, patients were divided into group A (≤ULN, upper limit of normal=50U/L, n=21), group B (1~2ULN, n=22) and group C (≥2ULN, n=18). Significant HBsAg decline was observed in group B and group C (3.63±0.68logIU/ml to 3.53±0.63logIU/ml; 4.15±0.57logIU/ml to 3.66±0.48logIU/ml, both P<0.05) early at 24 weeks.

Conclusions:
TAF is effective and safe in NA treat-naive CHB patients with HBsAg decline, improvement in liver fibrosis and stable renal safety. Patients with elevated ALT obtained significant HBsAg decline at 24 weeks.

H-25

Pharmacokinetics of VIR-2218, an RNAi therapeutic for the treatment of HBV infection, in healthy volunteers

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Objectives:
VIR-2218 is an investigational N-acetylgalactosamine GalNAc-conjugated ribonucleic acid interference (RNAi) therapeutic in development for functional cure of chronic hepatitis B virus infection (CHB). VIR-2218 is designed to silence all HBV transcripts, from both cccDNA and integrated DNA, across all 10 HBV genotypes. Preliminary pharmacokinetic (PK) data from the first-in-human Phase 1 randomized, blinded, placebo-controlled, dose ranging study of VIR-2218 in healthy volunteers are reported herein.

Materials and Methods:
Six cohorts of eight subjects (6:2 active:placebo) received a single subcutaneous (SC) dose of VIR-2218 ranging from 50 to 900 mg. Plasma samples were assessed to determine PK of VIR-2218 and an active metabolite.

Results:
VIR-2218 was absorbed after SC injection with median tmax of 4-8 hours. VIR-2218 was not measurable in plasma after 48 hours for any subject; the median apparent elimination half-life (t1/2) ranged from 2-8 hours. Following single SC dose of 50 to 900 mg, plasma area under the curve (AUClast) and mean-maximum concentrations (Cmax) increased with dose with mean exposures ranging between 1260 to 59,000 ng*hr/mL and 155 to 5014 ng/mL, respectively. Intersubject variability within each dosing cohort was generally low (CV ~35%). The PK Prof.ile of the most prevalent active metabolite AS(N-1)3'VIR-2218, was similar to VIR-2218 with AUClast and Cmax values of AS(N-1)3' VIR-2218 in plasma ≤10% of VIR-2218.

Conclusions:
VIR-2218 demonstrated favorable PK properties in healthy volunteers supportive of SC dosing and continued development. Evaluation of VIR-2218 in patients with HBV is ongoing.

H-26

Preclinical Efficacy and Pharmacokinetics of ALG-010133, an S-Antigen Transport-inhibiting Oligonucleotide Polymer (STOPS™) for the Treatment of Chronic Hepatitis B (CHB)

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Objectives:
To evaluate the preclinical in vitro efficacy and pharmacokinetics of ALG-010133, a STOPS molecule designed to reduce hepatitis B surface antigen (HBsAg) levels in patients with CHB.

Materials and Methods:
The effect of ALG-010133 on secreted HBsAg levels was assessed in HepG2.2.15, PLC/PRF/5, HepG2-GtA, HepG2-GtB, HepG2-NTCP and HBV-infected PHH systems. The pharmacokinetics of ALG 010133 was evaluated following single subcutaneous (SC) injections given to mice and monkeys, or intravenous infusions (IVinf) given to monkeys.

Results:
ALG-010133 inhibited HBsAg release with EC50 values of 3.9, 23.7, 3.2, and 5.9 nM in HepG2.2.15, PLC/PRF/5, HepG2-NTCP and PHH cells, respectively. ALG-010133 inhibited HBsAg release in HepG2 cells containing integrated genotype A, B, C and D genomes with EC50 values of 7.9, 9.25, 0.72 and 3.9nM, respectively. Intracellular HBsAg was concomitantly reduced.
ALG-010133 demonstrated a low overall exposure in plasma with a half-life of 4h in mice. Following IVinf in monkeys, plasma ALG-010133 exhibited low clearance and volume of distribution and a half-life of 2.3h. ALG-010133 was readily absorbed with high SC bioavailability (70%-87%). ALG-010133 plasma exposure increased linearly with dose and slightly greater than dose-proportional manner in the 5-50 mg/kg dose range.
ALG-010133 has a high exposure and long half-life (>6 days) in monkey liver, the target organ for efficacy, indicating low, once weekly SC doses have potential to be efficacious in patients.

Conclusions:
The combination of excellent in vitro efficacy and favorable pharmacokinetic Prof.ile has allowed ALG-010133 to advance into clinical development to be evaluated as a potential treatment for CHB.

H-27

Prevalence of hepatitis delta virus genotypes among patients with chronic viral hepatitis B with a Delta agent in Kazakhstan

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Background:
Liver cirrhosis and HCC in outcome of chronic hepatitis B with Delta agent (CHD) is the most common cause of liver transplantation in Kazakhstan.
Multivariate analysis identified age, HBV genotype C, and HDV genotype I as independent factors for poor outcomes.

The Aim:
to study the prevalence of genotypes of HDV in Kazakhstan

Methods:
Blood samples of patients with CHD from all regions of Kazakhstan were examined for the determination of genotypes of HDV by the PCR. Isolation of HDV RNA was performed using the GeneJETViral RNA Purification Kit, ThermoScientific. PCR was performed using specific primers. Purified PCR products were sequenced in two directions, using a forward and reverse primer.

Results:
In total, out of 294 samples, 256 samples were positive in PCR and genotyped (87%). We included 256 patients, including 40,0% men, 60,0% women. The average age was 42.9±12,0 years. Only 2 patient (0,8 %) were HbeAg-positive. Patients with CHD had the stage F0 of liver fibrosis (Metavir) in 23,3 %, F1 in 6,9%, F2 – 14,7%, F3 –14.7 %, F4 in 40,5% .
Comparison and phylogenetic analysis of the nucleotide sequences of the PCR products of the HDV isolates showed that they 100% belonged to genotype 1. The identity of the nucleotide sequences of isolates isolated on the territory of Kazakhstan was 75-95%.
The 82 patients with positive PCR of HBV DNA and HDV RNA has genotype D of HBV.

Conclusions:
Genotype 1 of HDV is the only common in Kazakhstan and is distributed in all regions.

H-28

Real-world Outcomes of Sequential Therapy with Tenofovir Alafenamide Following Long-term Entecavir

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Objectives:
Entecavir (ETV) and tenofovir alafenamide (TAF) are both first-line HBV therapies, but ETV-to-TAF switch outcome data are limited. We aimed to assess outcomes up to 96 weeks after ETV-to-TAF switch.

Material and Methods:
ETV-treated (≥12 months) CHB patients switched to TAF in routine practice at 15 centers (U.S., Korea, Japan, Taiwan) were included. Primary outcome was complete viral suppression rate (CVS, HBV DNA<20 IU/mL).

Results:
We analyzed 425 patients (mean age 60.7 ± 13.2 years, 60% male, 90.8% Asian, 20.7% diabetic, 27% hypertensive, 14.8% cirrhotic, 8.3% HCC, mean ETV duration before switch 6.16 ± 3.17 years). Mean baseline eGFR was 89 ± 19 (CKD stages: 55.6% stage 1, 35.7% stage 2, and 8.8% stage 3-5). CVS increased from 91.90% at switch (from 90.46% 24 weeks before switch) to 95.57% and 97.21% at 48 and 96 weeks after (P=0.03 and 0.02, respectively). Over the 96-weeks after switch, mean HBV DNA (P<0.001) but not ALT, or CKD stage decreased. Between switch and 96-week follow-up, 11% (26/235) of CKD stage 1 patients migrated to stage 2, 8% (12/151) stage 2 to 3-5, while 18% (27/151) from stage 2 to 1, and 19% (7/37) from stage 3-5 to 2. On multivariable generalized estimated equation analysis adjusted for sex, hypertension, diabetes, and cirrhosis, baseline eGFR, age (P<0.001) and CKD stage 2 and 3-5 (vs. 1) (both P<0.001) were associated with lower follow-up eGFR.

Conclusions:
After an average of 6 years on ETV, CVS increased from 91.9% at TAF switch to 97.2% 96 weeks later.

H-29

Extremely rare risk of hepatocellular carcinoma after naturally and Nucleos(t)ide Analogue induced Hepatitis B Surface Antigen Seroclearance

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Objectives:
Despite a favorable clinical course, the risk of hepatocellular carcinoma (HCC) still exists in patients achieving HBsAg seroclearance. Therefore, we investigated the incidence of HCC after naturally and nucleos(t)ide analogue (NA) induced HBsAg seroclearance in real-life clinical practice

Materials and Methods:
A cohort study was conducted using data from Gangnam Severance Hospital. We identified all subjects with positive HBsAg between January 1, 2001 and March 21, 2018. NA use, liver biochemistries, serial HBsAg and anti-HBs results were retrieved. The primary endpoint was the incidence of HCC after naturally and NA induced HBsAg seroclearance.

Results:
A total of 109 chronic hepatitis B patients with HBsAg seroclearance were included for analysis. Among them, 26 patients were excluded. HBsAg seroclearance was developed after liver transplantation in 13 patients and after the development of HCC in 10 patients. In patients with spontaneous HBsAg seroclearance (n=51), all patients had confirmed HBsAg seroclearance and there was no HBsAg seroreversion. In patients with NA-induced HBsAg seroclearance (n=32), all patients had confirmed HBsAg seroclearance and HBsAg seroreversion was not observed. During a median follow-up period of 9 years, only one patient with spontaneous HBs Ag seroclearance developed HCC at 6 months after HBs Ag seroclearance. There was no incidence of HCC in patients with NA-induced HBsAg seroclearance.

Conclusions:
The incidence of HCC was extremely rare after naturally and nucleos(t)ide analogue (NA) induced HBsAg seroclearance in real-life clinical practice. NA-induced HBsAg seroclearance is also as durable as naturally HBsAg seroclearance

H-30

Safety and Efficacy of Tenofovir Alafenamide in Geriatric Patients with Chronic Hepatitis B: Experience from 4 Ongoing Phase 2 and Phase 3 Clinical Trials

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Objectives:
TAF is a first-line treatment for CHB patients at risk for TDF-associated bone and renal effects, including advanced age. We reviewed data in the subset of geriatric CHB patients participating in ongoing TAF clinical trials.

Materials and Methods:
Included were patients age ≥65 y treated with TAF in 3 phase 3 trials; TAF naïve patients in Studies 108 and 110, and suppressed patients switched from TDF to TAF in Study 4018, and data from a phase 2 study (Study 4035). Efficacy (virologic suppression) and safety (AEs, SAEs, changes in BMD and changes in eGFRCG) were assessed for (≥65 y) vs (<65 y) patients. In Studies 108, 110, and 4018, results for TDF in patients ≥65 y were also determined for comparison.

Results:
124 patients ≥65 y were included. Rates of virologic suppression, AEs and SAEs were comparable in geriatric vs non-geriatric patients treated with TAF. There were no Grade 3/4 AEs related to study Dr.ug in patients ≥65 y. Compared with younger patients, declines in eGFRCG and BMD were greater in viremic older patients; however, the decreases were less than in older patients on TDF. In suppressed patients, eGFRCG increases were greater in younger vs older patients receiving TAF, while changes in BMD were similar; TDF treatment resulted in declines in BMD and eGFRCG.

Conclusions:
Efficacy and safety of TAF in geriatric CHB patients were generally similar to younger patients. Small improvements in renal/bone parameters can be seen in older patients switched from TDF to TAF.

H-31

Safety and pharmacokinetics of single ascending doses of ALG-000184, a Class II Capsid Assembly Modulator for the treatment of Chronic Hepatitis B, in healthy volunteers

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Objectives:
Evaluate the safety and pharmacokinetics (PK) in HVs of ALG-000184, a proDr.ug of a novel Class II Capsid Assembly Modulator (empty capsid formation), ALG-001075. ALG 001075 is a pangenotypic, potent inhibitor of HBV RNA encapsidation HBV DNA replication and cccDNA establishment (Debing Y, et.al AASLD 2019).

Methods:
In Part 1 of this ongoing multi-part, double-blind, randomized, placebo-controlled study, up to 7 cohorts of 8 HVs (≥3 Asians/cohort) will receive single ascending oral doses of ALG-000184 or placebo (3:1 ratio). Adverse events (AE), vital signs, ECG and laboratories and, plasma and urine PK samples were collected. Reported here are preliminary blinded results for the first 4 cohorts [40, 100 (fasted/fed) and 250 mg]. Additional cohorts results will be included at the time of presentation.

Results:
There were no serious adverse events. All AEs were mild. The only AE in ≥1 subject was headache (n=2). All laboratory abnormalities were Grade ≤ 2 except for one unrelated Grade 3 creatine kinase elevation. There were no clinically significant ECG or vital sign findings. Plasma ALG-001075 exposures following single fasted doses of ALG-000184 increased dose-proportionally between 40-250mg, with low PK variability. The plasma t1/2 was ~7.5 hrs, supporting once daily dosing. High-fat meal did not significantly impact ALG-001075 PK. ALG-001075 exposures achieved with the 100 and 250 mg doses are expected to result in antiviral activity in CHB patients.

Conclusions:
Single doses of ALG-000184 of up to 250 mg were well tolerated with a PK Prof.ile supporting further evaluation in HVs and CHB patients.

H-32

Kinetics of HBsAg and ALT decline in nucleos(t)ide analogue treated HBV subjects

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Background:
The ideal endpoint of Hepatitis B treatment with nucleos(t)ide analogue therapy is the loss of hepatitis B surface antigen (HbsAg). We performed serial HBsAg quantitations in nucleos(t)ide analogue treated HBV subjects to determine whether kinetics of HBsAg decline were predictive of HBsAg seroclearance and ALT improvement.

Methods:
316 HBV subjects received nucleos(t)ide analogues. Of these, 243 patients had ≥ 4 HBsAg quantitations data points and were used for analysis. We log-transformed the HBsAg and ALT data and correlated the kinetics of HbsAg/ALT declines.

Results:
21 patients showed HBsAg seroclearance. Among them, 10 showed a linear HBsAg decay pattern with half-life of 9 ± 7 months, achieving seroclearance after 46 ± 29 months.
Six patients showed a biphasic decay pattern with a slow first phase (half-life 27 ± 29 months) followed by a faster second phase (half-life of 5± 2 months).
Remaining patients showed a triphasic pattern, a slow first phase, a faster second phase (half-life 1.5 ± 0.2 months) and a slower third phase.
We found a statistically significant correlation (R=0.19, p=0.011) between HbsAg and ALT decays in the patients with a monophasic HBsAg decay pattern. There were too few patients with the biphasic and triphasic patterns for statistically significant correlations.

Discussion:
About nine percent of HBV subjects receiving nucleos(t)ide analogue therapy had HBsAg seroclearance. Most showed an exponentially linear pattern of decline. However, biphasic or triphasic patterns were also observed. Understanding the mechanism for the change in rate of HBsAg clearance might provide insights into HBsAg eradication.

H-34

Secular trend of disease burden in patients with chronic viral hepatitis – a territory-wide study of 143,701 patients with data from HADCL in 2000-2018

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Objectives:
World Health Organization (WHO) calls for the reduction of chronic viral hepatitis (CVH) incidence and mortality of 80% and 65% respectively by year 2030. Antiviral treatment is the key to reduce mortality. Patients with advanced liver fibrosis should be prioritized for antiviral treatment. We aimed to determine the secular trend of disease burden in the territory-wide CVH cohort in Hong Kong from year 2000 to 2018 with data retrieved from the Hospital Authority Data Collaboration Lab (HADCL).

Materials and Methods:
This was a territory-wide retrospective observational cohort study in Hong Kong. We identified CVH patients through HADCL, based on laboratory data of viral markers, diagnosis codes and medication record of antiviral treatment for chronic hepatitis B and/or C. Advanced liver fibrosis was defined by serum fibrosis scores (APRI, Forns index and FIB-4 scores).

Results:
143,701 CVH patients were included; 24,422, 33,503, 40,290 and 45,486 were identified in year 2000-2004, 2005-2009, 2010-2013 and 2014-2018 respectively. The prevalence of advanced liver fibrosis appeared to be decreasing over time, which coincided with an increasing trend of uptake rate of antiviral treatment (Table). At the earliest (2000-2004) and the latest (2014-2018) time periods, advanced liver fibrosis was found in up to 22.4% and 16.6% of CVH patients respectively.

Conclusions:
Prevalence of advanced liver fibrosis decreased over the last two decades, which was likely related to the increasing uptake rate of antiviral treatment.

Acknowledgement:
HADCL provided data, tools, platforms, heath informatics and Prof.essional support. All data were anonymized and not identifiable data were retrieved.

H-36

Significance of switching from ETV to TAF for CHB patients with suboptimal response to ETV: A Retrospective Cohort Study

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Background and Aims:
Entecavir is one of the first-line therapies for CHB patients and widely used in China. However, there are insufficient data on recommendation for patients with suboptimal response (SOR) to ETV after prolonged ETV monotherapy This study aims to compare the virological and biochemical response of switching to TAF versus continue ETV treatment in ETV suboptimal response patients.

Methods:
This single-center, retrospective study enrolled 499 suboptimal response patients receiving at least 1-year ETV treatment. These patients were divided into two groups based on physician s' decision: continue ETV group (n=395) and switch to TAF group (n=104). The HBV DNA undetectable rate (HBV DNA <30 IU/mL), and biochemical response (ALT<40U/L, AST<35U/L) are assessed at 12 weeks and 24 weeks in both groups.

Results:
The baseline characteristics are showed in the Table. Compared to ETV group, TAF group were significantly older (46.1 vs. 41.7, P=0.003). The baseline HBV DNA, ALT and AST levels are comparable between two groups. Virological response rate of TAF group was significantly higher than those of ETV group at 12w (41.8% vs. 8.0%, P<0.001) and 24w (79.4% vs. 9.1%, P<0.001). More patients in TAF group achieved normal ALT level than that in ETV group (12w: 91.8% vs. 82.8%; 24w: 92.6% vs. 80.6%, p<0.05). At 24w, TAF group had more patients with normal AST level than that in ETV group (97.1% vs. 81.8%, P=0.001).

Conclusions:
For the ETV suboptimal response patients, switching to TAF significantly increased the virological and biochemical response rates at 12w and 24w.

H-37

Simplified test & treat protocols to eliminate HCV & HBV in Uzbekistan

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Objectives:
An estimated 3.5 million people are infected with HBV or HCV in Uzbekistan. This study tested the feasibility of eliminating HBV & HCV if the testing and treatment protocols were simplified to support a national program.

Materials and Methods:
Nurses were trained to use rapid HCV antibody and HBsAg to screen patients at polyclinics. Rapid creatinine and HIV tests were used to test HBsAg+ patients before they were referred to GPs for treatment. Core antigen/PCR, creatinine and APRI was collected for HCV+ cases. Cirrhotic patients were referred to a specialist while other patients were referred to GPs who were trained by specialists to treat patients. A centralized registry was used to collect patient data as they moved from screening to prescription refill.

Results:
More that 50,000 people were screened over six months at polyclinics. 70% of HBV+ were linked to care and 86% of patients received a prescription. 57% of HCV+ were linked to care and 84% of viremic patients received a prescription in spite of lower patient engagement with healthcare systems due to COVID-19. There were large geographic variations in HBV and HCV prevalence across Tashkent and nationally.

Conclusions:
A simplified test/treat protocol can be used to screen, link to care and treat large numbers of HCV+ and HBsAg+ patients using nurses and GPs who are accessible throughout the country. Patients with advanced liver disease still require consultation with a Specialist. The study also highlighted hotspots in the country that could be prioritized in a national program.

H-38

Long-Term Renal Safety Of Tenofovir Disoproxil Fumarate In Chronic Hepatitis B Patients

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Introduction and Objectives:
The majority of chronic hepatitis B patients, required long term oral nucleotide, tenofovir disoproxil fumarate (TDF) for virus eradication. Safety data on the long-term use of TDF not available in this part of the world, where renal stones and other disorders are very common.
The aim of this study is to evaluate the long term renal safety of TDF in chronic hepatitis B patients.

Methodology:
This prospective observational study was conducted from January-2019 till-todate in the Department of Gastroenterology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan and at Dow University of Health Sciences Ojha campus Karachi, Pakistan. A total of 120 patients with CHB started on TDF therapy of both gender, age ≥ 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 213 patients, 122 (57%) were males and 91 (43%) were females, with a mean age of 36.50 ± 11.04 years. During follow-up at 3 months there was no difference in eGFR ≥60 mL/minute/1.73m2 from baseline. However, after 6 months of TDF therapy patients had significantly lower eGFR (43.5 mL/minute). Also, in a subanalysis, patients older than age 50 years had worse renal outcomes with TDF.

Conclusions:
Comparing with baseline a significant reduction of eGFR has been observed at the end of six months (p value <0.05).

H-39

Response to Antiviral Therapy of Naïve Chronic Hepatitis B Patients in Semarang, Indonesia: a real-case study

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Objectives:
The aim was to evaluate the virological and histological response of antiviral therapy using Peg-IFN or Nucleos(t)ide Analogue.

Methods:
This was a single centered retrospective study. The subjects were 1017 naïve CHB patients receiving treatment during 2018-2019, 472 patients had complete information. Patients received PEG-IFN α2a or Nucleos(t)ide Analogue based on indications and Dr.ugs availability. Virological and histological responses were defined according to EASL.

Results:
A total of 472 patients were enrolled, mean age was 46.97 ± 13.2 years, 70.3% (n=332) male, 64.2% HBeAg negative, and 22% had cirrhosis. Hypertension, DM, CKD, Hepatitis C, Cardiovascular, Pulmonary diseases, HIV, and malignancy were found comorbidities (13.6%, 7.6%, 2.5%, 1.3%, 2.8%, 2.5%, 0.4%, and 3.3% respectively). Antivirals received were Tenovofir (13,3%; n=63), Telbivudine (67.6%; n=319), Entecavir (2.7%; n=13), and Peg Interferon (16.3%; n=77). Mean baseline fibroscan in Tenovofir, Telbivudine, and Peg Interferon group was 18.7 kpa, 15.4 kpa, and 15.1 kpa respectively. Virological response (VR) was observed in 64.1% of the patients (302/472) and a histological response was observed in 71% of the patients (132/187). There was no significant difference in virological and histological response between Tenovofir, Telbivudine, and Peg Interferon (p=0.213 and p=0.105). Viral load<log 6 IU/ml was significantly associated with virological response (VR) in every group (p <0.001).

Conclusions:
Peg-INF and NA therapy showed good virological and histological response with no significant difference between each group. Low viral load at baseline was a significant factor in achieving virological response in each group.

H-40

Sequential Therapy with Tenofovir Alafenamide (TAF) in Patients with Chronic Hepatitis B (CHB): An Interim Analysis of an Ongoing Multinational Prospective Study

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Objectives:
Efficacy and safety data for sequential treatment of TAF after nucleos(t)ide analogue are limited.

Materials and Methods:
This is a prospective trial of adult CHB patients from Japan, Korea, Taiwan, and the US who switched to TAF after any nucleos(t)ide analogue. Primary outcomes were complete viral suppression (CVS, HBV DNA<20 IU/mL) and biochemical response (BR, ALT<35/25 U/L men/women). Written informed consent was obtained from all patients.

Results:
270 eligible patients (mean age 58.1±10.6, 58.1% male, 99.6% Asian, and 11.5% cirrhotic) were enrolled. 73.7% were switched from ETV monotherapy, 23% from TDF/ADV-based therapy (7.8%: combination therapy), and 3.3% from other nucleosides. BMD T-score and Z-score at baseline were similar between the prior ETV (-1.1±1.5 and 0.01±1.3) and prior TDF/ADV groups (-1.1±1.5 and -0.07±1.1). In prior ETV patients, CVS increased from 93.5% at switch to 96.8% at 12-months, but there was no change in ALT normalization rates (87.9%, 93.0%). In prior TDF/ADV patients, all already achieved viral suppression at switch and remained so at 12-months, while ALT normalization rate increased from 74.2% to 84.2%. In multivariable generalized estimating equation analysis, significant factors associated with changes in HBV DNA, ALT, and eGFR were baseline HBV DNA/eAg, baseline ALT, and age, respectively. There have been seven serious adverse events (none TAF related or resulted in discontinuation) and nine withDr.awals (4-change of care location, 3-nausea, and 2-body/abdominal pain).

Conclusions:
Switching from ETV or TDF/ADV-based therapy to TAF appeared safe and effective with continued viral suppression.

H-41

Sodium-glucose co-transporter 2 inhibitors reduce hepatocellular carcinoma incidence in diabetic patients with chronic hepatitis B

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Objectives:
Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are a novel class of anti-diabetic Dr.ugs that lower the blood glucose level by inhibiting the renal glucose reabsorption. We aimed to evaluate the effect of SGLT2i on the risk of hepatocellular carcinoma (HCC) in diabetic patients with chronic hepatitis B (CHB).

Materials and Methods:
This is a retrospective territory-wide cohort study. Entecavir (ETV)/Tenofovir (TDF)-treated diabetic patients with CHB were included. Patients used SGLT2i for more than 90 days were classified as SGLT2i users and those never use SGLT2i were defined as non-SGLT2i users. The primary endpoint was the cumulative incidence of HCC.

Results:
Among 6,852 ETV/TDF-treated diabetic patients with CHB, 419 (6.1%) patients were SGLT2i users and 6,433 (93.9%) patients were non-SGLT2i users. The corresponding number of patients developed HCC were 10 (2.4%) and 435 (6.8%) during the median follow-up of 23 and 30 months. The risk of HCC was marginally significantly lower in SGLT2i users by univariate analysis (subdistribution hazard ratio = 0.528; P = 0.074) compared with non-SGLT2i users and the correlation disappeared in multivariable analysis (adjusted subdistribution hazard ratio = 0.703; P = 0.324). Patients' clinical characteristics were comparable after propensity score weighting. Use of SGLT2i was not correlated with HCC incidence by Fine-Gray subdistribution hazard regression (weighted subdistribution hazard ratio = 0.488; P = 0.75).

Conclusions:
Use of SGLT2i is correlated with a lower risk of HCC in ETV/TDF treated diabetic patients with CHB. A larger study or a randomized control trial is warranted.

H-42

Switching from entecavir to tenofovir alafenamide for chronic hepatitis B patients with low-level viremia

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Background & Aims:
Patients receiving entecavir (ETV) treatment sometime showed a suboptimal virologic response with low-level viremia (LLV), which is associated with progression of liver fibrosis and high risk of hepatocellular carcinoma. We aimed to evaluate the effectiveness and safety of switching from ETV to tenofovir alafenamide fumarate (TAF) in ETV-treated patients with LLV.

Methods:
In this prospective study, ETV-treated patients with LLV, presented to our hospital from December 2018 to October 2019, were enrolled. Switching to TAF or continuing ETV was given. The primary effectiveness endpoint was complete virologic response (CVR) at 24 weeks, and the safety endpoint was the first occurrence of any clinical adverse event during the treatment.

Results:
Totally, 211 patients were recruited and propensity score matching (PSM) generated 75 patients in either TAF or ETV group. After PSM, baseline characteristics were balanced in two group. After 24-week treatment, the CVR and ALT normalization in TAF group were 62.7% and 47.6%, which were higher than 9.3% and 10.5% in ETV group (OR 16.4, 95% CI 6.6–40.0, P<0.001), respectively. Subgroup analysis showed that switching to TAF achieved favours CVR regardless of the status of sex, age, CHB family history, HBV DNA, HBeAg and liver cirrhosis. Whereas, alcohol consumption and diabetes mellitus might compromise the CVR of switching to TAF. Both therapies were well tolerated and had satisfying renal safety.

Conclusions:
For ETV-treated patients with LLV, switching to TAF is safe enough and superior compared with continuing ETV monotherapy regarding the virologic and biochemical benefits.

H-43

Switching to Tenofovir Alafenamide (TAF) from Entecavir in Chinese Chronic Hepatitis B (CHB) Patients

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Objectives:
To analyze the efficacy and safety of TAF in CHB patients previously treated with entecavir (ETV).

Methods:
This cohort study included 38 consecutive CHB patients who switched to TAF after previous treatment with ETV for over 96 weeks. Virological/laboratory response, LSM, CAP value and eGFR were evaluated for 24 weeks after switchover. According to HBV DNA level at switchover, they were divided into MVR (HBV DNA <20 IU/ml) group and LLV (HBV DNA 20-2000 IU/ml) group, and quantitative changes of HBsAg between two groups were compared.

Results:
Of 38 patients switched to TAF, 24 patients with MVR and 14 patients with LLV after 96 weeks ETV treatment. 17 patients switched to TAF for virological response, 9 cases for improve eGFR, and 12 cases for HBsAg decline. Compared with the baseline, both of ALT (<50 U/L) and AST (<40 U/L) normalization rate were well maintained at 94.74%, from 92.11% to 94.74%, repectively. HBV DNA suppression rate were significantly increased from 55.26% to 92.11% (P<0.05).Overall HBsAg declined significantly from 3.23 ± 0.74 log IU/ml to 3.09 ± 0.77 log IU/ml (P <0.05), meanwhile no significant difference in decline of HBsAg between MVR group and LLV group (P>0.05). There was no statistical difference in LSM, CAP value and eGFR after switchover (P> 0.05).

Conclusions:
CHB patients switched to TAF from long term ETV treatment maintained a high biochemical recovery rate, achieved significant improvement in virological response and decline in their HBsAg compared with the baseline of switchover, and demonstrated comparable safety Prof.iles.

H-45

Evolution of full-length hepatitis B virus quasispecies in HBeAg-negative patients during spontaneous viral reactivation and remission

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Objectives:
The viral evolutionary pattern in hepatitis B reactivation is unclear. This study aims to evaluate viral quasispecies evolutionary patterns before, during, and after HBeAg-negative reactivation.

Materials and Methods:
Three genotype B HBeAg-negative patients recovered from HBV reactivation were included. Full-length HBV DNA was amplified from 3 time-point sera per patient (before reactivation, during reactivation, and recovery), followed by cloning and sequencing. Sequences were aligned using Lasergene SeqMan Pro. Phylogenetic trees of the HBV genome were constructed using BEAST 2 under the general time-reversible model, using the Bayesian skyline plot as a coalescent prior. Mutations in the four open reading frames and enhancer (Enh) / promoter regions were analysed.

Results:
Phylogenetic tree analysis showed that the viral sequences from different time-point formed the distinct clusters within the tree. Premature stop codon in the preS1 gene was observed in 73% sequences at the recovery time-point. 72% of sequences at the recovery time-point had a deletion of the pre-S2 start codon. Other mutations in the HBV protein, P5T, Y38H, P/A50H, L60V, L84A, A177K in the core region, Q85K, K190E, P225L, N470D, I615L, S678R, R841K in the polymerase region, L45F in the preS1 region, and G44E in the S region were found in all patients during recovery. Several mutations are found in the regulatory regions in all patients during recovery.

Conclusions:
HBV evolves during reactivation in HBeAg-negative HBV patients. The nucleotide variability in the open reading frames and regulatory regions may play an important role in the progression of chronic HBV infection.

H-47

The incidence of hepatocellular carcinoma in patients with hepatitis B cirrhosis during long-term antiviral therapy: A real world cohort study

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Objectives:
In the era of antiviral therapy, the incidence and risk factors of hepatocellular carcinoma(HCC) in patients with hepatitis B cirrhosis in different clinical stages need to be further clarified.

Methods:
This is a retrospective-prospective cohort study between June 2014 to June 2020. The enrolled hepatitis B cirrhotic patients received TDF or ETV monotherapy for more than 12 months from June 2014 to December 2018 at outpatient or inpatient department. The average follow-up time is 2 years The endpoint of follow-up:(1) occurrence of hepatocellular carcinoma, (2)death or liver transplantation.

Results:
A total of 9601 hepatitis B cirrhotic patients were included, male/female 6593/3008, 47.57±13.13 years old. Of them, compensated(CC) and decompensated cirrhotic(DCC) patients were 2844 and 6757, respectively. Total 445 (4.6%: 445/9601) of enrolled patients were development to HCC during follow-up. Of them, 334 (4.9%: 334/6757) in DCC and 111 (3.9%: 111/2844) in CC patients respectively.
The 6-year cumulative incidence of HCC were singifcantly difference between DCC (60.07%) and CC (43.70%) .
Interesting,the 2,3,4,5,6-year cumulative incidence of HCC in ETV vs TDF treatment cirrhotic patients were4.35% vs 1.85%, 7.35% vs 3.82%, 11.62% vs 7.65% and 19.98% vs15.66%,55.99% vs56.52%.

Conclusions:
Whether it is CC or DCC patients, ETV or TDF antiviral treatment can significantly reduce the incidence of HCC. Moreover, the incidence of HCC in CC patients was significantly lower than that in DCC. Compared with ETV, TDF seems to reduce the incidence of HCC in patients with cirrhosis more significantly.

Key words: Hepatitis B cirrhosis; Hepatocellular carcinoma; Compensated; Decompensated; Antiviral therapy

H-49

Mother To Child Hepatitis B Virus Transmission: Analysis Of Toll-Like Receptor 2 (TLR2) Expression, HBsAg, HBeAg, ANTI-HBs, ANTI-HBc, And Hepatitis Virus DNA Identification

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Objectives:
To analyze the correlation of TLR2 protein, HBsAg, HBeAg, Anti-HBs, Anti-HBc and Hepatitis virus identification in women with hepatitis B virus infection, in order to gain the understanding of hepatitis B viral transmission from mother to child.

Materials and Methods:
We performed enzyme-linked immunoadsorbent assay of HBsAg titer, HBeAg, Anti-HBs, Anti-HBc to 59 HBsAg positive pregnant women, and identified DNA hepatitis virus using nested PCR in their cord blood during delivery. Detection of virus DNA in cord blood indicates intrauterine exposure to Hepatitis B virus. The expression of TLR2 protein in placenta was performed using immunohistochemistry stain.

Results:
Intrauterine exposure to Hepatitis B virus occurred in 69.5% of all pregnant women with HBsAg positive. The placental TLR2 expression was significantly associated with maternal Anti-HBc status (p= 0.027). However, the TLR2 expression has no statically significant correlation with HBsAg (p=0,400), HBeAg (p=0,506) and Anti-HBs (p=0,358). Statistic analysis results also showed that placental TLR2 expression did not indicate an association with Hepatitis B virus DNA identified in cord blood (p=0.402 OR 1.371 95%CI 0.432–4.344).

Conclusions:
TLR2 as Pattern Recognition Receptors (PRRs) induces the immune system and increases antibody products (Anti-HBc), it could be used to gain knowledge of the pathogenesis of Hepatitis B viral transmission form mother to child.

H-50

Comparison of Fibrosis Regression of Entecavir Alone or Combined with Pegylated Interferon Alpha2a in Patients with Chronic Hepatitis B

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Objectives:
Antiviral treatment with necleos(t)ide analogues contributes to histological improvement and virologic response in chronic hepatitis B (CHB) patients. However, whether adding pegylated interferon alpha2a (Peg-IFN-α-2a) can help additional clinical benefit, partically on fibrosis regression was still unknown.

Materials and Methods:
CHB patients with pre-treatment biopsy-proven Ishak fibrosis score 2, 3 or 4 were randomly assigned to entecavir (ETV) alone or ETV plus Peg-IFN-α-2a (Peg-IFN-α-2a add-on) group (1:2 ratio). Post-treatment liver biopsy was performed at week 78. Fibrosis regression was defined as decrease in Ishak fibrosis score by ≥ 1 stage or predominantly regressive categorized by P-I-R score. Serum HBV DNA levels were assessed at baseline and every 26 weeks, while HBsAg and HBeAg were evaluated at baseline and every 52 weeks.

Results:
A total of 218 treatment-naive CHB patients were randomly assigned to ETV alone or Peg-IFN-α-2a add-on group. Totals of 115 patients (ETV alone: Peg-IFN-α-2a add-on, 47:108) were included in statistical analysis. Fibrosis regression rates were 68% (32/47) in the ETV alone and 56% (60/108) in Peg-IFN-α-2a add-on group (P = 0.144). Both groups showed a similar trend of virological suppression during the process of 104-week's antiviral therapy (P = 0.132). HBeAg or HBsAg loss or seroconversion rates in the ETV alone group were lower than Peg-IFN-α-2a add-on group though without statistical significance.

Conclusions:
Peg-IFN-α-2a add-on therapy did not yield additional fibrosis regression and virologic response than ETV alone therapy.

H-51

Characteristics Of Hcc Patients With 'HBsAg-negative And Hbcrag-positive' Prof.ile Undergoing Tace

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Background:
Elevation of hepatitis B virus core-related antigen (HBcrAg) has been shown to be associated with hepatocellular carcinoma (HCC) development in patients with chronic hepatitis B (CHB). However, the prevalence and clinical characteristics of HCC patients with HBsAg-negative but HBcrAg-positive have not been well defined.

Methods:
A total of 196 Thai patients with HCC treated with transarterial chemoembolization (TACE) were included. The etiologies of underlying liver diseases were CHB (n=132), chronic hepatitis C (CHC, n=36) and non-B, non-C (NBNC, HBsAg/anti-HBc/anti-HCV-negative, n=28). HBsAg quantification and HBcrAg levels at baseline prior to TACE were determined by chemiluminescence enzyme immunoassay.

Results:
Serum HBsAg and HBcrAg levels were positive in 132 (67.3%) and 164 (83.7%), respectively. Among those with HBsAg negativity (64 patients), HBcrAg levels were detected in 32 (50%). Among the CHC and NBNC groups, the positivity of HBcrAg was 11 (30.6%) and 21 (75.0%), respectively. HBcrAg levels were positively correlated with HBsAg ($r=0.681$, $P<0.001$) and HBV DNA ($r=0.551$, $P<0.001$. There was no difference in baseline clinical characteristics and overall survival between the HBsAg-positive group and HBsAg-negative/HBcrAg-positive group. Among the NBNC group, patients with HBcrAg positivity tended to have a shorter overall survival than those without detectable HBcrAg (11.5 vs 23.0 months, $P=0.088$).

Conclusions:
The prevalence of 'HBsAg-negative/HBcrAg-positive' was high among Thai patients with HCC. This serological Prof.ile might represent 'occult hepatitis B infection' and could had an impact on overall survival of patients undergoing TACE.

H-52

Single Nucleotide Polymorphisms of TRAIL Receptor 1 are Linked to the Risk of Hepatitis B Virus-Related Hepatocellular Carcinoma

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Background:
Single nucleotide polymorphisms (SNPs) of tumor necrosis factor-related apoptosis inducing ligand receptor 1 (TRAIL-R1) have been involved in the etiology of various cancers. However, data of their associations with the risk of hepatocellular carcinoma (HCC) development in patients with chronic hepatitis B virus (HBV) infection are limited.

Methods:
A total of 684 Thai individuals were enrolled including 222 patients with HBV-related HCC, 369 HBV without HCC and 93 healthy controls. SNPs rs20575 and rs20576 of TRAIL-R1 were performed by TaqMan genotyping method.

Results:
Participants in all groups were predominantly male. The mean age of patients with HCC was significantly higher than the other two groups. The distribution of rs20575 GG, GC and CC genotypes in the HCC group was 4 (1.8%), 34 (15.3%) and 184 (82.9%), respectively, while the corresponding genotypes in the non-HCC group and healthy controls were 0 (0%), 39 (10.6%), 330 (89.4%) and 0 (0%), 10 (10.8%), 83 (89.2%), respectively. There was significantly different in frequencies of rs20575 genotypes between the HCC and the other two groups (p=0.007). Among patients with HCC, a correlation of rs20575 with HCC risk was observed when compared with the non-HCC group under recessive and allelic models (OR=0.57, 95% CI=0.35-0.93, p=0.023 and OR=0.53, 95% CI=0.34-0.84, p=0.007, respectively). However, no association was found between rs20576 and risk of HCC in this cohort.

Conclusions:
These results indicate that TRAIL-R1 rs20575 but not rs20576 might be linked to the risk of HCC development in Thai patients with chronic HBV infection.

H-53

Serum Hbcrag Levels Are Correlated With Intrahepatic Replication Activity In Patients With Hbeag-positive Chronic Hepatitis B

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Background:
Covalently closed circular DNA (cccDNA) is the template for hepatitis B virus (HBV) replication via pre-genomic RNA (pgRNA) transcription. This study aimed at determining the correlation between serum hepatitis B core-related antigen (HBcrAg), a novel serum marker of HBV, and replication activity (pgRNA/cccDNA) in patients with chronic hepatitis B (CHB).

Methods:
This study included 32 and 36 patients with HBeAg-positive and HBeAg-negative CHB, respectively. Liver biopsies were analyzed for intrahepatic cccDNA and pgRNA by real-time PCR. Serum HBcrAg level was measured by automated chemiluminescent immunoassay.

