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Diagnosis and treatment of hepatitis C virus in a Spanish jail

Multidisciplinary Support Program for patients with addictions and suspected chronic hepatitis C (MSP ADIC-C) to improve their evaluation and access to antiviral treatment

High SVR rates in patients with and without cirrhosis treated in real life with Sofosbuvir/Velpatasvir (SOF/VEL) combination for 12 weeks without Ribavirin (RBV)

Fast-track HCV check-up enhances possibility of sustained Virollogical response in HCV infected patients

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Parallel session: HCV: Striving towards elimination
South 2
Date & Time: Friday, 13 April 2018 - 17:00-17:15

HepFree: Screening migrant patients for viral hepatitis in primary care. A 90,000 patient randomised controlled trial indicates benefits are most obvious in older patients

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Background and Aims: Viral hepatitis prevalence is around 0.5% in the UK, but higher in migrant populations. No studies have identified strategies for testing and treating Hepatitis B (HBV) and Hepatitis C (HCV) in migrants in primary care. HepFree is a large, national screening trial involving 92,000 patients in control and intervention primary care practices.We report on characteristics and outcomes of patients attending for primary care viral hepatitis screening.

Methods: HepFree was a cluster randomised trial involving 58 primary care practices [8 control/50 interventional] in 3 areas of high density migrants (Bradford, East and South London) between 2013–2017. 59,390 eligible patients (aged over 18 and from a high-risk density migrants (Bradford, East and South London) between 2013–2017) were invited to control primary care practices who were paid per patient tested. In control practices where migrant population as per WHO prevalence by country ) who had never tested for HBV/HCV were invited by letter for screening at intervention practices who were paid per patient tested. In control practices where local protocols applied, screening rates were measured in the 32,722 eligible adults.

Results: In intervention practices, of 59,390 invited patients, 11,611 (19.4%) tested for both HBsAg and HCV Ab, compared with 555/32,722 (1.7%) in control practices (p = 0.011). In intervention practices, 57.5% of tested patients were female. 32% of eligible patients from the Indian sub-continent (Bangladeshi, Indian or Pakistani) were tested. 8.6% of eligible Black Afro-Caribbean patients were tested. 15% of patients aged 18–39 years were screened compared to 29% in patients older than 40 years. In control practices, testing rates were similar in the different ages (0.9% in patients aged <40 years, 1% in aged > 40 years). 115 patients (0.90%) tested HBsAg positive. 80 (69.5%) were male, 67 (58.2%) were East Asian, 26 (22.6%) Afro-Caribbean. 5 (4.35%) were eAg positive and 2 others (1.74%) delta positive. 6.1% had severe fibrosis or cirrhosis on ultrasound or transient elastography, mean age (MA) 46 years (range 18–83). 103 (0.81%) tested HCV Ab positive, of whom 38/103 (36.9%) were viraemic. 34 (89.5%) were South East Asian, and 15.8% had severe fibrosis or cirrhosis, MASO years (range 35–82). There were no cases of co-infection with HBV/HCV or HIV and no hepatocellular carcinoma. In 8 control practices, of 32,722 eligible patients 17/555 (3.1%) tested positive. Both testing and positivity rates were low in young (<40) indicating that screening in this group by GP invitation may not be cost-effective.

Conclusion: In this 92,000 patient study where doctors were encouraged and paid to test migrants almost 20% of eligible patients were tested. High rates of infection (1.7%) were found. Young patients are unlikely to present for testing and, if so, are unlikely to be positive. The converse is seen in older patients. These data indicate that screening in primary care should be targeted at older patients and alternative strategies applied for younger people where rates of infection are lower.

Figure: Relationship between PDGF-β serum concentration and platelet counts. (A) PDGF-β serum concentrations correlate with platelet counts, suggesting that platelets are a source of PDGF-β in humans. (B) The ratio of PDGF-β serum concentration divided through platelet count is higher in patients with liver fibrosis compared to patients without liver fibrosis. (Fib., fibrosis.)

Conclusion: There is a protective association between the usage of antiplatelet agents and occurrence of liver fibrosis. A randomized controlled trial is needed to explore the potential of antiplatelet agents as anti-fibrotic therapy in patients at risk for liver fibrosis progression.

Parallel session: Cirrhosis: Portal hypertension and complication
North 1
Date & Time: Saturday, 14 April 2018 - 08:00-08:15

A spleen stiffness measurement-based model for recognition of high risk varices: Baveno VI criteria and beyond

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Background and Aims: Recently, Baveno VI guidelines suggested that esophagegastroduodenoscopy (EGD) can be avoided in patients with cACLD who have a liver stiffness measurement (LSM) <20 kPa and platelet count >150,000/mm³. We aimed to assess the performance of spleen stiffness measurement (SSM) in ruling out patients with high risk varices (HRV); we also aimed to validate Baveno VI criteria in a large population and assess how the sequential use of Baveno VI criteria and SSM could safely avoid the need for endoscopy.

Method: We retrospectively analysed 498 cACLD patients who had undergone LSM/SSM by transient elastography (TE), platelet count and EGDs from 2012 to 2016 referred to our tertiary centre. We performed multivariate analysis and split validation to define the role of SSM in predicting HRV. The derivation dataset consisted of 54 randomly selected cases and 129 randomly selected controls from the original datasets of 100 cases and 398 controls; consequently, the validation dataset includes 46 cases and 123 controls.

Results: At the multivariate analysis, LSM (OR = 1.108; 95%CI = 1.072–1.145), LSM (OR = 1.068; 95%CI = 1.042–1.096), platelet count (OR = 0.985; 95%CI = 0.979–0.993) and Child-Pugh B (OR = 3.06; 95%CI = 1.654–5.692) were independent predictors of HRV. With the aim of identifying, by SSM ROC curves, the most accurate SSM cut-off to rule out patients with HRV [corresponding to a low probability (<5%) of HRV presence], a cut-off ≤ 46 kPa was chosen. The performance of SSM (≤46 kPa) in ruling out HRV showed a sensitivity of 97.8%, a specificity of 44.9%, NPV of 98.9% and an LR- of 0.05. Applying the newly identified SSM cut-off (≤46 kPa) or Baveno VI criteria, 36.7% and 21.7% of patients in the validation cohort could have avoided EGD, with HRV being missed in 1% in both cases. The combination of SSM with Baveno VI criteria would have made it possible to avoid an additional 22.5% of EGDs if compared with Baveno VI criteria alone, thus reaching a final value of 44.2% of avoided EGD, with <5% missed HRV.

Conclusion: The study indicates that SSM is not only an independent predictor of the presence of HRV but is also an accurate and noninvasive test for ruling out HRV and that combining it with Baveno VI criteria in a simple sequential algorithm makes it possible to safely avoid a significant larger proportion of unnecessary endoscopies.

Figure: (abstract: PS-135): Rate of spared endoscopies by each of the considered non-invasive models. All percentages (%) are referred to the entire population (n = 498), represented as the combination of the derivation and validation cohort. In the new combined model Baveno VI/SSM ≤ 46 kPa, the rate of the spared endoscopies is reported also in the column graphs as the sum of the patients that fulfill only the Baveno VI Criteria (SSM > 46 kPa), patients with SSM ≤ 46 kPa (outside Baveno VI Criteria) and patients that would have avoided endoscopy according to both models (in overlapping area).

Conclusion: Our study indicates that SSM is not only an independent predictor of the presence of HRV but is also an accurate and noninvasive test for ruling out HRV and that combining it with Baveno VI criteria in a simple sequential algorithm makes it possible to safely avoid a significant larger proportion of unnecessary endoscopies.
**Results:** Serum liver enzymes (ALT, AST, GGT, and ALP) were mostly within the normal range, but significantly higher in PiZZ carriers compared to non-carriers. Significant liver fibrosis (LSM ≥ 7.1 kPa) was observed in 24% of PiZZ subjects (95/403), whereas advanced liver fibrosis (LSM ≥ 10.0 kPa) was present in 13.2% PiZZ carriers (53/403) and in 1.3% of non-carriers (OR = 18.9 [4.4–80.3]). Severe liver steatosis (CAP ≥ 280 dB/m) was detected in 39% of PiZZ patients (157/403) vs. 31% of non-carriers (OR = 2.1 [1.4–3.3]). Likewise, PiZoverexpressing mice developed hepatic steatosis. Lower serum triglyceride, VLDL, and LDL cholesterol levels detected in PiZZ patients indicated impaired hepatic lipid secretion. The observed metabolic alterations and increased liver fibrosis/steatosis were also detected, when only patients without AAT augmentation therapy were considered. Moreover, the presence of liver fibrosis or steatosis was not associated with the severity of lung disease (COPD assessment test or need for long-term oxygen therapy). Several demographic and laboratory parameters discriminated between PiZZ carriers with and without significant liver fibrosis. Using a machine learning algorithm, a score consisting of gender, BMI, GGT and platelet count predicted the presence of significant liver fibrosis with 85% accuracy (AUROC 0.77). As only 45% of PiZZ adults receive regular assessment of liver enzymes, this score might help to determine which patients deserve further hepatologic workup.

**Conclusion:** This study defines the liver phenotype of adult PiZZ carriers and uncovers associated metabolic alterations. Together with the identified predictors, these findings facilitate the hepatologic assessment and counseling of PiZZ patients.

**PS-180**

Parallel session: NAFLD: Diagnostics and non-invasive assessment
South 2
Date & Time: Saturday, 14 April 2018 - 08:45-09:00

**Performance of controlled attenuation parameter (CAP) to assess steatosis in a large prospective multicentre UK study of patients with non-alcoholic fatty liver disease (NAFLD)**


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**Background and Aims:** The objective of this prospective study was to evaluate the diagnostic performance of CAP by FibroScan using either the M or XL probe, selected using the machine-embedded automated probe selection tool, in a cohort of patients with NAFLD versus steatosis at liver biopsy.

**Method:** According to the sample size calculation, 450 patients were enrolled to undergo FibroScan examination within 2 weeks of a clinically indicated liver biopsy (LB) for suspected NAFLD. Recruitment took place (Mar 2014–Jan 2017) at seven UK centres. LB were scored by two expert pathologists in a blinded manner with consensus using the NASH CRN system. NASH was diagnosed using the FLIP algorithm. Diagnostic performance was assessed using area under the receiver operating curve (AUC). Cut-offs are computed for the Youden index and a sensitivity and a specificity of 90%.

**Results:** Among the 408 patients who completed the study, 381 had a valid FibroScan examination with CAP and a LB interpretable according to pathologist. 45% were female, with a median age 54 [IQR 18] years and BMI 33.8 [9.3] kg/m². Steatosis distribution was: S0: 12%, S1: 23%, S2: 28%, S3: 36%. 64% had NASH. The performance of CAP in distinguishing categories of steatosis is shown in the figure below.

**Conclusion:** CAP had good performance to distinguish steatosis (S ≥ 1) but showed modest performance for the detection of higher grades of steatosis.
POSTERS

THU-050

Comorbid disease burden in patients with primary liver pathologies- data from a comprehensive analysis of serial transient elastography and other liver disease evaluations at the Toronto liver centre (CASTLE-TLC)

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Background and Aims: There is increasing interest in characterizing the burden of comorbidities in patients with diverse etiology. There is evidence that aging patients with chronic hepatitis B have a higher incidence of diabetes, hypertension and renal insufficiency. Similarly, clinical manifestations of late stage NAFLD and NASH have been associated with many aspects of metabolic dysfunction. This analysis, the first in an ongoing long-term retrospective analysis, aims to assess the burden of comorbidities in liver disease patients at a large urban liver clinic in Toronto, Canada.

Methods: 3,610 patient charts were retrospectively reviewed and was assigned to one of the following primary liver disease categories: chronic hepatitis B (HBV), chronic hepatitis C (HCV), NAFLD/NASH, autoimmune liver disease (AIH), alcoholic liver disease (ALD), and others. Patient age, sex, BMI, serial liver histology and serology were collected to look at the incidence of obesity (BMI > 29.9), hypertension (HTN), dyslipidemia, type II diabetes, gastroesophageal reflux disease (GERD), cardiovascular disease (CVD), thyroid disease, and various carcinomas.

Results: 3,610 patient charts reviewed: 56.2% males, 43.8% female; percent distribution of liver disease were as follows: NAFLD/NASH 47.7%, HCV only 16.1%, HBV only 16.2%, others 19.8%, with 52.9% ≥50 years of age at last visit. 58.9% of patientswere reported to have only 1 liver disease; and 41.1% were reported to have 2 or more liver conditions. The most frequently reported comorbidities were HTN (26.8%), dyslipidemia (26.6%), diabetes (16.1%), thyroid disease (14.4%), and GERD (11.3%). HTN, dyslipidemia and diabetes occurred with greater frequency in the NAFLD/NASH patients compared to those with viral hepatitis (HBV and HCV). Cancer of any type was reported in 6.8% of patients (246/3610), with the following cancers found most frequently: liver/HCC (28.9%) breast (21.1%), and thyroid (8.1%). NAFLD /NASH contributed to 42.2% of overall cancer incidence, with higher number of breast and thyroid cancer reported in NAFLD/NASH patients.

Conclusion: The burden of comorbidities is high among a large sample of liver disease patients of diverse etiology, and is particularly pronounced in patients with NAFLD/NASH, with slightly higher percentage of certain cancers seen in NAFLD/NASH patients compared to other liver disease patients, although the incidence of cancer reported in this cohort was low. While these data are in agreement with much of the emerging data in patients with NAFLD/NASH, data collection for this study will continue with future analyses currently being planned.

THU-073

Transient elastography for screening of liver fibrosis in the population: A cost-effectiveness analysis using prospective databases from 6 countries in Europe and Asia


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Background and Aims: The global epidemic of obesity and diabetes leads to an increased incidence of nonalcoholic fatty liver disease (NAFLD) posing a challenge to current hepatic clinical pathways in our healthcare systems. The aim of the present study is to explore the cost-effectiveness of transient elastography (TE) as screening method to detect advanced liver fibrosis in the general population.

Methods: Microdata from 7 independent prospective databases from 6 countries (5 in Europe and one in Asia) (n = 6,295), mean age = 54.7 (12.2), mean BMI = 27.0 (4.9) with mean liver stiffness measurement (LSM) value = 5.6 kPa (5.0) was merged and analyzed with data mining techniques (conditional inference trees, logistic regression and Heckman sample-selection models) to explore the relationship between socio-demographics, comorbidities, LSM, and hepatic fibrosis, as assessed by liver biopsy in 295 patients. The results were used in the parameter tuning of one cost-effectiveness model (Tanajewski L et al., BJM 2017) for a risk-based community stratification strategy in each of the populations.