Results:
The HBeAg-positive group had significantly higher levels of serum and intrahepatic viral markers than the HBeAg-negative group; HBcrAg (8.0±1.2 vs. 4.0±1.4 log10 U/ml, P<0.001), cccDNA (1.6±1.0 vs. 0.3±1.0 log10 copies/cEq, P<0.001) and pgRNA (4.4±1.1 vs. 1.4±1.2 log10 copies/cEq, P<0.001). In the HBeAg-positive group, log10 HBcrAg had positive correlation with log10 cccDNA (r=0.568, P=0.001), and log10 pgRNA (r=0.404, P=0.024). In the HBeAg-negative group, log10 HBcrAg tended to have weak correlation with log10 cccDNA (r=0.300, P=0.076) and log10 pgRNA (r=0.284, P=0.093), but did not reach significant difference. Additionally, serum log10 HBcrAg had positive correlation with replication activity in the HBeAg-positive group (r=0.375, P=0.038), but not in the HBeAg-negative group (r=0.163, P=0.342).

Conclusions:
The diverse levels of serum and intrahepatic markers reflected the differences in viral activity of the two groups. Positive correlation between serum HBcrAg and replication activity was found only in the HBeAg-positive group. Thus, serum HBcrAg could be a better surrogate marker of replication activity in HBeAg-positive CHB compared with HBeAg-negative CHB.

H-54

Serum Sulfatase-2 As A Novel Diagnostic And Prognostic Marker Of HBV-related Hepatocellular Carcinoma

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Background and Aims:
Recently, upregulated expression of sulfatase-2 (SULF-2), an extracellular enzyme promoting tumor proliferation, has been reported in liver tissues of hepatocellular carcinoma (HCC). The study was aimed at assessing the diagnostic and prognostic role of serum SULF-2 in patients with hepatitis B virus (HBV)-related HCC.

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 an independent prognostic factor in patients with HCC.

Conclusions:
These data suggest that SULF-2 might play important roles in promoting HCC progression. Our findings also indicate that serum SULF-2 could serve as a diagnostic and prognostic marker for HBV-related HCC.

H-55

Characterization of Serum HBV RNA Quantification in the Phases of Chronic Hepatitis B Infection

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Background and Aims:
This study was aimed at evaluating the correlation between serum hepatitis B virus (HBV) RNA quantification and other viral markers in patients with chronic HBV infection.

Methods:
Serum HBV markers of 434 treatment-naïve patients were analyzed. Patients were classified into 4 groups: phase 1; HBeAg-positive chronic infection (N=51), phase 2; HBeAg-positive chronic hepatitis (N=99), phase 3; HBeAg-negative chronic infection (N=159) and phase 4; HBeAg-negative chronic hepatitis (N=125). HBV RNA was quantified by a Dr.oplet digital PCR amplification.

Result: Levels of HBV DNA, HBV RNA and HBsAg were lowest in phase 3 and highest in phase 1. The mean HBV RNA in the respective 4 phases were 6.7±0.7, 5.1±1.8, 1.8±0.1 and 2.6±1.1 (log10 copies/ml). HBV RNA were positively correlated with HBV DNA in phase 1 (r=0.715, P=0.001), phase 2 (r=0.598, P<0.001) and phase 4 (r=0.793, P<0.001) but not in phase 3 (r=0.017, P=0.847). The correlations between HBV RNA and HBsAg were found only in phase 1 (r=0.790, P<0.001) and phase 2 (r=0.480, P<0.001). Among patients undergoing liver biopsy, HBV RNA had a good correlation with intrahepatic covalently closed circular DNA (cccDNA) in phase 2 (n=21, r=0.494, P=0.023) and in phase 4 (n=68, r=0.343, P=0.004). However, HBsAg levels correlated with cccDNA only in phase 2 (r=0.440, P<0.046) but not in phase 4 (r=0.067, P=0. 589).

Conclusions:
Serum HBV RNA levels varied among different phases of chronic HBV infection. Our findings suggest that serum HBV RNA quantification represents a surrogate marker reflecting cccDNA and is useful for disease monitoring.

H-56

ALT flare predicts hepatocellular carcinoma among antiviral treated patients with chronic hepatitis B: a cross-country cohort study

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Objectives:
Evidences regarding the interpretation of a flare of ALT level in Chronic hepatitis B (CHB) patients under NAs treatment for hepatocellular carcinoma (HCC) risk management remain inconstant. Hence, we aim to investigate the association between ALT flare and HCC progression.

Materials and Methods:
The study population included all CHB patients under NAs treatment and with once normalized ALT level. Data was extracted from the hospital medical records system at the Ruijin Hospital, China and Optum PanTher EHR database in US. ALT flare was defined as a flare level higher than 128 IU/L (2x local ULN) in China and 5x AASLD ULN in US. The highest ALT level during treatment were further categorized into ≤25, 25-40, 41-64, 65-80, 81-128, and >128 IU/L to explore the dose-dependent relationship between ALT level and HCC risk. The association between ALT flare and HCC occurrence were analyzed by Cox proportional hazards models and logistic regression model. The optimal cut-off point was determined by Youden index from ROC.

Results:
8,152 in Ruijin and 4,893 in US were included in the study. ALT flare was significantly associated with increased risks of HCC (HR 2.55, 95%CI 1.45-4.50) in China and in US (HR 7.62, 95%CI 4.85-11.98). A positive dose-dependent correlation (OR: 1.5-8.8) between the peak ALT level and HCC was identified in both cohorts. Optimal cut-off point of ALT is 30 in China and 45 in US.

Conclusions:
ALT flare is a strong signal calling for monitoring for HCC risk management in CHB patients under treatment.

H-57

Effect of Glycyrrhizin on fibrosis regression in chronic hepatitis B patients treated with Entecavir

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Objectives:
To compare the rate of fibrosis regression in chronic hepatitis B (CHB) patients treated with Entecavir alone vs in combination with glycyrrhizin.

Materials and Methods:
This perspective study included 296 liver fibrosis CHB patients. 148 patients were administrated with entecavir monotherapy or entecavir adding glycyrrhizin therapy, respectively. The value of liver stiffness was measured by FibroScan every 12 weeks. The regression of liver fibrosis is defined as a reduction of > 1 stage by liver stiffness at the end of the study.

Results:
At the baseline, there was no significant difference between the value of LS (15.6 Kpa vs. 14.7 Kpa) in two groups. After the treatment, the value of LS in combination therapy group decreased more Dr.amatically than momotherapy from the baseline (8.4 Kpa vs. 10.7 Kpa, P < 0.001). There were 81 (59%) and 71 (48%) patients diagnosed advanced fibrosis (F3 or F4) in two groups (P = 0.066). After the treatment, there were only 26 (19%) and 55 (38%) advanced fibrosis patients respectively. The patients in combination group had more fibrosis regression than in the monotherapy group (P < 0.0001). A multivariate logistic regression showed that the combination therapy was the regression of the most significant factor for the prediction of cirrhosis (OR: 3.8763, P < 0.001).

Conclusions:
Entacavir adding glycyrrhizin therapy is the efficient method to improve the liver fibrosis regression caused by HBV.

H-61

The Chinese herbal TiaoGanBuXuJieDu formula inhibits HBV replication and HBV-related hepatoma cell proliferation

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Objectives:
The Chinese herbal TiaoGanBuXuJieDu formula (TGBXJD) has been proven effective for the treatment of Hepatitis B virus (HBV) infection alongside with nucleoside analogues (NAs) in preliminary trial. Here we aimed to explore the functions of TGBXJD on HBV replication and HBV-related hepatoma cell proliferation.

Materials and Methods:
The hepatoma cells were maintained in DMEM supplemented with 10% fetal bovine serum. Placebo and TGBXJD granule were dissolved in dimethyl sulfoxide and added to the cell culture with 500 μg/mL final concentration. After treatment, the cell viability was detected by CCK-8 kit, the levels of hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), and HBV DNA in the cell culture supernatant were detected by the quantitative determination kits. The hepatitis B virus X (HBx) gene expression in the cell was examined by qRT-PCR.

Results:
The CCK-8 results showed that the TGBXJD could suppress proliferation of HBV replicating cells, including HepAD38 and HepG2.2.15, but it had no comparable inhibitory effect on none-HBV replicating hepatoma cells, including HepG2, Huh7 and SK-Hep1. After treatments, the levels of HBsAg, HBeAg and HBV DNA were downregulated significantly in TGBXJD group compared to placebo. Moreover, the mRNA level of HBx was lower expressed in TGBXJD group in both HepAD38 and HepG2.2.15 cells.

Conclusions:
TGBXJD exerted potent anti-HBV effect at the cell level. The inhibitory effect of TGBXJD on HBV-related hepatoma cell proliferation may achieved by downregulating HBx expression. The current study provided a basis for further clinical applications.

H-64

ALG-020572, a next generation antisense oligonucleotide (ASO) with bridged nucleic acid chemistry, has a significantly improved preclinical Prof.ile

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Objectives:
To develop a potentially best-in-class HBV ASO for the treatment of chronic hepatitis B.

Materials and Methods:
ALG-020572 was Prof.iled in the HepG2.2.15 cell line and AAV-HBV mouse model for in vitro and in vivo activity as a single agent or in combination with other anti-HBV compounds.

Results:
We developed ALG-020572, a 17-mer ASO based on Aligos' proprietary ASO platform technology containing 3rd generation bridged nucleic acids in the wing, novel nucleobases in the gap region and proprietary GalNAc4 for targeted hepatocyte delivery. ALG-020572 demonstrated significant reductions in hepatotoxicity from an all-LNA parent while maintaining in vivo activity as measured by ALT and HBsAg levels, respectively, in the serum of the AAV-HBV mouse model.
ALG-020572 targets the small HBsAg region and demonstrates a high degree of homology across >8000 HBV clinical isolates across genotypes A-J. In HepG2.2.15, the unconjugated form of ALG-020572, ALG-020579, exhibited an EC50 of 15 nM in reducing HBsAg. ALG-020572 demonstrated additivity to synergy in vitro when combined with ALG-010133 (STOPS™), ALG-020576 (ASO targeting HBx) and ALG-125097 (siRNA targeting HBx).
In the AAV-HBV mouse model, ALG-020572 (6x10mg/kg) reduced serum HBsAg by 1.2 log10 IU/mL without an increase in serum ALT. ALG-020572 also demonstrated additivity to synergy in vivo in reducing HBsAg levels when combined with ALG-125097 or ALG-020576 respectively. When combined with entecavir or an ALG-000184 analog (HBV capsid assembly modulator), ALG-020572 demonstrated additivity in reducing serum HBV DNA.

Conclusions:
ALG-020572 has a significantly improved preclinical Prof.ile and could be developed into a best-in-class HBV ASO.

H-67

Distribution of hepatitis B virus genotypes and subtypes in the general population of Kazakhstan

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Background:
Genotypes and subtypes of HBV have distinct geographical distribution, and are important in both clinical manifestation of infection and response to antiviral therapy. Strategy of antiviral therapy of CHB by PegINF depends on genotype of HBV (EASL2017)

The Aim:
To study the prevalence of genotypes and subtypes of HBV in Kazakhstan

Methods:
Blood samples of patients were examined for the determination of genotypes and subtypes of HBV by the PCR. Isolation of HBV DNA was performed using the GeneJETViral DNA. Purification Kit, ThermoScientific, PCR was performed using specific primers. Purified PCR products were sequenced in two directions, using a forward and reverse primer

Results:
324 patients CHB of 10 regions of Kazakhstan were examined, including 41,7% men, 53,8% women. The average age was 44.6±14,0 years. Only 4 patient (1,2 %) were HbeAg-positive. 19 patients had a viral load of less than 2000 IU. The 53.8% of patients had stage of fibrosis F0 (Metavir), 11.3% F1, 7% F2, 9.1% F3, 18.8% F4

In 91.3% of cases genotype D occurs. Only in 7.7% of cases were identified genotype A and 1.0% genotype C.
In the study of subtypes C1 was determined in the 1,0%, A2 in 7.7% of cases. Patients have D1 suptype in 61.5%, D2 in 10.6% and D3 in 9.6% . The combination D1D2D3 was found in 1.0%, subtypes D1, D2, D1, D3 in 2,9%. In 0.31% was found of D1, D3, D4, D6 combination. The prevalence of D1 subtype in the different regions of Kazakhstan ranges from 50 to 86%, D2 0-26%, D3 0.7-26.7%, A2 0-11.8%. C1 suptype was found only in Nur-Sultan and Atyrau

Conclusions:
In Kazakhstan the causes of CHB are genotypes A, C, D of HBV. HBV genotype D, subtype D1 is the most predominant variant in Kazakhstan and is distributed throughout in all regions.

H-68

Correlations between non-invasive biomarkers and fibrosis scores in chronic hepatitis B patients treated with tenofovir disoproxil fumarate and tenofovir alafenamide in Phase 3 clinical trials

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Objectives:
Noninvasive biomarker tests (NITs) such as APRI and FIB-4 are means for assessing fibrosis or cirrhosis in the clinical setting. We explored correlations between APRI and FIB-4 with fibrosis scores in HBV patients enrolled in TDF and TAF Phase 3 studies.

Materials and Methods:
Included were pooled data for HBeAg+ and HBeAg- CHB patients participating in TDF registration studies GS-US-174-0102 and GS-US-174-0103 (Studies 102/103) and the 2 TAF pivotal studies GS-US-320-0108 and GS-US-320-0110 (Studies 108/110). For studies 102/103, cirrhosis was defined as an Ishak score ≥5, while for studies 108/110, a FibroTest® score ≥0.75 was used. Correlations were performed for APRI and FIB-4 values at the following time points: studies 102/103: baseline (BL), Wk 48, Wk 240; studies 108/110: BL, and Wks 48, 96, and 144.

Results:
At BL and each posttreatment time point in all studies, cirrhosis patients had significantly higher values for both APRI and FIB-4 than non-cirrhosis patients ($p<0.001$). At BL, FIB-4 showed a higher AUC (95% CI) than APRI (studies 102/103: 0.75 [0.70, 0.79] vs 0.65 [0.60, 0.70]; studies 108/110: 0.88 [0.86, 0.91] vs 0.82 [0.78, 0.86]). In general, changes in APRI and FIB-4 from BL at Wk 240 (studies 102/103) and at Wks 48, 96, and 144 (studies 108/110) were positively correlated with changes in fibrosis scores.

Conclusions:
Using data derived from 4 Phase 3 studies with TDF and TAF, use of NITs (APRI and FIB-4) correlated reasonably well with fibrosis staging by liver biopsy or FibroTest, particularly for those with or without cirrhosis.

H-69

Impact of pre-treatment plasma HBV DNA levels on the rate of ALT normalization during antiviral therapy with TAF or TDF for CHB

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Objectives:
Early normalization of serum ALT levels is associated with improved clinical outcomes in chronic Hepatitis B (CHB) patients. We evaluated the impact of baseline (BL) HBV DNA levels on ALT normalization rates in a cohort of CHB patients treated with tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF).

Materials and Methods:
Two ongoing Ph3 studies (GS-US-320-0108, GS-US-320-0110) were included (N=1632; TAF 1093, TDF 539 patients). Randomized (2:1) to TAF or TDF, treated for up to 144 weeks in a double-blind fashion, followed by open-label TAF through Week 384. Normal ALT was defined by 2018 AASLD criteria. ALT normalization, viral suppression, and pre-treatment HBV DNA levels were assessed. Predictors for time to ALT normalization were also evaluated.

Results:
At BL, the TAF and TDF groups were well matched. Median (IQR) ALT and HBV DNA were 82 U/L (55-131) and 7.3 log10IU/mL (5.6-8.2), respectively. At Weeks 48 and 96, similar rates of viral suppression were observed for TAF vs TDF (77% vs 79% and 87% vs 88%, respectively). Overall, BL HBV DNA levels did not impact rates of ALT normalization with TAF treatment, whereas with TDF, a parabolic pattern was seen (higher rates at HBV DNA ≥7 to <8 and <5 log10IU/mL). Other factors associated with a reduced rate of ALT normalization were history of fatty liver (both treatments), increased prothrombin time (TDF), and HBeAg-positive status and diabetes (TAF).

Conclusions:
Pre-treatment HBV DNA levels impacted rates of ALT normalization in those treated with TDF; this effect was not observed with TAF.

H-70

Coadministration without or with food on the 96-week efficacy and safety of tenofovir alafenamide in virally suppressed chronic HBV patients switched from tenofovir disoproxil fumarate

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Objectives:
TAF has shown noninferior efficacy to TDF with superior bone and renal safety in a virally suppressed switch population of CHB patients taking TDF long-term. Unlike the registrational trials, switch study patients were permitted to take their study Dr.ug without or with food. This sub-analysis evaluates the impact of TAF once daily with/without food.

Materials and Methods:
In Phase 3 Study 4018 (NCT02979613), CHB patients virally-suppressed on TDF were randomized (2:1) to switch to TAF or remain on TDF for 48 weeks, after which patients received open-label TAF for an additional 48 weeks. Efficacy and safety were assessed over 96 weeks for patients taking study Dr.ug without vs with food

Results:
Of 488 patients randomized and treated, 162 (33%) continued taking study Dr.ug without food (n=81 each for the TAF-TAF and TDF-TAF groups). Antiviral efficacy was maintained at Week 96, in those taking study Dr.ug without vs with food. Adverse events (grade 3 or 4 and SARs) were generally comparable for those taking Dr.ug without vs with food. In patients who took TAF without food for 96 weeks (TAF-TAF) or for 48 weeks (TDF-TAF), improvements in eGFRCG and in hip and spine BMD were observed.

Conclusions:
In CHB patients taking TAF without food for up to 96 weeks, antiviral efficacy was maintained, renal and bone parameters improved, and safety and tolerability were comparable to those receiving TAF treatment with food. These results lend support for the administration of TAF without regard to food.

H-71

Phase 3 Study Comparing Switching from TDF to TAF with Continued TDF Treatment in Virologically-suppressed Patients with CHB: Final Week 96 Efficacy and Safety Results

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Objectives:
We demonstrated at Week 48 that switching from TDF to TAF in virally suppressed CHB patients on long-term TDF has shown noninferior efficacy, with superior bone/renal safety. Here we report the final, efficacy and safety results from this study at Week 96.

Materials and Methods:
Virally suppressed CHB patients were randomized (1:1) to TAF 25mg QD or TDF 300mg QD, each with matching placebo, and treated for 48 weeks in a double-blind (DB) fashion. At Week 48, all patients received open-label (OL) TAF 25 mg once daily for an additional 48 weeks. Changes in bone (BMD), renal function [eGFRCG], viral suppression, and serological and biochemical responses were assessed in all patients.

Results:
Of 488 (TAF 243, TDF 245) patients, 472 completed 48 weeks of DB treatment, and 465 completed study treatment through Week 96. Baseline patient characteristics were similar between groups. Virologic suppression was similarly maintained at Week 96 in patients switched to TAF treatment at BL vs those switched to TAF after 48 weeks of DB TDF treatment; ALT normalization increased in both groups at Week 96; Similar increases in spine BMD were seen while increases in hip BMD were smaller. In the TDF group, eGFRCG decreased at Wk48 (-2.7mL/min); improved after switching to TAF at Wk96 (-0.39mL/min).

Conclusions:
In CHB patients on long-term TDF treatment, viral suppression was maintained, ALT normalization increased, and bone and renal safety parameters were improved at Wk96.

H-72

Safety and Efficacy of 24 Weeks Treatment with Oral TLR8 Agonist, Selgantolimod, in Viremic Adult Patients with Chronic Hepatitis B: A Phase 2 Study

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Objectives:
Selgantolimod (SLGN) is an oral, selective, small molecule agonist of TLR8. Here we present safety and efficacy of SLGN after 24 weeks of treatment in viremic CHB patients.

Materials and Methods:
In double-blind, Ph2 study, viremic CHB (HBeAg-positive and -negative) patients randomized 2:2:1 to SLGN 3mg, 1.5mg, and PBO once weekly for 24 weeks with TAF. AE's were monitored. Primary endpoint was ≥ 1 log10 IU/mL decline in HBsAg. Secondary/exploratory endpoints assessed HBsAg, HBV DNA <20 IU/mL, and changes in IL-12p40 and IL-1RA.

Results:
67 patients; Asian (98%), male (58%) with a median age of 47 years, HBsAg level of 4.1 log10 IU/mL, and HBV DNA level of 7.5 log10 IU/mL. Dose-proportional increases in cytokines were observed 4 h post-dose on Day 1 for 3mg, 1.5mg, and PBO: median IL-12p40 of 5.4, 3.3, 1.0 pg/mL, respectively, with similar changes observed for IL-1RA. No tachyphylaxis observed. Grade ≥ 3 AE's in 0%, 0%, and 7.7% of patients treated with 3.0 mg, 1.5 mg, and placebo, respectively. Primary endpoint was not met. However, 3 SLGN-treated patients achieved HBsAg decline ≥ 0.5 log10 IU/mL. The proportion of patients with HBV DNA <20 IU/mL were similar between SLGN 3mg, 1.5mg, and PBO (37.5% vs 32.1% vs 33.3%) at Week 24. Higher baseline ALT and IFN-gamma levels were associated with HBsAg decline ≥ 0.3 log10 IU/mL.

Conclusions:
Oral SLGN up to 3mg once weekly for 24 weeks is safe and well-tolerated. SLGN can induce HBsAg decline in some patients. Week 48 studies are ongoing.

H-73

Safety and Efficacy of Switching to Tenofovir Alafenamide in Virally Suppressed Chronic Hepatitis B Patients with Hepatic Impairment: Week 48 Results from Phase 2 Study

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Objectives:
Chronic Hepatitis B (CHB) patients with impaired hepatic function who switch to TAF maintain viral suppression with stable or improved bone/renal safety at Week 24. Here we evaluated the efficacy and safety 48 weeks after switching to Tenofovir Alafenamide (TAF).

Materials and Methods:
In this phase 2 study (NCT03180619), all patients were switched to TAF 25 mg QD and were to be treated for 96 weeks. Safety assessments including changes in bone (hip/spine BMD), eGFRCG, viral suppression, and biochemical responses were assessed at Week 48.

Results:
90% of 31 patients completed 48 weeks of treatment. At baseline, 74% were ≥50 y, 68% male, 81% Asian, 90% were HBeAg-negative, with median fibrotest (FT) score 0.81, median CTP and MELD scores of 6 and 10, respectively, median eGFRCG 98 mL/min, and 19% had osteoporosis at spine. Prior use of TDF and entecavir was reported by 68% and 45%, respectively. By missing equals failure analysis, all patients had HBV DNA <20 IU/mL, 81% had normal ALT and CTP, MELD scores were stable. After switching to TAF in this population with liver impairment, CTP, MELD, and FT scores were unchanged while bone and renal parameters were stable. Few Grade 3 or 4 AEs (4 patients); no serious AEs related to study Dr.ug, and 1 patient discontinued, unrelated to TAF.

Conclusions:
CHB patients with hepatic impairment who were switched to TAF from TDF or other OAV showed high rates of viral suppression, normal ALT and bone and renal safety were stable at Week 48.

H-75

AB-729, a GalNAc-siRNA, results in robust reductions of HBV DNA and HBsAg in subjects with chronic hepatitis B infection

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Objectives:
AB-729 is a GalNAc-conjugated RNA interference therapeutic in development for the treatment of chronic hepatitis B (CHB). Preliminary results following single dose (SD) administration of AB-729 in HBV DNA+ subjects and repeat dose administration in virologically-suppressed CHB subjects are reported.

Materials and Methods:
AB-729-001 is an on-going study examining AB-729 in healthy (Part 1) and CHB subjects (Parts 2/3). In Part 2 Cohort D, 6 CHB subjects with HBV DNA >1,000 IU/mL not taking nucelos(t)ide analogues received AB-729 90mg SD. In Part 3, virologically-suppressed CHB subjects received AB-729 60mg every 4 weeks (Q4w, Cohort E) or Q8w (Cohort F).

Results:
One Cohort D subject was excluded as predose Day 1 results revealed a spontaneous HBV flare. There were no serious adverse events (AEs), discontinuations due to AEs, Grade 3 or 4 AEs or lab abnormalities. 22 TEAEs (9 related) were observed in 11/19 subjects; 91% were mild.

In Cohort D, 90mg SD (N=5) resulted in Week 12 mean (SE) HBsAg and HBV DNA declines of -1.02 (0.13) and -1.53 (0.24) log10 IU/mL. Week 16 mean HBsAg decline was similar between Cohort E (N=7) and F (N=6): -1.44 (0.18) and -1.37 (0.08) log10 IU/mL (p=0.7). AB-729 60mgQ4w resulted in continuous mean HBsAg decline at Week 24 [-1.84 (0.16) log10 IU/mL]. Dosing continues in both cohorts.

Conclusions:
AB-729 90mg SD reduces both HBV DNA and HBsAg, demonstrating rapid target engagement. Similar HBsAg declines between AB-729 60mg Q4w and Q8w provide further support that AB-729 may be dosed less frequently than monthly.

H-76

Characterization of Serologic Responses Following ALT Flares in >3000 CHB Patients Pooled from 5 Clinical Trials

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Objectives:
ALT flares in CHB treated patients have been associated with improvements in viral parameters. Here, we pooled data from phase 3 studies evaluating tenofovir-based regimens to determine the associations of ALT flares with treatment outcomes.

Materials and Methods:
Clinical data from 5 studies were evaluated for the presence of ALT flares on treatment, defined as ALT >5x ULN and >2x Baseline (Low Flares) or ALT >10x ULN and >2x Baseline (High Flares). Endpoints of HBsAg loss, HBeAg loss, and HBsAg decline of >=1log10 were evaluated at 12, 24, or 48 weeks after the flare.

Results:
3013 patients; 70% Asian, and 67% male. Overall, 58% were HBeAg positive at baseline and 8%, 22%, 41%, and 27% had Genotype A, B, C, and D infection, respectively. Low Flares were observed in 297 subjects; High Flares in 141 subjects. HBeAg and HBsAg loss was observed in 634 and 93 subjects, respectively, during the treatment. Serological events were significantly higher in the flare group (HBsAg loss 12%, 34/295; HBeAg loss 51%, 112/219; HBsAg decline 50%, 149/296) and similar for patients experiencing low and high flares; however, most patients with serologic outcomes did not have detectable ALT flares (HBsAg loss 2%, 57/2714; HBeAg loss 35%, 522/1514; HBsAg decline 23%, 611/2717). Timing of flare did not impact outcomes.

Conclusions:
HBeAg loss, HBsAg decline and loss occurred with or without on-treatment ALT flares. Relative to those not experiencing a flare, patients with an ALT flare were more likely to achieve positive serologic outcomes, including HBsAg loss.

H-78

Role of serum M2BPGi levels in predicting persistence of advanced fibrosis in chronic hepatitis B virus infection

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Background:
Mac-2-binding protein glycosylation isomer (M2BPGi) is a serum marker for liver fibrosis for various liver diseases including chronic hepatitis B (CHB). We aimed to evaluate its role in predicting persistence of advanced fibrosis (F3/F4) in CHB patients.

Methods:
CHB patients with F3/F4 who were treated with nucleos(t)ide analogues (NAs) for ≥3 years with normal alanine aminotransferase and undetectable serum HBV DNA were prospectively recruited. Paired assessment with transient elastography (TE) and M2BPGi measurements were performed and repeated at 3 years. F3/F4 was defined by liver stiffness (LS) ≥9 kPa.

Results:
A total of 143 patients (M:F= 101:42; median age 58.7 years) were recruited and completed paired assessment. The baseline median LS and M2BPGi values were 12 (IQR: 10.5-18.2) kPa and 0.99 cut-off-index (IQR: 0.75-1.74) (COI), respectively, with 96% concordance for diagnosing F3/F4. Multivariate analysis showed that baseline M2BPGi (OR 2.128, 95% CI 1.037-4.366) and presence of central obesity (OR 4.648, 95% CI 1.742-12.402) were significantly associated with persistent F3/F4 at 3 years. Baseline M2BPGi ≥1.265 COI has 50.6% sensitivity and 79.4% specificity for predicting persistent F3/F4 at 3 years (AUROC: 0.695). Combining both the presence of central obesity and baseline M2BPGi ≥1.265 COI, 95.7% patients had persistent F3/F4. Five patients developed HCC during follow-up and were associated with bigger median relative percentage increment of serum M2BPGi compared to patients without HCC (46% vs 6.2%, P=0.038).

Conclusions:
Among CHB patients with F3/F4 diagnosed by TE, high serum M2BPGi was associated with persistent F3/F4 after 3 years of ongoing antiviral therapy.

Hepatitis C

I-01

A Real-World Study of Treatment of Sofosbuvir/Velpatasvir on Chronic hepatitis C in Guangdong Province of China

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Objectives:
To evaluate the efficacy and safety of Sofosbuvir/Velpatasvir (SOF/VEL) on patients of chronic hepatitis C (CHC).

Methods:
48 CHC patients were analyzed retrospectively, who took SOF/VEL 12 weeks and followed-up 12 weeks. Genotype 3 patients with liver cirrhosis added ribavirin (1000-1200mg per day). Sustained virological response (SVR), safety and Dr.ug-Dr.ug interactions (DDI) were observed.

Results:
Of the 48 patients, 24 patients(50%) are HCV genotype 6a, 14 (29.2%) genotype 3a, 5 (10.4%) genotype 1b,4 (8.3%) genotype 3b and 1 (2.1%) genotype 2a. Among 8 patients with liver cirrhosis (16.7%), 4 cases are genotype 6a, 2 genotype 3a, and 2 genotype 1b. HCVRNA undetectable rate was 39.6% (19/48), 72.9% (35/48), 93.8% (45/48), 100.0% (48/48) and 100.0% (48/48) respectively at 1 ,2,4,8 and 12 weeks therapy, SVR12 was 95.8% (46/48). 2 cirrhosis cases of genotype 6a relapsed with HCVRNA detectable at 4 weeks therapy. Alanine aminotransferase and aspartate aminotransferase normalization rate was 97.9% (47/48)and 95.8% (46/48) at 12 weeks therapy, and 93.8% (45/48) and 95.8 %(46/48) after 12 weeks Dr.ug withDr.awal. At baseline, 2 patients with mild renal impairment completed treatment without dosage adjustment, estimated glomerular filtration rate (eGFR) of 1 patient decreased at 8,12 weeks , it returned normal without dosage adjustment after 12 weeks Dr.ug withDr.awal. Among the 48 patients, 16 cases had complication, 10 cases had combined medications, no DDI occurred during their treatments.

Conclusions:
CHC patients who took SOF/VEL treatment could have very high SVR12 and biochemical response, the therapy is also safe.

I-03

Comparison of the pharmacokinetic parameters of ASC18 tablets (ravidasvir and sofosbuvir fixed dose combination) with reference tablets (ravidasvir, sofosbuvir) for hepatitis treatment

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Objectives:
The objective of this study was to compare the pharmacokinetic parameters of ASC18 tablets (RDV and SOF fixed dose combination) with reference tablets (RDV, SOF) in healthy subjects after single and multiple oral dosing

Materials and Methods:
This was a single-center, randomized, open-label, two-treatment, two-period and crossover study. In each cycle, subjects received a single dose of ASC18 or RDV/SOF, and serial plasma samples were collected over 72 hours after the dose. On Day 4, subjects received multiple doses of ASC18 or RDV/SOF for 10 days, and serial plasma samples were collected over 96 hours after the last dose. There was a washout period of 14 days between the two cycles.

Results:
A total of 20 healthy subjects were enrolled in this study including 13 males and 7 females. In both single and multiple dose groups, the mean Tmax for RDV, SOF and GS-331007 (major metabolite of SOF) was 1.50-1.75 h, 0.50 h and 3.00 h after ASC18 administration and 1.75 h, 0.63-0.75 h and 2.75-3.00 h after RDV/SOF administration, respectively. The pharmacokinetic parameters such as Cmax or Cmax, ss, AUC0-t or AUC 0-Ţ, AUC0-∞, t1/2, R1ac and R2ac after administration of ASC18 were similar to those after administration of RDV/SOF ($P>0.05$). There were no serious adverse events observed after administration of ASC18 or RDV/SOF.

Conclusions:
The results demonstrated that similar pharmacokinetic parameters were observed after administration of ASC18 or RDV/SOF in healthy subjects and all regimes were well tolerated.

I-04

DAAs and NAFLD are associated with increased incidence of Hepatocellular carcinoma in patients with chronic HCV infection after sustained virologic response: a prospective multi-center study

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Background and aim:
The incidence of hepatocellular carcinoma (HCC) decreased significantly in chronic hepatitis C (CHC) patients with sustained virologic response (SVR). We studied our cohort of CHC patients to identify risk factors associated with HCC development after SVR.

Methods:
CHC patients with SVR from Fifth Medical Center of Chinese PLA General Hospital and Humanity and Health Medical Group, Hong Kong, China were followed up at 12-24 weekly intervals with surveillance for HCC by ultrasonography and alpha-fetoprotein(AFP). Multivariate Cox proportional hazards regression analysis was used to explore factors associated with post-SVR occurrence of HCC.

Results:
Between October 2015 and May 2017, SVR was observed in 519 of 533 (97.4%) and 817 of 1202 (68.0%) patients after DAAs and PR therapy respectively (P<0.001). After a mean post -SVR follow-up of 44.8 months, occurrence of HCC was significantly lower in patients treated with PR (3.3%) versus DAAs therapy (6.0%, P=0.024). By adjusted Cox analysis, DAAs therapy [HR 1.7, 95%CI(1.0-3.0)], older age (≥55 years) [HR 2.4, 95% CI (1.3-4.3)], NAFLD [HR 2.4, 95%CI (1.3-4.2), higher AFP level (≥20 ng/ml) [HR 3.4, 95%CI (2.0-5.8)], higher liver stiffness measurement (≥14.6 kPa) [HR 4.2, 95%CI (2.3-7.6)], diabetes mellitus [HR 4.2, 95%CI (2.4-7.4)] at treatment baseline were associated with increased risk of HCC. HCC patients in the DAAs group had a higher prevalence of NAFLD when compared with HCC subjects in PR group, 62% (18/29) vs 28% (7/25), P=0.026.

Conclusions:
DAAs therapy and NAFLD are associated with increased incidence of HCC in CHC patients after SVR.

I-06

Dynamic fibrosis features in HCV post-treatment liver biopsies and its interpretation

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Objectives:
Complex hepatic fibrosis patterns comprising progressive and regressive features are often observed, particularly in post-intervention samples. These dynamic fibrosis features are not specifically/adequately documented with conventional staging systems. The objective is to examine the heterogeneity of fibrosis features in pre- and post-treatment liver samples and its impact on fibrosis regression evaluation.

Materials and Methods:
Paired pre- and post-treatment liver biopsies from 58 HCV patients were staged (Ishak system) by independent and blinded pathologists. Fibrosis features, such as total collagen area and number of collagen intersections (#intersection), were measured in portal and septal compartments by qFibrosis.

Results:
For biopsies showing stages F5/6, the treated cases revealed significantly less total collagen area (48%) and #intersections (51%) across all compartments as compared to the non-treated biopsies. This indicates significant fibrosis reduction, such as septal thinning, in the treated cases despite being accorded F5/6 by conventional staging definitions. For the F0/1/2 cohort, more total collagen area (65%) and #intersection (68%) were observed in the treated cases, which could suggest residual fibrosis from more advanced fibrosis stages with breaking-up of septa.

Conclusions:
The paired HCV biopsies provide quantitative evidence for heterogeneity of fibrosis features which are the mainstay of histological scoring systems. There is a need to evaluate the finer aspects of regression. We propose an integrated semiquantitative scoring and quantitative qFibrosis approach for enhanced staging of fibrosis regression.

I-08

Effectiveness and safety of sofosbuvir/velpatasvir ± ribavirin in the treatment of Chinese adults with chronic HCV infection

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Objectives:
To investigate the effectiveness and safety of sofosbuvir/velpatasvir(SOF/VEL) ± ribavirin (RBV)in the treatment of hepatitis C virus (HCV) in China.

Methods:
From July 2018 to February 2020, 96 Chinese adults with HCV were treated with SOF/VEL ± RBV for 12 weeks. The laboratoryexamination were detected at baseline, 4 weeks of treatment, end of treatment and 12 weeks of follow-up. The adverse events and laboratory abnormalities were recorded.

Results:
93 (96.9%) patients achieved sustained virological response (SVR12), and 3 patients(3.1%) relapsed. Among the three patients, L80K,F28L and L31M mutant of two patients were detected.The proportion of rapid virological responses was 91.7%, and 100% achieved virological response by the end of treatment. In patients with decompensated cirrhosis, the mean baseline CP score was 7.4 ± 1.0, and the mean MELD score was 11.4 ± 1.7. Among them, 12 patients(100%) after treatment with SOF/VEL+ RBV achieved SVR12, and only 3 patients (60%) after 12 weeks of SOF/VEL achieved SVR12 .There was no significant difference of creatinine between baseline and 12 weeks after treatment. The incidence of adverse events was 5/79 (6.3%) in patients with chronic hepatitis C and compensated cirrhosis, and 6/17 (35.3%) in patients with decompensated cirrhosis. The most common adverse events were elevated bilirubin, fatigue and anemia. There was no serious adverse event, death or discontinuation of treatment caused by adverse events.

Conclusions:
Patients with chronic hepatitis C, compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma received sofosbuvir and velpatasvir combined with or without ribavirin showed higher SVR12, good tolerance and safety.

I-09

Molecular Epidemiology And Evidence Of Patient-to-patient Transmission Of Hepatitis C Virus Within Hemodialysis Units

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Background:
Patients with end-stage renal disease undergoing long-term dialysis 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 possibility of viral transmission, within several dialysis centers in Thailand.

Methods:
A cross-sectional study was performed among 3,305 patients at 15 dialysis centers. Patients with positive anti-HCV antibodies were assessed for HCV viremia using HCV RNA and HCV core antigen (HCVcAg). Nucleotide sequences of core and NS5B regions were analyzed for HCV genotype by phylogenetic analysis.

Results:
Among 140 (4.2%) patients with anti-HCV antibodies positive, HCV RNA was detected in 66/104 (63.5%) individuals. Compared to HCV RNA, HCVcAg testing displayed high sensitivity (92.4%), specificity (100%) and accuracy (95.2%) in determining HCV viremia. Patients with HCV infection had a significantly longer dialysis vintage compared with those without infection. The predominant HCV genotypes in this study were 1a, 1b, 3a, 3b and 6 (6f and 6n). Based on phylogenetic analysis, 3 separate clusters of HCV genotypes 3a, 6f and 6n isolates involving 7 patients with high sequence homology were identified, providing strong evidence of patient-to-patient transmission of HCV within HD facilities.

Conclusions:
The prevalence and genotype distribution of HCV in Thai patients undergoing dialysis differed to those of the general population. Patient-to-patient transmission of HCV sporadically occurred within dialysis units, indicating insufficient infection controls. Thus, improved preventive control measures and increased access to antiviral treatment eradication are essential for micro-elimination of HCV from dialysis centers.

I-10

Retreatment of Hepatitis C Failed a NS5A-containing DAAs Regimen

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Approximately 5-10% of patients treated with DAAs containing NS5A inhibitors cannot achieve a sustained virological response. Its treatment strategy is still challenging. We report three cases of failed treatment of DAAs containing NS5A inhibitors, including people with decompensated liver cirrhosis, who received SVR after 12 or 24 weeks of treatment with Sofosbuvir/Velpatasvir + ribavirin.

Case 1, male, 27 , chronic hepatitis C, genotype 1b, took oral dalatavir + azurevir for 24 weeks. The recurrence occurred 10 days after the Dr.ug was discontinued, and four mutations of S122G, L31V, Y93H and C316N were found. Eight months later, he took oral Sofosbuvir/Velpatasvir 1 tablet/d + ribavirin 900mg/d for 12 weeks, SVR24 was obtained.

Case two, male, 71, chronic hepatitis C, genetype 1b, primary liver cancer, had failed PEG-interferon + ribavirin treatment. In 2017, he took oral dalatavir 60mg/d + azurevir 100mg/time, twice a day. After 8 weeks of treatment, he had a virological breakthrough and the Dr.ugs were stopped. In November 2019, he started taking Sofosbuvir/ Velpatasvir + ribavirin for 12 weeks and obtained SVR24.

Case three, male, 60 , hepatitis C cirrhosis, decompensation stage, ascites, CTP C, GT 1b, self-administered sofosbuvir 400mg/d + dalatavir 60mg/d for 24 weeks, HCVRNA was positive again after 12 weeks of Dr.ug withDr.awal. In 2018, he was treated with Sofosbuvir/ Velpatasvir + ribavirin for 24 weeks, and obtained SVR24.

I-11

Scaling up in-hospital HCV care cascade in a medical center in Taiwan

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Objectives:
Obstacles exist in facilitating the hepatitis C virus (HCV) care cascade. To increase timely and accurate diagnosis, disease awareness and accessibility, an in-hospital HCV reflex testing followed by automatic appointment and late call-back strategy (R.N.A. model) was applied. The current study aimed to compare the uptake of HCV treatment for patients treated with the strategy compared to those without.

Materials and Methods:
One hunDr.ed and twenty-five anti-HCV seropositive patients who adopted the R.N.A. model in 2020 and another 1396 controls in 2019 were enrolled for comparing the gap from accurate HCV RNA diagnosis to final treatment allocation.

Results:
The HCV RNA testing rate was significantly higher in patients receiving reflex testing than those without (100 % vs. 84.8 %, P<0.001). While patients were stratified according to the sources of outpatient department visits, a significant improvement in the HCV RNA testing rate was particularly noted in patients from non-hepatology departments (100% vs. 23.3%, P<0.001). The treatment rate in HCV RNA seropositive patients was 83% (83/100) after the adoption of the R.N.A. model, with 96.1% and 73.9% of patients from the hepatology and non-hepatology departments, respectively. Compared to subjects without R.N.A. model application, a significant improvement in the treatment rate was observed for patients from non-hepatology departments (73.9% vs. 27.8%, P=0.001). The application of the R.N.A. model significantly increased the in-hospital HCV treatment uptake from 6.4% to 73.9% for patients from non-hepatology departments (P<0.001).

Conclusions:
The care cascade increased treatment uptake and set up a model for enhancing in-hospital HCV elimination.

I-12

Successful Direct-Acting Antiviral Therapy Improves Circulating Mucosal-Associated Invariant T Cells In Patients With Chronic HCV Infection

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Objectives:
Mucosal-associated invariant T (MAIT) cells have been shown to contribute in the pathogenesis of various liver diseases, including chronic hepatitis C virus (HCV) infection. This study was aimed at investigating the frequency, phenotype, and function of circulating MAIT cells, as well as their alterations after successful direct-acting antivirals (DAAs) in HCV-infected patients with or without HIV infection.

Methods:
A total 85 patients (51 HCV-monoinfection and 34 HCV/HIV-coinfection), who received elbasvir/grazoprevir from a clinical trial and 20 healthy controls were included. MAIT cells in blood were characterized using flow cytometry at baseline and 24 weeks post-treatment.

Results:
HCV-monoinfected and HCV/HIV-coinfected patients achieved similar sustained virological response rates (SVR24, 94.1% vs. 97.1%). Circulating MAIT cells in the monoinfection and coinfection groups were presented at low frequencies in comparison with healthy controls (median, 1.1% vs. 1.1% vs. 2.4%, $P<0.001$) and exhibited features of chronic activation and impaired functional capacity. A negative correlation between circulating MAIT cell frequency and liver stiffness assessed by magnetic resonance elastography was observed. Compared with baseline, increased in circulating MAIT cells after successful DAA therapy was mainly detected in HCV-monoinfected patients compared with HCV/HIV-coinfected individuals. Moreover, MAIT cell restoration was predominantly observed among patients with significant fibrosis to cirrhosis (F2-F4).

Conclusions:
These data indicated that dysregulation of MAIT cells might play a role in the progression of chronic HCV infection. Partial restoration of MAIT cell frequency and function was observed after successful DAA therapy, particularly in HCV-monoinfected patients.

I-13

Systematic Review with Meta-analysis: Non-invasive assessment of liver fibrosis for the prediction of liver-related outcomes in chronic viral hepatitis C patients

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Objectives:
Liver fibrosis leads to liver-related event (LREs) in patients with chronic hepatitis C (CHC) infection. Although non-invasive tests (NITs) could be critical to early identify the development of liver fibrosis, prognostic role of NITs remains to be consolidated due to limited types of NITs and liver-related outcomes in previous studies. We aimed to determine the prognostic values of NITs for risk stratification in CHC patients.

Materials and Methods:
We performed a literature search until February 25th, 2020, for the selection of CHC cohort studies reporting association between liver fibrosis assessed by NITs and the development of hepatocellular carcinoma (HCC), decompensation or mortality. Pooled hazard ratios (HR) and area under the receiver operating characteristic (AUROC) for each NIT were estimated using the random effects model.

Results:
The present meta-analysis included 29 cohort studies, enrolling 69,339 CHC patients. FIB-4 index, APRI score and liver stiffness measurement (LSM) were found to have HCC predictive potential with pooled adjusted HR (95%CI) of 2.46 (1.91-3.18), 4.24 (2.15-8.38) and 8.41 (4.01-17.64) and AUROC (95%CI) of 0.81 (0.73-0.89), 0.81 (0.76-0.87) and 0.79 (0.63-0.96), respectively. The pooled unadjusted and adjusted HRs of FIB-4 score of 3.25 before HCV treatment were 4.79 (95%CI: 3.58-6.42, I2=85%) and 3.34 (95%CI: 2.28-4.89, I2=83%), respectively, for prediction of HCC development. Additionally, FIB-4 and LSM were associated with overall mortality, with pooled adjusted HRs (95%CI) of 2.07 (1.49-2.88) and 4.04 (2.40-6.80), respectively.

Conclusions:
FIB-4, APRI and LSM could potentially be used for risk stratification in CHC patients. However, their cutoff levels need validation.

I-14

The Effectiveness of DAAs Treatment in Patients with Chronic Hepatitis C: A Multicenter, Prospective, Observational, Real-world Study in East China

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Objectives:
Direct-acting antiviral agents(DAAs) in the patients with chronic hepatitis C(CHC) recommended by several international guidelines widely used in China, there is still a lack of data from the multi-center, prospective real-world study in Chinese. Thus, this study aim is to investigate the effectiveness of DAAs in the treatment of CHC in the real-world in China.

Materials and Methods:
Since March 2019, a multi-center real-world clinical study has been launched with 10 hospitals in eastern China involving. Adult CHC patients who have received approved DAAs were enrolled. Patients with DAAs treatment-experienced, hepatocellular carcinoma, survival for less than 1 year or disable to follow-up have been excluded. The laboratory parameters were detected including HCV RNA(LLOQ=15IU/L), biochemical indicators, FibroScan®/ FibroTouch®, and abdominal ultrasound, and complicated diseases, combined medication, and DAAs regimen should be recorded.

Results:
A total of 159 patients had been followed-up for 12 weeks after the end of therapy by March 31, 2020. Among the 159 patients, males 46.5%, ≥65ys 17.6%, genotypes including 1/2/3/6(GT1b 75.5%, GT2 6.3%, GT3a 5.7%, GT3b 5.0%, GT6 6.3%); cirrhosis 51.6%, interferon-used 5.0%, HBV infection 5.0%, no HIV co-infection, diabetes 8.8%. Among them, 157 cases reached SVR12, and 2 cases failed, with an SVR12 rate of 98.7%(CI95% 96.9~100%). The failure rate was higher in non-GT1b infection(5.1% vs. 0%, p=0.059). There were no significant differences with SVR12 rate between gender, advanced age(≥65ys), liver cirrhosis, interferon-experienced, HBV co-infection, diabetes mellitus, high HCV RNA load, Pan-gene regimens.

Conclusions:
In the real-world, DAAs are effective in patients with CHC in China.

I-15

The Fibrosis Characters of Hepatitis C Patients in Community.

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Objectives:
Hepatitis C virus infection induces the liver cirrhosis. We collected HCV infected patients and performed the fibroscan to evaluate liver fibrosis characters in the high HCV incidence community.

Materials and Methods:
The screening program was implemented in Chidong/Chikan from January 2019. Fibroscan was performed to the chronic virus hepatitis patients and the abnormal liver function patients extensively.

Results:
By July 2020, 903 subjects were enrolled and successfully completed the fibroscan exam. The mean age was 57 years old with 477 (52.9%) male subjects. The mean AST and ALT level were 37.1 and 43.2 IU/L. 549 subjects were Anti-HCV Ab positive. 622 (68.9%) were fibrosis F0-F1, 137 (15.2%) were F2, 56 (6.2%) were F3 and 88 (9.7%) were F4. After the univariate and multivariate analysis, AST ($P<0.001$), r-GT level ($P=0.005$) and the numbers of Anti-HCV Ab positive ($P=0.001$) were the obvious factors related to the liver fibrosis grade from fibroscan. We further analyzed the Anti-HCV Ab positive subjects, AST ($P=0.003$) and r-GT ($P<0.001$) were also the obvious factors related to the fibrosis grade. The positive HCV RNA level was also the factor to the fibrosis grade according the univariate analysis, but the HCV RNA level was not related to the fibrosis severity grade.

Conclusions:
The HCV-Viremias subjects had higher grade liver parenchyma fibrosis change. Higher fibrosis change means high mortality and high primary liver malignant change. The virus eradication is important in the HCV viremias subjects.

I-16

The Role of Hepatitis C Virus Core Antigen in the Determination of Treatment Response after Direct Acting Anti-viral Agents.

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Objectives:
Hepatitis C virus core antigen (HCVcAg) has been proven to be a reliable and cost-saving method in the diagnosis of HCV. The evidence is, however, not clear whether HCVcAg can be reliably used to monitor treatment response with direct acting anti-viral agents (DAAs). The aim of this study was to determine the correlation between HCV RNA and HCVcAg at each time point during DAA treatment including the determination of sustain virological response at 12 and 24 weeks post-treatment (SVR12 and SVR24)

Materials and Methods:
Patients with HCV genotype 1 were enrolled. Treatment-naïve patients were treated with grazoprevir and elbasvir for 12 weeks. Treatment-experienced patients were treated with the combination plus weight-based ribavirin for 16 weeks. HCV RNA and HCVcAg were measured at baseline, week4, end-of-treatment, week 12 post-treatment and week24 post-treatment. HCV RNA level <12 IU/mL and HCVcAg < 3 pg/mL were considered undetectable.

Results:
One hunDr.ed and one patients were enrolled. The rate of SVR12 was 98%. Three patients who achieved SVR12 (3.0%) relapsed at week24 post-treatment. The correlation coefficient between HCV RNA and HCVcAg at baseline, week 4, end-of-treatment, week12 post-treatment and week24 post-treatment were 0.867 ($p<0.001$), 0.475 ($p<0.001$), 0.878 ($p<0.001$), 0.996 ($p<0.001$) and 0.994 ($p<0.001$), respectively. The concordance between HCV RNA and HCVcAg was 100% at SVR12 and 99% at SVR24.

Conclusions:
HCVcAg correctly predicted SVR12 with good correlation between HCVcAg and HCV RNA. HCVcAg is a potentially lower-cost alternative to HCV RNA in the determination of treatment response with DAAs.

I-17

The Safety and Efficacy of Direct-Acting Antivirals in HCV and HCV/HIV Patients with Blood Coagulation Disorders: A Systematic Review

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Objectives:
Direct-acting antivirals (DAAs) are currently on the rise as the Dr.ug of choice in hepatitis C virus (HCV) infection because of its high sustained viral response (SVR) rate and low rate of adverse effects (AEs). SVR-12 is defined as an undetectable HCV RNA level 12 weeks after treatment and is used as an indicator of efficacy. Data on SVR-12 and the safety of DAAs in HCV and HIV-coinfected HCV (HCV/HIV) patients with blood coagulation disorders are still limited. Therefore, the aim of this systematic review is to appraise the efficacy and safety of DAAs in this specific population.

Materials and Methods:
This systematic review was conducted in accordance with the PRISMA guidelines. The literature search was done in PubMed, ProQuest, and EBSCOhost without time, setting, and language restrictions up to 20th August 2020. Title, abstracts, and full texts were assessed for eligibility. All related clinical trials and cohort studies were included. ROBINS-I was used for bias assessment of the studies.

Results:
Three non-randomized clinical trials and six retrospective studies were included out of 86 studies. SVR-12 of HCV in patients with blood coagulation disorders was high (>94%). Several studies reported slightly lower SVR-12 in HCV/HIV patients, but most were not statistically significant. All studies reported little to none bleeding-related AEs associated with DAAs both in HCV and HCV/HIV patients. Mild adverse effects such as fatigue, headache, and nausea were frequently reported.

Conclusions:
DAAs are safe and effective to be used in HCV and HCV/HIV patients with blood coagulation disorders.

I-18

Impact of Sofosbuvir-based direct-acting antivirals on renal function in chronic hepatitis C patients - a large cohort study from the nationwide HCV Registry Program (TACR)

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Objectives:
The current study aimed to adDr.ess the impact of Sofosbuvir (SOF)- vs. non-SOF-based DAAs on serial change of renal function in chronic hepatitis (CHC) patients.

Materials and Methods:
CHC patients receiving DAAs were retrieved from the Taiwan nationwide real-world HCV Registry Program (TACR). Serial eGFR levels were measured at baseline (BL), end-of-treatment (EOT), and end-of-follow-up (EOF, 3 months post EOT).

Results:
11,376 patients were enrolled. Of which, 5,740 (50.5%) patients had eGFR < 90 ml/min/1.732 (Group A), while the other 5,636 (49.5%) had eGFR >= 90 ml/min/1.732 (Group B). The Group A were significantly older, with higher proportion of co-morbidity and severe liver diseases. In Group A, the eGFR continuous significantly increased from BL to EOT and EOF (68.9±18.4, 70.0±21.5, and 70.4±21.9, respectively, BL vs. EOT, and BL vs. EOF: P<0.001). The trend was similar between patients treated with SOF-based and non-SOF-based regimens. When breaking down the patients into eGFR < 30, 30-60, 60-90 ml/min/1.732, the trend remained in both subgroups. The increased eGFR between EOF and BL was significantly higher in SOF-based than non-SOF-based subgroups in patients with eGFR < 30 ml/min/1.732(18.3±37.0 vs. 4.1±20.2, P=0.001). By contract, in Group B, the eGFR significantly decreased from BL to EOT (P<0.0001), and substantially recovered at EOF, but not to the extent of BL levels (eGFR: 113.1±22.2, 105.6±23.3 and 106.2±23.8, respectively).

Conclusions:
Both of SOF-based and non-SOF-based DAA regimens restored renal function in CHC patients with chronic kidney diseases, especially in those with significant renal function impairment.

I-19

Treatment Outcomes Of Sofosbuvir And Velpatasvir In Chronic Hepatitis C Patients Undergoing Hemodialysis.

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Background:
Hepatitis C virus infection (HCV) is highly prevalent in patients with chronic kidney disease (CKD). The advent of direct-acting antiviral agents has revolutionized the therapy of HCV, including patients with advanced chronic kidney disease.

Objectives:
To determine the treatment outcomes Of SOF And VEL in Chronic Hepatitis C Patients Undergoing Hemodialysis.

Materials and Methods:
We enrolled 78 CKD patients at department of Gastroenterology , Jinnah Postgraduate Medical Centre, Karachi, Pakistan, All patients were ≥ 16 years old diagnosed cases of CKD (stage V) on maintenance hemodialysis. Evaluation of HCV infection by polymerase chain reaction HCV RNA were performed. All patients were treated with combination pill of SOF 400 mg and Velpatasvir 100 mg once daily taken per oral for 12 weeks. All laboratory values were repeated at 12 and 24 weeks to assess the efficacy and side effects of therapy.

Results:
Twenty eight patients, 20 (70.0%) were male while 8(30.0%) were female with a mean age of 40.84±10.52 years. Baseline investigations were Creatinine 7.5±3.75, urea 125.±36.5, s.albumin 3.35±0.62, Alanine Aminotransferase (ALT) 36.20±45.10, Alkaline Phosphatase (ALP) 535.64±720.Twenty seven (95%) of patients achieved End treatment response (ETR) at 12 weeks and 25 (91%) patients achieved Sustained virological response (SVR) at 24 weeks. There was no deterioration of hepatological status in any of the patients

Conclusions:
HCV is highly prevalent in patients undergoing hemodialysis and treatment with SOF and VEL demonstrates a good response 91% patients achieved SVR at 24 weeks.

I-20

Long term follow-up of safety and efficacy of sofosbuvir-based HCV DAAs in pediatric patients

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Objectives:
While high SVR rates and favorable safety with DAAs have been reported for pediatrics, data describing long term virologic outcomes and effects on growth and development of these regimens are needed.

Materials and Methods:
The registry enrolled pediatric HCV patients treated with SOF+RBV, LDV/SOF±RBV, or SOF/VEL in clinical trials. Durability of SVR and effects on growth are assessed at visits every 6 to 12 months, starting 24 weeks post-treatment in the parent trial. Height, weight and BMI z scores were calculated using the 2000 US CDC reference charts and shifts in Tanner pubertal stage were summarized for each study visit.

Results:
As of February 2020, 441 patients were enrolled in the registry study with a median(range) follow-up of 100 (0-238) weeks. At enrolment into the registry study, median(range) age was 11 (3-17) years, 57% were female, and 82% were white; the majority of HCV genotype (GT) was GT1 (69%) followed by GT3 (19%). At the time of this analysis, all patients had maintained SVR during their follow-up in the registry study. Across the combined age categories and DAAs through 144 weeks of follow-up, mean changes in height, weight, and BMI z scores were 0 (SD 0.61, 0.52. 0.63, respectively) and there were no apparent effects on development as assessed by Tanner stage.

Conclusions:
HCV treatment with SOF, LDV/SOF and SOF/VEL resulted in durable SVR in pediatrics aged 3-17 years and did not impact growth or development through a median of 3 years and up to 5 years post-treatment.

I-21

Real-world virological efficacy and safety of ledipasvir and sofosbuvir in patients with chronic hepatitis C virus genotype 2 infection in Japan: a multicenter study

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Objectives:
The real-world virological efficacy and safety of interferon-free direct-acting antiviral (DAA) therapy with ledipasvir (LDV) plus sofosbuvir (SOF) were assessed in patients who were chronically infected with hepatitis C virus (HCV) genotype 2.

Materials and Methods:
A total of 126 patients with chronic hepatitis C due to HCV genotype 2 infection who were treated with the LDV/SOF regimen were enrolled. The sustained virological response (SVR) rate and safety were analyzed. SVR was assessed in the intention-to-treat (ITT) population as well as in the modified intention-to-treat (mITT) population, which excluded patients with non-virological failure, including those who Dr.opped out before the SVR assessment.

Results:
In the mITT population, the percentages of patients with undetectable HCV RNA at 4, 8, and 12 weeks after the start of therapy were 92.9% (95% CI, 86.5–96.9) (105/113), 99.1% (95% CI, 95.2–100.0) (112/113), and 100.0% (95% CI, 97.4–100.0) (113/113), respectively. The overall SVR12 rates of the ITT and mITT populations were 87.3% (95% confidence interval [CI], 80.2–92.6) (110/126) and 97.3% (95% CI, 92.4–99.4) (110/113), respectively. Subgroup analyses of the mITT population showed no significant differences in SVR rates according to age, sex, HCV genotype (subtype), history of interferon-based therapy, baseline FIB-4 index, or baseline estimated glomerular filtration rate. In all subpopulations, the SVR rates were more than 90%. There were no severe adverse events associated with the treatment.

Conclusions:
The LDV/SOF regimen showed high virological efficacy and acceptable safety in patients with HCV genotype 2.

I-22

Risk of end-stage renal disease among hepatitis C patients with chronic kidney disease treated with and without sofosbuvir

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Objectives:
The predominant metabolite of Sofosbuvir (SOF) is renally eliminated. Using administrative claims data, we sought to characterize the risk of end-stage renal disease (ESRD) or dialysis among patients with chronic kidney disease (CKD) and HCV treated with SOF- and non-SOF-containing direct acting antiviral (DAA) regimens.

Materials and Methods:
2,359 HCV-infected CKD patients treated with interferon (IFN) -free DAAs were identified from a US administrative claims database. Patients were observed from initiation of the most recent DAA to the first of: a claim for ESRD/dialysis, kidney transplant, discontinuation of insurance enrolment, or last date of data availability. Absolute rates per 100 person-years (PYs) were calculated at all CKD stages combined and stratified for those patients with staging identified. Adjusted hazard ratios (aHRs) estimating ESRD/dialysis risk associated with SOF- vs non-SOF-containing DAAs were calculated using Cox proportional hazards methods, after adjustment for baseline health status and treatment propensity score weighting.

Results:
Overall, the unadjusted incidence of ESRD/dialysis was 3.88 (95%CI, 3.24-4.62) per 100 PY. For the 1,976 SOF and 383 non-SOF DAAs, the unadjusted rates of ESRD/dialysis were 3.53 (95%CI: 2.89–4.28) and 7.41 (95%CI: 4.65–11.22) per 100 PY respectively. After adjustment and propensity score weighting, there was no significant difference in risk of ESRD/dialysis with vs. without SOF (aHR=0.77, 95%CI: 0.43-1.36). Similar results were observed when stratified by CKD stage.

Conclusions:
This real-world data indicate no difference in risk of ESRD or dialysis in HCV-infected CKD patients treated with SOF- vs. non-SOF-containing DAAs.

I-24

Hepatitis C Genotype 3 subtypes and Y93H mutation in single center experience in Myanmar

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The first wave DAA regimen including Sofosbuvir and Daclatasvir is the mainstay of treatment for hepatitis C patients in Myanmar. Presence of NS5A resistance-associated substitutions (RAS) (Y93H) can influence the sustained virological response (SVR) after DAA in genotype 3 patients.

Objectives:
This study was performed to determine the subtypes and proportion of Y93H in genotype 3 patients and to evaluate the SVR after Sofosbuvir and Daclatasvir .

Materials and Methods:
The study was implemented at Yangon Specialty Hospital, from November 2017 to March, 2019. This study analyzed 112 treatment-naïve non-cirrhotic hepatitis C genotype 3 patients. Y93H mutation was tested by population sequencing method at baseline and Sofosbuvir and Daclatasvir were given for 12 weeks.

Results:
Among 112 genotype 3 patients, the majority (90%) had subtype 3b while 10% had subtype 3a. Population sequencing of NS5A region was successfully done in 80 samples and Y93H mutation was not detected. Among the study population, 91.1% achieved SVR12 while 6.3% did not. There was no association between SVR and age, sex, HCV RNA level and subtypes among the study population.

Conclusions:
Higher proportion of subtype 3b was detected in genotype 3 patients and this may account for the absence of baseline Y93H mutation in this study. Overall similar potency (SVR 91.1%) of Sofosbuvir and Daclatasvir regimen for 12 weeks was observed in non-cirrhotic genotype 3 patients which was comparable to international studies. Other NS5A RAS (A30K and L31M) which are common in subtype 3b patients should be investigated further for research purposes.

I-25

The Association of PNPLA3, COX-2 and DHCR7 Polymorphisms with Advanced Liver Fibrosis in Patients with HCV Mono- Infection and HCV/HIV Co-Infection

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Background:
There is increasing evidence that host genetic variations may influence the natural history of chronic hepatitis C virus (HCV) infection. The aim of this study was to determine the association between single nucleotide polymorphisms (SNPs) of PNPLA3 (rs738409), COX-2 (rs689465) and DHCR7 (rs12785878) and advanced liver fibrosis in Thai patients.

Methods:
A total of 220 patients with HCV mono-infection, 200 patients with HCV/HIV co-infection and 200 healthy controls were enrolled. The SNPs were detected by allelic discrimination using real-time PCR with TaqMan probes. Liver stiffness measurement (LSM) was assessed by transient elastography.

Results:
The results showed that the distribution of the studied SNPs were not significantly different between the HCV mono- and co-infected groups. The frequencies AG and GG genotypes of rs689465 and GG genotype of rs12785878 were less commonly found in the HCV mono- and co-infected groups compare with healthy controls ($P<0.01$). Among patients with HCV infection, older age, HIV co-infection, GG genotype of rs738409 and GG genotype of rs689465 were independently associated with advanced liver fibrosis (LSM≥9.5 kPa) in multivariate analysis. Moreover, the percentage of patients with advanced liver fibrosis increased significantly along with the accumulated numbers of these risk genotypes.

Conclusions:
PNPLA3 (rs738409) and COX-2 (rs689465) polymorphisms were associated with advanced liver fibrosis in patients with HCV mono- and co-infection, suggesting that these variants might play an important role in progressive liver fibrosis in these patients.

I-26

Treatment outcome with DAAs in a multinational cohort of 11,099 hepatitis C (CHC) patients with genotypes 1, 2, 3, 4 and 6: A REAL-C study

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Objectives:
The Western Pacific is a large region but few studies have examined the real-world outcomes of DAAs in a multinational study with diverse HCV genotypes (GT). This REAL-C study (Real-world Evidence from the Asia Pacific Rim Liver Consortium for HCV) will characterize CHC patients treated with DAAs in routine practice.

Methods:
We analyzed 11,099 CHC patients from 51 REAL-C clinical sites from Mainland China, Hong Kong, Taiwan, Korea, Japan, and Singapore. The primary outcome was SVR12.

Results:
The cohort had mean age of 64.0, 44.8% male, 24.2% Chinese (10.0% Mainland China, 1.2% HK, 13.0% Taiwan), 7.5% Korean, 68.1% Japanese, 32.6% with cirrhosis, 9.1% HCC, and 27.0% treatment-experienced (TE: 23.2% interferon, 3.8% DAA). The largest group was GT1 (7837 [70.6%]: 642 1a, 7195 1b), then GT2 (2945 [26.5%]: 1761 2a, 1184 2b), GT3 (211: 70 3a, 126 3b, 11 others), GT6 (91), GT4 (5), and mixed (10). DAA use was also diverse: 3349 (30.2%) SOF/LDF±RBV, 2437 (22.0%) SOF+RBV, 2251 (20.3%) DCV+ASV, 1270 (11.4%) 2D/3D±RBV, 633 (5.7%) GLE/PIB, 623 (5.6%) SOF/VEL±RBV, and others. Overall SVR12 was 96.2% (10674/11099). By cirrhosis and prior treatment, SVR12 was >96% for all groups, except GT1 cirrhosis/TE (93.4%, 759/813), GT2 cirrhosis/TE (89.0%, 146/164 [144 with SOF+RBV]), GT3 cirrhosis/TE (88.9%, 8/9), and GT6 no cirrhosis/TE (93.3%, 14/15). There was no treatment-related SAE.

Conclusions:
In this diverse cohort of Asian patients with genotypes 1, 2, 3, 4 and 6, the overall cure rate was 96.2%, despite large numbers of cirrhosis, HCC, prior treatment failure, and older DAA use.

I-27

Significant amelioration of hepatitis C virus infection in a hyper-endemic area: Longitudinal evidence from the COMPACT Study in Taiwan

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Objectives:
Hepatitis C virus (HCV) infection is the leading cause of cirrhosis and hepatocellular carcinoma worldwide. Tzukuan, located in the southwestern area of Taiwan, is an HCV hyperendemic area (>30%). This study aimed to assess the changing epidemiological characteristics of HCV infection and to evaluate the long-term outcomes after the implementation of public health strategies for two decades.

Materials and Methods:
A population-based retrospective cohort study under a comprehensive care program was implemented, namely COMPACT Study, in Tzukuan since 1997.

Results:
A total of 10,714 residents participated the screening.The HCV infection prevalence rates were 21.1% (1,076/5099) in 2000-2004, 18.8% (239/1,269) in 2005-2009, 14.1% (292/2,071) in 2010-2014, and 10.3% (234/2,275) in 2015-2019 (p for trend test<0.0001). Among them, 1,614 underwent repeated tests during the follow-up period. The annual incidence rates were 0.54% in 2005-2009, 0.4% in 2010-2014, and 0.22% in 2015-2019, respectively (p=0.01). In addition to old age, lower education level was a major risk factor for HCV infection across different periods. HCV infection prevalence rate among those illiterates reached 40.9%, followed by 28.5% in those with elementary school level, and <10% in those with high school or higher levels. The major risk factor has shifted from iatrogenic exposure in 2000-2009 to household transmission after 2010.

Conclusions:
HCV infection has been decreasing and the epidemiological features are changing in the hyper-endemic area by continuing education, prevention and treatment strategies.

Hepatobiliary Neoplasia

J-02

99m-Technetium Galactosyl Human Serum Albumin Scanning to Evaluate Liver Function After Stereotactic Body Radiotherapy for Hepatocellular Carcinoma: A Case Report

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Purpose:
The primary choice among treatment options for liver malignancies is surgery. However, if surgery cannot be performed, stereotactic body radiotherapy may be effective. 99m-technetium galactosyl human serum albumin single-photon emission computed tomography imaging is useful for the assessment of liver function before surgery.

Materials and Methods:
We report the case of a 77-year-old man who had undergone stereotactic body radiotherapy for hepatocellular carcinoma of the left lobe of the liver 2 years previously. Follow-up revealed a 15-mm hepatocellular carcinoma at the edge of the right lobe of the liver. 99m-technetium galactosyl human serum albumin single-photon emission computed tomography was performed before stereotactic body radiotherapy to confirm that there was no accumulation in the left lobe and to ensure that there was good function of the right lobe.

Results:
Three months after stereotactic body radiotherapy, the tumor had responded, and decreases in galactosyl human serum albumin accumulation were observed in line with the radiation beam. Because hepatocellular carcinoma often relapses, it is important to assess the anatomic site of liver dysfunction before and after radiation.

Conclusions:
This case demonstrates that 99m-technetium galactosyl human serum albumin single-photon emission computed tomography is useful for this purpose.

J-03

ABO Blood Group Differential on the Survival in Hepatocellular Carcinoma Patient Treated with Chemoembolization

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Objectives:
Recently the correlations of ABO blood group with survival have been evaluated in several malignancies. However, the associations of ABO blood group with the prognosis of hepatocellular carcinoma remains unclear. We investigate the impact of ABO blood group and prognostic factor in HCC patients treated with transarterial chemoembolization (TACE)

Materials and Methods:
We revisited records of all HCC patients undergone TACE between January 2007-December 2019 at our hospital. The inclusion criteria were unresectable HCC patients in BCLC- A and BCLC-B stage, Child-Pugh score < 7 and treated with TACE monotherapy. Background of the patients was compared against their blood group and survival analysis was carried out using Cox's regression. With Bonferroni adjustment for multiple comparisons, $P < 0.0125$ were considered statistically significant.

Results:
Of 211 study patients, frequency of blood group O, A, B and AB were 89, 54, 56 and 12, respectively. Their respective months of median survival were 41, 20, 21, and 42. After adjustment for Up-to-7 criteria, Child-Pugh score, using O as the referent group, coefficients/SE of group A, B and AB were 0.69/0.24, 0.47/0.23, and 0.49/0.49 respectively. The significant difference in survival was found only between patients with blood group O vs A (Hazard ratio 1.99, CI = 1.09, 3.60) and not among any other pairs

Conclusions:
In our data, patients with blood group O tended to have the best survival. However, only A and not other groups had significantly shorter. Further studies on the mechanisms of these differentials are needed.

J-04

Are Vitamin D Receptor Polymorphisms Associated with a Risk of Hepatocellular Carcinoma in Hepatitis C Related Liver Cirrhosis?

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Objectives:
HCV is a major risk factor HCC, however the exact mechanism of hepatocarcinogenesis is still not fully understood. Host genetic factors have been reported to play a significant role. Experimental studies support the tumor inhibitory effect of vitamin D on HCC cells. Several single nucleotide polymorphisms (SNPs) have been depicted in vitamin D receptor (VDr.) gene. We aimed to assess whether any of these polymorphisms could be significantly associated increased risk of HCC.

Patients and Methods:
This study was conducted on 76 patients with HCV-related liver cirrhosis (48 patients had HCC on top of cirrhosis and the other 28 had liver cirrhosis only). All patients underwent full medical history, clinical examination, laboratory investigations, abdominal ultrasonography and genotyping of VDr. gene.

Results:
HCC patients had significantly higher frequency of ApaI CC genotype compared with those patients without HCC. There is no statistically significant difference between the studied groups at any TaqI genotypes, but the carriage of ApaI CC genotype had significant association with of liver disease severity in both patients groups compared with ApaI CA/AA genotypes. The carriage of ApaI CC genotype was an independent predictor for HCC in HCV-related liver cirrhosis.

Conclusions:
VDr. ApaI polymorphism is significantly associated with development of HCC, thus ApaI CC genotype could be used as an important molecular marker to predict the risk of HCC in patients with HCV-related liver cirrhosis.

J-06

Combined hepatocellular-cholangiocarcinoma and its mimickers: diagnostic pitfalls in surgical pathology

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Objectives:
To perform a clinicopathologic study on combined hepatocellular-cholangiocarcinoma (cHCC-CCA) and its potential histopathologic mimickers at a tertiary referral hospital in Thailand.

Materials and Methods:
A 5-year retrospective review was performed of pathologically diagnosed cHCC-CCAs and other primary liver cancers (PLCs), including hepatocellular carcinoma (HCC) and cholangiocarcinoma, whose pathological features could mimic those of cHCC-CCAs. The pathological features and clinical characteristics of these cases were analyzed.

Results:
A total of 4 cHCC-CCAs and 4 PLCs whose pathological features closely resemble those of cHCC-CCAs were retrieved. cHCC-CCA accounted for 1.4% of total PLCs in our archives. Histologically, all of them showed a mixed epithelioid-glandular pattern with variable immunoreactivity. The provisional diagnosis usually failed to detect either the hepatocellular or bile duct component of such a rare neoplasm. The treatment modalities include liver resection and chemotherapy. One out of four patients expired four months postoperatively. The overall prognosis was worse than that of HCC, but better than intrahepatic cholangiocarcinoma (iCCA). PLCs that could have a morphologic resemblance of cHCC-CCA include iCCA with nodular regenerative hyperplasia, iCCA with background liver cirrhosis, mucinous iCCA, and adenosquamous iCCA.

Conclusions:
Routine histopathology is crucial for the diagnosis of cHCC-CCAs. Sampling error, intratumoral heterogeneity, and diversity in histomorphology of biphenotypic PLCs could lead to misdiagnosis. Thorough pathological evaluation with imaging studies helps arrive at the correct diagnosis of such an uncommon biphasic hepatobiliary neoplasm.

J-10

Evaluation of the differential diagnosis value of PIVKA-II in patients with liver disease

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Objectives:
Elevated PIVKA-II is not only seen in patients with HCC, but also in many patients with severe liver damage. This study intends to evaluate the differential diagnosis value of PIVKA-II in patients with severe hepatic impairment.

Materials and Methods:
This is a retrospective study to include patients diagnosed with liver failure among inpatients. 272 patients whose PIVKA-II> 400mAU/mL (10ULN), received vitamin K1 treatment were included in the study. According to the discharge diagnosis, they were divided into 3groups: cholestatic liver disease group (47 patients), liver failure group (29 patients), and HCC group (196 patients).

Results:
The value of PIVKA-II in patients with HCC was mostly higher, which was significantly higher than that of liver failure group and cholestatic liver disease group, which were 13768±5639mAU/mL,10986±9754mAU/mL, 2716±1324mAU/mL, respectively. Review the changes of PIVKA-II and PTA 7 days after vitamin K1 application. The changes of PIVKA-II and PTA in the HCC group were not obvious. In the liver failure group, the PIVKA-II decreased by <50% in the patients who died within 3 months, and the PTA was slightly increased or no change. In the liver failure group, PIVKA-II in surviving patients was reduced by more than 70%, PTA increased. The cholestasis group decreased by >85%, and the PTA increased by >150%.

Conclusions:
In the early stage of patients with severe liver disease, it's difficult to distinguish if the laboratory indicators are similar to liver failure. Observing the changes of PIVKA-II and PTA can help us to make the correct diagnosis and treatment, judge the prognosis.

J-11

Development and validation of artificial intelligence to detect and diagnose liver lesions from ultrasound images

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Objectives:
To develop and validate a convolutional neural network (CNN) for localization and diagnosis of focal liver lesions (FLLs) in ultrasonography (USG) still images.

Methods:
The CNN was developed by a supervised training method using 40397 images from 3487 patients, including 20432 FLLs (hepatocellular carcinomas (HCCs), cysts, hemangiomas, focal fatty sparings, and focal fatty infiltrations). The performance of the artificial intelligence (AI) system was evaluated on internal test set of 6191 images with 845 FLLs, then externally validated using 18922 images with 1195 FLLs in 2 other hospitals.

Results:
On the internal test set, overall localization rate, diagnostic sensitivity and specificity were 87.0% (95%CI: 84.3–89.6), 83.9% (95%CI: 80.3–87.4), and 97.1% (95%CI: 96.5–97.7), respectively. The CNN also performed consistently well on external validation cohorts, with localization rate, diagnostic sensitivity and specificity of 75.0% (95%CI: 71.7–78.3), 84.9% (95%CI: 81.6–88.2), and 97.1% (95%CI: 96.5–97.6), respectively. For diagnosis of HCC, the CNN yielded sensitivity, specificity, and negative predictive value (NPV) of 73.6% (95%CI: 64.3–82.8), 97.8% (95%CI: 96.7–98.9), and 96.5% (95%CI: 95.0–97.9) on the internal test set; and 81.5% (95%CI: 74.2–88.8), 94.4% (95%CI: 92.8–96.0), and 97.4% (95%CI: 96.2–98.5) on the external validation set, respectively.

Conclusions:
CNN can reliably localize and diagnose common FLLs in USG images with excellent specificity and NPV for HCC. Further development of AI system for real-time detection and characterization of FLLs in USG is warranted.

J-13

FGF19/FGFR4 Signaling in Hepatocellular Carcinoma

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Objectives:
FGF19/FGFR4 signaling plays an important role in development and progression of hepatocellular carcinoma (HCC). In this study, we conducted clinicopathological analyses based on FGF19/FGFR4 expression in tumor tissues and serological analyses based on serum FGF19 levels.

Materials and Methods:
Immunostaining for FGF19/FGFR4 was performed in surgical specimens. Serum FGF19 levels in various stages of HCC patients was measured by ELISA. In vitro assays of HCC cells treated with multi-kinase inhibitors was also conducted.

Results:
The expression pattern of FGF19 was significantly correlated to that of FGFR4, and the concomitant expression of FGF19/FGFR4 was detected in approximately 1/3 of the cases. Clinicopathological examination demonstrated that FGF19-highFGFR4-high HCC was significantly associated with a high serum level of AFP and low differentiation pathology. Serum FGF19 levels. The serum FGF19 levels in HCC patients were significantly higher than those in chronic liver disease patients without HCC. Although serum FGF19-high patients treated with sorafenib exhibited a significantly shorter progression-free survival and overall survival than FGF19-low patients, there were no significant differences between FGF19high and FGF19-low patients treated with lenvatinib. In culture, combined use of a selective FGFR4 inhibitor with sorafenib further suppressed FGFR4/ERK signaling and synergistically inhibited HCC cell growth. ELISA demonstrated that the increase in serum FGF19 levels was observed after lenvatinib administration in approximately 80% of cases examined, but not after sorafenib administration.

Conclusions:
FGF19/FGFR4 signaling is a key target for treatment of HCC. Serum FGF19 serves as not only diagnostic marker but also predicting markers for MKI treatment effects.

J-14

Hepatocellular carcinoma emergence in Armenia:
Outcome of multiple risk factors for the period January 2019 to March 2020, Nork Clinical Hospital of Infectious Diseases

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Background:
According to the most recent estimates of GLOBOCAN, primary liver cancer (PLC) emerged as a major health threat in Armenia. We intend to provide the first detailed description of PLC risk factors and clinical presentation in Armenia.

Methods:
A series of 69 patients were diagnosed with PLC using. Demographic data, risk factors, histology, PLC work-up, symptoms and biological variables were collected at the time of diagnosis and patient survival was determined long-term.

Results:
HCC was found in the majority of cases of PLC(95.6%) while tumors appeared in patients with cirrhosis in most cases (90.3%). The sex ratio of this series was (M:F=3.9) with the mean age of patients(56. 9±11.4 years). HCV was the main risk factor (68.1% of cases) followed by heavy alcohol consumption (51.7%) followed by HBV(18.8%). Metabolic disorders were prevalent with 63.7% of the patients with obesity being the most common(BMI≥30). The median overall survival time was 10 months(IQR:6-14). Younger patients (≤57.0 years) were characterized by an even high proportion of male sex (94.1% vs 65.7% for patients over >57 years old, P<0.01), as were frequent tobacco consumption (85% vs 58.8%, P<0.05). We noticed that HBV-infected patients self-reported significantly higher rates of somatic cancers in their families (92.3% vs 58.6%, P<0.05).

Conclusions:
The current problem of HCC in Armenia seems to be due to the presence of HCV spread with metabolic disorders and to the alcohol/tobacco use disorders. Further studies are warranted to characterize viral characteristics and molecular alterations that may promote liver tumorigenesis in Armenia.

J-15

Image-guided Locoregional Therapies in the Management of HCC

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Learning Objectives:
To describe various image-guided locoregional therapies in the management of hepatocellular carcinoma

Background Information:
Locoregional therapies are the mainstay of treatment in hepatocellular carcinoma as most patients are not candidates for surgical resection or transplantation. The ablative therapies can be classified as thermal, non-thermal or chemical in nature. Thermal ablative techniques use extreme temperatures to destroy the tumor cells. These include radiofrequency ablation (RFA), microwave ablation (MWA) and cryoablation (CA). Irreversible electroporation is a non-thermal technique, uses high voltage, high intensity electric pulses of short duration to create irreversible pores in the cell membrane resulting in cell death and apoptosis. Chemical ablation uses ethanol or acetic acid to produce cellular dehyDr.ation and coagulative necrosis to destroy tumor cells. Transarterial therapies for HCC include transarterial embolization (TAE), transarterial chemoembolization (TACE), DEB-TACE (Dr.ug eluding beads TACE) and transarterial radioembolization (TARE).