Results: Heckman’s inverse Mills ratio was −0.23, p = 0.343, indicating that the biopsied subsample of patients is consistent with no selection bias. A LSM cut-off of 9.1 kPawas found to provide the best discriminatory accuracy (DA) for advanced fibrosis (stages ≥ F2), AUC = 77.46% (95%CI 0.71–0.83). 343 (5.45%) patients of the whole sample presented LSMvalues above the selected threshold. The mean incremental cost-effectiveness ratios (ICER) of the risk-stratification strategy ranged from 4,034€ (95%CI 4,531–2,853€) per quality-adjusted life-year (QUALY) to 849€ (95%CI 1,533–603€) per QUALY depending upon the targeted population. For comparison we used the ICER of hepato cellular carcinoma screening published in 2016 that was found to be 39,825USD (Kuo et al., WJG 2016).

Conclusion: The evidence presented suggests that community risk factor-based TE screening pathways performed at primary care centres is a highly cost-effective intervention and potentially costsaving for health systems in need for better resource allocation within their provision of care. Compared to previous published in hepatocellular carcinoma screening, our findings suggest that an earlier detection of fibrosis associated with NAFLD leads to a 10-fold improvement in cost-effectiveness estimates in European and Asian contexts.

THU-106


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Background and Aims: HepCARE is an end to end viral hepatitis
(HBV and HCV) patient management tool. HepCARE enables simple, automated, rapid identification and analysis of patient cohorts and provides a single system for management of patients during clinic visits. Funding for HepCARE at our centre was provided by a service to medicine grant from Gilead Sciences. HepCARE can also assist in the provision of an outreach service for the treatment of HCV and HBV, through the analysis of geographical and liver health data.

Method: All patients with a positive marker of HBV and/or HCV were identified through read code searches to create the database. All relevant lab test results were then extracted and uploaded to HepCARE. New patient diagnoses of HBV and/or HCV are instantaneously transmitted to HepCARE through the hospitals electronic patient records. In parallel, transient elastography (Fibroscan), CAP score and clinically relevant laboratory results are also transfer electronically to HepCARE.

Results: HepCARE has collated data on 9,816 patients with viral hepatitis attending Liver Services at our centre (HBV: 6524; HCV: 3292). To date, 891 HCV treatment outcomes following direct-acting antiviral therapy have been identified by HepCARE. This includes 319 patients who have cirrhosis who have been identified for ongoing HCC surveillance and follow-up. A further 1,506 individuals with untreated HCV infection have been identified, of these, 1,094 were previously known to the service but have not attended their clinic appointments in the past 18 months. Of these, 294 have cirrhosis based on FIB-4 and/or Fibroscan data. 26.9% are thought to be alcoholic. Of those with HBV, 3,375 are currently engaged with our viral hepatitis service, and 481 are cirrhotic. Analysis of the geographic distribution of patients with HCV who are awaiting treatment is ongoing. Extraction of patients’ geographic and liver health data is enabling service redesign to ensure the provision of HBV/ HCV treatment services are directed towards high prevalence areas. Data will be presented on the impact of HepCARE on the redesign of HCV outreach services.

Conclusion: The use of HepCARE has reformed local clinical management, and will enable large-scale patient reengagement with our service. It also facilitates in-depth analysis of the patient cohort attending the viral hepatitis service at our centre. Future strategies include linking raw patient data from primary care to assist with case finding, and mapping of geographic inequalities in diagnoses and treatment, to ensure equity in access to care.

THU-236
Risk stratification using transient elastography and the new scoring systems for patients with primary biliary cholangitis
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Background and Aims: The recent EASL guidelines recommend the use of transient elastography (TE) to monitor PBC progression and the risk scores to better define the individual risk of development of complications.

Method: 154 PBC patients prospectively seen between January 2009 and July 2017 were enrolled into the study. TE was performed at baseline and every 2 years thereafter (in the follow-up 111 pts had 2 measurements, and 52 pts 3 measurements). A cut-off of ≥9.6 kPa was chosen to determine the risk of decompensation. Globe score and UK-PBC scores were calculated at each interval. Risk factors were assessed using Cox proportional hazard models. Longitudinal variations of liver stiffness (LS) were assessed with the following formula: ΔLS/Δt = (LS2 − LS1)/(t2 − t1).

Results: At baseline LS was positively correlated with the Globe score (r = 0.395, p = 0.01). UK-PBC score provided a survival outcome at 5, 10, and 15 years significantly correlated with the LS (p < 0.001).

Conclusion: LS measurements and risk stratification scores are useful tools in the follow-up of PBC patients to establish prognosis and for decision-making for second line therapy.

THU-287
Treatment of chronic hepatitis C with direct acting antivirals and its effect on body mass index and hepatic steatosis as measured by controlled attenuation parameter
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Background and Aims: Direct Acting Agents (DAAs) have high cure rate but still lack the knowledge of their effect on hepatic steatosis in chronic hepatitis C (CHC). Controlled Attenuation Parameter (CAP), evaluated with transient elastography, could help in assessment of steatosis grades. Aim: to evaluate the effect of DAAs on body mass index and steatosis in CHC using CAP.

Method: This cohort study included 155 CHC patients, divided into 3 groups according to the DAAs regimen. All patients were subjected to pre-treatment and 3-months post-treatment BMI, laboratory workup and liver stiffness measurement and CAP using the FibroScan® M probe. Cut off values for steatosis: S0: <238 dB/m = Grade 0, S1: 238–258 dB/m and S2: 259–291 dB/m = Grade 1 (mild-moderate steatosis) and S3: ≥292 dB/m = Grade 2 (severe steatosis). Changes in steatosis grades were defined as improvement or worsening (one grade or more change).

Results: Patients mean age was 45.78 ± 11.6 years, mean BMI 26.63 ± 2.75 and 18.1% were cirrhotic. Baseline assessment revealed no steatosis in 43.9%, 32.9% had mild-moderate steatosis and 23.2% had severe steatosis. The overall sustained virological response 12 was 93.6%. Followup revealed stationary steatosis in 56.7% and regression in 21.3%. Mean pre-treatment CAP were significantly lower in responders 244.9 ± 62.4 dB/m vs non-responders; 300 ± 28.4 dB/m (p = 0.04). ROC curve delineated 273 dB/m as best cut-off for detection of responders with an AUC of 0.81, sensitivity 68.2%, and specificity 100%. BMI significantly increased after treatment (p = 0.004) particularly in patients with worsened steatosis (p = 0.001). On the other hand, a decrease in BMI was found in 55% of patients with improved steatosis grade. Steatosis significantly correlated with BMI (r = 0.3, p < 0.001).
**THU-290**

**Diagnosis and treatment of hepatitis C virus in a Spanish jail**


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**Background and Aims:** HCV infection in prisoners is considered a special care group in the National Hepatitis C Plan in Spain with high risk of transmission. Our aim is to assess the efficacy and safety of new DAA in VHC patients of the Picassent’s Penitentiary Center (PPC) – 2,200 inmates - whose referral hospital is the University General Hospital of Valencia (CHGUV).

**Method:** All incoming inmates are screened for anti-HCV antibody and those with HCV viremia are remitted to CHGUV to undergo a full diagnostic study, including transient elastography (Fibroscan), before being treated according to current guidelines. 197 patients have been treated with DAA, 182 (92.4%) were males, the median age was 46 years (23–68), 77 (39%) had a history of drug addiction, 77 (39%) were HIV co-infected. 32 (16.2%) had received prior treatment. According to degree of fibrosis, 51 were F0-F1 (25.5%), 60 F2 (30.5%), 42 F3 (21.3%) and 44 F4 (22.3%). The most common HCV genotypes (G) were G1a (89 patients, 45.2%), followed by G3 (43 patients, 21.8%), G4 (36 patients, 18.3%), G1b (20 patients, 10.2%), G1 (5 patients, 2.5%), G2 (1 patient, 0.5%) and 3 coinfections (1.5%): 1 + 3, 1a + 4 and 1b + 4. The prescription and follow-up until viral response has been done by hepatologists and infectologists, and the clinical evolution by a physician of the CPP with controlled administration of the pills. Patients have been treated with different combinations of DAA according to current guidelines, taking into account comorbidities, interactions, and avoiding the use of RBV: 126 patients with SOF + LDV (63.95%), 2 to 24w, 94 to 12w, 21 to 8w); 34 with SOF + DAC (17.2%), 10 with SOF + VEL (5.1%); 9 with EBV + GZV (4.6%); 8 with SOF + SMV (4%); 10 with 3D or 2D regime (5%).

**Results:** 135 of 197 (68.5%) treated patients have reached 12w after treatment, showing an overall SVR of 97.8% (132 patients), and 3 relapses (2.2%), 1 to 12w SOF + DAC and 2 to 12w SOF + LDV, one of them retreated with 24w SOF + EBV + GZV + RBV. There hasn’t been any serious adverse drug event nor death, although a chronic myeloid leukemia and a laryngeal neoplasm were diagnosed, both with SVR. Follow-up was more difficult due to frequent transfers of inmates from one prison to another and prisoners released during treatment and lost in follow-up.

**Conclusion:** Most of our inmates were men, naive to treatment and infected with 1a, 3 and 4 genotypes. The most used treatment has been SOF + LDV. DAA show a high efficacy (97.8%) and good security profile, similar to general population.

**THU-316**

**Multidisciplinary Support Program for patients with addictions and suspected chronic hepatitis C (MSP ADIC-C) to improve their evaluation and access to antiviral treatment**


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**Background and Aims:** Patients with addictions (illicit drugs or heavy alcohol intake) have high chronic hepatitis C (CHC) prevalence (32% in our area) (Roncero et al. EJGH, 2017). Alcohol intake and HIV coinfection accelerate the progression to cirrhosis and hepatocellular carcinoma in patients with CHC. Thus, it is a priority to create Multidisciplinary Support Programs (MSP) to identify, evaluate and treat these patients with direct acting antivirals (DAAs). The aim of our study was to create a MSP including primary care physicians and specialists in Mental Health, Internal Medicine, Pharmacy and Hepatology, for the screening, diagnosis, evaluation, treatment and follow-up of patients with addictions and suspected CHC (MSP ADIC-C).

**Method:** Open prospective study since January 2016, including patients with addictions and suspected CHC (HCV + antibodies) from our hospital. Patients dependent in basic activities of daily living (DBADL), deceased or in jail during the study period were excluded. CHC was confirmed using a PCR test with 15 IU/ml sensitivity. Fibrosis stage was evaluated using transient elastography (TE).

**Results:** 110 patients with HCV+ antibodies and addictions have been evaluated. Nine patients were excluded. Among 101 included patients, 78 (77.2%) were male, with median (range) age of 45.6 (25.6–64.4), 19 (18.8%) consumed some illicit drug, 17 (16.8%) alcohol intake, 57 (56.4%) under opioid replacement therapy and 8 (7.9%) were abstinent. Forty-seven (46.5%) had a severe mental disorder. Only 6 (5.9%) had received previous antiviral treatment. HIV antibodies were determined in 100 (99%) patients, being positive in 42 (42%), HCV-RNA in 91 (90%) confirming CHC in 90 (98.9%), and HCV genotype in 60 (59.4%). Liver fibrosis was evaluated in 55 (54.5%) patients, showing advanced fibrosis or cirrhosis (TE > 9 kPa) in 23 (41.8%). Treatment with DAAs was started in 22 (21.8%): 7 are in treatment, 2 lost during follow-up and 13 are in week 12 after end of treatment; 12 of them (92.3%) have achieved SVR12.

**Conclusion:** A Multidisciplinary Support Program for patients with addictions and suspected HCV infection (MSP ADIC-C) has allowed to identify and to diagnose practically all patients. Liver fibrosis has been evaluated in more than a half of them, identifying advanced fibrosis or cirrhosis in 41.8%. Preliminary SVR rate is high (92.3%).

**THU-323**

**High SVR rates in patients with and without cirrhosis treated in real life with Sofosbuvir/Velpatasvir (SOF/VEL)**


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11. Internal Medicine, Canosa

**Open prospective study since January 2016, including patients with addictions and suspected CHC (HCV + antibodies) from our hospital. Patients dependent in basic activities of daily living (DBADL), deceased or in jail during the study period were excluded. CHC was confirmed using a PCR test with 15 IU/ml sensitivity. Fibrosis stage was evaluated using transient elastography (TE).**

**Results:** 110 patients with HCV+ antibodies and addictions have been evaluated. Nine patients were excluded. Among 101 included patients, 78 (77.2%) were male, with median (range) age of 45.6 (25.6–64.4), 19 (18.8%) consumed some illicit drug, 17 (16.8%) alcohol intake, 57 (56.4%) under opioid replacement therapy and 8 (7.9%) were abstinent. Forty-seven (46.5%) had a severe mental disorder. Only 6 (5.9%) had received previous antiviral treatment. HIV antibodies were determined in 100 (99%) patients, being positive in 42 (42%), HCV-RNA in 91 (90%) confirming CHC in 90 (98.9%), and HCV genotype in 60 (59.4%). Liver fibrosis was evaluated in 55 (54.5%) patients, showing advanced fibrosis or cirrhosis (TE > 9 kPa) in 23 (41.8%). Treatment with DAAs was started in 22 (21.8%): 7 are in treatment, 2 lost during follow-up and 13 are in week 12 after end of treatment; 12 of them (92.3%) have achieved SVR12.

**Conclusion:** A Multidisciplinary Support Program for patients with addictions and suspected HCV infection (MSP ADIC-C) has allowed to identify and to diagnose practically all patients. Liver fibrosis has been evaluated in more than a half of them, identifying advanced fibrosis or cirrhosis in 41.8%. Preliminary SVR rate is high (92.3%).
Background and Aims: Pangenotypic regimens are now available for treatment of patients with chronic HCV infection. However, for some of them, treatment duration needs to be adjusted depending on cirrhosis and/or genotype. To confirm in real life usefulness of “one size fits all strategy using SOF/VEL for 12 weeks regardless of baseline features, we analysed data on treatments performed in Puglia (Italy) in patients with and without cirrhosis regardless of HCV genotype.

Method: From the Regional register, 1,099 patients were started on treatment from May 15th to November 1st 2017. Patients were treated at physician discretion and data collected within a collaborative group. Diagnosis of advanced fibrosis/cirrhosis was based on transient elastography and APRI score according to the standard thresholds. This analysis refers to 513 HCV mono-infected patients who completed SVR4 by November 1st.