Teaching points:
We outline the various ablative techniques and endovascular therapies used at our institute in the management of hepatocellular carcinoma. Detailed discussion of the procedure, indications, contraindications, and limitations of each ablative technique will be provided. We will also describe the technical success, clinical outcome and potential complications of each procedure.

Conclusions:
Locoregional therapies have pivotal role in the management of hepatocellular carcinoma, and the type of therapy is based on the stage of the disease, tumor size, location and extension. They can be used as curative or palliative therapies or as bridge to transplant, and can be used in conjunction with other treatment modalities.

J-16

Impact of liver cirrhosis in patients with intrahepatic cholangiocarcinoma receiving systemic chemotherapy: a subgroup analysis of the JCOG1113 randomized phase III trial

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Objectives:
Liver cirrhosis (LC) is a risk factor for intrahepatic cholangiocarcinoma (ICC). Whether LC affects the safety and efficacy of systemic chemotherapy remains unclear.

Materials and Methods:
Data were analyzed from JCOG1113, a randomized phase III trial identifying the non-inferiority of gemcitabine plus S-1 (GS) to gemcitabine plus cisplatin (GC) for biliary tract cancer, including ICC. Differences in the safety and efficacy of GS and GC between LC and non-LC were investigated. LC was clinically diagnosed based on CT images and clinical findings.

Results:
Among 94 patients with ICC, 10 (GC, five; GS, five; Child–Pugh score 5/6/7/10:5/3/1/1) had LC. No remarkable differences were found in the backgrounds, including Child–Pugh scores, between patients with and without LC. The frequency of all grade 3–4 adverse events (LC [n=10] vs. non-LC [n=84], 20.0% vs. 38.1%) and serious adverse events (0.0% vs. 2.1%) tended to be lower in patients with LC, whereas grade 4 neutropenia was more frequently observed with liver atrophy (Present, 23.1%; Absent, 9.9%) or blunt edge (Present, 20.0%; Absent, 9.5%). The efficacy data were not worse in LC patients. The response rates were 20.0% and 30.0%, median overall survival was 19.0 and 13.8 months (hazard ratio of LC to non-LC 0.969; 95% CI: 0.482–1.948), and median progression-free survival was 7.1 months and 5.9 months (hazard ratio 0.995; 95% CI: 0.513–1.929) in LC and non-LC patients, respectively.

Conclusions:
Clinically diagnosed LC did not affect the safety and efficacy of systemic chemotherapy for ICC in JCOG1113.

J-17

Impact of multi molecular target agent therapy in advanced hepatocellular carcinoma

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Objectives:
Systemic chemotherapy for hepatocellular carcinoma (HCC) has been remarkably developed in these days. Currently, four molecular target agents (MTA) are available for the treatment of HCC in Japan. The present study aimed to clarify the current use of MTAs and its effect on HCC.

Materials and Methods:
This multicenter, retrospective study collected and analyzed the clinical data of 877 patients who underwent MTA therapy for HCC between 2009 and 2019 at several institutes in Japan. Patients were classified into three groups according to the period of MTA treatment (period 1, 2009 to 2012; period 2, 2013 to 2016; period 3, 2017 to 2019), with each period comprising 267, 352, and 258 patients, respectively. Patient characteristics, MTA use, and prognosis were analyzed.

Results:
The median overall survival was 11.8 months for the entire cohort and 10.4, 11.3, and 15.2 months, respectively, for each period. Prognosis of patients improved over time ($p = 0.016$). As for progression free survival, the median value was 3.0 months for the entire cohort and 2.8, 2,8, and 4.8 months for each period ($p < 0.0001$). The treatment duration was also prolonged with the passage of time (2.8, 3.3, and 6.7 months, $p < 0.0001$). Multivariate analysis showed that HCV infection, Child-Pugh score, performance status, α-fetoprotein ≥ 400 ng/mL, presence of macrovascular invasion, and period 3 for initial MTA introduction were independent prognostic factors.

Conclusions:
Sequential therapy with multiple MTAs has gained popularity with the passage of time, and has been noted to improve the prognosis.

J-18

Interpretation pitfalls in immunohistochemistry of primary liver carcinoma: a retrospective analysis of liver biopsy specimens

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Objectives:
To retrospectively analyze the interpretation pitfalls in immunohistochemistry (IHC) as an adjunct in assessing primary liver carcinoma (PLC) in liver biopsy specimens at a tertiary hospital in Thailand.

Materials and Methods:
The archives of the Division of Pathology, Thammasat University Hospital, were searched from 2015 to 2020 using a search tool from the pathology software system and a combination of codewords, including PLC, hepatocellular carcinoma (HCC), and intrahepatic cholangiocarcinoma (iCCA). Histomorphology of PLCs in liver biopsy specimens and the corresponding immunophenotypes were retrospectively analyzed. Clinical data for each patient was retrieved from the medical record.

Results:
A total of 153 liver biopsy specimens were retrieved. There were 128 (83.7%) iCCA, 23 (15%) HCC, and 2 (1.3%) combined hepatocellular-cholangiocarcinoma (cHCC-CCA). Six cases (3.9%) with interpretation pitfalls in IHC were analyzed. These pitfalls included incorrect subtyping of PLCs (2 cases, 1.3%) and PLCs misdiagnosed as metastatic cancers (4 cases, 2.6%).

Conclusions:
Interpretation pitfalls in IHC of PLCs were not uncommon, accounting for 3.9% in our series. Pathologists should be familiar with the histomorphology of PLCs together with their rare variants. Appropriate use of IHC as adjuncts for evaluating PLCs and correlation with clinical details are essential for rendering the correct diagnosis of PLCs.

J-19

Massive hepatomegaly and abdominal pain – An unexpected presentation of primary choroidal melanoma

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Teaching Points:
Uveal melanoma, although a relatively uncommon form of melanoma, is the most common ocular malignancy, usually presenting with ocular symptoms, namely metamorphopsia, photopsia or visual impairment. This type of melanoma has a predominance to metastasise to the liver due to the absence of lymphatic channels to the uveal tract, with surveillance strategies currently aimed at regular liver imaging due to the risk of micrometastasis in the early stages of disease. Extra-ocular symptoms resulting in the diagnosis of uveal melanoma are a rare occurrence, however, are associated with a dismal prognosis.

Background/Outline:
We present the case of a 71-year-old female with a two-month history of abdominal pain and progressive abdominal distension who presented to a metropolitan emergency department. Biochemical assessment on admission demonstrated significant derangement in liver function tests, hyperbilirubinaemia, hyperammonaemia, and a markedly elevate lactate dehyDr.ogenase. Computed tomography demonstrated marked hepatomegaly with heterogenous change, which after ultrasound guided biopsy was confirmed as melanoma on histopathological analysis. Subsequent MRI brain demonstrated a 15 mm lesion in the right globe with retinal detachment. Further ophthalmological assessment confirmed a diagnosis of metastatic choroidal melanoma. Retinal detachment secondary to mass-effect of choroidal melanoma was diagnosed on ultrasound of the right orbit. The patient was commenced on inpatient nivolumab however died five days after cycle one of therapy secondary to progressive disease resulting in hepatic encephalopathy.

J-21

Posttreatment after Lenvatinib in Patients with Advanced Hepatocellular Carcinoma

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Objevtices:
Establishment of a second-line treatment after the failure of lenvatinib treatment is an urgent clinical issue in patients with advanced hepatocellular carcinoma (HCC). The study was aimed to explore candidate Dr.ugs that might be appropriate as second-line treatment after Lenvatinib.

Patients and Methods:
We collected data on patients with advanced HCC who received lenvatinib as the first-line agent in seven institutions in Japan between March 23, 2018 and September 31, 2019.

Results:
During the study period, 178 patients received lenvatinib as first-line systemic therapy. Seventy-one of 151 patients (47.0%) who discontinued lenvatinib converted to posttreatment. The conversion rates from lenvatinib to second-line agent and from second-line agent to third-line agent were 41.4% and 42.4%, respectively. Based on multivariate analysis, response to lenvatinib and discontinuation of lenvatinib due to radiological progression were associated with a significantly higher probability of conversion to posttreatment after lenvatinib. Of 63 patients who received second-line systemic therapy, 53 (84.2%) were administered sorafenib. PFS and response rate (RR) for sorafenib treatment were 1.8 months (95% CI, 0.6–¬3.0) and 1.8%, respectively. According to Cox regression hazard model, discontinuation of lenvatinib due to radiological progression, significantly contributed to shorter PFS. Twenty-two patients received regorafenib after discontinuation of Lenvatinib. PFS and RR for regorafenib treatment were 3.2 months (range, 1.5–4.9 months) and 13.6%, respectively.

Conclusions:
Sorafenib was not a candidate as a posttreatment agent after lenvatinib, except in patients who discontinued lenvatinib without radiological progression. Regorafenib has the potential to become an appropriate posttreatment agent after lenvatinib.

J-22

Predict Early Recurrence of Hepatocellular Carcinoma Using Multi-dimensional Artificial Intelligence Analysis of Liver Fibrosis

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OBJECTIVES

Hepatocellular carcinoma is the third most commonly diagnosed cancer in the world, and surgical resection is the commonly used curative management of early-stage disease. However, the recurrence rate is high after resection, and liver fibrosis has been thought to increase the risk of recurrence. Conventional histological staging of fibrosis is highly subjective to observer variations. To overcome this limitation, we aimed to combine a fully quantitative fibrosis assessment tool, qFibrosis (utilising second harmonic generation and two photon excitation fluorescence microscopy), with multi-dimensional artificial intelligence analysis to establish a fully-quantitative, accurate fibrotic score to predict early recurrence of hepatocellular carcinoma after curative intent resection.

MATERIALS AND METHODS

The study included 81 hepatocellular carcinoma patients receiving curative intent hepatectomy. Detailed fibrotic features of resected hepatic tissues were obtained by qFibrosis, and we used multi-dimensional artificial intelligence analysis to create a recurrence prediction model “combined index” according to the morphological collagen features of each patient’s non-tumor hepatic tissues.

RESULTS

Our results showed that “combined index” can better predict early recurrence (area under the curve = 0.917, sensitivity = 81.8%, specificity = 90.5%), compared to alpha fetoprotein level (area under the curve = 0.595, sensitivity = 68.2%, specificity = 47.6%). Using a Cox proportional hazards analysis, higher “combined index” is also a poor prognostic factor of disease-free survival and overall survival.

CONCLUSION

By integrating multi-dimensional artificial intelligence and qFibrosis, we may locate patients with a higher risk of recurrence, follow these patients more carefully, and do further management if needed.

J-24

Proton beam therapy for hepatocellular carcinoma with bile duct invasion

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Objectives:
Patients with hepatocellular carcinoma (HCC) with bile duct invasion (BDI) have a poor prognosis. However, due to the paucity of the reports, there is not yet a consensus about the management of this clinical condition. The aim of this study is to clarify the efficacy and safety of proton beam therapy (PBT) for HCC with BDI.

Materials and Methods:
Between 2009 and 2018, 15 patients with HCC with BDI underwent PBT in our institution. The median age was 71 (range, 58-90) years and the majority of patients were Child class (n=8, 53.3%) and have solitary tumor (n=11, 73.3%). Most patients had central type BDI (n=11, 73%). A plastic stent was placed for 4 patients due to bile duct obstruction and/or cholangitis. The median size of tumors was 4.0 (range, 1.5-8.0) cm. The overall survival (OS) and local control (LC) curves were constructed by Kaplan-Meier method. Toxicities were assessed by Common Terminology Criteria of Adverse Events (CTCAE) version 4.0.

Results:
The median follow-up time was 23.4 (range, 7.9-54.3) months. The 1-, 2-, and 3-year OS rates were 80.0%, 58.7% and 40.2%, respectively and the corresponding LC rates were 93.3%, 77.0%, and 61.6%, respectively. Acute grade 1-2 dermatitis (n=7, 46.7%) and Grade 2 (n=1, 6.7%) and 3 (n=1, 6.7%) cholangitis were observed. In terms of late toxicity, a grade 3 gastric hemorrhage and pleural effusion were observed, respectively. No grade 4 or worse toxicity was observed.

Conclusions:
PBT was feasible with tolerable toxicities for the treatment of HCC with BDI.

J-26

Risk factors of cholangiocarcinoma in non-endemic area of liver fluke infection

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Objectives:
Thailand has the world's highest prevalence of cholangiocarcinoma (CCA), especially in the northeastern region, where is endemic area of liver fluke Opisthorchis viverrini (OV) infection. However, other regions of Thailand still have relatively high prevalence of CCA. We aimed to determine risk factors for CCA in non-endemic areas of OV infection.

Materials and Methods:
A prospective case-control study was conducted during December 2016 – December 2017. We collected blood samples and information from CCA (case group) and non-CCA subjects (control group). CCA risk factors were determined using logistic regression analysis. OV infection was defined by the positive IgG antibody to OV antigen using ELISA.

Results:
There were 153 participants (70 cases and 83 controls), with mean age of 62.2 years. The overall OV infection rate was 45.8%, which was higher in the case than control group (57.1% vs. 36.1%, p=0.01). By univariate analysis, male, OV infection, geographic region, smoking, alcohol consumption, and chronic biliary tract diseases were significant risk factors, whereas diabetes, obesity and chronic liver diseases were not correlated with CCA. By multivariate analysis, chronic biliary tract diseases and alcohol consumption were among the strongest risk factors for CCA, with adjusted odds ratio (aOR) of 11.4 (95% confidence interval (CI): 1.2-106.1, p=0.03) and 10.0 (95% CI: 1.2-86.6, p=0.04), respectively. Smoking was another factor independently associated with CCA (aOR 3.5, 95%CI: 1.2-10.0, p=0.02).

Conclusions:
Chronic biliary tract diseases and unhealthy lifestyles, including alcohol consumption and smoking, were major risk factors for CCA in non-endemic areas of liver fluke infection.

J-32

The prevalence of palliative presentation for HCC over 10 years in a Maori, Pasifika and Asian cohort

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Objectives:
Hepatocellular cancer (HCC) is the second most common cause of cancer-related mortality worldwide. Despite improved detection, mortality remains unchanged. There are ethnic and geographic differences in HCC presentation. We aimed to determine if there was a change in palliative presentations over 10 years in a centre with a large Maori, Pasifika and Asian cohort.

Materials and Methods:
Presentations for HCC between January 2010 and December 2019 were compared over two 5-year cohorts (2010-2014 and 2015-2019) for the prevalence of palliative cases (not suitable for any treatment). Data were stratified by 4 main ethnic groups – Maori, Pasifika, Asian (including Indian) and European.

Results:
Between 2010-2019 there were 310 HCC cases (25.2% Maori, 21.9% Pasifika, 25.2% Asian and 26.2% European). Of these, 115 (37.1%) were palliative. This did not differ between 2010-2014 and 2015-2019 (59/158 (37.3%) and 56/152 (36.8) respectively, p=0.93, Chi square test). Between 2010-2104, 45.2% of Maori (n=19), 42.3% of Pasifika (n=14), 20% of Asian (n=8) and 39% of Europeans (n=15) were palliative. This was significantly higher for Maori (p=0.02) and Pasifika (p=0.04) compared to Asian. Between 2015-2019, 38.9% of Maori (n=14), 48.6% of Pasifika (n=17), 28.9% of Asian (n=11) and 30% of Europeans (n=12) were palliative, with no difference between ethnicities (p>0.05). For each ethnicity, the proportion of palliative cases did not change over time (p>0.05).

Conclusions:
One third of HCC cases have no suitable treatment options at the time of presentation, and this has not changed over 10 years. Previous ethnic-specific differences are no longer apparent.

J-34

Volatile organic compounds as potential biomarkers for diagnosis of hepatocellular carcinoma (HCC)

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Objectives:
To identify potential VOC that can be used as biomarkers for HCC diagnosis in patients with cirrhosis.

Materials and Methods:
Breath samples were collected from 61 patients with HCC and 62 patients with cirrhosis (controls). Samples were analyzed by gas chromatography/mass spectrometry (Agilent 7890B GC system, 7000D GC/MS triple quaDr.upole) in nontargeted fashion. The abundance of each identified compound by NIST database were compared between the 2 groups. Support Vector Machine (SVM) algorithm was applied to classify the samples.

Results:
Baseline characteristics including age, gender, etiology of chronic liver diseases were not different between the 2 groups. HCC patients had a higher median Child-Pugh score than cirrhotic patients (6 vs. 5, P=0.002). Proportion of individuals with Child-Pugh class A, B and C were different between HCC cases and cirrhotic controls. Of the 61 HCC patients, there were 8 (13%), 15 (25%), 15 (25%), 17 (28%) and 6 (10%) patients with BCLC stage 0, A, B, C and D, respectively. Among the top 38 identified metabolites, 2-butanone, dimethyl sulfide, 1-propanol, d-limonene, sulfide allyl methyl, isopropyl alcohol, phenol, 1,4-pentadiene and acetone were found as potential markers. Among these, a combination of 6 VOCs including 1-propanol, benzene, cyclohexane, D-limonene, phenol and sulfide allyl methyl had the best diagnostic performance for differentiating HCC from cirrhosis, with the maximum accuracy of 75.6%, sensitivity and specificity of 72.1% and 79.0%, respectively.

Conclusions:
This study demonstrates the feasibility of using exhaled VOCs as non-invasive tool for diagnosis of HCC in high-risk patients.

J-35

Comparison of Lenvatinib versus Hepatic Arterial Infusion Chemotherapy for Unresectable Hepatocellular Carcinoma.

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Background & Aims:
After REFLECT trial, lenvatinib has been approved as a first-line multikinase inhibitor in advanced hepatocellular carcinoma (HCC). Here, we performed a multicenter comparative study of lenvatinib versus hepatic arterial infusion chemotherapy (HAIC) for unresectable HCC.

Patients and Methods:
A total of 244 patients with unresectable HCC whose been treated with HAIC (n = 173) or lenvatinib (n= 71) were enrolled between November, 2012 and November, 2020. To reduce confounding, we used a propensity score-adjusted analysis regarding on several parameters.

Results:
In whole cohort, median follow up duration was 7.000 and 4.033 months for HAIC and lenvatinib group, respectively. Before propensity matching, hepatic reserve, extent of HCC and history of previous treatment were significantly different between lenvatinib and HAIC groups. Median PFS was 4.100 months for lenvatinib group and 4.833 months for HAIC group (P=0.115), and there was also no significant difference in OS with 8.567 months for lenvatinib and 10.333 months for HAIC (P=0.066). After propensity matching, there were no statistical differences in PFS between lenvatinib and HAIC groups (4.967 vs 5.400 months, P=0.108), although HAIC had superior OS compared to lenvatinib (OS 14.233 vs 7.933 months, P=0.010).

Conclusions:
Our multicenter real-world, propensity-matched data demonstrate that lenvatinib is comparable to HAIC in terms of anti-cancer efficacy in unresectable HCC

J-36

Diagnostic Performance Of PIVKA-II And AFP In Relation To Underlying Etiological Factors Of Hepatocellular Carcinoma

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Background:
Although serum protein induced by vitamin K absence-II (PIVKA-II) represents a tumor marker for hepatocellular carcinoma (HCC), limited data are available about its diagnostic performance in relation to etiological factors. The study was aimed at comparing the diagnostic role of PIVKA-II and alpha-fetoprotein (AFP) in viral- and non-viral-related HCC.

Methods:
Group A included 278 patients with viral-related HCC and group B included 72 patients with non-B, non-C-related HCC. Serum samples for measuring PIVKA-II and AFP were collected at initial diagnosis of HCC.

Results:
Group A was younger and had higher percentage of female than group B. Additionally, group A had larger tumor size and more advanced BCLC staging than group B. A weak correlation between PIVKA-II and AFP was found ($r=0.374$; $P<0.001$). PIVKA-II and AFP were correlated with large tumor sizes and advancing BCLC stage. Serum PIVKA-II levels were higher in group A than in group B (24,426 ± 58,275.6 vs. 6,579.2 ± 17,153.2, $P<0.001$). However, there was no difference between groups regarding AFP (20,350.6 ± 62,848.6 vs. 25,743.9 ± 70,727.7, $P=0.528$). Among patients with BCLC stage 0 and A, 27/61 (44.3%) in group A and 14/18 (77.8%) in group B had AFP elevation (≥20 ng/mL) ($P=0.012$), while 31/61 (50.8%) in group A and 1/18 (5.6%) in group B had elevated PIVKA-II (≥60 mAU/mL) ($P=0.001$).

Conclusions:
Serum PIVKA-II could be a better marker for diagnosis of early stage of viral-related HCC. In contrast, serum AFP had a better performance for early detecting HCC in patients with non-viral-related HCC.

J-37

Complication Rates, Overall And Recurrence-Free Survival After Surgical Resection With Curative Intent For Hepatocellular Carcinoma: A Meta-Analysis Of 110 Studies And 82,392 Patients

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Objectives:
Hepatic resection (HR) outcomes for hepatocellular carcinoma (HCC) may have improved recently and may vary by region. Using a systematic review and meta-analytic approach, we determined outcomes for adult HCC patients undergoing HR.

Methods:
Two investigators independently searched PubMed, Cochrane, and Embase databases from 1 January 2010 to 15 May 2020 for relevant studies and abstracted the data. Pooled estimates were calculated using random-effects models.

Results:
From title/abstract screening of 3918 articles, 673 were identified for full-text review, and 110 eligible studies involving 82,392 patients were analyzed. The pooled 1-, 3- and 5-year rates were 89.45% (95% CI 87.61 – 91.04; 63 studies), 69.99% (95% CI 67.10 – 72.73; 68 studies), and 56.61% (95% CI 53.24 – 59.93; 83 studies) for overall survival (OS) (Table 1), and 71.50% (95% CI 68.20 – 74.58; 51 studies), 46.34% (95% CI 43.52 – 49.19; 56 studies) and 35.55% (95% CI 32.83 – 38.38; 66 studies) for recurrence free survival (RFS). There were no significant changes in OS from studies completed before versus after 2010 (all P>0.20). The total and major complication rates were 27.60% and 9.73% (95% CI 23.35 – 32.28 and 06.34 – 14.65; 20 studies), respectively. By region, there was significant variation for OS with higher OS in some Asian regions (P<0.0001) but not RFS (P=0.071).

Conclusions:
HCC resection results in good outcomes overall, but further studies are needed to identify factors associated with higher survival in some Asian regions.

J-39

HIF-1α-induced expression of m6A reader YTHDF1 Dr.ives hypoxia-induced autophagy and malignancy of hepatocellular carcinoma by promoting ATG2A and ATG14 translation

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Objectives:
N6-methyladenosine (m6A), the most prevalent chemical modification in eukaryotic mRNA, plays a pivotal role in human tumorigenesis. Autophagy activation is one of the ways by which cancer cells survive hypoxia. However, the possible involvement of m6A modification in hypoxia-induced autophagy is unexplored in human hepatocellular carcinoma (HCC).

Materials and Methods:
The prognostic value of YTHDF1 expression was evaluated using the tissue microarray (TMA). Autophagy was detected using GFP-mRFP-LC3 immunofluorescence staining, western blotting, and transmission electron microscopy (TEM). Chromatin immunoprecipitation (ChIP), RNA MeRIP-sequencing, proteomics, RNA immunoprecipitation (RIP), and polysome Prof.iling were used to explore both upstream and downstream regions of YTHDF1 in HCC.

Results:
A significant correlation between YTHDF1 and hypoxia-induced autophagy was observed in HCC cell lines. Significant overexpression of YTHDF1 was observed in the HCC tissues associated with poor prognosis. HIF-1α regulated YTHDF1 transcription by directly binding to its promoter region under hypoxia. Multiple HCC models including HCC cells, HCC organoids, YTHDF1hep-/- mice, and nude mice were employed to confirm that YTHDF1 deficiency inhibits HCC hypoxia-induced autophagy and autophagy-related malignancy. YTHDF1 contributes to the translation of autophagy-related genes, ATG2A and ATG14, in an m6A-dependent manner, thus facilitating autophagy and autophagy-related tumorigenesis and metastasis of HCC.

Conclusions:
HIF-1α-induced YTHDF1 expression was associated with hypoxia-induced autophagy and autophagy-related HCC progression via promoting the translation of autophagy-related genes ATG2A and ATG14 in a m6A-dependent manner, suggesting that YTHDF1 is a potential prognostic biomarker and therapeutic target for patients with HCC.

J-40

Kinesin family member 15 promotes cancer stem cell phenotype and malignancy via reactive oxygen species imbalance in hepatocellular carcinoma

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Objectives:
Accumulating evidence demonstrates that the development and progression of hepatocellular carcinoma (HCC) is associated with the presence of cancer stem cells (CSCs). However, it is unclear how the stem cell features of HCC cells are maintained.

Materials and Methods :
KIF15 expression was determined by real-time PCR and western blot analyses. Functional assays were performed in HCC cells, HCC organoids and mice. Immunoprecipitation (IP)/mass spectrum (MS), co-immunoprecipitation (co-IP), immunofluorescence (IF) and immunohistochemistry (IHC) analyses were conducted to evaluate the interaction between KIF15 and Phosphoglycerate dehyDr.ogenase (PHGDH). Intracellular reactive oxygen species (ROS) levels were determined using 2',7'-dichlorofluorescin diacetate (H2DCFDA).

Results:
In present study, kinesin family member 15 (KIF15) expression was shown to be overexpressed in HCC tissues, cell lines, and CSCs. Patients with HCC with high KIF15 expression had shortened overall survival (OS) and high recurrence probability. Downregulation of KIF15 in vitro as well as in HCC organoids resulted in a significant reduction in sphere formation and expression of stemness-related genes. KIF15 downregulation in human HCC xenograft models delayed tumor initiation, growth, and metastasis. KIF15 was also demonstrated to interact with phosphoglycerate dehyDr.ogenase (PHGDH) and inhibit proteasomal degradation of PHGDH, thus promoting CSC phenotype and malignancy via PHGDH-mediated intracellular reactive oxygen species (ROS) imbalance in HCC. Moreover, AAA nuclear coregulator cancer-associated protein (ANCCA) upregulation acts as a key mediator in KIF15 expression upregulation in HCC.

Conclusions:
We found that KIF15 promotes the CSC phenotype and malignancy via PHGDH-mediated ROS imbalance in HCC. These findings highlight potential therapeutic targets for HCC.

J-41

Yttrium-90 Radioembolization Is Associated with Better Overall Survival in Patients with Hepatocellular Carcinoma Compared with Conventional Chemoembolization: A Propensity Score-Matched Study

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Objectives:
It is not clear whether radioembolization (TARE) outperforms conventional chemoembolization (TACE) as first-line treatment in patients with HCC. The aim of the present study to compare effectiveness of TARE and TACE as initial treatment for HCC.

Materials and Methods:
We retrospectively reviewed data of patients who have received TARE or TACE as the first HCC treatment at Seoul National University Hospital from March 2012 to December 2017. A propensity score matching was performed to reduce selection bias. Overall survival (OS), progression-free survival (PFS), and intrahepatic PFS were compared. This research was approved by an ethical committee.

Results:
A total of 138 patients initially treated with TARE (n=54) or TACE (n=84) was included in this study. Baseline characteristics was well balanced between the two groups. Of 138 patients, median age was 59 years and the mean follow-up period was 27.6 months. TARE showed better OS (hazard ratio [HR]=0.54, 95% confidence interval [CI]=0.31–0.92, log-rank P=0.02), better PFS (HR=0.51, 95% CI=0.36–0.97, log-rank P=0.04), and better intrahepatic PFS (HR=0.51, 95% CI=0.30–0.88, log-rank P=0.01) compared with TACE. In multivariable analyses, TARE was an independent prognostic factor for OS (adjusted HR [aHR]=0.52, 95% CI=0.30–0.90, P=0.02), PFS (aHR=0.57, 95% CI=0.35–0.94, P=0.03), and intrahepatic PFS (aHR=0.49, 95% CI=0.28–0.84, P=0.01).

Conclusions:
TARE was associated with better overall survival than TACE as the initial trans-arterial treatment in patients with HCC. A randomized clinical trial is warranted to define optimal selection criteria of TARE to maximize the therapeutic effect.

J-42

Development of hand foot skin reaction is associated with good prognosis for HCC patients treated with Sorafenib ; A prospective cohort study

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Objectives:
Sorafenib is a standard first-line systemic therapy of advanced hepatocellular carcinoma (HCC). However there are few studies that have examined prognostic factors of sorafenib therapy in prospective cohort. 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 prospectively enrolled at 13 hospitals. We analyzed various prognostic factors of sorafenib for overall survival (OS) and progression free survival (PFS) of 115 patients at 3 hospitals by univariate and multivariate analyses using Cox proportional hazards regression model.

Results:
We included 115 patients in the present analysis. The univariate analysis identified presence of HFSR and distant metastasis as potential prognostic factor for PFS. In multivariate analysis for PFS, presence of HFSR (HR 0.597, p=0.103) was not statistically significant factors of PFS. Prognostic factors for OS were analyzed in the same method. In univariate analysis, presence of HFSR and distant metastasis, serum albumin level were potential prognostic factors for OS. In multivariate analysis for OS, presence of HFSR (HR 0.341; 95% CI: 0.187-0.621, p<0.001), albumin level (HR ratio 0.362; 95% CI: 0.201-0.654, p=0.01) were significant factors of OS. The median OS duration of HFSR group was 785 days. In the no HFSR group, median OS was 199 days

Conclusions:
Developing HFSR from sorafenib therapy was associated with good OS. Developing HFSR have been suggested as valuable indicator of good sorafenib prognosis.

J-43

Thymidine kinase 1 Dr.ives the malignancy and immunosuppression by regulating the PRMT1/YAP axis in Hepatocellular carcinoma

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Objectives:
Increasing evidence indicated that thymidine kinase 1 (TK1) is associated with the tumor-progression and poor prognosis of various cancers. However, the role of TK1 in hepatocellular carcinoma (HCC) remains elusive.

Materials and Methods :
TK1 was detected by analyzing HCC samples through quantitative real-time polymerase chain reaction (qRT-PCR), western blot assays and immunohistochemistry (IHC) assays. HCC cells were stably transfected with lentiviruses using TK1 interference or overexpression plasmid, and then Cell Counting Kit-8 (CCK-8) assay, , colony formation, tube formation assay, wound healing, transwell invasion assays, mouse subcutaneous tumorigenicity assays, orthotopic tumor transplantation models and lung metastasis assays were employed to assess the potential role of TK1. Proteomics, fluorescence in situ hybridization, immunoprecipitation coupled with mass spectrometry (IP/MS), co-immunoprecipitation (co-IP) assay and ubiquitination assay and were used to evaluate the underlying mechanism of TK1.

Results:
We identified that TK1, which was overexpressed in HCC, predicted shortened overall survival and high recurrence probability. Further functional experiments revealed knockdown of TK1 could inhibit the proliferation, migration, and invasion of HCC cells both in vitro and vivo. Mechanistically, TK1 physically interacts with tripartite motif 48 (TRIM48), which leads to degradation of protein arginine methyltransferase 1 (PRMT1) through ubiquitination. Finally, our data reveal that TK1 promotes immunosuppression activities through enhancing transcription of YAP, a core protein of the Hippo signaling pathway and associated with tumor progression and immune evasion.

Conclusions:
Our findings uncovered a mechanistic role for TK1/PRMT1/YAP axis in
HCC tumor-promoting and immunosuppression characteristics, providing a potential therapeutic strategy in HCC.

J-44

The Efficacy of Lapatinib as a Safer Therapeutic Agent in Hepatocellular Carcinoma Patients: A Systematic Review

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Objectives:
This systematic review aims to identify the use of lapatinib as a potent alternative in hepatocellular carcinoma therapy.

Materials and Methods:
Systematic review was conducted with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines. The literature search was done using four databases: PubMed, ProQuest, ScienceDirect, and EBSCO with “Carcinoma, Hepatocellular”, “lapatinib”, and “therapeutics” as the main keywords with no restriction on timing of published journals. Cochrane risk of bias (RoB) tool 2.0 was utilized in the quality assessment of the included studies.

Results:
Search strategy resulted in a total of 51 studies. Two relevant full-text articles met the authors inclusion criterias. Two important outcomes were sought, that is efficacy and tolerability of lapatinib. One study observes a 5% objective response with a progression free survival (PFS) of 2.3 (95% CI: 1.7–5.6) months and a median overall survival (mOS) of 6.2 (95% CI: 5.1–∞) months. Another study shows somewhat similar results of 0% objective response with a median PFS of 1.9 (95% CI, 1.8-3.6) months and mOS of 12.6 (95% CI, 7.8-22.4) months. Adverse events of lapatinib were well-tolerated with diarrhea as the most common side effect.

Conclusions:
The importance and needs of a safer and a more tolerable therapy that Dr.ives the usage of lapatinib. Although lapatinib was well-tolerated, its efficacy rates are still questionable.

Hepatobiliary Surgery

K-02

Multiple Gallstones And Bile Duct Stones In Chronic Myelogenous Leukemia

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Objectives:
Chronic myelogenous leukemia (CML) is a hematologic malignancy with splenomegaly came as its clinical finding. A few studies showed that gallstones and jaundice can occur in CML. Hereby we reported the case of jaundice in CML which was treated successfully by endoscopic retrograde cholangiopancreatography (ERCP) and Spyglass system.

Materials and Methods:
An 83-year-old male came with a colicky pain in his right upper quaDr.ant (RUQ) abdomen, nausea, vomiting, and jaundice. There was a history of CML treated with imatinib mesylate for 10 years. Physical examination showed icteric sclera and RUQ tenderness. Laboratory tests: total bilirubin 4.78 mg/dl; conjugated bilirubin 4.47 mg/dl; AST 131 U/l; ALT 120 U/l; gamma-GT 143 U/l; alkaline phosphatase 97 U/l. Magnetic resonance cholangiopancreatography showed bile ducts dilatation with multiple stones in common bile duct with the largest stone size was > 1.4 cm. ERCP was done and laser lithotripsy of stones was performed with SpyGlass system. Stone fragmentation was achieved followed by a placement of 7 Fr double-pigtail stent. Laparoscopic cholecystectomy was then successfully performed.

Results:
Studies showed that gallstones frequency were higher in CML. This may be explained with the hemolysis seen due to splenomegaly and splenic sequestration in CML. Older age and longer duration of disease are other findings related to stone formation. SpyGlass system in this report was also used in managing large bile duct stone in elderly.

Conclusions:
CML may increase the frequency of gallstones and bile duct stones. Cholangioscopy with Spyglass platform can be helpful in large bile duct calculi.

K-04

Somatostatin prevents clinically relevant pancreatic fistula in intermediate risk patients after pancreaticoduodenectomy (SPEED): a multi-center, randomized, controlled study

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Objectives:
Post-operative pancreatic fistula (POPF) remains one of the most lethal complications after pancreaticoduodenectomy (PD). The objective is to evaluate the preventive effect of somatostatin on POPF in intermediate-risk patients.

Materials and Methods:
A multi-center, randomized, controlled study was conducted in six high-volume pancreas centers in China between June 2018 and April 2019. Patients undergoing PD with intermediate risk of POPF were enrolled. Patients were randomly assigned to somatostatin group (intravenous somatostatin of 250μg/h for 120 hours) and control group. The primary endpoint was clinically relevant POPF (according to the 2016 International Study Group on Pancreatic Fistula criteria). This trial was registered with Clinical Trial (NCT 03349424).

Results:
205 patients were enrolled. 99 in somatostatin group and 100 in control group were included for final analysis. The rate of clinically relevant POPF in somatostatin group decreased significantly (13% vs 25%, p=0.032), both in open and laparoscopic PD. But the rates of overall POPF (65% vs 69%, p=0.51) and biochemical leak (52% vs 44%, p=0.29) were not significantly different. Medical costs (¥115069 vs ¥115803, p=0.92) and other complications: biliary fistula (6% vs 6%, p=0.99), abdominal infection (19% vs 18%, p=0.83), chylous fistula (5% vs 4%, p=0.75), late postoperative hemorrhage (7% vs 12%, p=0.24) had no significant difference. However, the somatostatin group had a higher rate of delayed gastric emptying (33% vs 21%, p=0.0504).

Conclusions:
In patients with intermediate risk after PD, prophylactic use of somatostatin can reduce the clinically relevant POPF, but seems to increase the rate of delayed gastric emptying.

Hepatotoxicity

L-01

Alpha-Methyldopa Induced Hepatotoxicity In Women With Hypertensive Disorders Of Pregnancy: A Systematic Review Of Case Reports

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Objectives:
As recommended by the American College of Obstetricians and Gynecologists (ACOG), alpha-methyldopa is frequently used for treating hypertension disorders of pregnancy due to its safety Prof.ile for both mother and neonate. However on rare occasions, alpha-methyldopa has shown to develop Dr.ug-induced hepatotoxicity during pregnancy. This study aims to assess the potential of developing alpha-methyldopa induced hepatotoxicity in pregnancy.

Materials and Methods:
This study uses Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines for literature search. PubMed, EBSCOhost, and Proquest search engines were used to find cases that are relevant to our study, dating up to November 2020. Criterias included are english articles, human studies, and full text papers.

Results:
Nineteen studies were identified from literature search and 6 studies were found that matched the criteria. All studies are case reports, with a total of 6 patients. All patients in the case reports were diagnosed with alpha-methyldopa hepatotoxicity. The mean onset of time for the symptoms to arise was 31.25 days across 4 studies. One patient uses labetalol in advance before combining its regiment with alpha-methyldopa. All patients reported an increase in ALT levels between 685 - 2780 U/L and AST levels between 421- 2701 U/L.

Conclusions:
This study emphasises that the possibility of developing alpha-methyldopa hepatotoxicity is very much present, but not the possibility to predict when and which patients may develop the disease. Therefore, regular monitoring of liver enzymes and screening should be implemented for effective treatment and prevent further complications.

L-02

Covid 19 Associated Liver Injury: Clinical Manifestations, Challenges And Outcome: A Real Life Experience From Pakistan

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Objectives:
The study was aimed to determine the clinical manifestations, challenges, and outcome associated with Covid 19 associated liver injury.

Materials & Methods:
This observational study was conducted on all admitted patients of COVID-19 PCR positive at corona isolation ward & ICU. A total of 103 patients were evaluated (n = 62 from ward and n = 41 from ICU). Statistical analysis was performed to compare clinical manifestations, challenges, and outcome associated with Covid 19 associated liver injury among these groups.

Results:
A total of 74 (71.84%) patients had liver injury during hospitalization. Among them COVID-19 severity of illness was mild in 54.05% (n=40), moderate in 28.37% (n=21), and severe in 17.56%-(N=13) of cases. Mean age of patients admitted in ICU 59.21±6.33 was higher than those admitted in ward 47.21±7.01 years-(p 0.002). Higher CTP score (≥2) was found in patients admitted in ICU with severe COVID-19 disease as compared to patients admitted in ward (≤1), p=0.002. Similarly, the AARC score was also observed to be higher-(≥2) in patients admitted in ICU with severe COVID-19 disease as compared to patients admitted in ward (≤1) with mid and moderate COVID-19 disease, p=0.0001. A total of 12/41 patients (29.26%) died admitted in ICU. Increased mean age, presence of SOB at presentation, and raised gamma glutamyl transferase were independent predictors of increased mortality in patients with COVID-19 (p=0.001).

Conclusions:
Multiple clinical and non-clinical factors associated with poor outcome in patients admitted in ICU with COVID-19 associated liver injury.

Keywords: COVID-19, Liver Injury, Mortality, Pakistan

L-03

Dr.ug- Induced Liver Injury in the Elderly – Do We Know What We Don't Know?

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Objectives:
Dr.ug-induced liver injury (DILI) is the most common cause of acute liver failure in the US. The proportion of elderly in the population is also growing, but it is unclear whether age is a risk factor for DILI.

Methods:
A systematic review of literature describing DILI in elderly was conducted. Relevant articles were summarized under the themes:Definition of elderly-biological age/frailty, Epidemiology, Polypharmacy and inappropriate prescribing, Specific Agents associated with DILI, Pathophysiology of aging liver.

Results:
107 of 194 (55.5%) reviewed were included. Age-related changes of the liver function most likely relate to the degree of frailty, assessed by the biological, as opposed to chronological age, and may be relevant in the context of DILI. Incidence of DILI ranges from 2.3 to 23.8 per 100,000, and 41 per 100,000 (over 80 years). Research is equivocal about the nature of liver injury in the elderly, predominantly hepatocellular (up to 70% of cases), cholestatic (up to 46% of cases) and mixed (up to 29% cases). Changes in the aging liver were structural (up to 40% reduced volume and 60% reduction in blood flow, "pseudocapillarisation") and functional (reduced phase II metabolism and mitochonDr.ial liability). Isoniazid and benoxaProf.en had established relationships with DILI in elderly. While polypharmacy is common in the elderly, inappropriate medication use, affecting 6.64 million older Americans, was noted as more relevant in context of DILI.