Results: The majority of patients were male (55%), of mean age 63.2 (18–90). High proportion of patients (38.9%) was older than 70 yrs. 223 (43.5%) had cirrhosis/advanced fibrosis as compared to 27.8% with stage 0–1; the remaining had fibrosis stage 2. The proportion of naive was 75.3%. Diabetes was present in 20.5%, history of IVDA in 19.5% and active IVDA in 8.8%. GT1 was represented in 36.2% of cases; however, as a consequence of high GT2 prevalence in our region, GT2 was the most frequent (46.8%). Of the remaining, 17.2% had GT3 and 9.8% GT4. All but 4 patients received 12 weeks of therapy without RBV. 4 patients prematurely discontinued treatment; in 2 of 4 HCV RNA is currently undetectable. Overall, SVR was 98.6% at ITT analysis and 99% at PP analysis. Rates were 97.9% in patients with advanced fibrosis/cirrhosis and 98% in those with mild fibrosis. Among fibrosis stage 2, 100% of patients achieved SVR. No differences in SVR rates were observed across HCV genotypes: SVR was 100% in GT1b, 98% in GT1a, 97.9% in GT2 and 100% in GT3 and GT4. SVR was 99.2% and 98.6% in naive and experienced respectively. No difference in SVR rates was observed between diabetic and non-diabetics (100% vs 98.6%). Among IVDA, 100% achieved SVR.

Conclusion: Pangenotypic SOF/VEL combination is associated with 98.6% SVR4 in patients with all HCV genotypes, with or without cirrhosis treated for 12 weeks. RBV is not needed in patients with compensated cirrhosis treated with this combination. SOF/VEL is a suitable treatment for HCV infected patients regardless of baseline characteristics.

THU-353

Fast-track HCV check-up enhances possibility of sustained Virological response in HCV infected patients

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Background and Aims: New direct acting antiviral (DAA) against chronic hepatitis C virus (HCV) have drastically changed and shortened duration of treatments. However, the “HCV care course” (from diagnosis to sustained virological response (SVR)), remains an important challenge.

Aims: To evaluate the impact of a new fast-track HCV check-up in terms of retention in care and SVR. In order to assess the efficacy we provide a comparison between the first 50 pts of the FT-HCV (Fast track HCV check-up) in 2016 to 50 pts followed in our “standard” out clinic practice (control group (CG)) in 2015.

Method: FT-HCV is a new assessment unit of our center. In the same half-day, pts benefit of a complete assessment of liver function: blood test with HCV-Ab and HCV viral load, genotype (G) determination, Fibrotest®R and transient elastography. Three hours after admission, we were able to confirm HCV and to discuss the eligibility to an HCV treatment in accord to regulatory framework.

Results: Groups were comparable for age and sex: 50 pts of each group were analysed (FT-HCV: Male n = 34 (68%), mean age: 49 ± 14 years; CG: Male n = 35 (66.6%), mean age: 53 ± 13 years). In FT-HCV and CG fibrosis (F) was: mild F0-F1 n = 15 (30%), F2 n = 12 (24%) F3 n = 10 (20%), F4 n = 13 (26%), and, F0-F1 n = 18 (36%), F2 n = 12 (24%), F3 n = 9 (18%), F4 n = 10 (20%), unknown n = 1 (2%) respectively. All cirrhotic pts had compensated cirrhosis (Child A/MELD 8–10). Six pts (12%) in the FT-HCV group were excluded because HCV viral load was negative. G distribution in the FT-HCV and in CGwas: G1 n = 25(50%), G3 n = 8 (16%), G4 n = 11 (22%), and G2 n = 29 (58%), G2 n = 5 (10%), G3 n = 7 (14%), G4 n = 7 (14%), G6 n = 6 (4%) respectively. Thirty (69%) and 26 (52%) pts received DAA in FT-HCV and CG. Mean delay and numbers of out-clinic visits in FT-HCV and CG for treatmentwere 108 days (± 84) versus 260 days (± 85) p = 0.009 and 2 (2–5) vs 4 (2–9) p = 0.0003, respectively. To date in FT-HCV pts: SVR was achieved in 22 pts (74%), waiting for SVR12 in 7 pts (23%) and 1 pt was not responder (3%). Complete results SVR 12 for all pts will be presented. In CG SVR was achieved in 23 pts (88%), 1 pt was non-responder (3%) and 2 pts (6%) were lost of follow-up.

Conclusion: FT-HCV is a performing assessment of HCV infected patients and improves retention in care, management and rates of SVR.

THU-361

Hepatitis C direct-acting antiviral failures: clinical characteristics and resistance testing from a real-world setting


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Background and Aims: A small proportion of patients fail Hepatitis C (HCV) treatment with direct-acting antivirals (DAAs) for various reasons. Real-world data on DAA failures and the development of resistance associated substitutions (RAS) are limited. This study aims to characterize clinical parameters and RAS patterns in patients who failed DAA regimens.

Method: Retrospective chart reviewat two tertiary hepatology clinics between 01/2015 and 11/2017. Patients treated with DAAs who did not achieve SVR12were included. Baseline clinical characteristics and RAS testing at SVR12 were collected. HCV sequence data were obtained from next Generation Sequencing. Mutations >5% of viral population were reported. Resistance phenotypes was predicted based on EC50 fold-shift in mutant vs. wild-type replicons.

Results: Sixty-three patients were included: mean age 59.7 years (range 43–84) and mostly male (82.5%). Genotypes (GT) included GT1a (n = 28; 44.4%), GT1b (n = 8; 12.7%), GT2 (n = 5; 7.9%), GT3 (n = 19; 30.2%), GT4 (2; 3.2%), GT6 (n = 1; 1.6%). DAA regimen durations were 8 weeks (n = 6; 9.7%), 10 weeks (n = 11; 1.6%), 12 weeks (n = 38; 61.3%), 16 weeks (n = 2; 3.2%) or 24 weeks (n = 15; 24.2%). Pretreatment fibrosis by transient elastography (n = 41) revealed F0–2 (39.0%), F3 (12.2%) and F4 (48.8%). Post-DAA RAS testing was available for 59 patients. In 21 GT1a patients treated with SOF/LDV, 16 had a NSSA RAS, 8 of which were 93 position variant. All 6 GT1b patients who failed SOF/LDV had a NSSA RAS, with 5 being at position 93. 17 of 21 GT1a patients had an N53 RAS, 10 were Q80K. Two GT1a EBR/GZR failures had both a NSSA and a non-Q80K N53 RAS. 2 of GT1a patients who failed OBV/PTV/r + DSV/RBV, 1 had NSSA. In 17 of 19 GT3 patients RAS testing was available. DAA regimes included SOF/RBV (n = 11), SOF/VEL (n = 2), SOF/VEL/RBV (n = 2), SOF/RBV/Interferon (n = 2) and SOF/LDV/RBV (n = 2). Three patients had NSSB RAS, conferring possible SOF resistance (159wt/F, 321wt/A,
1425). There were no S282T RAS. All 4 GT3 patients failing SOF/VEL +/- RBV had NSSA RAS, 3 were Y93H. Of 11 GT3 patients with SOF/RBV +/- IFN treatment and RAS testing, 2 had NSSA RAS (S62L, A30K).

Conclusion: Distinct RAS patterns are present depending on genotype and DAA regimen failed. Virologic failure with a NSSA based regimen confers a high risk of developing a NSSA RAS, which may have implications on future treatments in these patients. Additional analysis to explore baseline patient characteristics associated with RAS is pending.

THU-375
Prevalence of baseline NSSA resistance associated substitutions in a real world cohort of veterans with chronic genotype 1 HCV infection

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Background and Aims: Data examining prevalence of Hepatitis C virus (HCV) NSSA resistance-associated substitutions (RAS) are limited to clinical trial cohorts. The aim of this study is to characterize the prevalence of baseline and pre-treatment NSSA RAS in a real world veterans cohort.

Method: This retrospective chart review examined 793 veterans with chronic HCV from the Atlanta Veterans Affairs Medical Center from March 16, 2016 to present. A convenience sample of 415 patients with HCV genotypes 1a, 1b, or 3 was analyzed. These patients underwent baseline/pre-treatment NSSA RAS testing at the Public Health Reference Laboratory (PHRL) in Palo Alto, CA. PHRL uses RT-PCR and population-based sequencing to determine the HCV NSSA gene amino acid sequence. Mixtures are scored at positions where the minority population is 20% or more. Demographic information included sex, age, and race. Other clinical information included HIV status, pre-treatment HCV viral load, any prior HCV treatment, and pre-treatment fibrosis-4 (FIB-4) score. Cirrhosis (including F3, F4 stages) designation was based on clinical information, radiology, FIB-4 score, and/or transient elastography results. NSSA RAS testing detailed the presence of signature NSSA mutations at the Y93, L31, M28, and Q30 codon positions. Descriptive analysis was performed with Microsoft Excel (2010, version 14.6.5).

Results: The cohort included 415 veterans (Table). The average age was 63 years, and the majority was men (99%), African American (79.5%), and HIV negative (92%). Most patients were infected with HCV genotype 1a (87.4%), and cirrhosis was present in 33% of patients. Most patients were HCV treatment naive (84%), and of those with prior therapy, interferon-based therapy was the main regimen (9%). Baseline NSSA signature RAS were found 21.4% (89) of the total cohort. In patients with genotype 1a infections, NSSA signature RAS were found in 80 (22%) patients. The most common NSSA RAS in the total cohort and in genotype 1a patients was at the M28 codon (7.4% and 8.2%, respectively). In the genotype 1b group, RAS were mostly at the L31 position (10%). In treatment naive patients, NSSA RAS were found at the Y93 (10, 2.8%), M28 (25, 7%), Q30 (10, 2.8%), and L31 (9, 2.5%) positions. Of the patients with prior treatment, NSSA RAS were at positions Q30 (12, 18.4%), Y93 (10, 15.4%), L31 (7, 10.7%), and M28 (6, 9%). In 137 patients with cirrhosis, NSSA RAS were at positions Y93 (10, 7%), Q30 (12, 9%), L31 (6, 4%), and M28 (8, 6%). 74% of patients with cirrhosis were treatment naive.

Conclusion: In this real world cohort, veterans with chronic HCV commonly had NSSA RAS on baseline testing. Our study found signature NSSA RAS that often confer significant resistances to standard, first-line DAA therapy in 20% of patients tested at baseline, which could impact treatment success. Limitations include single center location and homogenous study population.

THU-400
Changes in hepatic steatosis measured by CAP-fibroscan in patients with chronic hepatitis C treated with direct action antivirals

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Background and Aims: The relationship between the hepatitis C virus (HCV) and the development of hepatic steatosis is well known, due to different mechanisms that include a direct cytopathic effect, interaction in the liver turnover of triglycerides, etc. Likewise, liver steatosis next to HCV can contribute to the progression of hepatic fibrosis. At present, the CAP (Controlled Attenuation Parameter) allows the quantification of hepatic steatosis in a non-invasive way at the same moment of the realization of fibroscan. Our aim is to analyze what happens with steatosis measured by CAP after treatment of hepatitis C with direct action antivirals (DAA) and its relationship with anthropometric variables, lipid profile, viral variables, elastometry and type of treatment used.

Method: retrospective study from January 2015 to March 2017 of the cases treated with DAA in which a baseline and 24 weeks posttreatment determination of a CAP-fibroscan was made.

Results: 364 patients were collected (40% women), mean age 57 years (20 to 88), 53% naive, 26% with hypertension, 12.4% diabetes, 12.8% with dyslipidemia and 28.2% cirrhosis, which reached the sustained viral response (SVR). The predominant genotype was 1b (48.6%) and genotype 3 was 11.6%. The mean basal fibroscan was 12.4 KPa and post-treatment was 9.19 KPa (p < 0.05). The baseline CAP was 239.1 ± 50 and after treatment was 246.27 ± 56 dB/m (p < 0.05). 38.66% of the patients had basal liver steatosis moderate-severe (CAP ≥ 248 dB/m) and this percentage increased to 44.63% after treatment (p = 0.004). A direct relationship was found between the basal quantification of steatosis and the degree of liver fibrosis (p < 0.05): F0 (216.5 dB/m), F1 (222.1 dB/m), F2 (239.2 dB/m), F3 (254 dB/m) and F4 (247 dB/m). 20% of patients with fibrosis F < 2 had steatosis grade 2–3 (CAP > 250 dB/m) vs 42.23% of patients with F ≥ 2, (p = 0.003). The same occurred in the post-treatment CAP (17.9% in F < 2 vs 52% in F ≥ 2, p = 0.009). 66.7% of patients with genotype 3 had basal steatosis grade 2–3 vs 34.5% of the rest of genotypes, (p = 0.023) and this difference decreased after treatment (55.9% vs 43.5%). In the multivariable analysis, the increase in basal CAP was significantly related to weight gain, high viral load, genotype 3, high HOMA, atherogenic index (HDL/total cholesterol), coronary risk (HDL/LDL) and degree of hepatic fibrosis. No association was found with age, sex, type of treatment used and other comorbidities.

Conclusion: In our cohort, 40% of the patients with hepatitis C had a moderate-severe steatosis measured by CAP, which was more evident in patients with genotype 3, high viral load and greater degree of fibrosis. The cure of hepatitis C was associated with an increase in liver steatosis, which was directly related to changes in lipid profile, insulin resistance, weight gain and increased atherogenic and coronary risk.

THU-407
Evaluation of APRI index to identify cirrhosis prior to direct-acting antiviral HCV treatment

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Background and Aims: Direct acting antivirals have been shown to be effective in treating hepatitis C (HCV) regardless of cirrhosis stage. However identifying cirrhosis prior to treatment is still important for clinical care and follow up. Liver biopsy (LB) and transient elastography (TE) are standard of care but access is limited by cost and training. Aspartate aminotransferase to platelet ratio index (APRI) is required only routine blood tests and is simple to calculate. We aimed to identify an APRI value where LB or TE may not be required to identify cirrhosis.

Method: An analysis of data pooled from 10 sofosbuvir-based interferon free clinical trials that included participants with and without cirrhosis was conducted. Participants who underwent cirrhosis screening by LB or TE were included in this analysis. Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were calculated for a range of APRI values and stratified by age (<50 or >50 years). Poisson regression adjusted for sex, body mass index, HCV genotype and IL28B genotype was used to identify associations with cirrhosis.

Results: APRI data and LB or TE results were available for 3,835 participants among whom 23% (n = 898) were identified to have cirrhosis. The mean age of participants was 54 years (range 18–85), 64% were male and 82% were white. Approximately 34% underwent LB and there was no significant difference in cirrhosis identification between LB and TE (x^2 0.138 p = 0.71). APRI value <0.5 had an NPV of 92% to exclude cirrhosis (95% CI: 91–94) among participants aged >50 and a NPV of 98% (95%CI 96–99) among those aged <50. Participants aged >50 with an APRI value <0.5 were 77% less likely to have cirrhosis (adjusted prevalence ratio [aPR] 0.23, 95%CI 0.18–0.30) compared to those with an APRI >0.5. Among those aged <50, an APRI <0.5 was associated with being 90% less likely to have cirrhosis (APR 0.10, 95%CI 0.04–0.20).