Conclusions:
The review highlights substantive gaps in all areas. There is need for researchers, regulators, and industry to expand the science surrounding DILI in elderly.

L-04

Hepatoprotectants Efficacy Against Anti-Tuberculosis Dr.ug-Induced Liver Injury: A Systematic Review Of Randomized Controlled Trial

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Objectives:
Tuberculosis (TB) is one of the highest pulmonary diseases in the world, especially in developing countries. The long-term anti-TB regimen can be resulting in a higher incidence of Dr.ug-induced liver injury because of Dr.ugs hepatotoxic effect—the systematic review aimed for the efficacy of hepatoprotectant that can protect the liver from the anti-TB regimen.

Materials and Methods:
The systematic review was conducted with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines. The literature search was done using four databases: PubMed, ProQuest, ScienceDirect, and EBSCO with “Hepatoprotectant,” “Dr.ug-induced liver injury,” and “anti-TB Dr.ug” as the primary keywords. Cochrane risk of bias tool 2.0 was utilized in the quality assessment of the studies.

Results:
The search strategy identified 910 studies. Four relevant full-text articles met our inclusion criteria. Overall studies had low risk, but some had unclear and high risk in the blinding of outcome assessment. Three substances already used in a clinical trial as hepatoprotectants: N-acetylcysteine (NAC), Silibinin, and silymarin. NAC combination with anti-TB regimen showed none patients with the hepatotoxic conditions, then without NAC, 12 patients suffered hepatotoxicity condition (37.5%). In contrast, silibinin showed no significant hepatoprotective effect after 2, 4, and 8 weeks of intervention ($p>0.05$). Same outcome with silymarin that showed RR 1.23 (95% CI = 0.94–1.54) from the experiment and control group.

Conclusions:
Our findings showed that only NAC that can be used as hepatoprotectants in Dr.ug-induced liver injury combined with an anti-TB regimen.

L-06

Remdesivir Associated Acute Liver Injury In Covid-19 Patients: A Case Based Systematic Review

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Objectives:
In this pandemic situation, finding the safe and effective therapy against Severe Acute Respiratory SynDr.ome Coronavirus 2 (SARS-CoV-2) is a priority. Remdesivir has shown some promise for COVID-19 treatment, despite potentially inducing liver toxicity. The study's aim is to review the effect of Remdesivir that causes Dr.ug-induced and acute liver injury in hospitalized COVID-19 patients.

Materials and Methods:
We used Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines during our literature search. PubMed, EBSCOhost, and Proquest search engines were used to find cases that are relevant to our study, dating up to October 2020. Criterias included are english articles, human studies, and outcome assessments.

Results:
We identified 78 studies from search strategies and found 7 studies that have relevant issues. All studies are case reports or case series with a total of 23 patients. Outcome of studies include AST/ALT levels before and after treatment. Six studies suggested that the use of Remdesivir is associated with elevation of ALT/AST > 3 times the ULN. Three studies showed an increase of total bilirubin levels. Only 1 study stated that the risk of elevated liver function tests is still poorly understood.

Conclusions:
Despite limited reports, we concluded that the use of Remdesivir as treatment in COVID-19 patients is associated with acute liver injury. We suggest the use of Remdesivir should be accompanied with close monitoring due to its hepatotoxicity potential. Further studies are needed for better understanding and management of Remdesivir associated liver injury.

L-07

Severity Of Covid-19 Is Associated With Liver Injury In Patients Without Pre-Existing Liver Disease

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Objectives:
Covid-19 is known to disturb Liver function tests (LFTs). Not much literature is available regarding the effect of COVID-19 on LFTs in patients without pre-existing liver disease. The study aimed to find the effect of COVID-19 in these patients.

Methods:
142 patients were admitted with SARS-COV-2 during the period of the pandemic. Seven patients were excluded due to a history of chronic liver disease.

Results:
A total of 135 patients were included in the study aged between 18-95 (mean 57.7± 15.6.) Male were 93 (68.9%). Hypertension was present in 74 patients (54.8%) and diabetes in 35.6%). Fever was the chief complaint in 112 (83%), followed by dyspnea 93 (68.9%) and cough 79 (58.5%). Elevate AST was seen in 82 (61%), GGT 82 (61%), ALT 61 (45%), alkaline phosphatase 19 (14%), bilirubin 6 (4%) and low albumin in 35 (26%). Severe COVID-19 when compared with mild to moderate disease was associated with elevated AST≥2-time upper limit normal (2ULN) (p=0.002), GGT≥2ULN (0.026), and lower albumin(p=0.020). AST ≥2ULN was associated with a high SIRS score (0.045), high procalcitonin (p=.045), higher ferritin (p-0.005), lower PO2 (p=0.044), and higher SOFA score (p=0.002) pointing to the inflammatory response as the cause of liver injury.

Conclusions:
Large number of patients suffering from COVID-19 have evidence of liver injury which appears to be secondary to an inflammatory response. The degree of liver damage correlates with the severity of COVID-19 hence close monitoring of these variables is important as a part of the assessment of vulnerable population.

L-08

Statin Related Dr.ug Induced Liver Injury: A Case Series

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Objectives:
To describe the clinical Prof.ile of patients presenting with statin induced Dr.ug induced liver injury (DILI)

Materials and Methods:
Patients admitted with statin induced Dr.ug induced liver injury (DILI) meeting CIOMS/RUCAM criteria, from 1st August 2018 to 31st January 2020, in a tertiary care centre were included in the study.

Results:
Four cases were identified as statin induced DILI meeting CIOMS/RUCAM criteria. Case A- 60-year-old male with alcohol related chronic liver disease (CLD) presented with acute on chronic liver failure (ACLF). Case B- 50-year-old female with acute liver failure. Case C- 65-year-old female with cholestatic liver injury. Case D- 62-year old male with acute hepatitis and severe myositis. Indication for statin was ischemic heart disease in cases A,B and C and dyslipidemia in case D. All four had received atorvastatin, at doses of 40mg, 80mg, 80mg and 40mg in cases A,B,C,D respectively. Time to first presentation was 8weeks, 6weeks, 5days, 13weeks and peak total bilirubin (mg/dl)/ALT (IU/l) / ALP (IU/L)/INR were 24.2/1751/640/1.89, 30/4580/370/7.5, 3.2/240/560/1.3, 0.5/368/89/1.05 in cases A,B,C,D respectively. All 4 patients complained of myalgia with peak CPK (IU/L) values at 4340/3220/880/6253 in cases A,B,C,D respectively. Case A and C recovered following withDr.awal of statin and supportive care. Case B expired due to multi organ dysfunction and case D expired following massive pulmonary embolism. Viral and autoimmune hepatitis was excluded in all four patients.

Conclusions:
Though rare, statin induced DILI should be closely watched for, given the increasing use of statins.

L-10

Intrahepatic infiltration of activated CD8+ T cells and macrophages is associated with the severity of liver injury in Dr.ug-induced liver injury: implications in steroid therapy

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Objectives:
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 February 2020, 41 consecutive patients with DILI who underwent liver biopsy were enrolled prospectively in this study. Liver biopsy was performed, and immunohistochemical stain and multicolor fluorescence-activated cell sorting (FACS) analysis were done with the biopsy specimen.

Results:
The number of intrahepatic T cells (CD3+) showed positive correlation with serum levels of total bilirubin, AST, ALT, and MELD score ($p<0.05$). The number of intrahepatic macrophages (CD68+), also showed positive correlation with serum levels of total bilirubin, AST, ALT, and MELD score ($p<0.05$). The frequency of activated CD8+ T cells (CD38+HLA-Dr.+) among the liver-infiltrating CD8+ T cells in DILI livers, was significantly higher than that in healthy livers ($p<0.01$). Importantly, the percentage of CD38+HLA-Dr.+ cells among intrahepatic CD8+ T cells in DILI livers showed positive correlation with ALT ($r=0.593$, $p=0.04$). Thirty patients were treated with steroid. Among them, 22 patients showed more than 50% of reduction of ALT level after 1 week of steroid treatment.

Conclusions:
In conclusion, we found the positive correlation between the number of intrahepatic macrophages, T cells, CD8+ T cells and activated CD8+ T cells 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.

L-11

To Study LFT Abnormality in Patients with Ischemic Hepatitis and Congestive Hepatopathy and 7 Days Predictor Of Mortality.

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Objectives:
To study clinical parameters and LFT in Ischemic Hepatitis(IH) and Congestive hepatopathy(CH) and LFT on Day 1, 3 and 7.To study the 7 days predictor of mortality.

Materials and Methods:
Clinical features -jaundice,Right upper quaDr.ant(RUQ) pain, pedal edema ,ascites and hepatomegaly.LFT was studied for day1, 3, and 7,LDH,blood urea and creatinine,PT/INR,t.protein and albumin.Patients were followed for 7 days from admission for predictors of mortality.

Results:
This study includes 78 patients with IH and 33 patients with CH.The most common age group in IH and CH is 41-50 years.In the IH group RUQ pain-2.6%,ascites-1.3%,hepatomegaly-5.1%,pedal edema-16.1%.The mean AST was highest on day 1with significant difference on(day 1 and 7) and (day 3 and 7).The mean ALT peaked on day 3 with significant difference on (day 1 and 7) and (day 3 and 7).For predictors of mortality ROC curve of blood urea and creatinine (with AUROC=0.736 and AUROC=0.734 respectively)significant.In IH mortality was 37.2%.In 33 patients with CH the mortality rate 15.2%. RUQ pain-21.2%,jaundice-9.1%,ascites-15.2%,pedal edema-42.4%.The bilirubin peaked on day 1,decreased on day 3 and 7 with significant difference on day 1and 7.The mean ALP levels peaked on day 1 with significant difference on day 1and7.For predictors of mortality bilirubinD-1(AUROC=0.811) blood urea and creatinine(AUROC= 0.836 and AUROC=0.875 respectively) were significant.

Conclusions:
The peak in AST is on day 1 and ALT on day 3,normalization in > 7 days in IH.The presence of renal dysfunction in IH is associated with increased mortality. In CH bilirubin and ALP were elevated. Bilirubin on day1 and elevated renal parameters were associated with increased mortality.

L-12

Dr.ug-induced liver injury registry and the study of factors associated with its clinical course: a multicenter study

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Background:
Dr.ugs and herbal supplement are the common causes of Dr.ug-induced liver injury (DILI). The prospective study of DILI has never been done in Thailand.

Objectives:
We identified causes, clinical courses and outcomes of DILI among Thai population.

Methods:
Thai Association for the Study of the Liver (THASL) DILI registry was established on 1 Dec 2018. The prospective multicenter study has been conducted. Patients with abnormal liver function test (LFT) from Dr.ug or herbal use are enrolled. Inclusion criteria of DILI follows the DILI Network. Data are collected at enrolment and followed up until LFT normalization. The Roussel-Uclaf Causality Assessment Method (RUCAM) is used. DILI severity is graded.

Results:
Until Nov 2020, there are 202 patients. 64 (31.68%) have chronic liver disease. Median time of Dr.ug initiation to the first presentation is 28 (1-1,695) days. 30 (14.85%) patients use more than 1 Dr.ugs. There are 130/214 (60.75%) Dr.ugs and 84/214 (39.25%) herbals. Among 130 Dr.ugs, antimicrobial [50 (38.46%)] (mostly anti-tuberculosis Dr.ugs), anti-neoplastic [18 (13.85%)], immunotherapy [10 (7.69%)] and lipidemic Dr.ugs [10 (7.69%)] remain the frequent causes of DILI. The median time from initiation to the onset of symptoms or abnormal LFT is 28 (1-1,695) days. LFT normalization is seen in 117 (57.92%) patients. 7 (3.47%) patients died and 5 (2.48%) patients developed liver failure. Patients who died were older, had higher malignancy and chronic liver disease.

Conclusions:
Anti-tuberculosis Dr.ugs and herbal use are the most common causes of DILI in Thailand. Though most patients recover, fatality occurs in some cases.

Human Cholestatic and Autoimmune Liver Diseases

M-02

Establishing a non-invasive diagnosis model of liver cirrhosis in patients with primary biliary cholangitis based on the liver disease research database

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Objectives:
PBC Patients have a poor prognosis when they progress to cirrhosis, Existing non-invasive diagnostic models are not effective enough. It is planned to establish a non-invasive diagnostic model for patients with PBC.

Materials and Methods:
Based on the liver research database established in the previous period, 380 PBC patients hospitalized in our hospital from 2011 to 2020 were screened out, of which 65% of the patients received liver biopsy. Divided into model group and verification group. Take the 10 most relevant indicators as the final screened sensitive indicators, apply the random forest method in artificial intelligence machine learning to establish a non-invasive diagnostic model, and then use the validation group of patients to verify the diagnostic efficacy of the model.

Results:
Non-invasive diagnosis model of liver cirrhosis in PBC patients, based on the random forest method, the influencing factors of liver fibrosis were screened out hematocrit (HCT), liver stiffness, cholinesterase, cholesterol , etc. the random forest model was used to establish the model, and the area under the ROC curve was 89.6%. Compared with traditional research methods, the research time is shortened by 70% according to collecting data from the liver disease research database established by our research group..

Conclusions:
This study is based on the random forest method in machine learning to construct a non-invasive diagnosis model for liver cirrhosis, which has high accuracy and good extrapolation, which may avoid part of liver biopsy. The use of liver disease research databases can greatly improve research efficiency.

M-04

The Potential of Soluble Programmed Cell Death Protein-1 (sPD-1) and Anti-PD-1 as Serological Markers of Autoimmune Hepatitis: A Systematic Review

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Objectives:
Autoimmune hepatitis (AIH) is an inflammation of the liver caused by the immune system. Soluble programmed cell death protein-1 (sPD-1) is a protein released by activated T cells. Evidence has shown some correlation between sPD-1 and anti-PD-1 to AIH, but their serological potentials are still unclear. Therefore, this systematic review aims to assess the potential of sPD-1 and anti-PD-1 as serological markers for AIH.

Materials and Methods:
This systematic review was conducted in accordance with the PRISMA guidelines. The literature search was done in PubMed, ProQuest, and EBSCOhost without time, setting, and language restrictions up to 22nd August 2020. Title, abstracts, and full texts were assessed for eligibility. All related observational studies were included. QUADAS-2 was used for bias assessment of the studies.

Results:
The search result yielded 245 studies, and four studies were included after the eligibility assessment. All studies found that sPD-1 was significantly higher in active AIH group compared with control and immunosuppressant responders AIH groups, but similar sPD-1 level was found in immunosuppressant non-responders AIH group. With a cutoff value of 1.73 ng/ml, the AUC of sPD-1 was 0.895. A positive correlation was also seen between sPD-1 and liver enzymes, fibrosis, and scoring systems. The prevalence of anti-PD-1 was significantly higher in AIH compared with control and other causes of hepatitis.

Conclusions:
These findings showed that sPD-1 could be reliably used as a serological marker of AIH for diagnosis and treatment follow-up. Anti-PD-1 can be used to differentiate AIH with other types of hepatitis.

M-05

Two autopsy cases with rare aetiologies for massive hepatomegaly in middle aged females

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Objectives:
to study the histomorphological features of liver in two patients who had unexplained hepatomegaly.

Materials and Methods:
H and E and immunohistochemistry (IHC) stained sections of autopsy liver and spleen were available for examination. 1st case: a 54 years old female, known case of haemolytic anaemia with hepatosplenomegaly and generalized lymphadenopathy suggestive of lymphoma. Bone marrow and flow cytometry suggested to be a case of marginal zone lymphoma. 2nd case: 45 years old female, known hypothyroid, came with moderate grade fever of 4 months, loose motion with .jaundice and hepatomegaly. Radiology showed liver with multiple 1 cm sized diffuse nodules. Sigmoidoscopy – a few irregular ulcers of 1 cms sizes, normal intervening mucosa. Infective aetiology was excluded. Put on wysolon, no response. She developed seticemia and worsening jaundice.

Results and conclusions:
1st case: Histology- portal tract heavily infiltrated by monomorphic cells spilling into adjoining lobules and sinusoids. Cells - variable types including megakaryocytes, immature erythroid and leukocytes. IHC excluded mantle cell lymphoma; Autopsy diagnosis - extramedullary haematopoiesis. Similar morphology in spleen and lymph nodes. 2nd case: liver - enlarged and bile stained with multiple 1 cm size whitish nodules. CBD and its major branches - normal. Liver histology: multiple compact reticulin rich epithelioid cell granulomas involving portal tracts with Langhan and foreign body giant cells and mixed inflammatory cells. No necrosis. Granulomas involve medium and small sized bile ducts with bile extravasation. Histology - consistent with Sarcoid granulomas. Colon ulcers - chronic active colitis, no granuloma. AFB negative.

M-06

Double negative T cells therapy alone or in combination with oral UDCA alleviates primary biliary cholangitis in mice

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Objectives:
Double negative T (DNT) cell, a unique regulatory T cell, could maintain immune system homeostasis. Our previous study showed that DNT cells in both peripheral circulation and liver were reduced in primary biliary cholangitis (PBC) patients. This study aims to explore the therapeutic effect of DNT cells in PBC.

Materials and Methods:
6-8-week-old dnTGFβ RII mice were received a single transfer of DNT cells alone or in combination with oral UDCA for 6-8 weeks.

Results:
Compared with untreated group, DNT cells therapy significantly decreased the levels of ALT, AST, AMA-M2, IgM and proinflammatory cytokines, including IFN-γ, TNF-α, IL-6 and IL-1β in plasma. Liver pathology showed DNT cells therapy markedly relieved liver fibrosis in PBC mice. In addition, DNT cells exhibited strong killing effect on hepatic T cells, and strong inhibition on their proliferation in vitro. Combination of DNT cells therapy and oral UDCA could more effectively ameliorate the liver inflammation, through inhibiting hepatic T and B cells in vivo.

Conclusions:
A single transfer of DNT cells significantly ameliorated liver fibrosis in dnTGFβ RII mice, and UDCA could augment the suppression function of DNT cells. This study suggests that DNT cells may be an alternative therapy for PBC.

Inflammation and Immunobiology

N-01

A Prospective Case Control Study Of Liver Dysfunction In Hyperthyroidism With Special Reference To Portal Venous Flow And Fibrosis Assesement And Its Reversal Following Treatment

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Objectives:
To determine the frequency of liver dysfunction in patients with hyperthyroidism with special reference to portal venous flow and fibrosis assessment and its reversal following treatment.

Methods:
In the present Cross Sectional study, samples of 55 cases (newly diagnosed hyperthyroidism) and 50 controls (normal healthy persons) were selected from MaDr.as Medical College, Chennai. Serum AST, ALT, and ALP levels were measured on XL-640 fully-auto biochemical analyser. Blood flow in the portal vein were investigated in fasting state by means of Doppler ultrasound. Fibrosis assessment done by Echosens FibroScan 502 Touch System at different points in the study.

Results:
Results showed increase in serum AST, ALT and ALP in patients with altered thyroid function compared to normal subjects. The overall incidence of any biochemical liver test abnormality within 3 months of thyrotoxicosis was 45%. 33% of the patients had an increased ALP. The liver blood flow as estimated Doppler ultrasound was not altered significantly after the treatment period. Reversal of liver stiffness was seen after anti thyroid medications but was not significant.

Conclusions:
These findings indicate that abnormal results of liver function tests are common in patients with new onset hyperthyroidism and make the diagnosis of concomitant, unrelated liver disease difficult until the euthyroid state has been established.

N-04

Impact of Systemic Inflammation on Liver Function as Assessed by ALBI Grade

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In cirrhosis (LC), the immune system is impaired and infections and inflammation affect the prognosis. Inflammation caused by immunodeficiency in LC has recently been proposed as CAID (cirrhosis associated immune dysfunction) and has attracted much attention. We investigated the effect of systemic inflammation on the ALBI grade.

Methods:
The subjects were 742 patients (non-LC/LC: 568/174, median 65 years, male 57%, HCC 98).Liver fibrosis was diagnosed by MRE and ALBI (mALBI) grade by blood tests. Inflammatory markers were assessed by neutrophil fraction of WBC (%Neu) and immune function was assessed by total lymphocyte count (TLC), and the diagnosis of CAID was set at %Neu > 70% & TLC < 1500/mm3 (Nakamura et al. Liver 2020).

Results:
Frequency by stage (non-LC/ALBI 1/2/3) was 568/56/86/32 . The ALBI score correlated with liver stiffness, and T.Bil, Alb, TC, Hb, PT (%) and Na were significantly worsened by grade ($p<0.01$). %Neu (non-LC/mALBI 1/2a/2b/3) was 56/55/55/61/74 (mean), progressively increasing from 2b ($p<0.01$), while TLC decreased from early LC (1923/1895/1583/1223/1083). And the frequency of CAID was 5/4/7/21/55 (%). In multivariate analysis, %Neu was associated with WBC (t=11.6), TLC (-11.7), ALBI score (2.43) and TLC was associated with WBC , %Neu and HCC (-2.65) ($p<0.05$). Kaplan-Meier curves were significantly stratified by ALBI grade (log-rank: $p<0.01$). HCC (HR 2.89) and CAID (2.97) were prognostic factors in Cox proportional hazards ($p<0.05$).

Conclusions:
Inflammation contributed to the severity of ALBI grade, and immune deficiency appeared to be related to the worsening of LC prognosis due to CAID as an inflammatory trigger.

N-05

Expression analysis by Nanostring nCounter system in non-alcoholic steatohepatitis identifies activated macrophages as key mediators of inflammation

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Background & Aims:
In this study, we aimed to demonstrate that activated macrophages are as key mediators of inflammation in NASH livers.

Methods:
Ninety-four, snap-frozen benign liver tissues with various chronic liver diseases in the different fibrosis stages (0: n=17, 1: n=12, 2: n=12, 3: n=25, 4: n=28) were subjected to the expression analyses using the nCounter PanCancer Pathway Panel. Immunohistochemistry and multicolor flow cytometry were performed with the biopsy specimen. Mouse model of NASH-induced liver cirrhosis was established using high-fat, high-cholesterol (HFHC) diet with intraperitoneal streptozocin injection.

Results:
Gene expression analysis with 94 diseased liver samples using the nCounter PanCancer Pathway Panel identified that expression level of IL12B, SOCS1, and CHIT1, which are robustly expressed in activated macrophages, was higher in the livers with advanced fibrosis (stage 3 and 4) than those with low-grade fibrosis (stage 1 and 2) or no fibrosis ($P < 0.001$). Flow cytometry using liver biopsy specimen from NASH livers demonstrated that macrophages in the livers with advanced fibrosis show higher expression of HLA-Dr. and PD-L1, suggesting that these macrophages contribute not only to the inflammation, but also to dismantling anti-tumor immune surveillance in fibrotic NASH livers. Mice fed with HFHC diet with intraperitoneal streptozocin injection developed NASH, liver cirrhosis, and hepatocellular carcinoma, and the number of activated macrophages increased as the disease progressed.

Conclusions:
Our data using expression analysis of immune markers showed that activated macrophages are key mediators of inflammation in NASH livers.

N-06

Inflammation-induced, IgA (+) PD-L1-high tumor-associated macrophages are the main targets of immune checkpoint inhibitors in hepatocellular carcinoma

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Objectives:
To investigate the roles of inflammation-induced intrahepatic IgA (+), PD-L1-high macrophages in development and immune checkpoint inhibitor (ICI) treatment of hepatocellular carcinoma (HCC).

Materials and Methods:
Serum ELISA and immunohistochemial staining were performed. Multi-color flow cytometry was performed with mononuclear cells isolated from surgical and liver biopsy specimens of chronic liver diseases and HCC. In vitro differentiation of TAMs, stimulation of TAMs with coated IgA, and RNA sequencing was done. Hepa1-6 syngeneic mouse model was established.

Results:
First, we identified that serum IgA levels predicted the progression of hepatic fibrosis and the development of HCC ($P < 0.001$, AUROC = 0.70). Immunohistochemical staining of IgA revealed the strong positivity of IgA in Kupffer cells or recruited macrophages and the intensity of IgA staining reflected serum levels of IgA and the fibrosis progression in the chronic liver diseases ($P < 0.05$). In HCC patients, intrahepatic macrophages expressed significantly higher levels of IgA than circulating cells, and expressed higher levels of PD-L1 and HLA-Dr. than those without. In vitro coated IgA complex stimulation to M2 macrophages caused activation of these cells (demonstrated by RNA sequencing) and PD-L1 upregulation via YAP/TAZ pathway. In vivo experiments demonstrated that blockade of IgA signaling using soluble FcαRI peptide or treatment of anti-PD-L1 resulted in the decreased tumor volume and decreased the number of IgA-high TAMs.

Conclusions:
TAMs with strong IgA positivity in human HCC microenvironment express higher levels of PD-L1 and ICI treatment may target these cells.

Liver Fibrogenesis and Non-Parenchymal Cell Biology

O-01

EPR-TSA method for the diagnosis of liver fibrosis

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Objectives:
The functional activity of albumin directly depends on the condition of the liver. EPR spectroscopy (MedInnovation GmbH) provides information about the transport properties of albumin in human blood. The analysis of EPR specters is performed using a developed program that automatically calculates the indicators of albumin functionality: binding efficiency (BE), transport efficiency (RTQ), detoxification efficiency (DTE) and indicator of native albumin conformation (Dr.).

Aim:
To identify the feasibility of using the EPR test for the diagnosis of liver fibrosis.

Materials:
The first study group consisted of 144 patients with various chronic liver disease (NASH, HCV, HBV, autoimmune hepatitis). This group consisted of 28 women and 116 men average age - 43.5±7.35 years, who underwent percutaneous liver biopsy. This group was divided into 5 subgroups depending on the degree of METAVIR fibrosis.
The control group consisted of 24 people (6 women and 18 men) - average age 31.95±4.66 years, where liver diseases were excluded according to the results of the medical expert Commission of healthy volunteers (cosmonauts).

Results:
Comparison of the results of the study in the control group and in patients of subgroup F2 fibrosis (clinically significant level of fibrosis) indicates a statistically significant difference in all parameters.

Conclusions:
Clinically significant liver fibrosis (F2) may be diagnosed by using the parameter BE≤91 (AUROC-0.963), sensitivity-92.1% and specificity- 91.7 and the parameter DTE ≤91 (AUROC=0.975, sensitivity-97.4 and specificity-91.7).The RTQ parameter cannot be recommended, since at the optimal threshold≤71.1, sensitivity and specificity are only 63.2 and 70.8, respectively (AUROC=0.683).

O-02

Fuzhenghuayu recipe alleviates DMN-induced mice liver fibrosis through regulating recruitment and phenotype polarization of Bone marrow-derived macrophages

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Objectives:
Our previous studies have showed that Fuzhenghuayu recipe (FZHY) might play anti-fibrotic effects by regulating immune cells function in the liver. However, the reversing mechanism of FZHY on liver fibrosis by regulating recruitment and phenotype polarization of Bone marrow-derived macrophages (BMDMs) is still unclear.

Materials and Methods:
Serum ALT and AST levels, liver Hyp content, hepatic inflammation and fibrosis degree of liver were measured. Liver CD206, ARG-1, CCL2 and iNOS protein productions were detected by immunohistochemical staining. The proportions of intrahepatic Kupffer macrophages (KCs), BMDMs and the subset changes of pro-inflammatory mononuclear macrophage, restorative mononuclear macrophage and denDr.itic cell were evaluated by flow cytometry. The gene expressions of TNF-α, TGF-β1 and MMP9/12 in macrophages were detected by RT-PCR.

Results:
The results demonstrated that serum ALT and AST levels, liver Hyp content, liver inflammation, collagen deposition, and liver CCL2 and iNOS protein productions were significantly reduced and liver CD206 and ARG-1 protein productions were significantly increased in FZHY-adminstered mice, compared with DMN-induced liver fibrosis mice. There was no marked change of KCs proportion in liver, but proportions of monocyte-derived macrophage and pro-inflammatory mononuclear macrophage were apparently reduced, and proportions of restorative mononuclear macrophage and denDr.itic cell were obviously increased. TNF-α and TGF-β1 gene expressions were significantly decreased and MMP9/12 gene expression was significantly increased.

Conclusions:
FZHY could reduce the monocyte recruitment to liver and reduce proportion of pro-inflammatory macrophage, meanwhile increase proportions of restorative macrophage and denDr.itic cell. Thus, it played a significant therapeutic effect on DMN-induced liver fibrosis.

O-05

miR-30d Alleviates Liver Fibrosis through Inhibiting Hepatic Stellate Cell Activation

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Objectives:
Liver fibrosis is a common pathological process of chronic liver diseases which may eventually develop into liver cirrhosis, liver failure, or even death. Currently, efficient and safe interventions to alleviate or reverse liver fibrosis are needed. Dysfunction of microRNAs is associated with many different liver diseases, but the function of microRNA-30d (miR-30d) in liver fibrosis remains unclear. The present study is in order to explore the function of microRNA-30d (miR-30d) in liver fibrosis and the underlying mechanism.

Methods:
Male adult miR-30d global knockout SD rats and age-matched wild type SD rats were divided into four groups randomly, and received CCl4 or olive oil intraperitoneal injection for 6 weeks. Meanwhile, we investigated the function of miR-30d in rat hepatic stellate cell line HSC-T6 activation and the upstream-downstream mechanism.

Results:
In the present study, we investigated that the expression of miR-30d was reduced and played an essential role in CCl4 induced liver fibrosis and TGF-β1 induced HSC-T6 activation. Based on the animal model of liver fibrosis, we found that knockout of miR-30d expression promoted CCl4-induced liver fibrosis in vivo. Furthermore, overexpression of miR-30d promoted HSC-T6 cells proliferation and increased the percentage of HSC-T6 cells in S phase. Conversely, HSC-T6 cells proliferation and cell cycle progression were inhibited under inhibition of miR-30d. Integrin subunit alpha 5 (ITGA5) was confirmed to be a target gene of miR-30d involved in liver fibrosis.

Conclusions:
The present study demonstrates that miR-30d inhibits hepatic stellate cell activation by targeting ITGA5 in liver fibrosis.

O-06

Small surgical incisions in the liver cause fibrotic response in adult and neonatal mice.

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Objectives:
Liver fibrosis generally results from persistent chronic injury and the fibrotic response. In contrast, in many forms of acute injury, liver regeneration occurs without the development of fibrosis. This leads to a fundamental question as to why in some settings does the liver heal without fibrosis whereas in other settings this is not possible. We hypothesized that a stromal injury is a key event that prevents the restoration of normal liver architecture.

Material and Methods:
We developed a model of stromal injury using a small surgical incision through the normal liver in adult and neonatal mice.

Results:
We found that even in response to a limited stromal injury, the liver responds with an inflammatory response similar to that seen during injury and healing in other tissues. This response culminates in fibrosis characterized by deposition of type I collagen, similar to the response seen during the development of cirrhosis. Studies in neonates reveal a similar fibrotic response.

Conclusions:
These studies suggest that in the setting of a stromal injury, the liver is not a uniquely regenerative organ, but rather scars like other organs. These findings may have implications for understanding the pathogenesis of chronic liver disease and may suggest unique therapies for chronic liver disease.

Liver Transplantation and Liver Surgery

P-04

Impact of intensive care unit discharge delay on outcomes after liver transplantation

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Objectives:
For general patients, discharge delay (DD) from the intensive care unit (ICU) is associated with increased hospital length of stay (LOS), and multi-resistant bacteria (MRB) infections. The impact of ICU DD has not been studied in liver transplant (LT) recipients.

Material and Methods:
We retrospectively studied consecutive adults who underwent deceased-donor LT 2011-2019. All patients went to ICU post-operatively followed by the transplant ward. DD was defined as >8hours between being cleared by ICU for discharge to ward post-LT and leaving ICU.

Results:
549 patients received LT and survived to discharge to ward. Median ICU discharge time was 25.5hours (IQR 6.6-38.0). Most patients (68.5%) experienced DD. No donor or recipient variables were associated with DD. Patients cleared for discharge early in the week (Sun-Tues) were more likely to experience DD than those cleared later in the week (Wed-Sat): 75.2%vs.62.2% (P<0.01). Patients cleared within routine work hours (8am-5pm) were less likely to experience DD than those cleared outside (66.1%vs.93.6%, P<0.01). Median hospital LOS were identical (18 days). No differences were seen in ICU/hospital readmission rates and graft/patient survival (Log-rank P=0.84 and 0.87, respectively) between delayed and non-delayed patients. Patients who became colonised with MRB in ICU spent longer time there compared to those who remained MRB-free (9vs.6 days, P<0.01), however this was not associated with DD (8.0% vs. 7.4% became colonised, P=0.82).

Conclusions:
Discharge delay from ICU post-LT is common (69%) and related to logistical factors. It does not prolong hospital LOS and is not associated with adverse patient outcomes.

P-06

Low Birth Weight And Preterm Delivery In Pregnancies Following A Liver Transplant: A Systematic Review Of Retrospective Cohort Studies

Mr Leonardo[1], Mr Archie Fontana Iskandar[1], Ms Angeline Ekafentie[1], Ms Jocelyn Lee[1], **Ms Stephanie Johanes[1]**, **Ms Stephanie Johanes[1]**, Mr Oscar Odillo Laman[1], Mr Jordan Budiono[1], Mr Fransiskus Xaverius Rinaldi[1]
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Objectives:
Despite the knowledge of several immunosuppressive medications being safe for pregnancy, there are various reports of poor pregnancy outcomes in liver transplant recipients. This study aims to evaluate the pregnancy outcomes of women who have undergone previous liver transplantation, focusing on two outcomes which are premature deliveries and low birth weight babies.

Materials and Methods:
Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines were used during literature search, along with search engines PubMed, EBSCOhost, and Proquest, with studies dating up to November 2020. Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were used to assess the risk of bias of each study. The studies selected for this study were english articles, human studies and studies published within the last 10 years.

Results:
A total of 194 studies were found and 19 studies met the criteria, all cohort retrospective studies. A prematurity rate of 34.4% was found out of 705 deliveries and a rate of 26.3% for low birth weight babies out of 315 live births. The calculated mean gestational age was 37.2 weeks out of 221 deliveries and mean birth weight was 2.847 grams out of 269 neonates.

Conclusions:
The rate of poor pregnancy outcomes, such as preterm deliveries and low birth weights in women liver transplant recipients are still high. However, it is still possible for women to conceive and have a successful pregnancy. Strict monitoring from specialised obstetricians is needed to ensure positive outcomes.

P-08

The Role Of Qt Prolongation And Nt-Probnp To Predict Mortality In Liver Transplant Patient: A Systematic Review And Meta Analysis

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Objectives:
There have been reports of QT prolongation and the increase of NT-proBNP in patients with End Stage Liver Disease (ESLD) and it is known that liver transplant (LT) is one of the best methods of therapy. However, the rate of mortality in liver transplant recipients is still high. This study aims to assess the role of QT prolongation and NT-proBNP to predict the mortality of liver transplant patients.

Materials and Methods:
Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines were used for literature research. PubMed, EBSCOhost, Proquest search database were used, with studies dating up to November 2020. To assess risk of bias Strengthening the Reporting of Observational studies in Epidemiology (STROBE) is used.

Results:
Out of 244 studies identified, 8 studies were relevant. Three studies showed no significant association between pre-LT QTc prolongation and mortality rate. However, one study reported increasing mortality in post-LT QTc prolongation group (HR, 1.78 [95%CI, 1.05-3.03]; P = 0.03). The meta-analysis from 3 studies showed high pre-LT NT-proBNP group has higher risk of all kind mortality (RR 7.01 [95%CI=5.28, 9.29]) and another 3 studies showed high post-LT NT-proBNP group has higher risk of all kind mortality (RR 4.38 [95%CI=2.69, 7.13]).

Conclusions:
Post-LT QTc prolongation and peri-LT NT-proBNP are associated with higher risk of mortality in LT patients. QTc interval and NT-proBNP evaluation can be considered in LT patients. A deeper research is needed for better understanding.

P-09

Trends in Etiology of Chronic Liver Disease referred for Liver Transplant evaluation in Pakistan 2020

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Objectives:
Liver cirrhosis (LC) is a major and life-threatening health problem worldwide. There is scanty data on changing trends in etiological distribution of LC. In this study we examined the liver disease etiology trends among adults who were referred for liver transplant evaluation.

Materials and Methods:
A descriptive study (prospective) was conducted at the Gastro-hepatology outpatient department of AIMS Hyderabad from August 2020 to September 2020. It's an ongoing study. Adults with liver cirrhosis were included in the study and were evaluated for liver transplant. The clinical characteristics, etiology, and laboratory data were documented, based on which MELD, CTP scores and BCLC stage were calculated. Descriptive analysis was performed using SPSS software.

Results:
A total of 202 cirrhotic patients, out of which 68.3% were males. The mean age of the participants was 48.62 years ± 12.4 (Standard deviation) with majority in 21-50 years of age group. The etiological agents were as follows: Hepatitis C virus (HCV) 61.9%, Hepatitis B virus (HBV) (13.9%), HBV+ HDV (11.9%), NASH (7.9%), HBV+HCV and NASH+ALD (1.3%) each, HCV+NASH (1%) and HBV+HCV+NASH (0.5%).
Twenty-seven percentage of patients had hepatocellular carcinoma (HCC) of which majority were in BCLC Stage D (11.9%).The underlying etiology in HCC was HCV (74.1%).

Conclusions:
Although HCV remains the leading etiology of cirrhosis among HCC and non-HCC patients, there is rise in the prevalence of NASH observed in our study. This could be attributed to the obesity epidemic and escalating prevalence of diabetes and metabolic synDr.ome worldwide including developing country like Pakistan.

P-10

Experience of Antiviral Therapy (AVT) Liver Cirrhosis (LC) in Outcome of Hepatitis B (CHB) and Hepatitis B with Delta Agent (CHD) in Patients on the Waiting List for Liver Transplantation

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Background:
LC and HCC in outcome of CHB and CHD are the most common causes of LT in Kazakhstan. The cause of terminal liver disease in patients on the waiting list in 25% - patients with CHB and in 21% CHD.

Objective:
to assess the effectiveness of AVT in patients with LC and HCC caused by CHB and CHD before and after LT

Materials and Methods:
253 patients with LC and HCC in outcome of CHB and CHD has been retrospectively analyzed

Results:
131 with LC caused by CHB were included to study, mean age 43±7 years. A group with CHD was 112, mean age 38±6 years. The average MELD in CHB group was 16±9.1, 2,2% belonged to class A by CTP, B 56%, C 30%. In CHD group MELD was 15±10.2, with class A (CTP) were 4.5%,B 83%, C 12.5%.
Patients have taken tenofovir 84%, entecavir 16%. All received a rapid virological response. From all 76 patients (CHD 59, CHB17) underwent LT. 16% received HBIG. From 4th POD all patients continued taking NA. One patient with CHD interrupted entecavir during 5 months. He has been estimated diagnosis “Recurrent CHB+D, HBV DNA(+) and HDV RNA(+), F4 (Metavir)”. He continued tenofovir but received virological response against HBV only.

Conclusions:
From 148 recipients 93 biopsies were performed after LT, including HBV patients 4, HDV 8. Patient who interrupted tenofovir was diagnosed Recurrent CHB, F4 according examination.

NAFLD and NASH

Q-03

A Double-Blind, Randomized, Placebo-Controlled, Phase II Study to Assess the Efficacy and Safety of Pioglitazone in Taiwanese Patients with Nonalcoholic Steatohepatitis

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Objectives:
We conducted the first randomized trial aiming to investigate the efficacy and safety of insulin sensitizer in Asian non-alcoholic steatohepatitis (NASH) patients.

Materials and Methods:
A total of 90 biopsy-proven NASH patients was randomized to receive either oral Pioglitazone 30 mg/day (Arm A) or placebo (Arm B) for 24 weeks. Liver biopsy, MRI-PDFF, clinical dat were collected in paired fashion.

Results:
Forty-three patients were randomized into Arm A, whilst 47 patients were in Arm B. The pre-treatment mean ALT level was 86.9 ± 34.3 IU/L in Arm A, and it significantly decreased to 45.7 ± 35.8 IU/L at end-of-treatment (P=0.003). There was no significant change of ALT level in 46 Arm B patients (88.5 ± 37.6 IU/L to 79.8 ± 48.0 IU/L. There was a significant decrease of fat content (20.2 ± 9.0% to 14.3 ± 6.9%, P<0.0001) in Arm A, whereas the change of fat content was not significant in Arm B patients (21.7 ± 7.6% to 20.1 ± 7.0%, P= 0.16). There were 66 patients who completed paired liver biopsies. NAS improvement was observed in 14 (46.7%) patients in Arm A, which was significantly higher than 4 (11.1%) patients in Arm B (P=0.002). No significant difference of AE development between groups (P=0.63) except that those patients in Arm A had a higher incidence of neuropsychiatric symptoms than Arm B (11.6% vs 0%, P=0.02).