Conclusion: In settings with limited access to liver biopsy or transient elastography, APRI could be used to triage further fibrosis assessment. An APRI of <0.5 among people over 50, and APRI <1.0 among under 50 years old may an appropriate cut-off to rule out cirrhosis and avoid additional fibrosis testing.

THU-410
Preliminary analysis of the Prime Study: A randomized controlled trial comparing the hepatitis C care cascade in primary care vs. tertiary care

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Background and Aims: In order to achieve the World Health Organisation hepatitis C virus (HCV) elimination targets, it is essential to increase access to treatment and retention in the HCV care cascade. The Prime Study is an Australasian study that aims to determine the effect of providing transient elastography (TE) and direct acting antiviral (DAA) treatment in the community on the proportion of people commencing treatment and achieving cure, especially amongst people who inject drugs (PWID).

Method: People with HCV infection were recruited at primary health care centres and randomized to receive eligibility assessment including TE (Australian sites only) and DAs at their primary health centre (intervention arm), or the local tertiary hospital (standard of care (SOC) arm). Participants assessed as cirrhotic (liver stiffness ≥ 12.5 kPa) were ineligible and were referred to tertiary care. Study endpoints included key milestones in the care cascade; eligibility assessment, commencing DAA and achieving cure. Participants could exit the study at any milestone by failing to attend or declining to schedule further appointments.

Results: We report preliminary findings from the first 120 participants. 97% had ever injected drugs; 48% had injected in the last six months. 116 participants were randomized; 59 to the intervention arm and 57 to the SOC arm. Of 59 participants in the intervention arm; 50 (85%) completed their eligibility assessment (37 were eligible, 13 were ineligible) and 9 exited the study. Of the 37 eligible participants, 31 commenced DAA and 6 exited the study. The overall treatment uptake rate, excluding ineligible participants, was 31/46 (67%). To date, 25 participants have reached their SVR12 time-point, of which 14 have completed an SVR12 test demonstrating cure and 11 are yet to have an SVR12 test. Of 57 participants in the SOC arm; 39 (68%) completed their eligibility assessment (26 were eligible, 13 were ineligible) and 18 exited the study. Of the 26 eligible participants 18 commenced DAA and 8 exited the study. The overall treatment uptake rate, excluding ineligible participants, was 18/44 (41%). 11 participants have reached their SVR12 time-point, of which 9 completed an SVR12 test demonstrating cure and 2 are yet to have an SVR12 test.

Conclusion: Preliminary analysis suggests that providing liver assessment and DAA in the community may increase treatment uptake, including in PWID – a key to achieving the elimination targets.

THU-422
Decrease in blood borne viral infections, liver fibrosis and drug use in a Danish prison population

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**Background and Aims:** Our study aimed to describe the current prevalence of blood borne viral infections and liver fibrosis in Danish prison inmates and to characterize their drug use behaviors and opioid substitution therapy (OST) coverage.

**Method:** In seven Danish prisons, prisoners ≥18 years were offered participation in the study. Participation included a questionnaire, testing for blood borne viral infections by Dried Blood Spot sampling and Vibration-Controlled Transient Elastography as a marker for liver fibrosis.

**Results:** Among 1,098 prisoners, 801 (73%) participated. Of these 618 (77%) had snorted cocaine. Heroin use was reported in 146 (18%). Only 68 (8.5%) had ever injected drugs, 29 (3.5%) had injected while incarcerated and only one (0.1%) was currently injecting, compared to the 43%, 22% and 14% measured 20 years earlier in the same population. Median duration of injecting drug-use was 10 (IQR 4–18) years. The people of who inject drugs (PWID) 58 (85%) had received OST compared to 13% 20 years earlier. The prevalence of chronic viral infections was: hepatitis C (HCVRNA) 3.2% (26/801), hepatitis B (HBsAg) 1.1% (9/801), and antiHIV 0.2% (2/801) compared to 29%, 4.3% and 0% 20 years ago. The prevalence of HCV among PWIDs was 28% compared to 56% 20 years ago. Median age of the HCV infected prisoners was 44 years, IQR 24–38) p < 0.001. Of the HCV infected prisoners 92% had previously been tested for HCV and 62% were aware of being infected. Prisoners with viral hepatitis (n = 35) had significantly higher liver stiffness measurements with 68% < 7 kPa, 26% 7–10 kPa and 6% > 10 kPa compared to 95%<7 kPa, 2% 7–10 kPa and 3% > 10 kPa among non-infected prisoners (n = 763), p = 0.001.

**Conclusion:** We found a ninefold decline in the prevalence of HCV among PWIDs and a twofold decrease in prevalence of HCV among PWIDs in Danish prison inmates over the last two decades. There was a more than sixfold increase in OST coverage in the same period. The prevalence of fibrosis was low among the HCV infected prisoners probably reflecting a short duration of infection. Almost all prisoners with chronic hepatitis C had been tested previously but only two-thirds were aware of their infection. The decreasing HCV prevalence in prisons suggests that the WHO target of 90% reduction in prevalence by 2030 may be within reach in Denmark.

**THU-432**

Has increased rollout of DAA therapy decreased the burden of late presentation and advanced liver disease in patients starting HCV therapy in Germany?


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**Background and Aims:** Direct-acting agents (DAAs) against HCV have impressively improved treatment outcome of HCV therapy including patients with cirrhosis. To date, it remains unclear if widespread DAA usage has already led to a reduction in HCV-positive patients presenting with advanced liver disease. More recently, a consensus definition of advanced liver disease has been developed which defines advanced liver disease due to chronic viral hepatitis as a patient with chronic hepatitis B, C or D who shows significant fibrosis (≥F2 assessed by APRI score >1.5, FIB-4 > 3.25, Fibrotest >0.59 or alternatively a transient elastography (FibroScan) >9.5 kPa) with no previous antiviral treatment. Therefore, we assessed the proportion of HCV-positive patients presenting with advanced liver disease at DAA treatment initiation over time in the German hepatitis C cohort (GECCO).

**Method:** The GECCO cohort is a multicenter cohort from 9 German sites. All treatment-naive HCV mono- (n = 1.168) and coinfected (n = 282) patients (n = 1450) initiating DAA-based treatment since 2014 were analysed. Advanced liver disease was considered a liver stiffness ≥9.5 kPa in transient elastography (n = 1.036) or APRI score ≥1.5 (n = 414). Fisher’s exact, chi-square and Mann-Whitney U test were used for statistical analysis.

**Results:** 938/1.450 (65%) patients were male, median age was 50 years (IQR: 41–57). HCV genotype (GT) distribution was: GT1a60%, GT2 5%, GT3 29%, GT4 5%. 157/478 (33%) had IL28B C/C GT polymorphism. Median baseline HCV RNA was 1.097.704 Mio IU/ml (989.320–1.243.600). Median baseline ALT was 69 UI (66–73). Liver cirrhosis was present in 323/1.450 (22%). Median baseline CD4 was 569/ul (554–632). 353/1450 (24%) were on opiate substitution therapy (OST). Overall SVR rate was 95.8%. In 2014 35% (94/272) of all patients presented with advanced liver disease. In the following years that proportion decreased to 24% (149/631) in 2015, to 26% (92/357) in 2016 and to 20% (37/357) in 2017 (p = 0.001).

**Conclusion:** In line with recommendations from clinical guidelines our real life data confirm that initially DAA therapy was prioritized to HCV patients with advanced liver disease. As a consequence the proportion of patients initiating DAA-based therapy with no or minimal HCV related liver disease has increased in recent years. The use of a consensus definition for advanced liver disease outweighs contribute to both improving the epidemiological understanding of viral hepatitis and other liver diseases as well as testing policies and linkage to care.

Table: Distribution of DAA-treated HCV patients with/without advanced liver disease over time

<table>
<thead>
<tr>
<th>year</th>
<th>optic/minimal fibrosis (%)</th>
<th>advanced fibrosis (%)</th>
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</thead>
<tbody>
<tr>
<td>2014</td>
<td>65 (178)</td>
<td>34 (9)</td>
</tr>
<tr>
<td>2015</td>
<td>76 (142)</td>
<td>24 (6)</td>
</tr>
<tr>
<td>2016</td>
<td>64 (104)</td>
<td>22 (6)</td>
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<tr>
<td>2017</td>
<td>80 (135)</td>
<td>22 (6)</td>
</tr>
</tbody>
</table>

**FRI-016**

Outcomes of liver transplantation in patients with non-alcoholic steatohepatitis: High recurrence rate in ultrasound and transient elastography


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**Background and Aims:** Non-alcoholic steatohepatitis (NASH) is a rapidly increasing indication for liver transplantation surpassing other causes of liver cirrhosis. Recurrence of diseases like autoimmune hepatitis and primary sclerosing cholangitis have been reported after liver transplantation. This study aimed to investigate outcomes including recurrence of disease after liver transplantation in patients with NASH.

**Method:** In a cross-sectional study, adult (>18 years) patients with liver cirrhosis underwent liver transplantation at Shiraz Transplant Center, Shiraz, Iran between January 2011 and March the 2017 were included. Recurrence of steatosis in patients with NASH was evaluated by ultrasound and transient elastography (TE). Kaplan-Meier curve was used for analysis of post-transplant survival of patients.
Results: Totally 1950 patients were included. 71 patients with NASH underwent liver transplantation during the study period, 14 patients passed away during the study period. Mean post-transplant survival was 42.38 ± 2.35 months in NASH patients and 47.71 ± 2.98 in non-NASH patients (p = 0.558). From 57 patients underwent ultrasound evaluation in a mean follow-up of 15.5 ± 12.6 months after liver transplantation, 33 (57.8%) patients had recurrence of hepatic steatosis. 12 patients had grade II and III and 21 patients had grade I steatosis. In univariate analysis, lower high density lipoprotein (HDL), higher low density lipoprotein (LDL) and warm ischemic time were associated with recurrence of hepatic steatosis (p < 0.05). In regression analysis, none of these factors were independent predictor of recurrence in our study population (p > 0.05). From 18 patients who underwent TE, one patient had no steatosis (50), 2 patients had S1 steatosis, 3 patients had S2 steatosis and 12 patients had S3 steatosis. 13 patients had different degrees of liver fibrosis. Posttransplant hypertension (OR: 5.3; p = 0.016), diabetes mellitus requiring insulin therapy (OR: 4; p = 0.034) and higher body mass index (BMI) (p = 0.015) were associated with significant fibrosis in TE.

Conclusion: Long-term survival of patients with NASH is comparable with other causes of liver cirrhosis. Recurrence of steatosis both in TE and ultrasound is prevalent and patients with hypertension, DM on insulin therapy and high BMI are susceptible to significant fibrosis.

FRI-091 RNA-sequencing analysis of biopsies from chronic liver disease patients identifies gene signatures associated with progressive liver disease

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Background and Aims: Liver fibrosis, resulting from injury- and inflammation-driven production and accumulation of extracellular matrix proteins, is characteristic of most type of chronic liver diseases (CLD). Although our understanding of the cellular and molecular mechanisms of liver fibrosis has greatly advanced, current methods for diagnosing and treating liver fibrosis are limited. Existing noninvasive methods of liver fibrosis diagnosis involve transient elastography and certain serologic tests such as the enhanced liver fibrosis (ELF) score; however, these methods are not able to reliably detect fibrosis stage. Liver biopsy still remains the only effective way to accurately determine the stage of fibrosis, but it is an invasive procedure, which can be accompanied by complications such as internal bleeding. In this study, we aimed to identify the core gene signature associated with liver fibrosis to identify novel biomarkers and/or therapeutic targets for liver disease.

Method: In this study, we performed RNA-sequencing using liver tissue RNA from 69 chronic liver disease patients at different stages of fibrosis and with different aetiologies to identify gene signatures associated with advanced liver disease.

Results: RNA-sequencing analysis identified 171 genes that were differentially expressed between early versus advanced stages of fibrosis, 60 of which encoded extracellular proteins. By gene correlation analysis with matched patient ELF score data, we identified 52 genes that strongly correlate with advanced fibrosis. One such gene represents a candidate master transcriptional regulator of the profibrogenic gene signature associated with liver fibrosis. By comparing gene profiles of HCV or HCV with steatohepatitis patient biopsies, we also identified a steatohepatitis-enriched set of genes associated with progressive fibrosis.

Conclusion: In summary, our approach of using samples from patients with different CLD aetiologies has enabled us to deconvolute the inherent heterogeneity that exists within clinical samples, and has led to the identification of a core set of liver fibrosis-associated genes. Several of these encode immune-related proteins that may represent tractable targets and/or biomarkers for chronic liver disease.

FRI-094 SWAVE: Steady State Shear Wave Elastography for Fibrosis Evaluation in Liver Disease

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Background and Aims: Non-invasive liver elasticity measurements have previously been shown to be correlated with histologic liver fibrosis stage on biopsy. Measurement of the propagation speed of shear waves within the liver is directly related to the accumulation of fibrosis within the liver. Herein we present initial results of a new technology developed to non-invasively measure deep volumetric liver elasticity using steady state shear waves, known as shear wave absolute vibroelastography, or SWAVE. This technology enables measurements of liver elasticity to a depth equal to the B-mode image, or in excess of 15 cm.

Method: The system consists of an ultrasound machine, a vibration device to excite shear waves in the patient and a 3D ultrasound transducer (m4DC7-3). The vibration device induces shear waves in the liver at four different frequencies between 40Hz and 70Hz simultaneously. The ultrasound volume is acquired through the ribs at the same location as a typical transient elastography (TE) measurement. Volumes are collected in a fan of approximately 15 degrees and taken at a depth of 15cm. SWAVE (Sonic Incytes), TE (FibroScan), and magnetic resonance elastography (MRE) were performed on a cohort of healthy volunteers. A second cohort of patients with chronic liver disease (Hepatitis C (HCV), Hepatitis B (HBV), or Non-alcoholic steatohepatitis (NAS)) were evaluated with SWAVE and TE.

Results: 12 healthy volunteers (mean age 37 years [range 25 to 49], 25% female) and 8 patients (mean age 56 years [range 34 to 65], 37% female, diagnosis of HCV (n = 3), HBV (n = 2) and NAS (n = 3)) were included in the study. Of the volunteers the mean elasticity and standard deviation measured with SWAVE was 3.9 ± 0.4 kPa, with TE was 4.5 ± 0.7 kPa and with MRE was 4.9 ± 0.3 kPa. Figure 1a compares the SWAVE, TE and MRE results. For the cohort of patients, the mean elasticity was 5.4 ± 0.7 kPa withSWAVE and 8.4 ± 1.5 kPa with TE, with staging ranging from F0-F3. Since each elastography measurement algorithm is unique, the correlation between theSWAVE and TE for all patients with chronic liver disease (Hepatitis C (HCV), Hepatitis B (HBV), or Non-alcoholic steatohepatitis (NASH)) were evaluated with SWAVE and TE.