Conclusions:
Twenty-four weeks of insulin sensitizer treatment significantly improved liver function, decreased liver fat and NAS with a safe and well-tolerated Prof.ile in Asians.

Q-04

A New Method For Early Diagnostics Of Obesity In Non-Alcoholic Fatty Liver Disease

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Objectives:
The aim of the research was to create an algorithm for the management of patients with NAFLD, taking into account the indices of the bioelectrical impedance analysis.

Materials and Methods:
The study included 80 patients with NAFLD (25 men, 55 women), the mean age was 38.2 ± 16.6 years. The indicators of 20 persons without pathology of the hepatobiliary zone served as a control.

Results:
Anthropometric studies of patients with NAFLD showed that about 22.5% of the examined individuals have normal body weights, 22.5% are overweight. Obesity of the 1st, 2nd and 3rd degrees was detected only in 30%, 15% and 8.7% of people, respectively. The study showed that in 42% of patients with NAFLD, the level of the phase angle of impedance was within the normal range, in 51% it corresponded to a low level of physical activity, a high level of physical performance was noted in 7% of individuals. Normal fat mass were determined in 7.6% of patients, in 15.3% - increased content and in 76% obesity. In the control group, 80% of patients had a normal fat content, and 20% increased it. Patients with NAFLD, the % fat content was 61% higher than in the control group.

Conclusions:
Thus, the impedance-metric method for determining the component composition of the human body will allow therapists, gastroenterologists and general practitioners to correctly interpret the indicators of physical development, differentiate the constitutional norm and early manifestations of excessive fat deposition, and also conduct adequate therapy in patients with NAFLD.

Q-07

Association Between Chronic Hepatitis B And Human Immunodeficiency Virus Infection With Hepatic Steatosis And Fibrosis By Non-invasive Assessment

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Objectives:
Prior studies showed chronic hepatitis B (CHB) or HIV infection is associated with hepatic steatosis and fibrosis. To investigate liver steatosis and fibrosis in chronic HBV-HIV co-infected Chinese individuals using non-invasive tools, as compared to CHB and HIV mono-infected counterparts; whether coinfection would synergistically increase degree of steatosis and fibrosis.

Methods:
In a pilot cross-sectional study at a local hospital, CHB and/or HIV infected patient were recruited. Non-invasive assessments with transient elastography (TE) and controlled attenuation parameter (CAP) performed to assess hepatic steatosis and fibrosis.

Adjusted CAP computed according to Karlas et al, to correct for diabetes or extremes of BMI. A decisional flowchart used to correct for overestimates in TE for those with high CAP values ≥300dB/m as liver stiffness measurement has been found to be falsely high in these individuals

Results:
Liver fibrosis is associated with hepatic steatosis, hypertension and waist circumference. Hepatic steatosis is associated with metabolic risk factors in line with prior studies; there being no difference in steatosis between groups according to their infection status. With adjusted TE and CAP values, the relationships still hold true.

Conclusions:
Liver steatosis is common in both CHB and HIV infected individuals, and is associated with metabolic risk factors in all three groups, whereas fibrosis is linked to underlying steatosis. There is no significant increase in fibrosis in the co-infection group.

Future longitudinal studies with larger cohorts would be helpful to study relationships between steatosis, fibrosis, CHB and HIV infections, and derive cutoffs and algorithms for specific groups.

Q-08

BioFibroScore®: a new non-invasive method for diagnosing hepatic fibrosis in NAFLD and NASH

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Objectives:
Through analysis of candidate genes by scanning the sera of fibrosis and combining matrix-assisted laser desorption ionization-based proteomics, we have identified novel markers including uPA (FibA), MMP-9 (FibB), and β2M (FibC), which are highly useful to predicate the severity of hepatic fibrosis. By evaluating the serum levels of uPA, MMP-9, and β2M, we developed the BioFibroScore® as a novel noninvasive serum marker to assess the severity of hepatic fibrosis.

Materials and Methods:
Collect the medical records and serum samples of 60 NAFLD patients. The serum samples will be tested by BioFibroscore, and the test results will be correlated with the patient's medical records using statistical methods.

Results:
Diagnostic accuracy of hepatic fibrosis detecting by biopsy or fibroscan (F0/F1-4 and F0-1/F2-4) is evaluated by BioFibroScore and 6 biomarkers (leptin+Adiponectin+GOT+GPT+GGT+APTT). BioFibroScore® is about 73.47% accuracy for the diagnosis of hepatic fibrosis in patients with fatty liver.

Conclusions:
- Five parameters: age, GOT, GPT, GGT, HbA1c and insulin were correlated with hepatic fibrosis stages.
- BioFibroScore® is about 73.47% accuracy for the diagnosis of hepatic fibrosis in patients with fatty liver by using LDA method.

Q-09

Changing Clinicopathological Prof.ile Of Nonalcoholic Fatty Liver Disease In India - Interim Results Of The Icon-d (Indian Consortium On Nafld) Study

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Objectives:
Previous data from India had shown that patients with NAFLD have mild severity. Objective was to analyse the clinicopathological Prof.ile of NAFLD in a large real-life Indian cohort.

Methods:
In an on-going study [Indian Consortium on NAFLD (ICON-D)], interim data captured across 20 centres in India over 18 months was analysed. Severity of NAFLD was assessed on non-invasive scores, Fibroscan, histology and CT/MRI where indicated. The study had ethical approval at respective centers and patients gave informed consent.

Results:
Of 4313 patients with NAFLD (Mean age 45±12.2, Males 52%) anthropometry/metabolic synDr.ome data in 3553 (82.3%) patients (mean BMI 27.6 ± 5.7Kg/m2) revealed 378 (10.6%) were lean, 575(16.2%) overweight, 2580 (73%) obese. Metabolic synDr.ome was present in 1518 (42.7 %); at least one metabolic risk factor in 3292 (92.6%); commonest being central obesity [2981 (89%)]. As per AST to platelet ratio index (APRI) [n=3196 (74%)], 682 (21.3%) patients had significant fibrosis (APRI>1.5); Fibrosis-4 (FIB-4) data [n=3554 (82.4%)] showed significant fibrosis (FIB-4 > 3.25) in 676 (19%) patients. Fibroscan data [n=2475, (57.3%)] revealed significant fibrosis (≥ 8kPa) in 715 (29 %) and cirrhosis (≥ 12.5kPa) in 246 (10%); imaging showed HCC in 22 (0.5%) patients. On histology [n=267 (6.2%)], 57 (21.3%) had no-NASH, 89 (33.3%) borderline NASH and 131 (49 %) definite NASH; 80 (30%) F1, 51 (19%) F2, 19 (7.1%) F3 and 22 (8.2%) F4 fibrosis.

Conclusions:
In a large real-life cohort, a significant number of NAFLD patients from India have NASH, significant fibrosis or cirrhosis at presentation.

Q-10

Clinical Outcomes In A Real-world Cohort Of Patients With Non-alcoholic Fatty Liver Disease In South Asia

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Objectives:
There is lack of data regarding clinical outcomes in patients with NAFLD from South Asia. The objective was to study the clinical outcomes in a real-world cohort of patients with NAFLD.

Methods:
In an on-going study [Indian Consortium on NAFLD (ICON-D)], interim data captured across 20 centres in India over 18 months was analyzed for hepatic/extra-hepatic events. The study had ethical approval at respective participating centers and patients were included after informed consent.

Results:
Of 4313 patients, follow up data and hepatic/extra-hepatic events were recorded in 1353 (31.3%) patients. Overall, 255 (18.8%) had follow up of 3 months, 379 (28%) 6 months, 242 (17.8%) 1 year, 408 (30.2%) 1-5 years, 65(4.08%) 5-10 years and 4 (0.2%) more than 10 years (mean follow up 43.5 months). In patients without significant fibrosis [LSM<8 Kpa, n=1114 (82.3%)], 1 (0.09%) had hepatic (jaundice) and 1 (0.09%) had extra-hepatic event (bone fracture); in significant fibrosis [LSM 8-12.5 kPa, n= 162 (12%)], 2 (1.2%) had hepatic (ascites 1, HCC 1) and one (0.6%) had extra-hepatic event (myocardial infarction); in compensated cirrhosis [LSM≥ 12.5 kPa, n=71 (5.2%)], 26 (36.7%) had hepatic events (jaundice-3, UGI bleed– 3, HCC-2, HE- 8 and ascites-10) and 8 (11.3%) had extra-hepatic events (CKD-5, MI-2, and bone fracture -1) ($p<0.0001$).

Conclusions:
In a prospective analysis of clinical outcomes in a real-world cohort of patients with NAFLD in India, patients with NASH related compensated cirrhosis had higher hepatic and extra-hepatic events on follow up in comparison to those without cirrhosis.

Q-14

Efficacy of saroglitazar in non- alcoholic fatty liver disease using real world clinically relevant non- invasive parameters

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Objectives:
Saroglitazar is a novel dual peroxisome proliferator activated receptor α/γ agonist approved in India for the treatment of Non-Cirrhotic NASH. We evaluated the efficacy of saroglitazar in non-alcoholic fatty liver disease (NAFLD) patients in real world clinical settings using clinically meaningful non-invasive parameters.

Materials and Methods:
A retrospective analysis was conducted in 58 consecutive patients with documented ultrasonographic fatty liver changes and dyslipidemia who were prescribed Saroglitazar 4 mg once day. Obese patients (BMI: 31.31 ± 5.16) having Fatty Liver with or without type 2 diabetes who received Saroglitazar 4 mg once daily for at least 6 months from April 2018 to October 2019 were retrospectively included in this data analysis. Change in APRI (AST Platelet Ratio Index), CAP (Controlled Attenuated Parameter), LSM (Liver Stiffness Measurement), AST, ALT, TG, TC, LDL, HDL, and FIB 4 from baseline to 6 month was analyzed using paired t- test. This retrospective analysis has been approved by Ethics Committee (Medical) SMC/UECM/2019/86/81.

Results:
The mean age of patients analyzed is 42.72 ±10.01 year. There was a significant reduction of APRI (44.30%), FIB- 4 (23.42%), CAP (16.24%), LSM (18.68%)., AST (38.05%), ALT (51.54%), TG (22.7%), TC (12.37%) and LDL (18.16%) at 6 month compared to baseline. There were no serious adverse events reported.

Conclusions:
Saroglitazar was found to be safe and effective in management of NAFLD patients in this analysis of 6 months follow up. It can be used as potential option for management of NAFLD/NASH.

Q-15

Empagliflozin Effect of Reducing Liver Fat in NAFLD Patients with DM type 2: A Systematic Review of a Potent Therapeutic Agent

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Objectives:
This systematic review aims to identify and summarize the potential of empagliflozin in treating Nonalcoholic fatty liver disease (NAFLD) patients with diabetes mellitus (DM) type 2 by reducing liver fat.

Materials and Methods:
Systematic review was conducted with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines. The literature search was done using five databases: PubMed, ProQuest, ScienceDirect, EBSCO, and GoogleScholar with “empagliflozin”, “NAFLD”, and “Diabetes Mellitus, Type 2” as the main keywords with no restriction on timing of published journals. Cochrane risk of bias (RoB) tool 2.0 was utilized in the quality assessment of the included studies.

Results:
Search strategy resulted in a total of 105 studies. Three relevant full-text articles met the authors inclusion criterias. Overall studies measure similar outcomes but with different parameters. Using MRI-derived proton density fat fraction (MRI-PDFF) parameter shows a significant reduction of liver fat at the end of the treatment compared to baseline for the empagliflozin group (16.2–11.3%; $P < 0.0001$). Significant result was also seen using liver fat content (LFC) parameter which is a reduction of 22% (7–36%; $P = 0.009$). Last study using volumetric liver fat fraction also shows significant reduction compared to baseline (18.6–11.6%; $P = 0.017$).

Conclusions:
Uncertainty cannot be ruled out when dealing with treatment of NAFLD since there is still no definitive treatment today. However, a big part of it can be filled in with empagliflozin since it shows potential in reducing liver fat.

Q-19

Japanese subjects have moderately higher plasma exposures of the acetyl CoA carboxylase (ACC) inhibitor firsocostat (FIR) than Caucasian subjects

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Objectives:
Firsocostat (FIR) is an oral, liver-targeted inhibitor of acetyl-CoA carboxylase (ACC) in clinical development for the treatment of nonalcoholic steatohepatitis (NASH). This study evaluated the pharmacokinetics (PK) and safety of FIR and GS-834773 (primary metabolite) in Japanese and Caucasian subjects to support the clinical development of FIR in Japan.

Materials and Methods:
A single dose of FIR (20 mg) was administered to Japanese and Caucasian healthy subjects (n=20/group). Japanese subjects were defined as born in Japan, not lived outside Japan >5 years, and able to trace Japanese ancestry of parents and grandparents. Safety assessments were performed throughout the study. Plasma concentrations of FIR and GS-834773 were determined and geometric least squares mean ratios (%GLSMR) and 90% confidence intervals were calculated for PK parameters. FIR and GS-834774 are substrates of OATP and UGT; genotyping of these transporters/enzymes was performed. This research has been approved by an ethical committee

Results:
A total of 42 subjects were enrolled in the study; 3 subjects discontinued study early. Ten subjects experienced an AE (Grade 1) and 19 subjects experienced a graded laboratory abnormality (mostly Grade 1). The distribution of OATP and UGT genotypes were as expected for the Japanese and Caucasian populations. FIR AUCinf and Cmax increased 98% and 33%, respectively. GS-834773 AUCinf and Cmax increased 105% and 26%, respectively.

Conclusions:
FIR was generally well-tolerated with no clear difference in AEs or laboratory abnormalities between Japanese and Caucasian subjects. The ~2-fold exposure difference is not considered clinically relevant and does not warrant dose adjustment.

Q-20

Lack of Clinically Meaningful Differences in Pharmacokinetics and Pharmacodynamics of the FXR agonist Cilofexor in Japanese and Caucasian Participants

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Objectives:
Cilofexor (CILO) is an oral, farsenoid X receptor (FXR) agonist in development for treatment of primary sclerosing cholangitis (PSC) and nonalcoholic steatohepatitis (NASH). CILO causes release of fibroblast growth factor 19 (FGF19), regulating hepatic metabolic homeostasis and changes in bile acids. Thus, FGF19 and bile acid intermediate 7α-hyDr.oxy-4-cholesten-3-one (C4) levels inform on its pharmacodynamic (PD) effects. The pharmacokinetics (PK), PD, and safety of CILO and its inactive metabolites (GS-716070 and GS-1056756) were evaluated in Japanese and Caucasian participants to support development in Japan.

Materials and Methods:
Healthy Japanese and Caucasian participants (N=20/group) received a single dose of CILO 100 mg. Japanese subjects were defined as born in Japan, not lived outside Japan >5 years, and able to trace Japanese ancestry of parents and grandparents. Safety was assessed throughout the study. PK parameters and changes in PD parameters (Day -1 vs Day 1) were compared between Japanese (test) vs Caucasian (reference) participants using geometric least-squares mean ratios and 90% confidence intervals. This research has been approved by an ethical committee.

Results:
39/40 participants completed the study. 5 participants (13%) had an adverse event (all Grade 1). CILO and GS-1056756 exposures (AUC) were higher (24% and 118%, respectively) with no difference in GS-716070 exposures in Japanese vs Caucasian participants. Baseline-corrected FGF19 and C4 responses to CILO were similar in both groups.

Conclusions:
CILO was well tolerated. There were no clinically meaningful differences in its PK or PD in Japanese and Caucasian participants, supporting no dose adjustment.

Q-23

New Possibilities Of Saliva Investigation For Diagnosis Of Steatohepatitis

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Objectives:
To conducted microscopy of saliva in patients with morphologically proven steatohepatitis and elevated levels of transaminases.

Materials and Methods:
80 patients with metabolic synDr.ome and characteristic
ultrasound criteria for NAFLD were included. All patients underwent a puncture biopsy of the liver, followed by histological examination. Microscopic examination of patient's saliva was performed after applying a Dr.op of an alcoholic 3% solution of copper chloride. The characteristic feature of steatohepatitis was the presence of amorphous dark yellow masses superimposed on crystals in the form of "panicles" or "bunches".

Results:
Patients were divided into 2 groups: The first group included 24 (30%) patients who had morphological signs of liver steatosis. The second group included 56 (70%) patients with characteristic morphological signs of steatohepatitis. 56 patients with steatohepatitis, 24 (42.9%) had normal level of transaminases, but the median histological activity was 5.5 [5.0; 8.0], fibrosis 1.5 [1.0; 2.0]. Microscopic examination of saliva in patients of the first group did not have characteristic amorphous dark yellow masses superimposed on saliva crystals. On the contrary, in patients with steatohepatitis amorphous dark yellow masses superimposed on saliva crystals were revealed regardless of the level of transaminases. The amount of amorphous masses differed depending on the degree of histological activity ($p < 0.05$).

Conclusions:
The presence of amorphous dark yellow masses superimposed on crystals in the form of "panicles" or "bunches" in microscopic examination of saliva indicates the presence of steatohepatitis in a patient with metabolic synDr.ome regardless of the level of transaminases.

Q-30

Safety and efficacy of combination therapies including semaglutide, cilofexor, and firsocostat in patients with NASH

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Objectives:
To evaluate safety and efficacy of semaglutide (sema), a GLP-1 receptor agonist, alone and combined with the FXR agonist cilofexor (CILO) and/or the ACC inhibitor firsocostat (FIR), in patients with NASH.

Materials and Methods:
This Ph2 trial randomized, equally, 108 non-cirrhotic patients with NASH (F2-F3 on biopsy, or MRI-PDFF ≥10% and liver stiffness by transient elastography ≥7 kPa) to sema, sema+CILO 30 mg, sema+CILO 100 mg, sema+FIR 20 mg, or sema+CILO 30 mg+FIR 20 mg for 24 weeks (W24). CILO and FIR were taken daily and sema subcutaneously weekly (dose escalated to 2.4 mg over 16 weeks). The primary endpoint was safety; exploratory endpoints included changes in liver biochemistry and MRI-PDFF. Least square mean (LSmean) changes based on post-hoc ANCOVA models adjusted for baseline (BL) value and diabetes.

Results:
At BL, median age and BMI were 54 yrs and 34 kg/m2, respectively; 55% had diabetes. All regimens were well tolerated. The most common adverse events (AEs) were gastrointestinal; 5–14% discontinued any Dr.ug due to AEs. LSmean change in LDL from BL to W24 ranged from –9 mg/dL with sema to 7 mg/dL with sema+CILO+FIR, and 23 mg/dL with sema+CILO 100 mg. At W24, greater LSmean improvements in ALT were observed with all combinations vs sema, and in MRI-PDFF with sema+FIR (-11.6%) and sema+CILO+FIR (-12.6%) vs sema alone (-8.6%) (all $p<0.05$).

Conclusions:
In patients with NASH, combinations of sema with CILO and/or FIR were well tolerated and may provide additional benefits vs sema monotherapy.

Q-31

Screening Colonoscopy and Colorectal Cancer Incidence in Patients with Non-Alcoholic Fatty Liver Disease: A Retrospective Cohort Study

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Objectives:
We aimed to estimate the risk of incident colorectal cancer (CRC) in non-alcoholic fatty liver disease (NAFLD) patients who did and did not undergo colonoscopy.

Materials and Methods:
We conducted a retrospective cohort study for patients aged over 40 years with NAFLD based on ICD9-CM codes between January 1, 2000 and December 31, 2014. The patients were followed until CRC diagnosis, death, or December 31, 2017. We estimated CRC incidence and standardised incidence ratio (SIR) using the general population of Hong Kong as reference.

Results:
We included 8,351 NAFLD patients in the final analysis [median (IQR) age 56.2 (49.2-65.3) years, 45.4% male, median (IQR) follow-up 7.4 (5.4-9.6) years]. Compared with patients who did not undergo colonoscopy, patients who underwent colonoscopy were older, less likely to be males, more likely to have type 2 diabetes, hypertension, dyslipidemia and obesity. Compared with the general population, NAFLD patients who did not undergo colonoscopy had increased incidence of CRC (SIR 1.86, 95% confidence interval [CI] 1.34–2.50), whereas NAFLD patients who underwent colonoscopy had lower incidence of CRC (SIR 0.69, 95% CI 0.50–0.92), especially among those aged ≥ 50 years. After adjusting for demographic and metabolic factors, age ≥ 50 years (HR 9.64; 95% CI 1.28-72.87), male gender (HR 2.75; 95% CI 1.13-6.67) and type 2 diabetes (HR 5.02; 95% CI 1.15-21.90) were associated with a higher risk of CRC.

Conclusions:
NAFLD patients who underwent colonoscopy had a lower incidence of CRC than the general population, especially among those aged ≥ 50 years.

Q-32

Semaglutide Treatment in Subjects with Nafld: Effects Assessed by Magnetic Resonance Elastography and Magnetic Resonance Imaging Proton Density Fat Fraction

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Objectives:
To investigate the effect of semaglutide on non-alcoholic fatty liver disease (NAFLD) using magnetic resonance imaging (MRI) and biomarkers.

Materials and Methods:
Sixty-seven subjects with NAFLD (MRI proton density fat fraction [MRI-PDFF] ≥10%) and increased liver stiffness (magnetic resonance elastography [MRE] 2.50–4.63 kPa) were randomised to subcutaneous semaglutide 0.4 mg/day or placebo for 72 weeks. MRE and MRI-PDFF were assessed after 24, 48 and 72 weeks.

Results:
No difference in MRE values were observed with semaglutide and placebo at week 48 (primary endpoint; estimated treatment ratio [ETR]: 0.96; 95% CI 0.89–1.03; p=0.2798) or week 24 and 72. Fewer subjects had a ≥15% increase in MRE with semaglutide vs placebo at week 72 (1 vs 8, respectively). MRI-PDFF was significantly reduced with semaglutide vs placebo at week 48 (ETR 0.47; 95% CI 0.36–0.60; p<0.0001), which was maintained to week 72. Over 70% of subjects had a ≥30% reduction in liver fat with semaglutide. At each time point, total liver volume, liver fat volume, and visceral and subcutaneous abdominal fat volumes decreased with semaglutide vs placebo (all p<0.0001). FibroScan® results were consistent with MR findings. Semaglutide vs placebo significantly reduced bodyweight (p<0.0001), HbA1c (p<0.0001; subjects with T2D) and liver enzymes (p<0.05). Inflammatory biomarkers decreased with semaglutide treatment. There were no safety concerns.

Conclusions:
Semaglutide significantly reduced liver fat, which together with other findings, suggests a positive impact on NAFLD. No apparent improvement in liver stiffness was observed with semaglutide, although fewer subjects had substantial MRE increases.

Q-33

Significant Liver Fibrosis is Associated with Increased Risk of Advanced Adenoma in Average-Risk Population with Metabolic Associated Fatty Liver Disease

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Background:
Metabolic associated fatty liver disease (MAFLD) shares similar risk factors with colorectal neoplasia. This prospective study was conducted to evaluate the relationship between MAFLD and colorectal neoplasia.

Methods:
We invited patients aged ≥50 years who underwent colonoscopy for colorectal cancer screening during 2018-2020 to determine the presence of steatosis and fibrosis with transient elastography. Logistic regression models were used to calculate the odds ratio (OD) for the effect of steatosis and fibrosis on colorectal neoplasia after adjusting for confounders (age, gender, smoking, and metabolic parameters).

Results:
956 participants (mean age 62.0±7.1 years, 33.3% male) were enrolled. Adenomatous polyps were observed in 412 (43%), 66 of them had advanced adenoma, and 3 were diagnosed with colorectal cancers. 480 (50.2%) participants had steatosis (controlled attenuation parameter ≥248 dB/m), with 279 (29.5%) presenting with severe steatosis (≥280 dB/m) and 45 (4.7%) having significant fibrosis (liver stiffness ≥7.9 kPa). The presence of steatosis was not associated with the detection of adenomatous polyps (OD=1.26, 95% CI, 0.94-1.70) and advanced adenoma (OD=1.26, 95% CI, 0.72-2.20). MAFLD patients with significant fibrosis did not have a higher detection rate of adenomatous polyps (OD=1.61, 95% CI, 0.85-3.04) but had an increased incidence of advanced adenoma (OD=2.61, 95% CI, 1.11-6.12) after adjusting for all confounders.

Conclusions:
Among the average-risk population, steatosis was not associated with adenomatous polyp detection, but advanced adenoma was higher in those with MAFLD and significant fibrosis. Thus, liver fibrosis assessment may add some value in predicting advanced adenoma in MALFD individuals during colon cancer screening.

Q-35

The plasma and liver triglyceride subclass of nonalcoholic steatohepatitis and fibrosis in morbidly obese patients

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Objectives:
The prevalence rate of nonalcoholic steatohepatitis (NASH) has been reported in 50% to 70% of morbidly obese patients. This study aims to use lipidomic analysis to investigate triglyceride (TG) subclass between healthy obesity (HO) and NASH with advanced liver fibrosis in morbidly obese patients.

Materials and Methods:
Lipidomics was performed using ultra-high-performance liquid chromatography–tandem mass spectrometry on plasma and liver samples from a prospective cohort study involved morbidly obese patients who underwent bariatric surgery at Taipei Medical University Hospital. Wedge liver biopsy was performed during surgery, and advanced liver fibrosis was defined as a fibrosis score 3. We selected HO (n=8) and NASH with advanced liver fibrosis (n=8) patients.

Results:
94 and 64 TG species were identified in plasma and liver, respectively. In plasma, the fold changes of TG (50:1), (52:2), (54:3), and (54:4) were significant higher and TG (55:2) was significant lower in the NASH with advanced liver fibrosis than HO group ($p < 0.05$). In liver, the fold changes of TG (48:3), (50:3), (50:4), and (54:2) were significant higher in the NASH with advanced liver fibrosis than HO group ($p < 0.05$). Furthermore, these TG species in plasma and liver had several highly positive correlation with parameters related to hepatic steatosis and fibrosis and liver functions, especially TG (50:1).

Conclusions:
TG subclass were associated with NASH and liver fibrosis. Among the TG species in plasma and liver, TG (50:1) may be proposed as a lipid metabolite to predict NASH with liver fibrosis in morbidly obese patients.

Q-36

Triple combination therapy of GLP-1 receptor agonist semaglutide with an FXR agonist and ACC inhibitor reverses non-alcoholic steatohepatitis (NASH) in diet-induced and biopsy-confirmed mice

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Objectives:
Semaglutide (SEMA), FXR agonists and ACC inhibitors are under clinical investigation for the treatment of NASH, however, the effects of combining these agents are unknown. We hypothesize that combination treatments are needed to reduce NAFLD activity score (NAS) and fibrosis stage.

Material and methods:
SEMA (0.12mg/kg, s.c.), FXR agonist (cilofexor, CILO; 30mg/kg, p.o.) and/or an ACC inhibitor (firsocostat-analog GS-834356, ACCi; 5mg/kg, p.o.) were administered daily to AMLN diet-induced and biopsy-confirmed DIO-NASH mice (n=15-16/group) for 12 weeks.

Results:
Liver triglycerides were reduced by SEMA (38% vs. vehicle). Addition of CILO, ACCi or both to SEMA reduced liver lipids by 64%, 73% and 81%, respectively. NAS was reduced in 19% of controls and in all SEMA or triple therapy-treated. Further, the number of mice exhibiting 3+ point improvement in NAS was higher with the triple combination (75%) vs. SEMA (13%). Likewise, triple therapy resulted in the greatest improvements in fibrosis (44% improved, 6% worsened), followed by the SEMA group (38% improved, 0 worsened) relative to vehicle (13% improved, 44% worsened). Collagen-1a and a-SMA (% area) were improved with SEMA (4.2%, and 1.4%) and triple therapy (3.9% and 0.9%) vs. vehicle (6.3% and 4.6%). Transcriptomic analyses revealed changes in gene expression related to inflammation, fibrosis, and metabolism were more pronounced in combination groups compared to monotherapy.

Conclusions:
SEMA improved NAS and fibrosis. Addition of ACCi or CILO, further reduced liver steatosis, and triple therapy had the strongest effect on NAS and fibrosis in DIO-NASH mice, supporting development of combination approaches for NASH.

Q-37

Diagnosis of Nonalcoholic Steatohepatitis with Mr-based Nonalcoholic Steatohepatitis Score

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Objectives:
As about 30% of the general population worldwide has nonalcoholic fatty liver disease (NAFLD), it is important to find a non-invasive biomarker for diagnosing nonalcoholic fatty hepatitis (NASH). This study is cross-sectional and designed to develop a scoring system for NASH diagnosis through multiple parametric magnetic resonance (MR) and clinical indicators.

Materials and Methods:
MR parameters, laboratory tests and clinical history of patients with NAFLD were assessed. Logistic regression model was used to develop a scoring system. In total, one hunDr.ed thirty patients were enrolled (sixty with nonalcoholic fatty liver disease [NAFLD] and seventeen with NASH). After assessing twenty-three clinical characteristics of the patients (four categorical and nineteen numeric variables) for the NASH diagnostic model, an equation was obtained using four demographic factors, two laboratory variables, and two MR parameters for MR-based NASH score.

Results:
For NASH diagnosis, the MR-based NASH score showed a satisfactory accuracy (c-statistics, 0.892; 95% CI, 0.834-0.950). At a cut-off MR-based NASH score of 0.73 for NASH diagnosis, its sensitivity was 0.67 and specificity was 0.90. When an MR-based NASH score of 0.37 was used as a cut-off for NASH exclusion, the sensitivity was 0.90 and specificity was 0.78. Only 17% (22/130) of patients were in the gray zone (between 0.37 and 0.73). Internal validation via bootstrapping also showed satisfactory accuracy for NASH diagnosis (c-statistics, 0.909; 95% CI, 0.855-0.964).

Conclusions:
For diagnosis of NASH in patients with NAFLD, MR-based NASH score is a novel non-invasive biomarker.

Q-38

Serum Mirna as a Useful Diagnostic Biomarker for Non-alcoholic Steatohepatitis and a Predictor for Disease Progression in Patients with Non-alcoholic Fatty Liver Disease

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Objectives:
Non-alcoholic steatohepatitis (NASH) is a subtype of non-alcoholic fatty liver disease (NAFLD). We evaluated the diagnostic value of serum miRNAs for differentiating steatosis simple (SS) from NASH.

Materials and Methods:
RNA extraction and small RNA sequencing were done using sera from twenty-four biopsy proven NAFLD patients. miRNA expression levels were compared between twelve SS and twelve NASH patients. Highly expressed miRNAs in NASH group compared to SS group were selected. miEAA database was used for assessing the functional relationship between miRNAs and specific signaling pathways significantly elevated in the serum of NASH patients.

Results:
miRDeep2 Quantifier module was used to obtain a total of 2,588 mature miRNA reads. Twenty-six miRNAs were significantly highly expressed in NASH group than in SS group, however, welve miRNAs showed lower expression compared to the SS group. Total thirty-eight miRNAs showed significance and eight miRNAs which showed higher expression within the top 25% of all miRNA were selected and analyzed. Four miRNAs showed a significant area under the receiver operating characteristic (AUROC) value for NASH diagnosis ($P<0.05$). There was no significant difference when AUROC values NASH diagnosis between eight miRNA combinations (AUROC: 0.924; 95% CI: 0.739-0.992) and four miRNA combinations (AUROC: 0.875; 95% CI: 0.676-0.973). In Twenty-six miRNAs which showed higher expression levels in NASH group, seventeen miRNA groups included ten meaningful miRNAs, such as adipocytokine and thyroid hormone signaling pathways.

Conclusions:
Serum circulating miRNA combination could be a novel diagnostic tool for NASH and its expression has related with specific signaling pathways.

Q-39

The Proportions and Functions of CD4-CD8- Double Negative T Cells during Non-alcoholic Fatty Liver Disease Development

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Hepatic inflammation is the Dr.iving force for the progression of non-alcoholic fatty liver disease (NAFLD). Double negative T cells (DNT), which are characterized as CD3+CD4-CD8-NK1.1-, play critical roles in regulating inflammation. However, the roles of DNT in NAFLD are still unknown.

In this study, C57BL/6 mice consumed methionine-choline deficient diet (MCD) for 4 weeks, and the proportions and immunoregulatory molecules of intrahepatic DNT cells were determined. Then, the intrahepatic DNT in NCD- or MCD-fed mice were compared in transcriptome sequencing. Meanwhile, we also adoptively transferred intrahepatic CD45.1+ DNT to mice with NAFLD, the progression of NAFLD were evaluated.

The proportion of intrahepatic DNT cells increased in NAFLD. RNA sequencing showed that chemokine receptor expression increased, indicating that DNT proportion may be associated with chemotaxis. Prf1, GZMB, Fasl expression decreased, while IL-17A expression increased, indicating that intrahepatic DNT cells were divided into two subsets (pro-inflammatory and anti-inflammatory) with distinct functional properties. Flow cytometry showed the expression of Prf1 and GZMB which were mainly secreted by TCRαβ+ DNT cells decreased and the expression of IL-17A which was mainly secreted by TCRγδ+ DNT cells increased in NAFLD. The adoptive transfer of TCRαβ+ DNT rather than TCRγδ+ DNT cells could alleviate MCD-induced inflammation, increase liver CD4, CD8 T cells apoptosis and CD8 Treg cells proportions.

Our data reveal two subsets of intrahepatic DNT cells in NAFLD: TCRγδ+ DNT cells which induced liver inflammation with upregulating IL-17A secretion and TCRαβ+ DNT cells which could prevent NAFLD development with high expression of perforin/granzyme B.

Q-41

Validation Model of FIB-8 Score to Predict Significant Fibrosis Among Patients with Non-alcoholic Fatty Liver Disease

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Objectives:
Identifying hepatic fibrosis is crucial for non-alcoholic fatty liver disease (NAFLD) management. Fibrosis 8 score (FIB-8) recently developed by incorporating four addition variables into fibrosis 4 score (FIB-4) showed better performance in prediction of significant fibrosis in NAFLD. We aimed to validate FIB-8 in biopsy-proven NAFLD cohort and compare diagnostic performance of FIB-8, FIB-4 and NFS for predicting significant fibrosis.

Materials and Methods:
We collected data of biopsy-proven NAFLD patients from 2 Asian centers. All patients with available variables for FIB-4 (age, platelet, aspartate and alanine aminotransferase), and FIB-8 (additional 4 parameters: body mass index, albumin to globulin ratio, gamma-glutamyl transferase, and presence of diabetes mellitus) were included. Fibrosis stage was scored using NASH CRN criteria and significant fibrosis was defined as at least fibrosis stage 2.

Results:
A total of 690 patients with biopsy-proven NAFLD were included. 55.4% were female, with mean age 47.7+13.1 years. Mean BMI was 32.8+10.5 kg/m2 and 50.7% had diabetes. 274 patients (39.7%) had significant fibrosis. The AUROC of FIB-8, FIB-4, and NFS for predicting significant fibrosis were 0.7361, 0.7199, and 0.6015, $p<0.016$ respectively. Both FIB-8 and FIB-4 had significant better performance for predicting significant fibrosis compared to NFS (FIB-8 vs NFS, $p=0.004$ and FIB-4 vs NFS, $p=0.001$). However, FIB-8 and FIB-4 had no significant difference in performance for predicting significant fibrosis (FIB-8 vs FIB-4, $p=0.924$).

Conclusions:
We demonstrated that FIB-8 had better performance for predicting significant fibrosis in NAFLD patients compared to NFS, but FIB-8 was not superior to FIB-4.

Q-43

Development and validation of a robust predictor for the carcinogenesis potential of non-alcoholic steatohepatitis patients: NASH-related Carcinogenesis Score (The NASH-C Score)

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Objectives:
Hepatocarcinoma is one of the most lethal cancers. NASH has been proved a strong relationship with HCC. Our study aims to establish and validate a novel predictor system to estimate the tumorigenesis potential and the prognosis of NASH patients.

Materials and Methods:
Our study established and validated a robust model to predict NASH patients' prognosis. Clinical and RNA-Seq data that came from TCGA, ICGC, and GEO were explored. An Optimal Subset-LASSO Cox regression model and GDSC Dr.ug prediction were used to choose prognostic genes and potential Dr.ugs, respectively.

Results:
We establish a 6-mRNA robust model which can distinguish high-risk patients from low-risk patients with different prognosis by using the Optimal Subset-LASSO Cox regression algorithm. The AUC of the Kaplan-Meier curve in 1 year, 3 years, and 5 years are all higher than 0.7. GO Enrichment showed several non-fat metabolism pathways are significantly associated with high NASH-C score, which means the tumorigenesis not only works in a metabolic way. The potential Dr.ugs are shown in the GDSC Dr.ug-sensitive prediction.

Conclusions:
NASH-C Score can evaluate the tumorigenesis ability and prognosis of NASH. According to the pathway enrichment results and GDSC Dr.ug-sensitive predictions, new therapeutic targets or Dr.ugs will be discovered and developed.

Other Viral Hepatitis

R-03

Clinical characteristics and risk factors of liver injury in COVID-19: a retrospective cohort study from Wuhan, China

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Background:
Coronavirus Disease 2019(COVID-19) has rapidly become a major international public health concern. This study was designed to evaluate the clinical characteristics and risk factors of COVID-19 associated liver injury.

Methods:
A fraction of 657 COVID-19 patients were retrospectively analyzed. Clinical and laboratory data were derived from electronic medical records and compared between patients with or without liver injury. Multivariate logistic regression method was used to analyze the risk factors for liver injury.

Results:
Among 657 patients, 303 (46.1%) patients had liver injury with higher rate in severe/critically ill patients (148/257 (57.6%)) than those in moderate cases (155/400 (38.8%)). The incidence of liver injury was much higher in male(192/303 (63.4%)) than female (111/303 (36.6%)), and in severe/critical patients(148/303 (48.8%)) with percutaneous oxygen saturation≤93% (89/279 (31.9%)) or peak body temperature≥38.5˚C(185/301 (61.5%)) on admission. Liver injury related inflammations included increased white blood cells, neutrophils and decreased lymphocytes. More patients with liver injury than without had increased serum IL-2R, TNFα, ferritin, hsCRP, PCT, ESR, γ-GT, and LDH. Multivariate regression analysis revealed that increasing odds of liver injury was related to male, higher serum hsCRP(≥10mg/L), and neutrophil to lymphocyte ratio (NLR) (≥5). Moreover, more deceased patients (14/82 (17%)) had significantly elevated serum TBIL than discharged patients (25/532 (4.7%)).

Conclusions:
Liver injury is a common complication in COVID-19 patients. The potential risk factors of liver injury include male, hsCRP and NLR score. A close monitor of liver function should be warned in COVID-19 patients, especially in severe/critical individuals.

R-04

Clinical Prof.ile and factors influencing mortality of patients diagnosed with acute Hepatitis E in a tertiary center in South India

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Objectives:
To explore the clinical and epidemiological Prof.ile of patients with hepatitis E virus (HEV) who were admitted to a tertiary care hospital in Chennai, India and to further assess various factors that influence the prognosis.

Materials & Methods:
Hospital records of patients who presented with features of acute hepatitis taking into consideration inclusion and exclusion criteria was taken from medical records from 2018-2020. History and clinical examination including presence of signs of organ failure was obtained. Investigations collected included routine parameters with viral markers for HBV, HAV, HCV, HEV. Outcomes be recorded in the form of discharge or death.

Results:
43 patients were analysed. Males had higher (81.39% n=35) incidence of HEV infection. Yellowish discoloration of urine was the most common symptom (n=19, 44.19%) and icterus was the most common sign at presentation (n=28, 65.11%). Hepatomegaly was the most common finding on abdominal examination (n=10, 22.72%). Overall, mortality observed was 13.90% (n=6). Higher mean INR (2.08 vs 1.41), total bilirubin (11.94 vs 11.01 mg/dL), were associated with higher mortality, whereas lower mean serum albumin (2.86 vs 3.06 gm/dL) was associated with higher mortality. Increase in renal parameters (ie,BUN [44.17 vs 14.46 mg/dL] and creatinine [1.98 vs 1.08 mg/dL]) and electrolyte imbalances (ie, hyponatremia [128.5 vs 132mmol/L]) were associated with higher mortality.

Conclusions:
Higher mean age, PT-INR, total bilirubin,blood urea, serum creatinine, lower mean serum albumin, and sodium values were associated with higher mortality along with co-morbidities especially chronic liver disease which can result in ACLF cause higher mortality.

R-12

Incidence and characteristic of Dengue hemorrhagic fever with severe hepatitis

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Objectives:
This study was aimed to evaluate the incidence and pattern of DHF with severe hepatitis.

Material and Methods:
This is a retrospective cohort study at Siriraj Hospital, Mahidol University, Bangkok, Thailand from January 1, 2015, to December 31, 2019. Patients of all ages were included if they were diagnosed DHF based on lab tests and had severe hepatitis. Patients were excluded if there were other causes of hepatitis or had no follow-up on liver enzymes after discharge.

Results:
There were 1,912 patients diagnosed with DHF. Nineteen patients had severe hepatitis. The mean age was 31.9 years old with 8 males and 11 females. All patients had a high-grade fever from 1 to 6 days. Most did not have any underlying disease (two had Thalassemia and one was pregnant). Ten patients were admitted. Seventeen patients had AST/ALT peaked around 3 days after diagnosis without clinical jaundice. Those who developed jaundice had total bilirubin peaks of 14.9 and 24.2 mg/dL. All patients had higher AST than ALT. Both liver enzymes returned to pretreatment levels after 7-39 days along with the normalization of platelet count and clinical symptoms. Only 1 patient who had DSS developed DIC, multi-organ failure, and died.

Conclusions:
Incidence of severe hepatitis, defined as AST/ALT > 300 IU/mL was 0.94% and usually occurred at the time of presentation. Most patients with hepatitis did not associate with Dengue shock synDr.ome and were asymptomatic. AST was higher than ALT and both returned to normal within 2 weeks.

R-13

Inhibitory effects of zinc chloride on hepatitis A virus replication through the cytokines in hepatocytes

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Objectives:
Hepatitis A virus (HAV) infection is still one of the major causes of acute hepatitis worldwide. Patients with acute hepatitis A have higher fever, indicating that interferon and cytokines play a role in the pathogenesis. We examined the effects of zinc chloride (ZnCl2) on HAV replication and the mechanism in hepatocytes.

Materials and Methods:
1) Human hematoma Huh7 cells were infected with HAV genotype IIIA HA11-1299.
2) After 3 cell passage with or without ZnCl2/interferon α-2a (IFN), HAV RNA were measured by RT-PCR assay. 3) We examined the 84 inflammasome-associated gene expression in HAV-infected Huh7 cells treated with or without ZnCl2. 4) We also compared the 84 toll-like receptor-associated gene expression between in Huh7 or PLC/PRF/5 cells treated with and those without 5 µM ZnCl2. 5) $P<0.05$ was considered as a statistically significant difference.

Results:
1) After 3 cell passage with ZnCl2/IFN, HAV RNA disappeared. 2) In HAV-infected Huh7 treated with ZnCl2, BIRC3, IL1B, PSTPIP1, PTGS2, PYCARD and TNF significantly decreased (4.34, 2.08, 4.22, 4.16, 2.10 and 3.95, respectively), and MAPK12 2.47-fold increased significantly, compared with HAV-infected Huh7 treated without ZnCl2. 3) Treatment with ZnCl2 could result in the reduction of MAP2K3 expression in both Huh7 and PLC/PRF/5 cells.

Conclusions:
ZnCl2 downregulates MAP2K3 expression, upstream of p38 MAPK which has shown to be involved in viral replication. ZnCl2 inhibits the production of several inflammatory cytokines and could suppress HAV replication.

R-18

SARS-cov2 infection and liver dysfunction

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Objectives:
Novel viral infection of SARS-cov2 is spreading worldwide and many mortal case have been seen. The aim of this study is to clarify the relation between SARS-cov2 infection and liver dysfunction.

Materials and Methods:
In April 2020, patients suspicious of covid 19 were consulted to our department. Liver function of these patients were collected. The extent of liver function was compared between patients with or without SARS-cov2 infection. Serum ALT levels were compared between two groups using student t-test. SARS-cov2 infection was confirmed with PCR.

Results:
Sixty-eight patients were consulted to our department within a month. Forty-one patients were positive for SARS-cov2. Sixteen out of 41 (39%) SARS-cov2 positive patients showed liver dysfunction (ALT>40), 2 out of 27 (7%) SARS-cov2 negative patients showed liver dysfunction. Mean±STDV of ALT level was 53.1±66.6 in viral positive patients and 19.7±14.3 in viral negative patients (p=0.013).

Conclusions:
Liver dysfunction was seen higher rate in SARS-cov2 positive patients than in negative patients. We need to scrutiny the status of Dr.ug taking and blood pressure deterioration to clarify the impact of this virus on liver dysfunction.

R-19

Screening for inhibitors of hepatitis A virus internal ribosomal entry site and HAV replication

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Objectives:
Hepatitis A virus (HAV) infection is still one of the major health concerns and causes acute hepatitis and acute liver failure, resulting in death or liver transplantation. HAV vaccine is available but expensive. Therefore, the development of anti-HAV Dr.ugs is important. Translation of HAV genomes is cap-independent mechanism, that is, internal ribosomal entry site (IRES) dependent translation. Our aim is to perform the screening of the Dr.ugs which inhibit HAV IRES activity and HAV replication.

Materials and Methods:
Stable cell lines COS7-HAV-IRES were incubated with 1,158 various types of Dr.ugs, which included 179 anti-diabetic mellitus Dr.ugs, 326 anti-virus Dr.ugs, 313 anti-cancer approved Dr.ugs and 340 stem cell differentiation compounds (TargetMol, Wellesley Hills, MA, USA). After 24 hours, HAV IRES activities were measured by luciferase assay. Cell viabilities were evaluated with MTS assay. The effects of promising Dr.ug candidates on HAV genotype IIIA HA11-1299 replication were also examined in human hepatocytes.

Results:
We screened 77 Dr.ugs which inhibit HAV IRES activity as follows: 13 anti-diabetic mellitus Dr.ugs, 21 anti-virus Dr.ugs, 23 anti-cancer approved Dr.ugs and 20 stem cell differentiation compounds. It is possible that 10 Dr.ugs could inhibit HAV replication among them. Further studies are now going on.

Conclusions:
Screening for inhibitors of HAV IRES and HAV replication were performed. 10 promising Dr.ug candidates were found, and these may be useful for treatment of HAV infection.

Pediatric Hepatology

S-01

A Thai Girl Fever with Hepatosplenomegaly and Liver Cyst

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Case Report:
A 4-year-old boy presented with fever 4 days, malaise, and mild abdominal pain poor appetite. Physical examination revealed mild hepatosplenomegaly. Laboratory investigation showed eosinophilia (17,000 white blood cells/µl, absolute eosinophil count 1585 cells/µl). Abdominal ultrasound showed liver 4-cm cyst at segment VII was found. He immediately started antimicrobial therapy. Lack of response to the empirical antimicrobial medication, and the imaging findings were indicative for hydatid cyst, so albendazole (20 mg/kg) was added.

The diagnosis of hydatiform cyst was confirmed with enzyme-linked immunosorbent assay (ELISA) detection of IgG antibodies against E. granulosus antigens (titer 1/4000).

Reevaluation of our patient 1 month after with albendazole follow up by ultrasound revealed 3 more cysts each 4-5 cm at Segment VII, VIII and this patient was underwent percutaneous aspiration cyst by PAIR procedure(Percutaneous aspiration injection and reaspiration) injection with absolute alcohol (scolicidal agent)and follow up cyst was subsided to 1 cyst 0.6 cm of size and continue 1 month with albendazole

Conclusion:
In children, the most involved organ was lung and liver. Surgical therapy in hydatid disease is indicated for large cysts with multiple daughter cysts, a risk of rupture, complicated cysts such as those accompanied by infection, compression or obstruction. However, surgical therapy carries high risk of mortality, morbidity or recurrence. Therefore, medical therapy may be an alternative option in uncomplicated cysts and in patients at high risk from surgery. The PAIR procedure and chemotherapy with albendazole was higher success rate of treatment than surgery and also be recommended for some patients.

S-07

Prevalence And Long-Term Outcome Of De Novo Hepatitis B Infection In Pediatric Liver Transplant Recipients

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Objectives:
We aim to study the prevalence and long-term outcome of De novo hepatitis B infection (DHB) in pediatric liver transplant (LT) recipients.

Methods:
Medical records of pediatric LT recipients at Ramathibodi Hospital between 2001-2019 were reviewed with regards to demographics, liver chemistries and histopathology, hepatitis B-related serology of donor and recipient, prophylaxis, and treatment for DHB. Patients who survived < 12 months after LT were excluded.

Results:
We reviewed 150 pediatric LT recipients with the median age at LT of 1.6 years (IQR 1.2, 2.8). We found seven cases (4.7%) with DHB at the median time of 6 years post LT (IQR 2.6, 8.8). Three cases received allograft from anti-HBc-positive donors, three with unknown donor's serology, and one with anti-HBc-negative donor. Overall, twenty cases (13.3%) received anti-HBc-positive allografts; three of them did not receive prophylaxis. The rates of DHB in patients received anti-HBc-positive allografts with and without prophylaxis were 5.8% (1/17) and 66.7% (2/3) (P=.046), respectively. At DHB diagnosis, 2/7 chilDr.en had F2 (METAVIR) on liver biopsy. At the median follow up time of 6.3 years after DHB diagnosis, all patients had viral suppression (HBV DNA < log2) and 29% (2/7) achieved HBsAg loss. There was no HBV-related mortality.

Conclusion:
Rate of DHB can be decreased with the use of prophylactic treatment in recipients who received anti-HBc-positive allografts. Pediatric LT recipients with DHB have good long-term outcome. However, allograft fibrosis should be monitored.

S-08

Low Psoas Muscle Index As An Unfavorable Factor In ChilDr.en With End-Stage Liver Disease Undergoing Liver Transplantation

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Background and Objectives:
Sarcopenia is common in cirrhotic adults and associated with waitlist mortality and worse outcome after liver transplantation. Psoas muscle mass has been used to define sarcopenia. Therefore, we aimed to determine the association between psoas muscle mass and waitlist mortality as well as post-transplant outcome in chilDr.en with end-stage liver disease.

Methods:
Medical records and abdominal imaging of pediatric liver transplant candidates during 2010 - 2019 were reviewed. A subset of images was measured by two radiologists to determine inter-rater reliability. Psoas muscle surface area was determined at intervertebral lumbar disc 3-4 (L3-4) and 4-5 (L4-5) levels. Psoas muscle index (PMI) was calculated by psoas muscle surface area divided by height squared.

Results:
We included 105 chilDr.en, most with biliary atresia (84%). Patients with waitlist mortality had lower PMI compared to the ones who survived to transplantation (PMI at L3-4 levels 352.8 ± 162.5 vs. 416.8 ± 136.2 mm2/m2 and at L4-5 levels 497.3 ± 167.8 vs. 571.4 ± 163.4 mm2/m2, both p=.04), but not in the multivariate analyses. For transplanted patients (n=75), a higher rate of re-operation (39 % vs. 15 %, p=.03) and longer hospital stay (53 vs. 45 days, p=.02) were found in patients with lower PMI.

Conclusions:
Lower PMI is associated with higher re-operation rate and longer hospital stay following transplantation, but not waitlist mortality. PMI may be taken into consideration with other biomarkers to predict post-transplant complications.

Portal Hypertension and Other Complications of Cirrhosis

T-02

A Comparative Study on the Diagnostic Accuracy of Non-Invasive Scoring Tests in detecting Esophageal Varices in patients with Liver Cirrhosis – A Retrospective Study

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Objectives:
Esophageal varices (EV) are the most common complication of portal hypertension secondary to liver cirrhosis and may cause life threatening complications. The current gold standard for diagnosis is esophagogastroduodenoscopy. Several readily available noninvasive scoring tests have been developed for the diagnosis of liver fibrosis, namely: APRI,FIB-4,AAR and LOK Index. The goal of this study is to evaluate the diagnostic accuracy of these non-invasive scoring tests in predicting presence of esophageal varices.

Materials and Methods:
All patients with liver cirrhosis who underwent surveillance video gastroscopy in Cardinal Santos Medical Center from January 2016 to January 2020 with complete demographic, endoscopic, clinical and laboratory data were included in this retrospective study. Areas under the curve (AUC) were calculated and the corresponding diagnostic accuracy parameters were obtained.

Results:
A total of 192 cirrhotic patients with complete data were included in this study. Sixty-eight and eight tenths (68%) were males with mean age of 62 years old. The most common etiology of cirrhosis was secondary to viral hepatitis (37%). All non-invasive scoring test ranges were of significant difference. The area under the curve calculated for these non-invasive scoring tests: APRI,AAR,FIB-4 and LOK Index, to predict the presence of EV were 0.573, 0.409, 0.554 and 0.481 respectively.

Conclusions:
APRI,AAR,FIB-4 and LOK Index had average diagnostic accuracy of predicting EV in liver cirrhosis. The most reliable non-invasive scoring test was APRI having the largest area under the curve. Although its utility as a diagnostic tool is still subpar when compared to the gold standard, esophagogastroduodenoscopy.

T-03

A status survey of albumin infusion and its relationship with prognosis in cirrhotic patients with ascites in China

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Objectives:
There is limited evidence of long-term albumin treatment in cirrhotic patients with ascites in China. Therefore, this study aims to analyze the impact of current albumin treatment on patients' prognosis in order to update clinical practice of albumin treatment in China.

Materials and Methods:
Cirrhotic patients with ascites treated with albumin infusion at Beijing Friendship Hospital (Beijing, China) from 1 January 2014 to 31 December 2019 were enrolled. Decompensated events and clinical data were retrospectively collected from hospital medical records. All patients were observed until the end of the study, liver transplantation or death. Linear regression analysis was used to identify the effects of albumin infusion to serum albumin concentration. Cox proportional hazard models were used to identify the effects of albumin infusion to survival.

Results:
A total of 205 patients were included in this study. The way of albumin infusion was intermittent mainly for once or twice, median treatment duration was 6 days. The initiation of albumin infusion was associated with the occurrence of cirrhotic complications (mainly due to ascites). The changes of serum albumin concentration before and after treatment were positively correlated with the amounts of albumin infusion ($r=0.649$, $P<0.001$), which was more obvious in patients with lower baseline albumin concentration ($P=0.001$). However, the current albumin treatment had no significant effect on patients' survival ($P>0.05$).

Conclusions:
The intermittent infusion of albumin is unsatisfied in improving the survival of cirrhotic patients with ascites, which indicated for further explored study of albumin in China.

T-05

Liver Biochemical Abnormality and In-hospital Outcome in COVID-19 Patients with Liver Cirrhosis

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Background:
Coronavirus disease (COVID-19) is a great threat for global public health. COVID-19 patients frequently develop liver biochemical abnormality, which is associated with poor outcomes. However, liver biochemical abnormality in COVID-19 patients with liver cirrhosis is under-recognized.

Methods:
All of 17 COVID-19 patients with liver cirrhosis consecutively admitted to the Wuhan Huoshenshan Hospital from February 2020 to April 2020 were included. Meanwhile, 17 age-, sex-, and severity-matched COVID-19 patients without liver cirrhosis admitted to this hospital during the same period were selected as a control group. Additionally, all of 14 cirrhotic patients without COVID-19 consecutively admitted to the Department of Gastroenterology of the General Hospital of Northern Theater Command during the same period were selected as another control group. Incidence of liver biochemical abnormality was compared among the three groups.

Results:
Among the COVID-19 patients with liver cirrhosis, the incidence of liver biochemical abnormality at admission and during hospitalization were 76.50% and 84.60%, respectively; 7 (41.20%) had decompensated events at admission; 1 was transferred to intensive care unit due to gastrointestinal bleeding; and all were cured. Among the COVID-19 patients without liver cirrhosis, the incidence of liver biochemical abnormality at admission and during hospitalization were 58.80% (P=0.271) and 60.00% (P=0.150), respectively; and none died. Among the cirrhotic patients without COVID-19, the incidence of liver biochemical abnormality at admission and during hospitalization were 69.20% (P=0.657) and 81.80% (P=0.855), respectively; 11 (78.60%) had decompensated events at admission; and none died.

Conclusions:
Liver biochemical abnormality is common in COVID-19 patients with liver cirrhosis.

T-06

Adherence to Non-Selective Beta Blockers in Cirrhotic Patients with Esophageal Varices

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Background and Aims:
Long-term use of non-selective beta blockers (NSBBs) is essential for preventing esophageal variceal bleeding in liver cirrhosis, which may impair the patient adherence. The aim of the present study was to investigate the adherence to NSBBs in cirrhotic patients with esophageal varices.

Methods:
All patients who had an indication of NSBBs for prophylaxis of variceal bleeding were screened between February 2018 and June 2019. Clinical pharmacists gave pre-medication education and recorded the adherence to NSBBs during the patients' hospitalizations. Factors associated with poor adherence were evaluated by univariate logistic regression analysis. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. The relationship between poor adherence and variceal bleeding during follow up was also evaluated.

Results:
Overall, 108 patients were included, of whom 12 were intolerant to NSBBs. Among the 96 remaining patients who could take NSBBs, the average change of heart rate before and after medication was -10.49 b.p.m (95%CI: -8.88 to -12.11, P<0.001) Twenty-two (22.9%) patients had poor adherence to NSBBs due to their refusal to take NSBBs (n=2), complete forgetfulness of NSBBs (n=11), and refusal or forgetfulness to monitor heart rate (n=9). Univariate logistic regression analysis demonstrated that only older age was significantly associated with poor adherence (OR: 1.065, 95%CI: 1.019-1.114, P=0.005). Patients with poor adherence were more likely to develop variceal bleeding during follow up.

Conclusions:
A significant proportion of cirrhotic patients with esophageal varices had poor adherence to NSBBs during their hospitalizations. Further studies should explore how to improve the patient adherence.

T-07

Anticoagulant Therapy for Cirrhosis-related Portal Vein Thrombosis: A Meta-Analysis

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Objectives:
Portal Vein Thrombosis (PVT) remains a devastating complication in liver cirrhosis (LC) patients. It is associated with poor outcome and high short-term mortality rates, as it may enhance the risk of bleeding aside from the already established mechanism; portal hypertension. Treating cirrhosis-related PVT with anticoagulants is difficult because of the patient's nature of coagulopathy-related disorders. Thus, a systematic review and meta-analysis was done to assess the efficacy and safety of anticoagulant in cirrhosis-related PVT.

Materials and Methods:
A search on PUBMED and EMBASE was conducted. The efficacy and safety outcomes were any recanalization (partial and total) and variceal bleeding, respectively. Data were pooled to determine the odds ratio (OR) and its 95% CI.

Results:
One RCT and 8 observational studies comprising 516 patients were included. Pooled analysis showed that recanalization was more likely to happen in patients who received anticoagulants than in no treatment group (OR=6.59; 95%CI=3.18-13.64). Occurence of variceal bleeding was lower in the anticoagulant group (OR=0.5; 95%CI=0.25-0.97; p=0.04).

Conclusions:
Preliminary analysis showed that anticoagulant therapy may be beneficial and safe for cirrhosis-related PVT. Further studies with RCT-design and bigger samples are needed to better elucidate its efficacy and safety.

T-13

Clinical value of liver stiffness measurement combined with spleen stiffness measurement for predicting esophageal-gastric varices in patients with cirrhosis

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Objectives:
To investigate the clinical value of liver stiffness measurement (LSM) combined with spleen stiffness measurement(SSM) for predicting esophageal-gastric varices (EGV) in patients with cirrhosis.

Materials and Methods:
A total of 98 patients with cirrhosis from October 2018 to May 2020 were enrolled. According to gastroscopy, all patients were divided into EGV group (n=55) and EGV-free group (n=43). The general information and laboratory parameter were collected. The LSM and SSM value were teseted with FibroTouch®. ROC curve was used to analyze the clinical value of LSM combined with SSM in predicting EGV in patients with cirrhosis.

Results:
Compared with EGV-free group, LSM and SSM values in EGV group were both higher significantly. In EGV group, SSM was positively correlated with LSM (R=0.506, P<0.001), EGV severity (Rs=0.566, P<0.001), portal vein width (R=0.485, P<0.001), spleen thickness (R=0.562, P<0.001), and negatively correlated with PLT (R=-0.503, P<0.001). When used to predict the EGV, the AUC of LSM was 0.748 (95%CI: 0.602-0.895), the AUC of SSM was 0.798 (95%CI: 0.666-0.929) and the AUC of LSM combined with SSM was 0.895 (95CI: 0.801-0.989). When used to distinguish the moderate EGV from severe EGV, the AUC of LSM was 0.756 (95%CI: 0.701-0.831), the AUC of SSM was 0.785 (95%CI: 0.712-0.821) , and the AUC of LSM combined with SSM was 0.887 (95%CI: 0.824-0.921) for LSM combined with SSM.

Conclusions:
There was a potential value of LSM combined with SSM uesd for prediction of EGV in patients with cirrhosis as a non-invasive evaluation method.

T-14

Comparative Analaysis On Efficacy Of Losartan Versus Propranolol As Portal Pressure Reduction Therapy In Cirrhotic Patients With Portal Hypertension: A Systematic Review Of Randomized Controlled Trial

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Objectives:
The easiest preventive management of portal hypertension is still unknown. The systematic review aimed for comparable efficacy of both Dr.ugs, losartan vs. propranolol in cirrhotic patients with portal hypertension that complicated as esophageal varices and also to note the adverse effects of the Dr.ugs.

Materials and Methods:
The systematic review was conducted with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines. The literature search was done using four databases: PubMed, ProQuest, ScienceDirect, and EBSCO with “Losartan,” “Propranolol,” “Liver Cirrhosis,” and “Portal Hypertension” as the primary keywords. Cochrane risk of bias tool 2.0 was utilized in the quality assessment of the studies, which covers the following seven domains of risk.

Results:
The search strategy identified 173 studies. Four relevant full-text articles met our inclusion criteria. Overall studies had a low risk of bias based on Cochrane risk of bias tool 2.0. The main findings from available data are as follows: (a) Losartan has been found to be more effective than propranolol among nonascitic and alcohol-abusing cirrhotic patients ($p<0.05$) (b) Losartan showed higher reduction in HVPG than propranolol, but the comparable differences were statistically insignificant in all studies (c) Losartan had more systemic effect than propranolol and only caused a reduction of MAP in Child B/C Pugh score from cirrhotic patients ($p = 0.003$).

Conclusions:
Our findings showed that overall losartan had the same efficacy as propranolol in lowering portal pressure. Both had systemic effects that can cause the hypotensive condition, but more severe in losartan administration.

T-15

Alterations in the Cardiovascular System in Patients with Cirrhosis - Assessment of a Haemodynamic Prof.ile.

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Aim of the study:
The aim of the study is to screen patients with cirrhosis, which may lead to earlier diagnosing CCM and hyperdynamic synDr.ome.

Material and Methods:
The study included 106 patients with cirrhosis, caused by alcohol ([ALD], 31), autoimmune (43), viral (18) other reasons (14), qualified for liver transplantation. 60 (56%) of them were male. Median age was 51. Each patient had a 6-minute walking test (6MWT) done and a hemodynamic monitoring using CNAP device was also performed.

Results:
Basic group characteristic differs between aetiologies of liver diseases. Patients in ALD group and viral had more advanced liver cirrhosis stage. Median NTproBNP level was highest in ALD group (239pg/ml). Median QTc interval was the most prolonged in patients with viral aetiology (456ms). Highest median CO were observed in viral group (5,7L/min). Median SVRI was lowest in viral aetiology (1785 dyn- s/cm–5/m2). The haemodynamic parameters (CO, SV, SVRI) were not correlated with MELD score and Child Pugh score (p=NS). DBP was positively correlated with MELD score (r=-0,23; p<0,05) and Child-Pugh score (r=-0,31; p=<0,05). Preliminary results show statistically significant correlations between distance in 6MWT and Diastolic Blood Pressure (DBP) (r=0,2; p=<0,05) and NT-proBNP level (r=-0,27 ;p<0,05) and BMI (r=-0,27; p<0,01).
Conclusions:
Preliminary results show that we can detect subclinical alterations in patients' circulatory parameters by non-invasive haemodynamic monitoring. In our study patients with viral and ALD etiology presented more advanced liver cirrhosis stages and more pronounced manifestations of hyperdynamic synDr.ome which may later progress to CCM.

T-16

Difference in Characteristics and Clinical Outcomes among Six Organ Failures of Cirrhotic Patients Hospitalized with an Acute Decompensation with and without Acute-on-Chronic Liver Failure (ACLF)

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Objectives:
Acute decompensation (AD) of liver cirrhosis and Acute-On-Chronic Liver Failure (ACLF) are life threatening events in cirrhotic patients. The studies in differences in clinical outcomes among liver, kidney, cerebral, coagulation, circulation and pulmonary failures are limited. We aim to compare clinical outcomes among these six organ failures in AD cirrhotic patients with and without ACLF.

Materials and Methods:
Retrospective-prospective cohort study from multicenter across 9 hospitals in Thailand was performed in cirrhotic patients with AD between January 2014 to December 2020. Clinical, laboratory data and survival rate were collected from patients admitted due to AD of liver cirrhosis (n=638), in which 345 patients (54.1%) have ACLF.

Results:
The ACLF group had significantly more six organ failures than non-ACLF group (P < 0.001). The most common organ failure in the ACLF group was kidney (42.6%). The ACLF group also had significantly more 30th and 90th days mortality than non-ACLF group (56.0% vs 42.0%; P = 0.001 and 66.8% vs 50.6%; P < 0.001, respectively). The kidney failure with ACLF had the highest 30th and 90th days mortality rate (odd ratio (OR) 4.66 (1.78-12.24), P = 0.001 and 4.12 (1.66-10.22), P = 0.001) followed by cerebral failure (OR 3.17 (1.44-7.00), P = 0.003 and 3.04 (1.36-6.77), P = 0.006) and liver failure (OR 2.89 (1.27-6.59), P = 0.009 and 2.52 (1.13-5.62), P = 0.022), respectively, while the coagulation, circulation and pulmonary failures are no significantly different.

Conclusions:
The kidney failure with ACLF had the highest 30th and 90th days mortality rate.

T-17

Elevated Serum Ferritin And CRP Levels As Prognostic Markers In Decompensated Cirrhosis: A Prospective Cohort Study

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Objectives:
The aim of the study was to analyse serum ferritin and CRP levels as prognostic markers in patients with decompensated cirrhosis and compare it with MELD and CTP scores.

Materials and Methods:
220 consecutive patients with decompensated cirrhosis were included. Serum Ferritin and CRP levels at presentation and factors predicting mortality at 3 months were assessed.

Results:
Patients with decompensated cirrhosis (n=220) (M:F 168:52 ,mean age 55.7 yrs +/- 11) were followed up for a period of 3 months. At presentation, median serum ferritin level was 321.45 (7.4-750) ng/ml in survivors and 725(275-3000) ng/ml in non-survivors, and median serum CRP level was 9 (2-60) mg/L in survivors and 18.5 (6-64) mg/L in non-survivors. Serum ferritin levels were significantly different between survivors and non-survivors [p <0.05] and showed significant correlation with CRP levels (p <0.01). Serum ferritin, CRP, total leucocyte count, MELD score, CTP score, presence of hepatorenal synDr.ome, spontaneous bacterial peritonitis, hepatic encephalopathy and ACLF were significant predictors of mortality on univariate analysis. Ferritin, MELD and presence of hepatorenal synDr.ome were significant predictors of mortality on multivariate analysis. Serum ferritin [AUROC 0.91, 95% CI 0.87-0.95] was comparable to MELD score [AUROC 0.92, 95% CI 0.891-0.961] and better than CRP [AUROC 0.74, 95% CI 0.67-0.80] and CTP score [AUROC 0.847, 95% CI 0.79-0.89], in predicting death at 3 months.

Conclusions:
Elevated serum ferritin level is an independent prognostic marker in decompensated cirrhosis. Elevated serum CRP levels did not show association with mortality at three months in decompensated cirrhosis.

T-19

Endoscopic Management of Portal Cavernoma Cholangiopathy: A Single Center Experience

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Objectives:
To study the efficacy and complications associated with the endoscopic management of portal cavernoma cholangiopathy (PCC).

Materials and Methods:
The present study is retrospective analysis of prospectively collected data of patients with symptomatic PCC who underwent endoscopic therapy between January 2011 to January 2020. Diagnosis of PCC was made based on ultrasonography, doppler and MRCP imaging. All patients underwent endoscopic therapy which included biliary sphincterotomy, extraction of stones/sludge and biliary stenting with multiple plastic stents. Patients were followed quarterly or when new symptoms developed.

Results:
Total 30 patients (24 males, mean age 37 years) with symptomatic PCC underwent endoscopic therapy. Jaundice was seen in all patients with mean bilirubin of 9.64 mg %. 40% patients had cholangitis at presentation, 63% had CBD stones and 26% had CBD sludge. Total 124 ERCP procedures with CBD stenting/stone or sludge removal were done. The most common cholangiographic finding was type I PCC. 7 (23.3%) patients are asymptomatic after stent removal during follow up period of 22 months. 4 (13.4%) patients underwent shunt surgery, required mean 3 ERCP procedures post-surgery due to persistent biliary obstruction and rest 19(63.3%) who refused shunt surgery are requiring periodic stenting and are asymptomatic. Post ERCP haemobilia and pancreatitis were seen in 2 patients each, which was managed conservatively. One patient developed pancreatic ascites following shunt surgery.

Conclusions:
Endoscopic therapy is safe and effective with minimal complications in patients with PCC.

T-20

Gastroesophageal varices evaluation using a novel spleen-dedicated stiffness measurement by Fibroscan

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Objectives:
Liver stiffness measurement (LSM) and spleen stiffness measurement (SSM) using standard Fibroscan (liver shear wave frequency: 50Hz, stiffness range 1.5-75 kPa), have been proposed as a non-invasive tests for screening of gastroesophageal varices (GEV) in chronic liver disease (CLD). Recently a novel spleen-dedicated Fibroscan (spleen shear wave frequency: 100Hz, stiffness range 6-100 kPa), has been developed. The aim of this study is to evaluate GEV using a novel spleen-dedicated Fibroscan.

Materials & Methods:
89 patients (mean age 67.7±13.2 years, male 74%) with CLD (including hepatocellular carcinoma) enrolled in a single center prospective study. The patients were underwent screening esophagogastroduodenoscopy for assessment of GEV within 3 months of LSM and SSM. SSM@50Hz and LSM@50Hz using liver mode, and SSM@100Hz using spleen mode were measured by a novel Fibroscan.

Results:
GEV were present in 46 (51.6%). The area under the receiver operating characteristic (AUROC) for GEV with LSM@50Hz was 0.692. The success rate and the interquartile range/median ≤0.3 rate were significantly higher in SSM@100Hz than that in SSM@50Hz ($P < 0.05$). The AUROC for GEV with SSM@50Hz or SSM@100Hz was 0.878 or 0.912. In the patients with LSM ≥11.8kPa, who were diagnosed cirrhosis, the AUROC for GEV with SSM@50Hz or SSM@100Hz was 0.846 or 0.915. SSM@100Hz were increased in a stepwise manner from the grade I to III GEV (Kruskal-Wallis test, $P < 0.001$).

Conclusions:
SSM@100Hz had a higher applicability than LSM@50Hz or SSM@50Hz. SSM@100Hz can select high-risk patients to be referred for esophagogastroduodenoscopy. These results have to be validated in another population.

T-21

Is It Necessary To Transfuse FFP And Platelets Before Band Ligation in Acute Variceal Bleeding Patients? South East Asia Experience. RIP FFP And Platelets Transfusion!

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Objectives:
Patients with liver cirrhosis undergo derangements in International Normalized ratio (INR) and platelet count for which fresh frozen plasma (FFP) and platelets transfusion is recommended prophylactically. Whether these measures are truly indicated and beneficial for a favorable prognosis is still debatable. We aimed to study the use of prophylactic administration of blood products in patients with cirrhosis undergoing endoscopic band ligation (EBL).

Materials and Methods:
A prospective study, conducted at AIMS Hyderabad from August to September 2020 in cirrhotic patients with upper gastrointestinal bleeding who underwent EBL. It's an ongoing study. They were evaluated for indications of transfusion such as INR>1.5 and platelets <50 × 109/L. The clinical characteristics, etiology, and laboratory data were documented, based on which MELD and CTP scores were calculated.

Results:
A total of 112 patients underwent EBL procedures: (70.5% male), (Age 48.94 ± 11.8 years), the main etiology was HCV (61.9%), median MELD 11, and Child A/B/C (42/38/20%). Prophylactic transfusion of FFP and platelets were needed in 31% and 12% with high INR (>1.5) and low platelets <50 × 109/L but could not be administered due to affordability issues. Rebleeding (3.5%, n=4) occurred in HCC patients with or without portal vein thrombosis. There was no association between platelet count and INR with bleeding events. The mean MELD and CHILD scores were not significantly different in patients with or without rebleeding.

Conclusions:
There was no association between baseline INR/platelet count and post EBL rebleeding. The majority didn't satisfy the criteria for transfusion protocol.

T-25

Natural history and predictors associated with the evolution of portal venous system thrombosis in liver cirrhosis

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Background:
Portal venous system thrombosis (PVST) will progress in some cases, indicating worse outcome and the necessity of antithrombotic treatment, but will spontaneously improve in others. It is crucial to understand the natural history of PVST in liver cirrhosis. However, the knowledge regarding how to predict the evolution of PVST in cirrhotic patients is very scant.

Methods:
Sixty-nine cirrhotic patients without malignancy, who had undergone repeated contrast-enhanced computed tomography or magnetic resonance imaging to evaluate the severity of PVST at the first and last admissions, were included. Logistic regression analysis was performed to identify the risk factors for evolution of PVST in liver cirrhosis. Odds ratios (ORs) were calculated.

Results:
Among 42 patients without PVST at the first admission, 10 (23.8%) developed PVST at the last admission. Serum albumin level (OR=0.873), prothrombin time (OR=1.619), activated partial thromboplastin time (OR=1.169), Child-Pugh score (OR=1.560), and model for end-stage liver disease (MELD) score (OR=1.292) at the last admission were significant risk factors associated with the development of PVST. Among 27 patients with PVST at the first admission, 11 (40.7%), 4 (14.8%), and 12 (44.4%) had improvement, stabilization, and progression of PVST at the last admission, respectively. ΔMELD score (OR=0.714) was the only significant risk factor associated with the improvement of PVST; additionally, serum albumin level at the first admission (OR=1.236) was the only significant risk factor associated with the progression of PVST.

Conclusions:
Aggravation and amelioration of liver dysfunction may predict the development and improvement of PVST in liver cirrhosis, respectively.

T-26

No association of homocysteine, anticardiolipin antibody, and anti-β2 glycoprotein I antibody with portal venous system thrombosis in liver cirrhosis

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Background:
Portal venous system thrombosis (PVST), a common complication of liver cirrhosis, is closely associated with thrombophilia.

Objectives:
To explore the association of homocysteine (Hcy), anticardiolipin antibody (aCL), and anti-β2 glycoprotein I antibody (aβ2GPI), which are possible thrombophilic factors, with PVST in liver cirrhosis.

Methods:
Overall, 654 non-malignant patients (219 with and 435 without liver cirrhosis) admitted between January 2016 and June 2020 were retrospectively evaluated. Presence of PVST, degree of main portal vein (MPV) thrombosis, and clinically significant PVST were identified. Hcy level, hyperhomocysteinemia (HHcy), aCL positivity, and aβ2GPI positivity were compared according to the presence of liver cirrhosis and PVST.

Results:
Positive aβ2GPI was significantly more frequent in patients with liver cirrhosis than those without, but Hcy level and proportions of HHcy and positive aCL were not significantly different between them. PVST could be evaluated in 136 cirrhotic patients. Hcy level [10.57 umol/L (2.71-56.82) versus 9.97 umol/L (2.05-53.44); P=0.796] and proportions of HHcy [4/44 (9.1%) versus 13/81 (16.0%); P=0.413] and positive aCL [1/23 (4.3%) versus 10/52 (19.2%); P=0.185] and aβ2GPI [9/23 (39.1%) versus 21/52 (40.4%); P=0.919] were not significantly different between cirrhotic patients with and without PVST. There was still no significant association of Hcy level, HHcy, aCL, or aβ2GPI with PVST based on Child-Pugh classification, MPV thrombosis >50%, and clinically significant PVST.

Conclusions:
Hcy, aCL, and aβ2GPI may not be associated with PVST in liver cirrhosis, suggesting that routine screening for Hcy, aCL, and aβ2GPI should be unnecessary in such patients.

T-28

One month and three month readmission rates in cirrhotic patients were not changed during past seven years

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Background:
Liver cirrhosis is a major complication of chronic liver disease. Early hospital readmission for patients with cirrhosis continues to challenge the healthcare system. We aimed to investigate readmission rate and cause of cirrhotic patients during year 2013-2019.

Methods:
Medical records of patients with cirrhosis who admitted to Konkuk University Medical Center during past seven years were analyzed. This research has been approved by an ethical committee.

Results:
Total 1,842 admission cases were analyzed. Most common etiology was alcoholic liver disease (51.1-70.0%) and male was predominant (61.3-72.8%). Mean ages were 55.1-58.5 years and mean Child-Pugh scores were 8.0-8.5. Mean admission durations were 9.4-11.0 days. One month readmission rate was 9.4% in year 2013 and 12.0% in year 2019 (9.4-14.8% during 7 years). Common causes of readmission were conservative management (22.2-38.1%) and hepatic encephalopathy (14.3-37.5%). Three month readmission rate was 16.9% in year 2013 and 27.0% in year 2019 (16.9-27.0% during 7 years). Common causes of readmission were conservative management (23.2-38.9%) and variceal bleeding (19.6-29.0%).

Conclusions:
Despite of antiviral treatment era, readmission rate of cirrhotic patients was not decreased because main etiology of these patients was alcohol. Management strategy for these patients is warranted.

T-29

Outcomes of early versus delayed endoscopy in cirrhotic patients with acute variceal bleeding: A systematic review and meta-analysis

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Background:
Endoscopy is the mainstay treatment option for acute variceal bleeding (AVB) in liver cirrhosis. However, the optimal timing of endoscopy in such patients remains unclear.

Methods:
PubMed, EMBASE, and Cochrane Library databases were searched. We compared the mortality, incidence of rebleeding, length of stay, endoscopic hemostasis, need for salvage, and units of transfusion between cirrhotic patients with AVB who underwent early and delayed endoscopy. Meta-analyses were performed by using a random-effect model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Subgroup analysis was performed in studies with a definition of early endoscopy (<12 hours).

Results:
Nine retrospective studies involving 2824 patients were included. Early endoscopy group had a significantly lower overall mortality than delayed endoscopy group in overall analysis (OR=0.56, 95%CI=0.33-0.95, P=0.03), but the difference was not significant between the two groups in subgroup analysis (OR=0.72, 95%CI=0.38-1.38, P=0.33). In-hospital (OR=0.77, 95%CI=0.26-2.32, P=0.65) and 6-week (OR=0.78, 95%CI=0.42-1.47, P=0.45) mortality were not significantly different between them. Overall rebleeding was not significantly different between early and delayed endoscopy groups in both overall (OR=0.86, 95%CI=0.48-1.54, P=0.62) and subgroup (OR=1.04, 95%CI=0.53-3.04, P=0.91) analyses. In-hospital (OR=1.41, 95%CI=0.67-2.96, P=0.37) and 6-week (OR=0.93, 95%CI=0.40-2.17, P=0.86) rebleeding remained not significantly different between them. Additionally, the length of stay, endoscopic hemostasis, need for salvage, and units of transfusion were not significantly different between the two groups.

Conclusions:
Early endoscopy may decrease the mortality of cirrhotic patients with AVB, but has no remarkable benefit on the prevention of rebleeding. More high-quality evidence should be very required in future.

T-31

Portal venous system thrombosis after bariatric surgery: A systematic review and meta-analysis

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Background and aims:
Portal venous system thrombosis (PVST) can develop after bariatric surgery. A systematic review and meta-analysis was conducted to evaluate the incidence of PVST after bariatric surgery and clarify the role of anticoagulation for the prevention of PVST after bariatric surgery.

Methods:
PubMed, EMBASE, and Cochrane Library databases were searched. The incidence of PVST after bariatric surgery was pooled by a random-effect model. Subgroup analyses were performed to explore the incidence of PVST according to the use of prophylactic anticoagulation. Meta-regression and sensitivity analyses were performed to explore the source of heterogeneity.

Results:
Among 2714 papers initially screened, 68 studies were included. Among 100,964 patients undergoing bariatric surgery, 300 developed PVST. The pooled overall incidence of PVST after bariatric surgery was 0.419% (95%CI: 0.341%-0.505%). The pooled incidence of PVST was similar between patients who received and didn't receive prophylactic anticoagulation after bariatric surgery (0.328% versus 0.303%), but it was lower in patients who received extended prophylactic anticoagulation protocol after bariatric surgery than those who received short-term prophylactic anticoagulation protocol (0.184% versus 0.459%). Meta-regression analyses demonstrated that sample size (P=0.006) might be a potential source of heterogeneity, but not region, publication year, history of bariatric surgery, follow-up duration, or prophylactic anticoagulation. Sensitivity analyses could not identify any source of heterogeneity. The estimated mortality of PVST after bariatric surgery was 1.33%.