Method: The system consists of an ultrasound machine, a vibration device to excite shear waves in the patient and a 3D ultrasound transducer (m4DC7-3). The vibration device induces shear waves in the liver at four different frequencies between 40Hz and 70Hz simultaneously. The ultrasound volume is acquired through the ribs at the same location as a typical transient elastography (TE) measurement. Volumes are collected in a fan of approximately 15 degrees and taken at a depth of 15cm. SWAVE (Sonic Incytes), TE (FibroScan), and magnetic resonance elastography (MRE) were performed on a cohort of healthy volunteers. A second cohort of patients with chronic liver disease (Hepatitis C (HCV), Hepatitis B (HBV), or Non-alcoholic steatohepatitis (NAS)) were evaluated with SWAVE and TE.

Results: 12 healthy volunteers (mean age 37 years [range 25 to 49], 25% female) and 8 patients (mean age 56 years [range 34 to 65], 37% female, diagnosis of HCV (n = 3), HBV (n = 2) and NAS (n = 3)) were included in the study. Of the volunteers the mean elasticity and standard deviation measured with SWAVE was 3.9 ± 0.4 kPa, with TE was 4.5 ± 0.7 kPa and with MRE was 4.9 ± 0.3 kPa. Figure 1a compares the SWAVE, TE and MRE results. For the cohort of patients, the mean elasticity was 5.4 ± 0.7 kPa withSWAVE and 8.4 ± 1.5 kPa with TE, with staging ranging from F0-F3. Since each elastography measurement algorithm is unique, the correlation between theSWAVE and TE for all subjects is shown in Figure 1b. This correlation yields an R2 value of 0.64.
Conclusion: These initial results demonstrate promise for SWAVE as a new technique for non-invasive fibrosis assessment in chronic liver disease. SWAVE is volumetric, works at depth, uses the same principle as MRE, and is suitable for point-of-care diagnosis and regular patient monitoring during and after treatment.

FRI-186

Risk assessment of hepatocellular carcinoma in chronic liver disease patients with a combination of liver stiffness measurement and controlled attenuation parameter by FibroScan

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Background and Aims: Patients with chronic liver disease (CLD) have hepatocellular carcinoma (HCC) causing risk. Recent advantage based on ultrasound technology provide us to evaluate liver stiffness measurement (LSM) and amount of hepatic fat quantitatively. This study aimed to investigate the applicable cutoff values of LSM and CAP for primary HCC development, and evaluate its clinical usefulness for risk assessment of HCC in hepatitis C virus (HCV), hepatitis B virus (HBV), and non-alcoholic fatty liver disease (NAFLD) patients.

Method: 1054 patients (88 with primary HCC and 966 without HCC) with a clinically evident CLD (HCV, 419; HBV, 377; NAFLD, 258) were enrolled in this retrospective and cross-sectional study. Results: In HCV, LSM of more than 8.0 kPa (OR: 4.06, 95%CI: 1.46–13.19, p = 0.0066) and CAP of less than 221 dB/m (OR: 2.80, 95%CI: 1.07–8.81, p = 0.0355) were independent risk factors for primary HCC development. In HBV, LSM of more than 6.2 kPa was an independent risk factor for primary HCC development (OR: 11.22, 95%CI: 4.10–34.49, p < 0.0001). In NAFLD, LSM of more than 5.4 (OR: 7.53, 95%CI: 1.97–49.81, p = 0.0018) and CAP less than 265 dB/m (OR: 4.56, 95%CI: 1.80–12.46, p = 0.0012) were independent risk factors for primary HCC development. Other risk factors for primary HCC development were low albumin and elevated α-fetoprotein for HCV, old age and low platelet counts for HBV, low albumin and complication with high blood pressure for NAFLD.

Conclusion: The cutoff values of LSM and CAP for the risk of HCC development were different depending on the etiology. The determining the cutoff values of fibrotic stage and hepatic steatosis for HCC occurrence and its combination use would be useful in daily clinic in assessing HCC risks among CLD patients.

FRI-278

Impact of gender, menopause status and age at menarche on severity of liver fibrosis among patients with chronic hepatitis B

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Background and Aims: The role of menopause status and age at menarche in the development of chronic hepatitis B (CHB) remain poorly understood. We performed a cross-sectional study to assess the role of menopause status and age at menarche in relationship to advanced liver fibrosis in CHB cases prior to antiviral therapy.

Method: Seven hundred and sixty-four consecutive female and one thousand three hundred and thirty-six age-matched male patients during the same period of time were prospectively evaluated, which all had positive serum HBsAg over 6 months and without antiviral therapy. Liver fibrosis was assessed by Liver stiffness measurement (LSM) using transient elastography (Fibroscan®). Menopause status and age at menarche were collected and documented from all female patients using a standardized questionnaire.

Results: 129 (16.9%) patients were postmenopausal, 98 (12.8%) had advanced fibrosis in females. The median age of overall, had menopause and age at menarche was 35, 49 and 14 years among women, respectively. Prevalence of advanced liver fibrosis increased from premenopausal to postmenopausal women (9.0 vs. 31.8%, p < 0.001, figure 1). Moreover, the menarche age was positively associated with liver fibrosis, the frequency of advanced fibrosis in groups of menarche age < 13,13 or 14, and >14 years were 5.9%,10.7% and 18.8% (p < 0.001, figure 2), respectively. Menopause status (postmenopausal vs. premenopausal, OR = 2.12–4.02, p < 0.05) and age at menarche (>14 vs. <13 years, OR = 2.38–3.83, p < 0.05) were consistently independent risk factors of advanced liver fibrosis across all four multivariate logistic regression models in female patients (table 1). Compared to premenopausal women, men and age < 50 (OR = 1.84–2.86, p < 0.05) had higher odds of advanced liver fibrosis. However, compared to postmenopausal women, men and age > 49 (p = 0.402) had a similar prevalence of advanced liver fibrosis (figure 1).

Table 1: Associations between the advanced liver fibrosis and menopause or age at menarche

<table>
<thead>
<tr>
<th>N</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menopause Model 1</td>
<td>764</td>
<td>2.22</td>
<td>1.10–4.49</td>
</tr>
<tr>
<td>Model 2</td>
<td>763</td>
<td>2.12</td>
<td>1.04–4.34</td>
</tr>
<tr>
<td>Model 3</td>
<td>654</td>
<td>2.91</td>
<td>1.51–5.65</td>
</tr>
<tr>
<td>Model 4</td>
<td>665</td>
<td>4.02</td>
<td>2.50–6.55</td>
</tr>
</tbody>
</table>

| Age at menarche Model 1 | 755 | 1.89 | 0.81–4.41 | 0.139 |
| Model 1 | 754 | 2.38 | 1.05–5.52 | 0.047 |
| Model 2 | 754 | 2.08 | 0.84–4.95 | 0.096 |
| Model 3 | 687 | 2.67 | 1.11–6.39 | 0.028 |
| Model 4 | 599 | 2.13 | 0.85–5.33 | 0.106 |
| Model 1 | 599 | 2.61 | 1.02–6.05 | 0.045 |
| Model 2 | 599 | 2.37 | 0.90–6.80 | 0.076 |
| Model 3 | 599 | 3.85 | 1.25–11.78 | 0.019 |

Model 1 was adjusted for age; model 2: model 1 plus adjustment for BMI, Diabetes and Hypertension; model 3: model 2 plus adjustment for ALL, model 4: model 3 plus adjustment for HBsAg status and HBV DNA level.
**Conclusion:** Menopause status and age at menarche were associated with advanced liver fibrosis in antiviral treatment naive female patients with CHB. The protective effect of female gender against severity of liver fibrosis was lost for postmenopausal women.

**FRI-289**

**The WHO guidelines for chronic hepatitis B fails to detect half of the patients in need of treatment**

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**Background and Aims:** Patients with chronic hepatitis B (CHB) who have liver fibrosis and/or ongoing necroinflammation of the liver are at increased risk of disease progression. Antiviral treatment can stop the progression to cirrhosis and reduce the risk of hepatocellular carcinoma. In 2015, the World Health Organization (WHO) issued guidelines for the management of CHB in low- and middle-income countries. Antiviral treatment was recommended based on 3 criteria: (i) clinically diagnosed cirrhosis, (ii) aspartate aminotransferase to platelet ratio index (APRI) >2.0, or (iii) age ≥30 years with abnormal ALT and viral load >20,000 IU/ml. The aim of this study was to evaluate the performance of the WHO guidelines in a large cohort of CHB patients in Ethiopia.

**Method:** Out of 1303 HIV-negative CHB patients enrolled at St. Paul's Hospital Millennium Medical College in Addis Ababa, 1213 treatment-naïve patients aged 18 years and older were included in this study. All patients underwent a standardized evaluation at baseline, including blood tests and transient elastography (Fibroscan, Echosense, France). A Fibroscan threshold of 7.9 kPa was used to define significant fibrosis and 9.9 kPa to define cirrhosis. Treatment eligibility was assessed using the most recent guidelines from the European Association for the Study of the Liver (EASL) as the “gold standard”.

**Results:** Out of 1213 patients with CHB, 317 (26.1%) were eligible for treatment according to the EASL 2017 guidelines. For comparison, only 159 (13.1%) were eligible according to the WHO2015 guidelines. Most patients (112 of 159, 70.4%) who fulfilled the WHO criteria were patients with uncompensated cirrhosis, who might have a dismal prognosis even with therapy. Only 23 of 105 patients (21.9%) with compensated cirrhosis, who are likely to benefit the most from therapy, were eligible for treatment according to the WHO criteria. APRI lacked sensitivity in this setting: only 23 of 317 (7.3%) in need of treatment had an APRI value >2.0.

**Conclusion:** The WHO guidelines for CHB fails to detect a considerable proportion of patients in need of treatment. A revision of the WHO treatment criteria should be based on local data.

**FRI-300**

**Disease progression is affected by pattern of serum alanine aminotransferase dynamics in a cohort of patients with hepatitis B e antigen-negative chronic infection: 4 years follow-up of a prospective longitudinal study (ALBATROS study)**

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**Background and Aims:** Disease progression is affected by pattern of serum alanine aminotransferase (ALT) dynamics for the outcome of long-time follow-up. The aim of the present study was to investigate the clinical significance of ALT changes between baseline (BL) and 4 years follow-up (FU4) for hepatitis B e antigen (HBsAg) seroconversion as well as for disease progression in a cohort of European untreated HBeAg-negative infected patients.

**Method:** Patients with HBeAg-negative low-replicative chronic HBV were enrolled for long-term follow-up over 10 years. Definition of low-replicative HBV without indication for antiviral therapy at study inclusion was based on EASL guidelines. Biochemical and virologic parameters as well as transient elastography (TE) were performed at BL and 1/year.

**Results:** Data of FU4 were available in 227 patients, mainly infected with HBV genotype A and D. Patients were classified according to ALT levels into the following groups: patients with constantly normal ALT ≤ 0.5 × ULN [group A; 18/227 (7.9%)], constantly normal ALT > 0.5 × ULN [group B; 151/227 (66.5%)], transient ALT elevation [group C; 51/227 (22.5%)] and persistent ALT increase [group D; 7/227 (3.1%)]. Overall, HBsAg seroconversion and reactivation with start of antiviral therapy was observed in 12/227 (5.3%) and 14/227 (6.2%) patients, respectively. HBsAg seroconversion was not significantly affected by ALT dynamics during 4 years FU [2/18 (11.1%), group A; 9/151 (6%), group B; 1/51 (2%), group C; 0/7, group D]. Patients with transient or persistent ALT elevation [group C and D] had a significant higher risk of disease progression with parallel increase of HBV DNA >2000 IU/ml and started with antiviral treatment compared to group A and B patients [6/51 (11.8%) and 4/7 (57.1%) in groups C and D versus 0/18 and 4/151 (2.6%) in groups A and B, respectively; p < 0.0001]. Single-point measurement of ALT showed significant correlations with liver stiffness by TE (r = 0.34; p < 0.0001), BMI (r = 0.269; p < 0.0001), triglycerides (r = 0.229; p = 0.001), quantitative HBsAg (r = 0.207; p = 0.004) and LDL cholesterol (r = 0.145; p = 0.045).

**Conclusion:** In our study cohort with 4-year period of follow-up patients with transient or persistent ALT elevation were shown to have a higher risk of disease progression. ALT levels ≤ 0.5xULN appeared to be no further advantage for the long-term outcome. Beside viral factors transaminase levels were also correlated to metabolic parameters, such as LDL cholesterol and BMI.

**FRI-301**

**Serum Mac-2-binding protein glycosylation isomer in assessing liver fibrosis in chronic hepatitis B infection**

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**Background and Aims:** Mac-2-binding protein glycosylation isomer (M2BPGi) is a novel serum marker for diagnosis of liver fibrosis in various liver diseases, while data in chronic hepatitis B (CHB), especially longitudinal data, is limited. We aimed to evaluate the role of M2BPGi in diagnosing advanced fibrosis (F3) and cirrhosis (F4) in HBeAg-ve CHB using liver stiffness measurement (LSM) as the reference.

**Method:** We performed transient elastography for HBeAg-ve CHB patients who were managed in Queen Mary Hospital, Hong Kong. LSM was performed by FibroScan® (Echosens, Paris, France) and presence of no/minimal fibrosis (F0/F1), grey area and F3/F4 was defined using the alanine-aminotransferase-based EASL-ALEH criteria. Serum M2BPGi was measured using a commercial immunoassay kit.
were measured using the HISCL-800 immunoanalyzer (Sysmex Corporation, Hyogo, Japan).