Conclusions:
PVST after bariatric surgery is rare, but potentially lethal. Extended prophylactic anticoagulation protocol may be considered in patients at a high risk of developing PVST after bariatric surgery.

T-33

Prediction of Esophageal Varices Grading in Cirrhotic Patients using Liaoning, Albumin-Bilirubin and Platelets-Albumin-Bilirubin Score

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Objectives:
Esophageal varices and variceal bleeding are the most common and life-threatening complications of liver cirrhosis. The risk of bleeding emphasizes the importance of screening for esophageal varices grading. This study aimed to evaluate correlation of different grades of esophageal varices and Liaoning, ALBI and PALBI score as 3 new non-invasive parameters in liver cirrhosis patients.

Methods:
This was a cross-sectional study of patients at the Hasan Sadikin hospital Bandung between January to December 2019 with a diagnosis of cirrhosis based on clinical, biochemical examination, ultrasound, and esophagogastroduodenoscopy. Liaoning, ALBI and PALBI score were calculated for all patients, tabulated, and analyzed.

Results:
We gathered 139 patients with mean age 51 ± 12 years with Child-Pugh B (49.6%), Child Pugh C (23%), Child-Pugh A (27.3%). The causes of liver cirrhosis were Hepatitis B 45 (32.4%), Hepatitis C 17 (12.2%) and others 77 (55.4%). Esophageal varices grades were F3 90 (64.7%), F2 36 (25.9%), F1 13 (9.4%). The Liaoning Score was significantly higher in large esophageal varices compare to small esophageal varices. 1.63(0,89-2,15) vs 0.09 (-0.60- 0.68) (p-value<0.001). Liaoning score with cut-off points > 0.49 was highly predictive in the diagnosis of variceal esophageal with a sensitivity of 91.1%, specificity of 40.8%, positive predictive value of 73.9% and negative predictive value of 71.4%. However, there were no correlation for ALBI and PALBI score to the grading.

Conclusions:
Liaoning score is significantly associated with esophageal varices. Liaoning score is a good noninvasive predictor of large esophageal varices in cirrhosis patients.

T-34

Presence of Atrial Fibrillation is Associated with Increased Mortality Risk in Cirrhosis Patients: Meta Analysis

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Objectives:
Cirrhosis remains to be one of the leading causes of mortality around the world. Cirrhosis patients get hospitalized because of various complications. These complications also can affect the heart, resulting fatal arrythmias and electrocardiographic changes. Previous studies reporting that atrial fibrillation (AF), atrial flutter, premature atrial and ventricular contraction, and ventricular arrhythmias can be observed in cirrhosis patients. There were no sufficient studies reporting these association, including the increasing risk in mortality. Thus, meta-analysis was conducted to identify the association between AF and mortality risk in cirrhosis patients.

Materials and Methods:
A literature search was conducted on Pubmed and EMBASE. Risk of bias was assessed using The Newcastle-Ottawa Scale (NOS). Outcomes were prevalence of AF and risk of mortality in cirrhosis patients. Using random-effects meta regression model, data were pooled to determine the odds ratio (OR) and its 95%CI. Meta-analysis was conducted using Revman 5.3 software.

Results:
Eight cohort studies comprising 695,825 cirrhosis patients were included. Risk of bias according to NOS mostly achieved 7 and 8 stars. Pooled analysis showed that prevalence of AF in cirrhosis patients was 7% (95% CI=0.04-0.10). AF was significantly associated with increased risk of mortality in cirrhosis patients (OR=1.29; 95%CI=1.06-1.57; p<0.00). This finding may be related with an autonomic dysfunction and increase levels of vasoactive substances from the intestinal.

Conclusions:
AF was associated with increased mortality risk in cirrhosis patients. Further studies need to be conducted to suggest a proposed model in which AF can be implemented in clinical setting.

T-35

Prevalence, characteristics and prognosis of bacterial infection in patients with decompensated cirrhosis and acute-on-chronic liver failure: a multi-center study

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Objectives:
We aimed to investigate the prevalence, outcomes and predictors of mortality of bacterial infection (BI)-related acute decompensation (AD) and acute-on-chronic liver failure (ACLF) in patients with cirrhosis.

Methods:
We included 310 ACLF patients and 260 AD patients admitted to 9 tertiary hospitals in Thailand from January 2014 - August 2020 using data collected by the Thai Association for the Study of Liver (THASL) or Acute-on-Chronic Liver Failure: multicenter study group (ACLF-TM).

Results:
BI was the most frequent cause of ACLF (61.9%) and AD (48.1%). The prevalence of BI in ACLF-1, ACLF-2 and ACLF-3 were 58.7%, 69% and 60.5%. Spontaneous bacterial peritonitis was the most common identified cause. Patients with infection-related ACLF had more encephalopathy (24.2%vs12.8%,p=0.02), higher CLIF-C ACLF score (47.7±9.4 vs 43.3±7.7,p<0.001), worse clinical course (ACLF2-3: 39.5%vs26.9%,p=0.03), higher 30-day mortality (62.9%vs48.6%, p=0.02) and 3-month mortality (65.4%vs50.6%,p=0.03) than ACLF patients without infection. While the 30-day mortality (39.4%vs43%, p=0.58) and 3-month mortality (53.1% vs45.7%, p=0.31) were not different between AD with and without infection. BI (OR=1.72,95%CI 1.05-2.83,p=0.03) and MELD score (OR=1.04,95%CI 1.01-1.08, p=0.01) were independent risk factors of 30-day death in ACLF patients. MELD score (OR=1.06, 95%CI:1.02-1.11,p=0.01) and respiratory failure (OR=4.19, 95%CI: 1.27-13.85) were the independent predictors for 30-day mortality in ACLF patients precipitated from infection. Baseline MELD (OR =1.27, 95%CI:1.20-1.34, p=0.000) was an independent predictor for the ACLF development in cirrhosis patients with BI.

Conclusions:
BI is prevalent in patients with AD and ACLF. Patients with infection-related ACLF have poor characteristics and high short-term mortality. MELD score is helpful predictor for poor prognostic outcomes.

T-36

Role of Lactulose for Prophylaxis on Hepatic Encephalopathy in Cirrhotic Patient Presented with Upper Gastric Intestinal Bleeding

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Objectives:
To assess the effect of lactulose for prophylactic effect on hepatic encephalopathy (HE) in cirrhotic patients with acute upper gastrointestinal bleeding (AUGIB).

Materials and Methods:
We conducted a randomized, double-blinded, placebo controlled clinical, multicenter study between October 2012 to February 2014. Cirrhotic patients presenting with AUGIB (age 18-80 years who had no HE at the time of admission) were enrolled and randomized to receive blinded medication, namely “Lactulose A” and “Lactulose B” for 5 days along with standard treatment depend on type of bleeding (variceal and nonvariceal bleeding_. Both intervention agents were physically indistinguishing, in the term of gross appearance, smell and taste. Primary endpoint was development of overt HE according to West-Haven criteria. Modified intention to treat analysis was performed.

Results:
Finally, 46 patients completed protocol: Lactulose A (placebo, n=22) and Lactulose B (lactulose, n=24). There were no significant differences in baseline characteristics and clinical outcomes between the two group. Nine (19.6%) patients had developed HE: Five patients (22.7%) in the placebo group and 4 patients (16.7%) in the lactulose group, P=0.718. One patient (2.2%) died (in lactulose group). All patients could tolerate medication and no significant differences in adverse effects detected (59.1% of placebo group VS 50.0% of lactulose group, P=0.536). On unconditional logistic regression analysis, baseline decompensated cirrhosis (Child-Turcotte-Pugh ≥ 8) and presence of diarrhea were significantly associated with development of HE.

Conclusions:
Lactulose is ineffective for prophylaxis on hepatic encephalopathy in cirrhotic patients with acute upper gastrointestinal bleeding.

T-38

SARC-F score: A quick bedside questionnaire to assess sarcopenia in Cirrhosis

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Objectives:
The aim of present study was to discern the utility of SARC-F score, a simple five-item questionnaire, to screen patients with chronic liver disease for sarcopenia.

Materials and Methods:
100 patients of Cirrhosis (Mean age 44 years; 86% males; etiology- 80% alcohol, 8% Hepatitis B, Hepatitis C each; 58% Child Pugh C, 40% Child Pugh B, 2% Child Pugh A) were enrolled from 1st Jan 2018 to 31st Dec 2019. SARC-F score (five variables: strength, assistance walking, rise from chair, climb stairs and falls, with score from 0-10), mid arm muscle circumference, hand dynamometer and CT scan psoas muscle cross-sectional area were done. Data was analyzed to calculate sensitivity of SARC-F score as a predictor of sarcopenia.

Results:
The sensitivity and specificity of SARC-F score for sarcopenia with a cut off ≥4 was found to be 72.58% and 68.42% respectively with Area under the ROC curve (AUC) of 0.744 (P value <0.001, significant). 69% patients had sarcopenia with SARC-F score ≥ 4. The frequency of SARC-F score ≥ 4 was higher with higher CTP class, (CTP class C:B:A - 74.1%: 62.5%: 50%). There was a negative correlation found for SARC-F score with Psoas muscle area with Spearman's correlation coefficient of -0.295, (p value 0.003, statistically significant). All five variables of SARC-F score were found to have good correlation with sarcopenia (p value of ≤ 0.05).

Conclusions:
SARC-F score can be used as a reliable bed side screening tool for predicting sarcopenia in chronic liver disease patients.

T-39

Spontaneous splenorenal shunt may decrease the long-term survival of liver cirrhosis by compromising liver volume

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Background & Aims:
Spontaneous splenorenal shunt (SSRS) is one of the manifestations of portal hypertension in liver cirrhosis. However, the impact of SSRS on long-term survival of cirrhotic patients remains unclear. We hypothesize that SSRS may worsen liver dysfunction and deteriorate prognosis in liver cirrhosis by decreasing hepatic perfusion.

Methods:
Patients with liver cirrhosis who were admitted to our department between December 2014 and August 2019 and underwent contrast-enhanced CT or MRI scans were prospectively collected. The maximum diameters of SSRS and portal vein system vessels were retrospectively measured. Liver-to-abdominal area ratio (LAAR), Child-Pugh, and MELD scores were calculated.

Results:
Overall, 122 cirrhotic patients were included. The prevalence of SSRS was 30.3% (37/122). Median diameter of SSRS was 13.5 mm. Patients with SSRS had significantly thinner diameters of right portal vein (9 mm versus 11.2 mm, P=0.001) and main portal vein (15.3 mm versus 16.8 mm, P=0.017) than those without SSRS. Patients with SSRS had significantly lower LAAR score (25.39 versus 31.58, P<0.001) and higher Child-Pugh (7 versus 6, P=0.046) and MELD (12.17 versus 9.79, P<0.006) scores than those without SSRS. Patients with SSRS had a significantly lower cumulative survival rate than those without SSRS (P=0.014). Cox regression analysis also showed that SSRS was a risk factor of death of cirrhotic patients (hazard ratio=4.161, 95% confidence interval=1.215-14.255, P=0.023).

Conclusions:
SSRS may narrow portal vein diameter and shrink liver volume, thereby worsening liver function and increasing mortality in liver cirrhosis.

T-41

The Association Between Hepatic Cirrhosis Complications and Total Lymphocyte Count in Hepatic Cirrhosis Patients at Saiful Anwar Hospital Malang

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Objectives:
Lymphopenia can be found in many chronic diseases, such as malignancy, tuberculosis, viral infection, and peripheral vascular disease. Lymphopenia is also found in patients with liver disease. It is caused by immune dysfunction which can affect the clinical outcome of cirrhosis patients. This study aim is to knows the association between hepatic cirrhosis complications and total lymphocyte count (TLC) in hepatic cirrhosis patients.

Methods:
This observational cohort retrospective study used complete blood count examination and differential counting to get TLC value, and interview to collect data about history of cirrhosis hepatis diagnosis, etiology, and complication which occured in the last 1 month, such as hematemesis melena, Hepatic Encephalopathy (HE), and ascites. The data had been analyzed using Chi Square with CI 95%, $p < 0.05$.

Result:
We had 52 cirrhosis patients, with 21 patients had TLC <1000/µL and 31 had TLC >1000/µL. 31 patients had bleeding complication, 10 had HE, and 35 had ascites. Normal TLC is a protective factor for HE, with likelihood ratio 1.944. Although, this value is not statistically significant (p=0.163). Bleeding and Ascites seems like did not affected by TLC numbers

Conclusions:
No difference between the frequency of gastrointestinal bleeding, HE, and ascites in hepatic cirrhosis patients with and without lymphopenia.

T-42

The clinical Prof.iles and in-hospital clinical outcome in young adult patients with esophageal varices: one-year observation

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Objectives:
This study was aimed to investigate clinical Prof.iles and in-hospital clinical outcomes in young adult patients with esophageal varices (EV) at limited resources hospital in Indonesia.

Materials and Methods:
A descriptive study was conducted during January-December 2019 using secondary data from medical records. We recruited hospitalized patients diagnosed through endoscopic examination as EV in Waled General Hospital, Cirebon, West Java, Indonesia. The subjects were divided into age groups, those were young adult group (YAG) for 20-40 years old and senior adult group (SAG) for more than 40 years old. Clinical Prof.iles encompassed clinical characteristics, etiology, and in-hospital clinical outcomes. Data were analyzed using descriptive statistics.

Results:
Of total 34 patients with EV, there were 7 (20.59%) young adult subjects in this study. There was no significant difference on melena (p=1.0), hematemesis (p=0.682), and jaundice (p=0.511). YAG showed higher AST (p=0.00), higher ALT (p=0.00), higher total bilirubin (p=0.00), and less hypoalbuminemia (p=0.00). Compared to SAG, non-cirrhotic liver was predominant etiology in YAG (p=0.001). There was no significant difference on EV severity (p=0.807), blood transfusion (p=0.211), and endoscopic ligation treatment (p=1.000). YAG underwent lesser volume of blood transfusion (p=0.002) and had shorter length of stay (p=0.045). No death was reported.

Conclusions:
The proportion of EV in young adult was relatively high. EV in young adult showed higher transaminase elevation and higher bilirubin level. The etiology of EV in young adult was mostly associated with non-cirrhotic liver. Young adults with EV had less volume of blood transfusion and shorter hospitalization.

T-43

The Effectiveness Of Oral Thrombopoietin Receptor Agonist, Lusutrombopag For The Treatment Of Thrombocytopenia In Chronic Liver Disease Patients Undergoing Invasive Procedure In Japan.

Mr Manami Yoshida[1,2], Dr. Ryosuke Tateishi[2], Dr. Shinzo Hiroi[1], Ms Yoshie Hongo[1], Mr Masakazu Fujiwara[1], Mr. Yoshitake Kitanishi[1], Mr. Kosuke Iwasaki[3], Ms Tomomi Takeshima[3], Dr. Ataru Igarashi[2,4]

[1]Shionogi & Co., Ltd, Osaka, Japan, [2]The University of Tokyo, Tokyo, Japan, [3]Milliman Inc., Tokyo, Japan, [4]Yokohama City University, Kanagawa, Japan

Objectives:
Thrombocytopenic patients with chronic liver disease (CLD) are at risk of bleeding related to invasive procedures (IPs) and often receive prophylactic platelet transfusion (PT). Lusutrombopag has been approved for thrombocytopenia in CLD patients undergoing planned IPs. 7 days administration should be started 8-13 days before the IP. The effectiveness of lusutrombopag versus PT was evaluated.

Materials and Methods:
Planned IPs in CLD patients were extracted from a Japanese health insurance claims database provided by Medical Data Vision. The analysis included IPs performed within 13 days after the hospital admission, age > 18 years, and having >30 days of observation period prior to the IP. Date of IP was defined as the index date. IPs with lusutrombopag prescription between 30 to 5 days prior to the index and matched IPs having PT on -1 and/or index day without lusutrombopag prescription were classified as lusutrombopag and PT group, respectively. The frequency of bleeding events during the hospitalization, mean medical costs during 30 days after the index and length of stay (LOS) were compared between 2 groups.

Results:
379 IPs were included in each group. The frequency of bleeding events was significantly lower in the lusutrombopag group (3.7%) than in PT group (8.2%) ($p=0.0006$). The mean medical cost in the lusutrombopag group and PT group were 0.73 and 0.79 JPY million, respectively ($p=0.0107$). The mean LOS was 11.8 days in lusutrombopag group and 13.9 days in PT group ($p<0.0001$).

Conclusions:
This analysis highlights lusutrombopag reduces bleeding, medical costs and LOS versus PT.

T-46

The Value of Platelet Parameters and Related Scoring System in Predicting Esophageal Varices and Collateral Veins in Patients with Liver Cirrhosis

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Objectives:
To explore the value of platelet parameters and related scoring system in predicting esophageal varices and collateral veins in patients with liver cirrhosis.

Methods:
A total of 94 patients with liver cirrhosis diagnosed in our hospital from March 2017 to July 2018 were divided into without esophageal varices group (NEV) and esophageal varices group (EV) into mild, moderate and severe subgroups according to the results of general gastroscopy. The differences of biological indexes among different degrees of esophageal varices and collateral veins were analyzed, and the related factors of esophageal varices and collateral veins were analyzed.

Results:
PLT count and PCT decreased gradually with the increase of esophageal varices in EV group. There were significant differences in PLT count and PCT, which were negatively correlated with the degree of collateral vein in esophageal collateral vein group. The maximum cross-sectional diameter and mean diameter of esophageal collateral veins in EV group were wider than those in NEV group. Further study showed that the maximum cross-sectional total diameter and mean diameter of esophageal collateral veins in severe esophageal varices group were wider than those in NEV group and mild esophageal varices group. The diagnostic efficiency of Lok score of 2/19 was the highest.

Conclusions:
Platelet parameters and related scoring system have a certain predictive value for the degree of esophageal varices and collateral veins. In many scoring systems, Lok score is the most effective in predicting esophageal varices and collateral veins, which has a certain clinical guiding value.

T-47

Thirty-Day Readmission after Esophageal Variceal Hemorrhage and Its Impact on Outcomes in the Tertiary care Hospital

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Objectives:
Esophageal variceal hemorrhage (EVH) is a potentially fatal Gastro-intestinal emergency, which is a complication of liver cirrhosis. The aim of this study was to evaluate the 30-day readmission rate and its impact on mortality and morbidity in EVH patients.

Materials and Methods:
A descriptive study (prospective cohort) was conducted at the Gastro-hepatology department of AIMS Hyderabad from September 2019 to February 2020. Adults with EVH with urgent/emergent admission needed were included in the study. The clinical characteristics and laboratory data at admission were documented, based on which MELD, and CTP scores were calculated. The surviving patients were then followed via telephone after 30 days and readmission and its reasons, mortality (in-hospital and readmission) and morbidity within 30-days were determined.

Results:
A total of 160 EVH patients were included in the study, out of which 75% (n=120) were males. The mean age of the participants was 50.33 years ± 12.9 standard deviation (SD). The etiology was Hepatitis C in 69.4% (n = 111) patients. The in-hospital mortality was 8.8% (n=14). Of those who survived, 15% (n=22) had re-admissions with rebleeding as cause in 4.4% (n=7) patients. Rest of the patients were admitted with other complications of end-stage liver disease.

Conclusions:
The all-cause 30-day readmission rate after EVH was 15% with m one-third of the cases due to re-bleeding. The readmission was not associated with higher rates of mortality (in-hospital mortality rate vs readmission mortality rate).

T-48

To Study the Prevalence of Hepato-ADr.enal SynDr.ome & Low HDL Value<40 mg/dl in Hemodynamically Stable Liver Cirrhotic Patients

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[1]*Yashoda Hospital, Secunderabad, India*

Objectives:
To Study the prevalence of ADr.enal Insufficiency & low HDL value<40 mg/dl in hemodynamically stable liver cirrhotic patients

Materials & Methods:
100 patient of liver cirrhosis who are hemodynamically stable indoor patient who may admitted with GI Bleed, hepatic encephalopathy, ascites, SBP or for any other complication.We measured serum basal cortisol level at morning after overnight fasting state, after that we gave injection actum prolongatum(Corticotrophin carboxymethylcellulose) 25 unit intramuscularly, after 1 hour we measured serum random cortisol level.
The cut off for basal cortisol is >5 microgram/dl, peak stimulation after one hour ACTH stimulation,cortisol is > 18 microgram/dl and delta cortisol(Peak level after stimulation- basal cortisol) > 9 microgram/dl
If basal cortisol level < 5 or delta cortisol < 9 or peak cortisol after one hour is < 18 microgram/dl is defined as a aDr.enal insufficiency

Results:
- The prevalence of ADr.enal Insufficiency by Basal, Delta & Peak cortisol level is 18%, 44% & 52% respectively
- The prevalence of ADr.enal Insufficiency in CTP class A.B & C is 55.6%, 60.5% & 65.9% respectively
- The prevalence of low HDL is found to have 89%
- Among ADr.enal Insufficiency patients, 90.32% have low HDL level

Conclusions:
- Patients with chronic liver disease are at increased risk of developing ADr.enal Insufficiency & low HDL level
- As the severity of liver disease increases, the prevalence of ADr.enal Insufficiency & low HDL increases.
- Peak & Delta Cortisol level can identify the prevalence of relative aDr.enal insufficiency which cannot be identified by Basal cortisol level

T-49

To Study The Prevalence Of Hepato-ADr.enal SynDr.ome In Hemodynamically Stable Liver Cirrhotic patients

Dr. Dipen Agrawal[1], Dr. Ravi Shankar B[1], Dr. Srinivas Rao[1], Dr. Viswanath Reddy[1], Dr. Rami Reddy[1], Dr. Bharani I[1]
[1]*Yashoda Hospital, secunderabad, India*

Objectives:
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Materials & Methods:
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- Among ADr.enal Insufficiency patients, 90.32% have low HDL level

Conclusions:
- Patients with chronic liver disease are at increased risk of developing ADr.enal Insufficiency & low HDL level
- As the severity of liver disease increases, the prevalence of ADr.enal Insufficiency & low HDL increases.
- Peak & Delta Cortisol level can identify the prevalence of relative aDr.enal insufficiency which cannot be identified by Basal cortisol level

T-51

Efficacy of zinc supplement in minimal hepatic encephalophathy : A prospective, randomized controlled trial

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Objectives:
Minimal hepatic encephalopathy (MHE) in cirrhosis has an impact on quality of life (QOL) by impaired attention, visuomotor coordination and cognitive decline. Zinc is one of cofactor enzyme to conversion of ammonia to urea. Aim of the study was to assess effect of zinc supplementation on psychomotor performance in patients of cirrhosis with MHE.

Methods:
Prospective, randomized controlled trial, recruited 69 cirrhotic patients with diagnosis of MHE by neuropsychometric (NP) tests which consists of Number connection test A(NCT-A), number connection test B(NCT-B), serial dot test(SDT), line tracing test(LTT) and digit symbol test(DST). Eligible patients were randomly assigned (1:1) to receive 45 mg of elemental zinc or placebo for 12 weeks. The primary endpoint was absolute change in NP tests from baseline to 12-week of zinc supplement compared with placebo. Assess change of QOL by SF-36, was also done in both groups.

Results:
Between January to December 2020, 69 patients had cirrhosis with MHE were randomly assigned to treatment: 35 patients receive zinc, 34 patients receive placebo. Significant improvement of NP tests was established in zinc group when compared with placebo (NCT-A,p=0.029; NCT-B,p=0.008; SDT,p=0.002 ; DST,p=<0.001). Significant improvement of QOL assessed by SF-36 score was seen only in zinc group,p<0.001. In zinc group, not only improvement of psychomotor performance but quality of life were achieved irrespective baseline zinc level.

Conclusions:
Twelve weeks of zinc therapy in cirrhotic patient with MHE not only had a positive effect to psychomotor performance but also improved QOL irrespective to baseline zinc level.

T-52

The Impact Of Frailty On Decompensation And Survival In Patients With Cirrhosis: A Prospective Cohort Study

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Objectives:
We aimed to study the prognostic impact of frailty on the natural history of stable cirrhotic patients.

Materials and Methods:
Stable cirrhotic patients attending outpatient clinic were prospectively enrolled. Objective frailty measurement was performed using: (1)Liver Frailty index (LFI) and (2)Short Physical Performance Battery (SPPB). Decompensation was defined as new-onset ascites, portal hypertension-related gastrointestinal bleeding, hepatic encephalopathy or acute kidney injury. Overall survival (OS) and probability of decompensation-free at 1-year were evaluated and compared between frail and non-frail patients by log-rank test.

Results:
A total of 158 cirrhotic patients were included (age 62.5±9.4 years, male 57.6%, MELD 9.3±3, Child A/B/C 81.6%/15.2%/3.2%). Main causes of cirrhosis were alcohol (29.7%), HCV (27.8%) and HBV (25.3%) infection. Mean follow-up duration was 10.1±3.9 months. The proportion of frail patients were 26.6% by LFI and 41.8% by SPPB criteria. By using LFI criteria, those who fail were older, female preponderance, had higher MELD, lower hemoglobin, higher serum creatinine, lower serum albumin, and higher INR. The cumulative 1-year OS of total population was 93.2%. The cumulative 1-year OS was significantly lower in frail patients (81.12% vs 96.75%, $p<0.01$ by LFI criteria, and 100% vs 83.22%, $p<0.01$ by SPPB criteria). The cumulative probability of 1-year decompensation-free was significantly lower in frail patients (60.53% vs 85.1%, $p<0.01$ by LFI criteria, and 67.12% vs 87.14%, $p<0.01$ by SPPB criteria).

Conclusions:
Frailty status is commonly found in stable cirrhotic patients, and is a poor prognostic factor of decompensation and survival. Prompt intervention might improve long-term prognosis in these patients.

T-53

Repeated versus Single Treatment of Esophageal Variceal Ligation after Esophageal Variceal Bleeding: Multicenter Retrospective Study

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Objectives:
International guidelines recommend repeated esophageal variceal ligation (EVL) for treatment of esophageal variceal bleeding. However, due to patient compliance and complications of repeated EVL procedure, many physicians perform single EVL treatment after varix bleeding. We aimed to compare the risk of variceal re-bleeding after repeated EVL versus single EVL.

Materials and Methods:
This retrospective study included consecutive patients who underwent initial esophageal variceal ligation (EVL) for the first esophageal variceal bleeding. Primary endpoint was the recurrence of variceal bleeding and uni-/multi-variate analyses were conducted to find independent predictors.

Results:
A total of 210 patients were included: 133 in the repeated EVL group and 77 in the single EVL group. During follow-up duration (median=46.5 months), 17 (12.8%) in the repeated EVL group and 36 (46.8%) in the single EVL group developed re-bleeding (P<0.01 by log-rank test). However there were no difference of overall survival between the two groups (P=0.05). Multivariate analysis showed that the single EVL group compared to the repeated group (adjusted hazard ratio [aHR]=3.372, 95% confidence interval [CI]=1.824–6.234, P<0.001) was the only independent risk factor after adjustment for alcohol etiology (HR=3.370, 95% CI=1.717–6.618, P<0.001), combined gastric varix (HR=1.333, 95% CI=1.250–9.612, P=0.017) and high MELD score (HR=2.379; 95% CI=1.192–4.748; P=0.014).

Conclusions:
Repeated EVL after esophageal varix bleeding can improve re-bleeding. However, there was no difference in overall survival. Further randomized control studies are needed.

T-54

Hepatic Encephalopathy in ACLF – Is intravenous BCAA the answer? Interim analysis of the BCAA-ACLF Trial

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Objectives:
A prospective, randomized controlled clinical trial was conducted to study efficacy of intravenous branched chain amino acids (BCAA) with lactulose versus lactulose alone in treatment of hepatic encephalopathy (HE) in acute on chronic liver failure (ACLF). Improvement in encephalopathy at 72-hours and survival at day 7 and 28 was measured.

Materials and Methods:
CANONIC ACLF patients with HE grades ≥ 2 received IV BCAA (500mL/day for 3 days) + Lactulose (Treatment Arm, n=34) or Lactulose alone (Control Arm, n=34). Six patients developed COVID-19 & were excluded after enrollment (4-treatment arm & 2-control arm). Grade of HE was assessed by West Haven Classification and Hepatic Encephalopathy Scoring Algorithm (HESA). ACLF severity was determined by CLIF-C ACLF, MELD and Child-Pugh's Score. All patients received standard of care for HE and ACLF management.

Results:
Both groups were similar in baseline characteristics including grade of HE (2.9 ± 0.7 vs 2.8 ± 0.6; p = 0.613) and CLIF-C ACLF score (54 ± 5.9 vs 55.34 ± 5.4; p = 0.383). Overall survival was 40% at 28 days (50% vs 31.2%; HR – 1.7 [0.88-3.28]; p=0.113). Significant improvement in HESA score by ≥1 grade at 24 hours was seen in 14 patients (46.7%) in treatment group and 6 patients (18.7%) in control group (p=0.029). Median change in HESA score at 24 hours was significantly more in treatment group than control group (p=0.003) however, this was not sustained at day 3 or 7.

Conclusions:
Intravenous BCAA does not improve HE or survival in ACLF.

T-55

Utility of Bispectral Index for objective assessment of Hepatic Encephalopathy in Acute on Chronic Liver Failure

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Objectives:
A prospective, observational, single center study to objectively assess hepatic encephalopathy (HE) in patients with acute-on-chronic liver failure (ACLF) by using the Bispectral index (BIS) was designed. The primary outcome was correlation of BIS with grade of HE.

Materials and Methods:
Sixty-two patients of CANONIC ACLF with HE grades ≥2 were prospectively recruited and followed sequentially for 28 days. Assessment of HE was done using West Haven Classification (WHC) and Hepatic Encephalopathy Scoring Algorithm (HESA). Optic nerve sheath diameter (ONSD) was available for 26 patients. Average BIS over 10 minutes was assessed on day 0, 1, 2, 3 and 7. In patients on mechanical ventilation, BIS was measured 1 hour after stopping sedation.

Results:
Sixty-two patients were included in the study (Mean Age – 48.1 ± 11.9; 87% Males). 23 patients (37%) required mechanical ventilation. Mean MELD score was 24.23 ± 7.02 while mean CLIF-C ACLF score was 54.7 ± 5.67. Mean baseline ammonia level was 140.5 ± 56.2. Mean baseline HESA grade was 2.85 ± 0.67. Median BIS was 82 [78-84]. Mean baseline ONSD was 3.59 ± 0.46. Total BIS recordings were 292 at different time points. However, 49 recordings (16.78%) were excluded due to presence of artefacts or EMG ≥ 45. BIS had significant negative correlation with HESA (r2 = -0.79), WHC (r2 = -0.81), CTP score (r2 = -0.54) and ONSD (r2 = -0.53).

Conclusions:
BIS may be used objectively for HE assessment, however presence of artefacts and muscle activity hampers its clinical utility.

T-56

Platelets In Chronic Liver Disease: Beyond Numbers…

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Objectives:
Thrombocytopenia, a complication of Chronic Liver Disease (CLD), is considered to be a marker of advanced disease and an independent predictor of mortality. But this is disputable and hence is this study 1. To find out prevalence of thrombocytopenia in CLD; 2. To find out association with severity of liver disease and other variables like age, duration of illness, etiology.

Materials and Methods:
This was a descriptive study analyzing CLD patients diagnosed by clinical, biochemical, serological and radiological evaluation in our institution between March 2019 and December 2020.

Results:
There were 48 patients; M:F 43:5; mean age 51.7±12.4 years; Thrombocytopenia: Mild (149999-75000/cu.mm) in 45.8%, moderate (74999-50000/cu.mm) in 12.5% and severe (<49999/cu.mm) in 8.3%. There was no association of thrombocytopenia with severity indices like Child-Pugh Class and MELD-Na score (Model for End-stage Liver Disease Sodium). There was no association with etiology, BMI, and duration of illness. International Normalized Ratio was associated with MELD-Na score and Child-Pugh Class.

Conclusions:
The prevalence of thrombocytopenia in CLD is 66.6% in this study. Thrombocytopenia is not associated with severity of disease. This necessitates larger studies and analyzing the factors other than number of platelets. This includes 1. functional status of platelets (thrombocythemia) 2. In a stable CLD, hemostasis and coagulation pathways achieve a delicate “rebalance state” (new normal) which may be tilted even by trivial insult. 3. Platelets also secrete platelet derived growth factor, transforming growth factor β, hepatocyte growth factor which can influence liver fibrosis and regeneration.

T-57

The prediction of liver decompensation using hepatic collagen deposition assessed by computer-assisted image analysis with Masson-trichrome stain

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Background & Aim;
There could be disagreement of fibrosis staging by METAVIR among pathologists. Quantification of fibrosis using computer-assisted image analysis can offer relative objective information for liver fibrosis. We measured hepatic fibrosis quantitatively using collagen proportionate area (CPA) and assessed its impact on predicting the development of liver decompensation (LD).

Methods:
During January 2010 to June 2018, we assessed 582 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 LD. Forty-two patients were excluded.

Result:
The mean age was 45.3±13.7 years, and most common etiology of liver disease was chronic hepatitis B (28.6%). Median follow-up duration was 37 months during which 28 out of 540 patients experienced LD. Mean analyzed dimension of collagen was 5653362±2423925 μm2 and included portal tract was 8.9±3.9. Mean CPA was 8.91±7.10 %. Albumin at baseline (HR: 0.257, 95% CI: 0.094-0.701, p=0.008), CPA (HR: 1.107 per 1% increase, 95% CI: 1.059-1.157, p<0.001), presence of diabetes mellitus (HR: 4.315, 95% CI: 1.063-17.510, p=0.041), and presence of alcoholic hepatitis (reference : chronic hepatitis B) (HR : 5.811, CI : 1.351-24.987, p=0.018) were independent predictors of LD on multivariate Cox-regression analysis. The concordance indices of CPA and METAVIR stage for progression to LD were 0.803±0.044 and 0.758±0.041, respectively, without significant difference.

Conclusions:
The CPA is an independent predictor of clinical outcomes in liver disease.

Training and Education (Career Development)

U-01

Assessing the knowledge of trainee residents for liver involvement and related issues in COVID-19 pandemic.

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Objectives:
To assess the knowledge of internal medicine and gastroenterology trainees regarding liver involvement and related issues in the current COVID-19 pandemic.

Methods:
This online survey comprised of 10 questions designed to examine the basic knowledge of Sars-Cov-2 virus, knowledge regarding liver involvement in COVID-19, and the ability to decide on patient care.

Results:
A total of 100 responses were collected. Most of the responses were from Pakistan (n=75). More than 80% of trainees responded correctly regarding the accurate indication of endoscopic procedures during COVID-19 pandemic, absence of ACE-II receptor expression on astrocytes, upper respiratory secretions being an eligible sample for SARS-COV-II, avoiding regular outpatient follow up, avoiding hyDr.oxychloroquine as a prophylactic Dr.ug, and azithromycin in decompensated cirrhosis, continuing beta-blockers and lactulose in a decompensated patient, melena being an accurate indication for screening endoscopy and the choosing right set of PPEs. Less than 50% of responders knew correctly regarding NAFLD being a notorious factor for COVID-19 related complications, ACE-II receptor expression by cholangiocytes and enterocytes, saliva and stool being an eligible sample for SARS-COV-II detection, palliative approach as an appropriated management step for decompensated-CLD patients and history of ascites as an appropriate indication for screening endoscopy. GI trainees performed better in some areas of knowledge

Conclusions:
Trainees were updated in many aspects of the recent guidance in the management of COVID-19 but there were many lacunae in the knowledge. So, continuous medical education activities are essential to keep the residents updated about the changing developments in the management of COVID-19.

U-04

Video-assisted Liver Ultrasound Training for Non-radiologists

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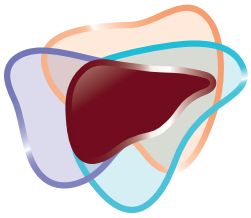
Objectives:
Ultrasound is a useful tool that helps the physicians for bedside diagnosis in several conditions. The limitation of ultrasound training in non-radiologists is time constraints. We conducted a prospective study to assess those physicians' ability in identifying the organ structures during a liver ultrasound performing after studying the self-learning ultrasound lessons in a video format.

Materials and Methods:
We developed a short video-lecture on liver ultrasound and a portable guidebook for image acquisition. Eighteen non-radiologist physicians studied the course and attended hands-on liver ultrasound examinations to capture the assigned images and label the acquired organ/structures, which were evaluated and scored by an expert radiologist.

Result:
130 liver ultrasound examinations were performed. The overall mean image acquisition score was 84.5±9.7%. The mean score of the 1st examination was 75.2±16.4%. The mean score was >80% since the 2nd examination. Eleven (61%) participants had initial low score (the 1st examination score less than 80%). The 2nd examination score significantly increased from the 1st examination score in the participants with an initial low score (84.7±14.1% vs. 64±8.6%, p=0.002). When performing ultrasound in cirrhotic cases, the score was significantly lower than non-cirrhotic cases (78.8±17.3% vs. 88.3±14.4%, p=0.001). The participants' year of study and experience in previous ultrasound training did not affect the image acquisition score.

Conclusions:
The liver ultrasound training course in a short video format with a portable guidebook is effective and relatively low time-consuming for teaching non-radiologists to perform bedside liver ultrasound.



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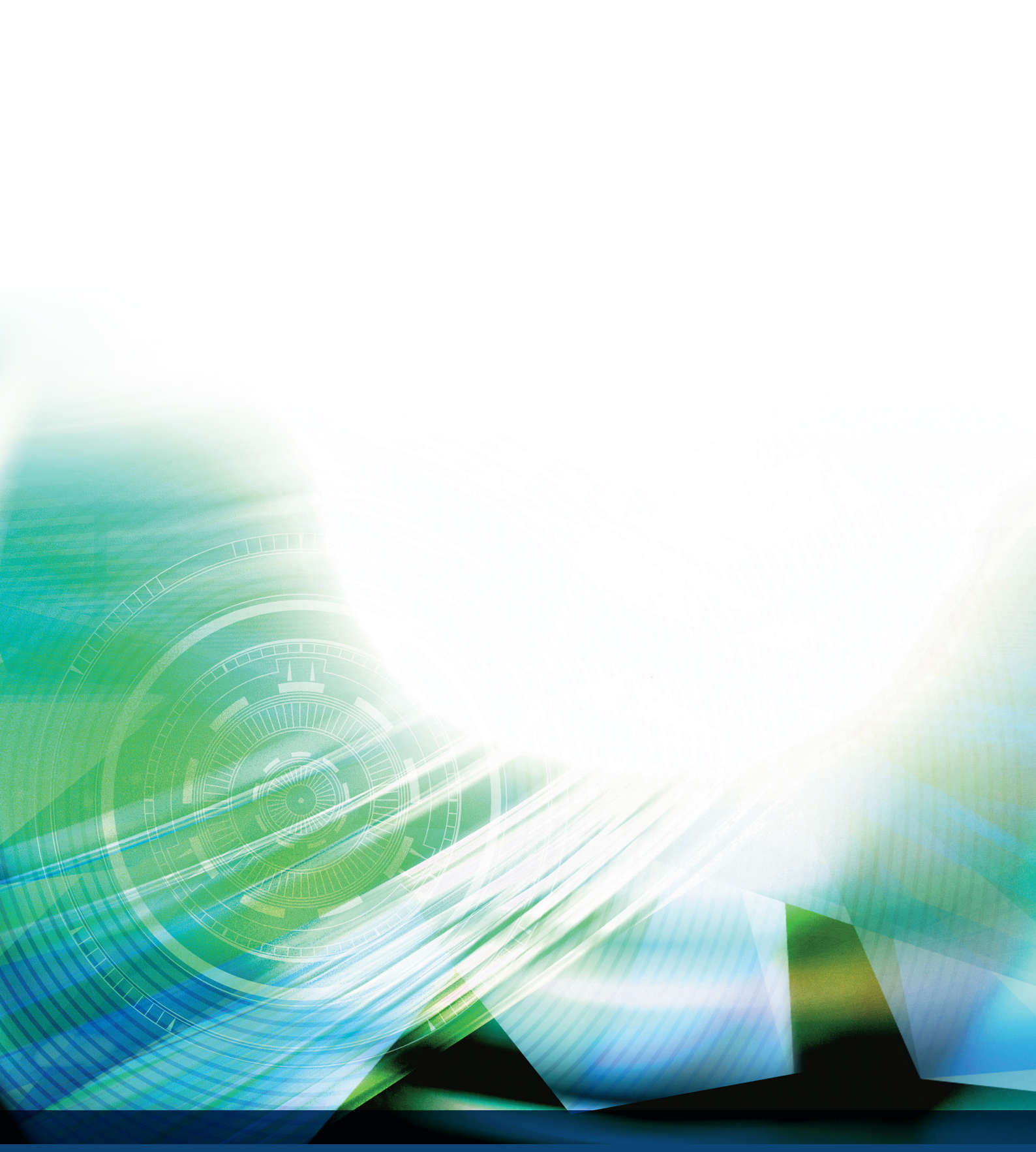

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