Results: 240 HBeAg-ve CHB patients (M:F = 116:124) of median age 47.5 years were recruited. The majority were treatment-experienced (85.8%). The median ALT was 26 U/l (range: 10–180 U/l). The median liver stiffness was 6.9 kPa (IQR 4.9–11.7 kPa) and 78 of them (32.5%) had F3/F4 by transient elastography at baseline. The corresponding median M2BPGi values for F0/1/2, F3 and F4 progressively increased in parallel with more advanced stages of liver fibrosis: 0.39, 0.46 and 0.82 COI, respectively (p < 0.01) (Figure 1A). The AUROC for diagnosing ≥ F3 by serum M2BPGi was 0.754. Using a cut-off value of 0.605, the sensitivity, specificity, PPV and NPV for ≥ F3 was 62.5%, 79.4%, 60.3% and 80.9%, respectively. In a subgroup of 86 patients who had repeated LSM 10 years after the initial LSM, the proportion of patients with F3/4 was reduced from 36.7% to 16.3% (p < 0.001). The median serum M2BPGi levels were significantly different between patients with F3/4 compared to those with F0/1/2 at baseline (0.67 COI vs. 0.41 COI, p < 0.05) and also at 10-year (0.62 COI vs. 0.48 COI, p = 0.039). 21 (24.4%) showed significant fibrosis regression (i.e. F3 or F4 → F0 or F1). The median change in serum M2BPGi level was -0.11 compared to +0.03 COI in the other patients who did not showed significant fibrosis regression (p = 0.011). (Figures 1C-1D)

Conclusion: Serum M2BPGi was an accurate serum marker for liver fibrosis in HBeAg-ve CHB patients. Using a cut-off level of 0.605 COI, 80.9% patients without ≥ F3 can be excluded. Serum M2BPGi levels remained significantly higher for patients with ≥ F3 compared to those with F0/1/2 even after 10 years. Serum M2BPGi levels also decreased significantly in patients who had fibrosis regression after 10 years.

FRI-333

Comparison of fibrosis-adjusted long-term clinical outcomes in patients with minimally active chronic hepatitis B who did not undergo antiviral therapy vs. those with complete virological response by antiviral therapy


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Backgrounds and Aims: The optimal criteria for commencement of antiviral therapy in patients with chronic hepatitis B (CHB) remain to be determined yet. Here, we aimed to compare the risk of hepatocellular carcinoma (HCC) and liver-related event (LRE) between patients with minimally active CHB who did not undergo nucleos(t)ide analog (NUC) therapy according to the current treatment guidelines (MA group) and those with complete virological response by NUCs (VR group).

Methods: We enrolled consecutive patients with CHB who underwent liver stiffness (LS) values by transient elastography between 2006 and 2015. Patients with a history of cirrhosis or hepatocellular carcinoma at the enrollment were excluded. To adjust for imbalances between the MA and VR groups, propensity-score matching (PSM) models with 1:1 ratio were performed based on age, gender, HBeAg, presence of diabetes, and LS value. Cumulative risks of HCC or LRE development were assessed using Kaplan-Meier method.

Results: A total of 915 patients were enrolled. The mean age was 54.2 years old, and 61.2% were male. MA group (n = 209) had higher serum HBV DNA level, alanine aminotransferase (ALT), total bilirubin, LS value and the lower proportion of positive HBeAg compared to VR group (n = 706). Regarding HCC development, MA group had the trend toward the higher risk compared to VR group (p = 0.087). Regarding LRE development, MA group was at the significantly higher risk than VR.
group (p = 0.003). On the contrary, after PSM, 206 pairs were generated, showing the similar risks between two groups in terms of the cumulative risk of both HCC (p = 0.782) and LRE (p = 0.796) development.

**Conclusion:** After adjusting the fibrosis degree, the potential prognostic factor for HCC and LE development, MA group also showed similar cumulative risks compared to VR group, supporting the appropriateness of the current treatment guidelines in patients with CHB.

**FRI-341**

**Association of metabolic adipokines with persistence of fibrosis in chronic hepatitis B during long-term nucleoside analogue therapy**

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**Background and Aims:** Liver fibrosis progression during nucleoside analogue (NA) treatment in chronic hepatitis B (CHB) is not guaranteed. There is emerging evidence on metabolic factors being associated with persistence of fibrosis in on-treatment CHB. There are emerging interests in metabolic biomarkers that reflect adipokine dysregulation, e.g. adiponectin, fatty acid-binding protein 4 (FABP4), fibroblast growth factor (FGF-21) and homeostatic model assessment-insulin resistance (HOMA-IR). Their role in CHB-related liver injury has not been well investigated.

**Method:** We recruited 414 on-treatment CHB patients and performed transient elastography for liver stiffness and controlled attenuation parameter (CAP). Significant fibrosis was defined based on the alanine aminotransferase (ALT)-based EASL-ALEH criteria, while severe steatosis was defined as the presence of CAP ≥ 280 dB/m. Logistic regression was used to investigate the risk factors associated with the development of severe steatosis and significant fibrosis. Apart from the above four variables of interest, we also considered clinical, metabolic, biochemical and virologic parameters. Results: Therewere 296 (71.5%) male patients, and the median age of the cohort was 60.2 years (interquartile range [IQR]: 54.2–65.3 years). The median duration of NA treatment was 73.6 months (IQR: 43.0–93.4 months); 73 (91.3%) patients had undetectable HBV DNA (<200 IU/mL) at assessment. Severe steatosis and significant fibrosis were found in 89 (21.5%) and 167 (56.4%) patients, respectively. The median adiponectin level was significantly lower among patient severe steatosis than those without severe steatosis (7.6 vs 11.4 µg/mL, p < 0.001), while there were no statistically significant differences for other adipokines (Table 1a). The median FABP4 level was significantly higher among patients with significant fibrosis than those without significant fibrosis (126.8 vs 73.7 pg/mL, p < 0.001), and the median HOMA-IR level was significantly higher (6.6 vs 5.1 µU/mL, p = 0.006), while there were no statistically significant differences for other adipokines (Table 1b). Independent risk factors for significant fibrosis included severe steatosis (OR: 2.22, 95% CI: 1.45–3.44), DM (OR: 1.90, 95% CI: 1.03–3.53), thrombocytopenia (OR: 3.78, 95% CI: 2.19–6.65), a lower albumin level (OR 0.90, 95% CI: 0.82–0.98), a higher AST level (OR 1.05, 95% CI: 1.01–1.10), a higher GGT level (OR: 1.02, 95% CI:1.01–1.10) and a higher FABP4 level (OR: 1.0016, 95% CI: 1.0003–1.0032).

**Conclusion:** Both a higher FABP4 level and severe steatosis were independently associated with the presence of severe fibrosis in NA-treated CHB. FABP4 is a marker of fatty acid uptake, transport and metabolism; its role in the fibrogenesis process of CHB requires further investigation.

**Table 1. Comparison of the median levels of various adipokines between (a) patients with and without severe steatosis; (b) patients with and without significant fibrosis**

<table>
<thead>
<tr>
<th></th>
<th>Serum adipokine</th>
<th>Absence of severe steatosis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>FGF-21 (pg/mL)</td>
<td>361.2</td>
<td>231.0</td>
</tr>
<tr>
<td></td>
<td>FABP4 (pg/mL)</td>
<td>138.0</td>
<td>93.6</td>
</tr>
<tr>
<td></td>
<td>Adiponectin (µg/mL)</td>
<td>7.6</td>
<td>11.4</td>
</tr>
<tr>
<td></td>
<td>HOMA-IR (µU/mL)</td>
<td>6.6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

**FRI-343**

**Therapy with oral directly acting agents in hepatitis C infection is associated with reduction in fibrosis and increase in hepatic steatosis**

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**Background and Aims:** Novel directly-acting antivirals (DAAs) are now the standard of care for hepatitis C (HCV) infection and are associated with high sustained viral response at 12 weeks (SVR12).

The aim of this study was to evaluate the change in liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) by transient elastography (FibroScan™) post DAA therapy.

**Method:** LSM and CAP were measured serially (baseline, 12 weeks post completion of therapy and at one year after completion of therapy) in a prospective cohort of 372 chronic hepatitis C (CHC) treated with DAAs. Patients with at least two FibroScan measurements were included. Linear regression was used to assess for factors predictive of dynamic change in LSM and CAP values.

**Results:** A total of 372 patients were included; mean ± SD age 38.3 ± 12.6 years; 58.3% were males. Cirrhosis-defined by biopsy or fibroscan measurement (≥212.5 kPa)- was present in 25.5%. Overall, on paired analysis (n = 317), the LSM (IQR) decreased from baseline value 7.1 (5.3–13.8) kPa to 12 weeks post therapy 6.2 (4.8–11.2) kPa; median decline 0.7 (−0.6–2.6) kPa, p < 0.001. On paired analysis (n = 105), the LSM value decreased from 12 weeks post therapy 6.8 (4.9–11.8) kPa to 1 year LSM 6.6 (4.9–8.7) kPa; median decline 0.6 (−0.5–2.6) kPa, p = 0.002. Similarly, on paired analysis (n = 160), LSM decreased from baseline value 6.9 (5.1–12.7) kPa to 1 year, 6.1 (4.8–9.4) kPa; median decline 0.9 (−0.6–3.2) kPa, p < 0.001. In contrast, on paired analysis (n = 317), CAP value increased from baseline 213.0 (180.0–254.5) dB/m to 12 weeks post therapy 225.0 (190.0–269.0) dB/m; median increase 7.0 (−23.5–45.5) dB/m, p = 0.001. On paired analysis (n = 105), CAP value increased from 12 weeks post therapy 234.0 (182.5–268.5) dB/m to 1 year 244.0 (206.0–286.0) dB/m; median increase 15.0 (−17.5–43.5) dB/m, p = 0.003.

**Conclusion:** Treatment with DAAs reduces liver stiffness, but is associated with increase in hepatic steatosis. Future studies are needed to evaluate the factors associated with increase in hepatic steatosis.
Long-term changes of liver elasticity in HVC-infected patients with SVR after treatment with direct-acting antivirals

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Background and Aims: Interferon-free antiviral therapy is associated with high rates of sustained virologic response (SVR). SVR has been associated with a significantly decreased liver stiffness; however, follow-up was mostly limited to 24 weeks after end of treatment (FU24). The aim of this work is to investigate long term liver stiffness changes in SVR patients using both, transient elastography (TE) and ARFI.

Methods: 171 patients (mean age 59 years, 54% male, 81% HCV genotype 1) with chronic HCV infection who achieved a SVR with IFN-free therapies were examined prospectively. 96 patients (56%) had liver cirrhosis (F4) at start of treatment. The duration of therapy was 8 to 24 weeks. All patients underwent liver elastography using TE at baseline and ARFI was performed at baseline in 169 patients, at FU24 in 126 patients and at FU96 in 92 patients.

Results: TE correlated with ARFI elastography at baseline, FU24 and FU96 (r = 0.779; r = 0.768; r = 0.629, respectively). TE and ARFI values decreased significantly from baseline to FU24 (20.7 ± 16.5 kPa to 14.2 ± 11.4 kPa, p < 0.001; 1.95 ± 0.64 m/s to 1.75 ± 0.64 m/s, p = 0.001). Importantly, neither mean TE nor mean ARFI values showed significant changes from FU24 to FU96 (14.2 ± 11.4 kPa to 13.3 ± 11.5 kPa, p = 0.08; 1.80 ± 0.73 m/s to 1.88 ± 0.88 m/s, p = 0.40). However, between FU24 and FU96 TE decreased in 43% and increased in 23%. ALT levels at baseline were significantly different in patients with and without liver stiffness regression from baseline to FU96 (93 ± 63 U/l vs. 57 ± 33 U/l, respectively, p = 0.036). Albumin, bilirubin and INR revealed no significant differences between FU24 and FU96. In cirrhotic patients TE changed only significantly from baseline to FU24 and not from FU24 to FU96 (31.3 ± 15.7 kPa to 20.2 ± 12.4 kPa, p = 0.001; 20.2 ± 12.4 kPa to 18.8 ± 12.6 kPa, p = 0.11). At treatment start 16% of patients suffered from Child B/C cirrhosis. 81% of these patients improved to Child A cirrhosis at FU96. Cirrhotic patients at baseline improved to TE values <14.5 kPa in 34% at FU24 and in 48% at FU96.

Conclusions: Using TE and ARFI, we identified a bi-phasic decline in liver stiffness with a more rapid decline observed in almost all patients until FU24 probably driven by decreased inflammation followed by rather flat phase during further follow-up. TE values may even increase during follow-up in up to 25% of patients.

The role of hepatitis C virus eradication with DAA on insulin resistance regulation

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Background and Aims: Insulin resistance (IR) is a common extrahepatic manifestation of Hepatitis C virus (HCV) infection. The aim of this research was to evaluate if viral eradication obtained with DAA plays a role in the development and/or improvement of IR; we also evaluate if IR improvement reduces hepatic complications incidence.

Method: All HCV patients treated with DAA from May 2015 to December 2016 were prospectively included in the study. For each patient, we analyzed blood test and HOMA score before therapy and at 3, 6 and 12 months after its completion. Liver fibrosis was quantified by stiffness with Transient Elastography before treatment, 6 and 12 months after antiviral therapy. IR has been defined as HOMA score ≥2.5. All patients were treated with DAA drugs.

Results: 161 patients were included in the study, between these 117/ 161 (72.7%) had IR and 44/161 (27.3%) not. Before receiving antiviral therapy patients with IR had higher BMI (p=0.0094) and liver stiffness (p < 0.0001) levels compared to those without IR. 158/161 (98.1%) patients obtained viral eradication. We observed a significant IR improvement both at 6 months (p = 0.0412) and 12 months (p = 0.0045) after therapy completion. 4 diabetics patients before therapy obtained resolution of diabetes. High BMI before antiviral therapy was the only predictive factor related to failure of IR improvement. All patients obtained significant liver stiffness reduction after DAA therapy (p < 0.0001), significant improvement in serum albumin levels and platelets count and transaminases normalization. 8/161 (3.9%) patients were cirrhosis the evolution of endoscopic features of portal hypertension induced by SVR obtained with DAA.

Method: 263 consecutive patients (mean age 65.0 ± 10.6, males 56%) with HCV Child-Pugh A cirrhosis treated with DAs were enrolled between January 2015 and May 2016. All patients underwent esophagogastroscope (EGS), liver ultrasound (US), liver stiffness measurement (LSM) by Transient Elastography and laboratory tests before the starting DAs and after achieving SVR. LS * spleen diameter/platelet ratio (LSPS) was calculated as previously described (1).

Results: Twenty-nine patients were excluded from the analysis, 20 (7.6%) since they had F2/F3 OV; baseline and were treated with betablockers (88), and 9 (3.7%) since they did not achieve SVR. Overall, 234 SVR patients were analysed. At baseline, 83 patients (35.5%) did not have OV and 151 (64.5%) had small OV. None received betablockers. After a median time of 24.5 months EGS showed de novo development of OV in 17/83 (20.5%) patients and progression from F1 to F2/F3 OV in 27/151 patients (17.9%), p = 0.58 by Kaplan Meier. By Cox regression analysis, LSPS as continuous variable (HR: 1.05, CI95%: 1.01–1.10, p = 0.046) or at a cut off ≥3 (HR: 2.87, CI95%: 1.44–5.72, p = 0.003) was associated with OV progression. Age (p = 0.15), gender (p = 0.93), BMI (p = 0.84) and SVR did not correlate with progression of OV.

Conclusion: Progression of clinically significant portal hypertension, as assessed by the evolution of oesophagogastrectic varices, is not uncommon among patients with HCV cirrhosis after HCV clearance. Non-invasive evaluation using combined data of LS, spleen diameter, and platelet count can assist in identifying patients in whom portal hypertension is likely to progress notwithstanding SVR.

had hepatocellular carcinoma (HCC) after the end of therapy (4/8 de novo HCC, 4/8 HCC recurrence); 7/8 of these patients had IR.

Conclusion: Viral eradication with DAA leads to IR improvement. High BMI is a risk factor for IR and a negative predictive factor for IR improvement. Persistence of IR after DAA therapy is a risk factor for liver disease complications, such as HCC.

FRI-385
In hepatitis C patients with cirrhosis who achieve SVR with treatment, reduction in transient elastography measures does not translate to reduced risk of hepatocellular carcinoma: A prospective cohort study

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Background and Aims: Achieving sustained virologic response (SVR) with interferon-based therapy in hepatitis C (HCV) reduces risk of hepatocellular carcinoma (HCC). However, in the era of direct acting antivirals, real-world risk of HCC post SVR is unknown, particularly in patients with reductions in transient elastography (TE) readings post SVR.

Method: In this prospective cohort study conducted between January 1st 2001 and November 8th 2017, HCV patients with cirrhosis (confirmed by TE, ultrasound and/or liver biopsy) who achieved SVR post treatment underwent HCC surveillance with 6 monthly ultrasounds and clinic review. Patients with previous HCC (including <6 months post SVR) were excluded. A subset of participants had TE performed 6–12 months post SVR. HCC diagnosis per international guidelines was recorded.

Results: 281 patients with cirrhosis who achieved SVR were prospectively followed with a total follow-up time of 8892 person-months at risk (median 15, IQR 12–26 months). Mean age was 58 years (+/-9.4 years), 216 (70%) were male and 266 (87%) were Caucasian. The majority were genotypes 1 (154, 51%) and 3 (120, 39.5%). 146 (48%) had significant alcohol intake and 25 (8.1%) were decompensated. 227 (74.2%) had received direct-acting antiviral therapy, the remainder having received pegylated interferon-based regimens. 15 (5%) developed new HCC post SVR (incidence rate 2.0 cases per 1,000 person-months at risk (95% CI 1.22–3.35), median time to diagnosis 22 months (IQR 15–86 months). 5/15 (33%) had received DAAs (30%). 77 patients had TE performed post SVR (follow-up time of 1,970 person-months at risk). 55 (71.4%) had post-SVR readings <12.5 kPa and 13 (17%) had readings <7.1 kPa. 36/55 (66%) had cirrhosis on imaging despite fall in TE to <12.5 kPa. 5/77 patients (6.5%) developed HCC, incidence rate 2.5 per 1,000 personmonths at risk (95%CI 1.1–6.1). 3/5 cases had TE readings <12.5 kPa: liver biopsy revealed two cases (TE 10.1 kPa and 12.4 kPa) had cirrhosis and one case (TE 6.5 kPa) had NASH without cirrhosis. None had clinical evidence of portal hypertension, or significant alcohol intake.

Conclusion: In a real-world population with universal access to DAA therapy, HCC risk diminishes, but persists in patients with HCV cirrhosis after SVR. Importantly, HCC can occur in patients whose post-SVR TE readings fall below <12.5 kPa post SVR. Therefore, HCC surveillance should continue irrespective of improvements in post-SVR TE readings.

FRI-398
The impact of direct antiviral agent therapy on liver fibrosis in patient with advanced fibrosis related chronic hepatitis C

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Background and Aims: The impacts of sustained virologic response (SVR) after direct antiviral agents (DAA) therapy in patients with chronic hepatitis C virus (CHC) remain unclear. The regression of cirrhosis and portal hypertension demonstrated in interferon therapy, are expected in the DAAs therapies. Transient Elastography (TE) is a noninvasive method ultrasound based, for assessment liver stiffness (LS). The aims of this study were: (1) evaluated the changes in liver stiffness and fibrosis stage (2) to examine factors influencing changes in liver stiffness measurements after DAA treatment.

Methods: We prospectively consecutive patients treated with DAAs in our department between January 2013 and September 2016. 643 patients who received a DAA based treatment for CHC were screened and 417 were included. TE values recorded before therapy initiation and within 24 months after therapy were analysed. In addition, predictors of fibrosis regression were evaluated in multivariate analysis.

Results: A total of 417 patients (375 have TE and 42 have paired biopsy) were included. Baseline characteristic: 71% were men, 54% had cirrhosis and the median age was 53 years. Median TE before DAA treatment was 12.85 kPa (IQR 9.75–19.2 kPa) and decreased to 8.55 kPa (IQR 5.87–15.23) post-treatment. This finding is statistically significant (p < 0.001) and equals a TE regression of 33.5% after DAA treatment. Median FIB-4 and APRI values significantly decreased from 2.53 (IQR 1.64–4.42) and 1.13 (IQR 0.67–2.45) to 1.78 (IQR 1.27–2.90, p < 0.001) and 0.48 (IQR 0.33–0.81, p < 0.001) respectively. Cirrhosis regressed in 15/24 patients (62%), but advanced fibrosis regressed 14/18 cases (78%) among 42 patients with liver biopsy. Multivariate analysis found a lower BMI and gender female as factors independently associated with fibrosis regression (odds ratio (OR) 0.68, 95%CI 0.48–0.97, p = 0.037 and [(OR: 0.51, 95%CI 0.36–0.89), p = 0.0221] respectively.

Conclusion: Patients with SVR after DAA therapy showed significant regression of TE values and fibrosis regression according liver biopsy. Rapid decrease in TE was in concordance with the improvement of liver function. It remains to be examined whether this indicates a true regression of fibrosis or merely resolution of chronic liver inflammation with subsequent improvement of biopsy values in large cohort.
after DAA-treatment. Soluble (s)CD163 is released from activated liver macrophages and serum levels reflect liver disease severity. We aimed to investigate changes in sCD163, liver stiffness, metabolic liver function, and portal hypertension with DAA-treatment in CHC patients with liver cirrhosis.

**Method:** Between 2015–2017, we assessed 14 Danish CHC patients with cirrhosis before and immediately after DAA-treatment including ombitasvir, paritaprevir, ritonavir, and dasabuvir. 

**Results:** The patients had a mean age of 56 years (SD 9); 9 males and 5 females. Eleven had genotype 1a hepatitis C virus and 3 had genotype 1b. Five were abstinent from alcohol, 8 had a previous over-intake and one drank 1 unit/week of alcohol until enrolment. All patients had Child-Pugh A cirrhosis with a mean MELD-score of 8 (1.7). All patients received 12 weeks of DAA-treatment except for one patient, who died within two months of treatment initiation. All patients, who completed treatment, achieved sustained virological response (SVR) 12 weeks after treatment cessation. The mean sCD163 level decreased from 6.8 mg/L (4.8) to 4.5 (4.9) (p = 0.005). The mean liver stiffness decreased from 22.8 kPa (11.8) to 11.0 (3.5) (p = 0.008). There was a trend for improved metabolic liver function (GEC) 60.0 (11.5) vs. 55.6% (9.1), p = 0.10. There was no significant effect on the hepatic venous pressure gradient after treatment (11.6 mmHg (5.9) vs. 9.8 (3.0), p = 0.50).

**Conclusion:** DAA-treatment leads to increased macrophage activation and reduced liver stiffness indicating reduced inflammation and beneficial effects in the liver right after DAA-treatment. Further, DAA-treatment had no significant effects on metabolic liver function or portal pressure; however, long-term follow-up studies may demonstrate further improvements in these parameters.

**FRI-404**

**Controlled attenuation parameter values of FibroScan® compatible with steatosis in patients with chronic hepatitis C and changes after sustained virological response**

**Background and Aims:** Steatosis worsen the prognosis of chronic hepatitis C (CHC) (Everhart et al; Gastroenterology 2009). Controlled attenuation parameter (CAP) of FibroScan® evaluates and quantifies steatosis non-invasively. In patients with CHC a CAP (db/m) value >250, correlates with significant steatosis (over 33% of hepatocytes). Aim of the study was to identify significant steatosis by CAP before and after achieving sustained viral response (SVR12) in patients with CHC and to recognize independent variables related to steatosis increase.

**Method:** Patients with CHC, treated with direct acting antivirals (DAA) between April 2015 and December 2016, were retrospectively included. Steatosis was defined as a CAP >250 at baseline (CAPb) or after SVR12 (CAPf).

**Results:** 350 patients with SVR were evaluated. 60 (17%) patients were excluded due to the lack of CAPb and/or CAPf. The median (range) age was 55 (24–86). The median (range) body mass index (BMI), waist circumference (WC) and skin-capsule distance (SCD) at baseline were 26.5 (16–41) kg/m², 98 (70–128) cm and 16 (8–30) mm, respectively. At baseline, transient elastography (TE) was 9.8 (2.8–72) kPa and CAPb was 229 (129–374) db/m. Patients with a CAPb >250 (n = 94, 32%) showed independently (OR, 95% CI, p) higher values of WC (1.5, 1.01–1.09, p = 0.011), SCD (1.3, 1.2–1.5, p < 0.001) and GGT (1.01, 1.01–1.01, p < 0.001). After SVR12, values of TE decreased to 7.1 kPa (2.8–57) (p < 0.001). However, median (range) CAPf did not change after SVR12 being 234 (100–394) (p = ns). Among patients with a CAPb <250 the CAPf increased in 21.4%. Patients with increasing CAPf showed higher values of WC (1.11, 1.06–1.16, p < 0.001) at baseline and weight increase during antiviral treatment (1.12, 1.05–1.195, p < 0.001).

**Conclusion:** A third of patients with chronic hepatitis C have significant steatosis according to the Controlled Attenuation Parameter (CAP) values with FibroScan®. Moreover, around 21% of patients with low values of CAP before antiviral treatment showed steatosis after SVR12, especially in those with a high waist circumference or weight gain during treatment. Long-term followup of these patients would be recommended to know the clinical implication of these findings.
Changes in liver steatosis and lipid metabolism accompanied by successful interferon-free DAAs therapy in HCV infected patients; a comprehensive analysis

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Background and Aims: HCV hijack hepatocyte lipid metabolism, resulting in liver steatosis and decrease in serum LDL level. After successful HCV eradication, existence of liver steatosis is associated with hepatocarcinogenesis, and elevated LDL might cause vascular event. Thus, to clarify the factors associated with those disorders after successful HCV eradication is required. We conducted comprehensive analysis to clarify the factors associated with those disorders after HCV eradication in patients treated with IFN-free DAAs.

Method: Patients who were treated with IFN-free DAAs therapy between 2014 and 2016 in Hokkaido University Hospital, and were conducted transient elastography including Controlled Attenuation Parameter (CAP) at pre- and post-treatment, and achieved SVR were enrolled. Liver steatosis was evaluated by CAP value. Changes in liver steatosis, lipid metabolism, blood test, and genetic factor, including PNPLA3:rs738409, MTP493:rs1800591, TMS6FS2:rs58542926, ALDH2:rs671 were analyzed.

Results: A total of 117 patients were included. 79 and 38 patients were infected with genotype 1 and 2 respectively and treated with DCV/ASV, SOF/RBV, SOF/LDV or OBT/PTV/r. Overall, mean CAP value and serum LDL levels were significantly elevated at post treatment point. However, in patients with baseline CAP value >220 dB/m, mean CAP value were significantly decreased. In patients with baseline LDL value >108 mg/dl, mean LDL values were significantly decreased. At baseline, LDL value and CAP value didn’t have significant association, however, after HCV eradication both values were significantly associated (r = 0.317 p = 0.01). Univariate analysis revealed that patients with liver steatosis (CAP > 248 dB/m, n = 21 (18%)) after HCV eradication both values were significantly associated in HIV/HCV post SVR are warranted. Interestingly, switching from a HIV PI to an integrase inhibitor based regimen was associated with a significant decrease in CAP®, which might indicate a beneficial effect on HS.

Conclusions: In HIV/HCV, achieving SVR to IFN-free therapies had no impact on CAP® values. Thus, the proportion of HIV/HCV affected by HS remained high after SVR. Moreover, HCV eradication increased CHOL and LDL levels. Hence, further studies investigating metabolic changes in HIV/HCV post SVR are warranted. Importantly, switching from a HIV PI to an integrase inhibitor based regimen was associated with a significant decrease in CAP®, which might indicate a beneficial effect on HS.

Impact of SVR to IFN-free DAA therapy on steatosis in HIV/HCV coinfected patients

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Background and Aims: Hepatic steatosis (HS) and dyslipidemia contribute to the burden of liver disease among HIV (HIV)/hepatitis C (HCV) coinfected patients (HIV/HCV). Previous studies suggested a steatogenic effect of HCV. We evaluated the impact of sustained virologic response (SVR) to IFN-free direct-acting antivirals (DAAs) on HS and dyslipidemia in HIV/HCV.

Methods: HIV/HCV attending our HIV/Liver outpatient clinic and achieving SVR to IFN-free DAA treatment were assessed. Patients with paired controlled attenuation parameter (CAP®, FibroScan®), Echosense, France) measurements pre and post SVR were included in this retrospective study. CAP® values were adjusted according to Karlas et al (J Hepatol 2017).

Results: The majority of all HIV/HCV (73%; 62/85) were male and (52%; 44/85) had intravenous drug abuse as suspected route of transmission. Patient characteristics: Median age at baseline (BL): 50 (15) years; median BMI: 23.9 kg*m-2 ± 4.52; PNPLA3 genotype (GT): C/G 41% (34/82) and G/G 4% (3/82); HCV-GT-1a 51% (43/85), HCV-GT-1b 14% (12/85), HCV-GT-3 20% (17/85) and HCV-GT-4 14% (12/85). Liver transaminases and bilirubin levels showed a significant decrease after SVR. Furthermore, total cholesterol (CHOL; 154 ± 40.6 vs. 172 ± 44.6; p < 0.001) and low density lipoprotein (LDL; 69.4 ± 46.3 vs. 98.6 ± 60.4; p < 0.001) levels significantly increased after SVR (Figure), while no changes in triglycerides (TG), high density lipoprotein (HDL) levels, or CAP® were observed. The prevalence of HS (defined by CAP® ≥ 248 dB/m) at BL and SVR was 35% (30/85) and 41% (35/85), respectively. Predictive factors for a decrease in HS after SVR were high BL CAP® values (253 dB/m ± 55.7 vs. 210 dB/m ± 47.6; p < 0.001) as well as protease inhibitor (PI) intake (47% (18/38) vs. 20% (9/46); p = 0.007) as part of antiretroviral therapy (ART) at BL. Noticeably, HIV PI were discontinued in 16% (14/85) to avoid drug-drug interactions with DAAs. In these patients, CAP® values decreased from 252 dB/m ± 51.3 at BL to 210 ± 64.3 dB/m (p = 0.046) at SVR.

Conclusions: In HIV/HCV, achieving SVR to IFN-free therapies had no impact on CAP® values. Thus, the proportion of HIV/HCV affected by HS remained high after SVR. Moreover, HCV eradication increased CHOL and LDL levels. Hence, further studies investigating metabolic changes in HIV/HCV post SVR are warranted. Importantly, switching from a HIV PI to an integrase inhibitor based regimen was associated with a significant decrease in CAP®, which might indicate a beneficial effect on HS.

Sustained virological response predicts fibrosis regression in chronic hepatitis C patients treated with direct acting antivirals-a single tertiary care centre experience

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Background and Aims: Treatment with Direct Acting Antivirals (DAA) results in sustained viral response (SVR) in more than 90% of treated individuals with subsequent improvement in liver function and fibrosis. The aim of our study was to assess changes in liver fibrosis by transient elastography (TE) and fibrosis-4 (FIB-4) score and AST-Platelet ratio (APRI) in patients with chronic hepatitis C (CHC) treated with DAA.

Method: Between April 2015 to April 2017, 110 consecutive CHC patients treated with DAAs at our centre were included. TE, FIB4, APRI
score were performed before treatment and after 12 weeks of completion of therapy, the time of assessing sustained virological response (SVR12) and after 24 weeks of completion of therapy. Changes in scores were analysed by paired t test.

**Results:** The median age of the patients was 51 years, 57% had compensated cirrhosis, 79% were treatment naive, 92.7% achieved SVR12. Most common genotype was type 3 (62%). There was significant improvement in fibrosis scores among all patients. Median TE improved from 18 kPa to 13.4 kPa (p < 0.01), median FIB4 score from 28.5 to 1.90 (p < 0.01), median APRI score from 0.95 to 0.54 (p < 0.01) before treatment to 12 weeks post treatment. Patients with advanced fibrosis (F3-F4, TE > 9.5 kPa) had significant improvement in fibrosis scores compared to those without advanced fibrosis (F0-F2, TE < 9.5). For F3-F4 patients median TE, FIB4, APRI scores improved from 23.8 kPa, 3.97, 1.73 before treatment to 17.8 kPa, 2.44, 0.63 at 12 weeks post treatment respectively. For F0-F2 patients median TE, FIB4, APRI scores improved from 6.7 kPa, 1.17, 0.34 before treatment to 6.5 kPa, 0.97, 0.28 at 12 weeks post treatment respectively. Patients who have not achieved SVR12 had increment in fibrosis scores. Median TE increased from 19.7 KPa to 28.8 KPa, median FIB4 from 3.6 to 4.3, median APRI from 1.35 to 2.07 before treatment to 12 weeks post treatment respectively. In the patients who had completed 24 weeks post treatment (78.4%), median TE, FIB4, APRI scores improved from 10.6 kPa, 1.95, 0.52 at 12 weeks post treatment to 9 kPa, 0.85, 0.32 at 24 weeks post treatment respectively. Trend for these patients has been shown in figure below.

**Conclusion:** SVR12 using DAA therapy predicts a significant regression in liver fibrosis, particularly in those with advanced fibrosis. A nonsignificant trend towards continued regression of fibrosis was maintained at 24 weeks post treatment.

**FRI-416**

**Long-term evolution of thrombocytopenia in patients with chronic hepatitis C and advanced fibrosis after sustained virological response with direct antiviral agents**

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**Background and Aims:** Thrombocytopenia (TP) is frequent in patients with hepatitis C virus infection (HCV) and advanced fibrosis. The platelet count (PC) evolution after the elimination of HCV infection with direct antiviral agents (DAA) is fairly unknown. The aims of the present study were to analyse the changes of PC and TP in patients with sustained virological response (SVR) after treatment of HCV infection with DAA and their relationship with fibrosis evolution.

**Methods:** Multicentric, prospective, observational study performed in patients with HCV infection and advanced fibrosis (F3/F4 measured by transient elastography, TE, Fibroscan, EchoSens, Paris) who were treated with DAA in a real-world setting. The study was carried out in 4 hospitals from Castilla y León, Spain. PC and TE values at baseline, 24 (W24), 48 (W48) and 72 (W72) weeks after the end of treatment were collected. As patients without SVR were retreated during the follow-up period, we considered for the analysis only patients with SVR after the first DAA treatment. We studied the evolution of PC and TP (PC < 150 x109/l) along the time and the relationship between these variables and the changes in fibrosis (cutoff values: F3 ≥ 9 kPa, F4 > 12.5 kPa).

**Results:** From April 2015 to November 2016, 386 consecutive patients were included; 366 (95%) achieved SVR. A) Baseline characteristics: 67% men, mean (SD) age 57 (11.7) years, BMI 26 (4.4) kg/m2, ALT 81 (60) UI/ml and HCV RNA 2725329 (3879053) UI/ml; 74% of patients had genotype 1 HCV and 65% had received a previous treatment. Median (IQR) fibrosis was 16 (9.5–75) kPa; 71% of patients had cirrhosis (91% Child-Pugh A). The most frequently used AAD combinations were: SOF+SMV (32%), 3D/2D (26%) and SOF+LDV (19%).

B) PC: At baseline, W24, W48 and W72 median (IQR) PC was 147.5 (117–198)x109/l, (p = 0.000); median (IQR) fibrosis was 16 (12–23) kPa, 10.8 (11–18) kPa, 12 (8–20) kPa and 10.5 (7.5–15) kPa, respectively (p = 0.007). PC at W72 was directly correlated with baseline albumin (rho = 0.29; p = 0.001) and inversely correlated with baseline INR (rho = −0.20; p = 0.021), bilirubin (rho = −0.18; p = 0.036) and with W72 fibrosis (rho = −0.37; p = 0.002). At this point of the study, in W72 64 patients have TE measurement. Median (IQR) PC at W72 was 126 (84.5–167.5)x109/l in patients who remained at F3-F4 stage vs 176 (151–213)x109/l in those whom moved to F0-F2 (p = 0.000). C) TP: TP was present in 191(52%) patients at baseline; at W72 only 26.5% had TP. The proportion of patients with TP decreased from 73% in those who stayed at F3-F4- 19% in those who improved to F0- F2 stage (p = 0.000).

**Conclusion:** In clinical practice, PC increases progressively until W72 after the end of treatment in patients with chronic hepatitis C and advanced fibrosis who achieve SVR. Both PC and TP improve significantly in patients who obtain fibrosis decrease after DAA treatment.
determined by analyzing LS in 92 subjects in whom liver fibrosis was assessed by liver biopsy.

Results: The overall prevalence of liver fibrosis in the whole series was 3.2%, and was due to non-alcoholic fatty liver disease (NAFLD) in most cases. The prevalence of liver fibrosis in patients with at least one risk factor for NAFLD (obesity, type-2 diabetes, hyperlipidaemia, arterial hypertension or metabolic syndrome) was 5.0%, compared to only 0.4% in patients with no risk factors (1,269 subjects, 42.1%). We then analyzed the accuracy of the following variables in predicting liver fibrosis in patients with risk factors for NAFLD: AST/ALT, NAFLD fibrosis score, fib-4, and FLI (fatty liver index, a score that estimates the amount of fat in the liver that includes body mass index, waist circumference, and serum GGT and triglycerides). Among these factors, FLI had the best negative predictive value 99.7%. Patients with a FLI value lower than 60 had very low prevalence of liver fibrosis (2 out of the 628 subjects, 0.3%). By contrast, the prevalence of liver fibrosis among subjects with FLI > 60 was 8.6% (p < 0.001). With this approach, only 35.7% of the population from our series (18–75 years) would have to be screened for presence of liver fibrosis with TE. The algorithm performed equally well if subjects younger than 45yrs were excluded.

Conclusion: An algorithm based on assessment of liver fibrosis using TE in subjects with risk factors of NAFLD and FLI > 60 allows the identification of the majority of subjects with liver fibrosis and reduces markedly the number of subjects to be screened.

FRI-428
Comparison of ElastPQ Shear-wave Elastography (ElastPQ-SWE) and FibroScan Transient Elastography (F-TE) for liver fibrosis staging in patients with NAFLD

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Background and Aims: Shear wave Elastography with ElastPQ (ElastPQ-SWE) is a recently introduced elastography-based technique for non-invasive fibrosis assessment. We compared liver stiffness evaluation by ElastPQ-SWE and Fibroscan (F-TE) in a cohort of consecutive patients with NAFLD. We further evaluated the performance of ElastPQ-SWE in a subgroup of patients with available histology.

Method: Anthropometric parameters (weight, height, BMI and waist circumference (WC)) were measured together with routine bloods including a lipid profile. Transient elastography (TE) was measured by FibroScan (Echosens) and ElastPQ-SWE (Affiniti 70G, Philips) in all recruited patients.

Results: We enrolled 319 consecutive patients with NAFLD, mean age 54 ± 13y, BMI 31.7 ± 5.8 kg/m2, waist circumference (WC) 107 ± 15 cm, 56.3% male, 44% with diabetes, 55.7% hypertension, 81% hyperlipidaemia. ElastPQ had a good correlation with F-TE (Spearman’s r = 0.740, p < 0.0001), which was better for mild and moderate stages of fibrosis (Figure 1). A ± 2 kPa difference between the two techniques was found in 89 patients. On the univariate analysis predictors of such a difference were diabetes (p = 0.004), BMI (p = 0.032), AST (0.021) and F-TE ≥ 10 kPa (p < 0.0001) compatible with advanced fibrosis. On the multivariate analysis the only independent predictor was F-TE ≥ 10 kPa (OR: 6.891, 95% CI 3.538–13.422, p < 0.0001).

In the subgroup of 112 patients with available histology, the distribution of fibrosis was as follows: F0 = 14 (12%), F1 = 40 (36%), F2 = 21 (19%), F3 = 17 (15%), F4 = 20 (18%). The optimal cut-off values of ElastPQ-SWE for individual stages of fibrosis were lower than those of F-TE. ElastPQ showed the same diagnostic performance for F ≥ 2 and a better diagnostic performance for F ≥ 3 and F4 compared to F-TE (Table 1).

Conclusion: ElastPQ and F-TE showed a good correlation in patients with NAFLD, which is better for low values of liver stiffness. The optimal cut-off values of ElastPQ are lower than those of F-TE for individual stages of fibrosis. ElastPQ seems to have a better diagnostic accuracy than F-TE in diagnosing advanced fibrosis and cirrhosis but this finding needs to be confirmed in larger cohorts.

FRI-431
New diagnostic method for hepatic steatosis using attenuation measurement by B mode ultrasound: Comparison with controlled attenuation parameter

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Background and Aims: Findings such as hepatic kidney contrast etc. have been used to diagnose fatty liver in B mode ultrasound, but they are based on subjective interpretation by the operator, and diagnostic accuracy is unsatisfactory. In recent years, it has become possible to measure hepatic steatosis (Controlled Attenuation Parameter: CAP) by measuring liver hardness using vibration-controlled transient elastography (VCTE) and attenuation of the ultrasonic signal. However, since VCTE cannot observe the measured section in real time, it has the disadvantage that it cannot be measured in postoperative cases or ascites. To overcome these disadvantages, we have developed a function (Attenuation: ATT) that transmits ultrasonic waves of different frequency components when measuring in B mode, and it estimates hepatic steatosis from the difference in attenuation of the received signal. The aim was to clarify the usefulness of ATT by comparing fat quantitative diagnosis by ATT and by CAP.

Method: All participants provided written, informed consent, and the study protocols were approved by the institutional ethics committee. Liver biopsies were performed from July 2015–March 2017, and 366 ATT and 105 CAP measurements were conducted. ATT measurements were performed five times with the ultrasonic
diagnostic apparatus (HI VISION Ascendus; Hitachi, Ltd., Tokyo, Japan) with a convex probe (EUP-C715), avoiding the vessels in the liver from the right intercostal space, and the median was calculated. The CAP measurement was measured using M and XL probes. Steatosis grades obtained from pathological tissues were compared with the ATT and CAP values.

**Results:** The steatosis grades of the cases were: S0 303 cases; S1 43 cases; S2 14 cases; and S3 15 cases. In all cases, ATT measurement was possible. The area under the receiver operating characteristic curve (AUC-ROC) for ≥ S1 was 0.77, 0.80, and 0.83 for ATT, CAP M probe, and CAP XL probe, respectively. The AUC-ROC for ≥ S2 was 0.85, 0.83, and 0.84, respectively. The AUC-ROC for S3 was 0.95, 0.98, and 0.92, respectively. Significant differences in AUC-ROC between ATT and CAP were examined by the DeLong test, and no significant differences were found for ≥ S1 (ATT vs M probe: p = 0.257, ATT vs XL probe: p = 0.061), ≥ S2 (ATT vs M probe: p = 0.385, ATT vs XL probe: p = 0.717), and S3 (ATT vs M probe: p = 0.515, ATT vs XL probe: p = 0.143). From these results, the diagnostic ability for hepatic steatosis was considered to be comparable between ATT and CAP.

**Conclusion:** The steatosis diagnostic grade ability of ATT was similar to that of CAP. ATT does not require dedicated equipment for lipid diagnosis, it can be measured simultaneously with normal observation in B mode, and it is a useful modality considered to be measurable even in cases where measurement is impossible or difficult by CAP.

**FRI-433**

**Electronic-nose breath print distinguishes non-alcoholic fatty liver disease from healthy lean control: A pilot study**


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**Background and Aims:** Human breath contains numerous volatile compounds which reflect metabolic activity. Electronic nose (eNose) technology can rapidly detect these volatile metabolites to provide breath prints non-invasively. Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome. We hypothesized breath prints obtained from eNose could distinguish healthy individuals from those with NAFLD.

**Method:** The study was prospective single-center cohort study (ClinicalTrials.gov: NCT02950610) with training cohort and one against all (leave-one-out) cross validation verification (CVV). eNose (SpiroNose) is a custom-made device made up of five-sensor arrays each containing four sensors, previously validated in respiratory and liver disease [1, 2]. eNose on exhaled breath was performed on well characterised NAFLD patients; (a) NAFLD Child’s A cirrhosis (n = 30; n = 4, liver biopsy; n = 20, endoscopic features of portal hypertension; n = 6, radiological features), (b) NAFLD non-cirrhosis (n = 30; n = 8, liver biopsy; n = 22, non-invasive markers e.g. NAFLD fibrosis score, Fib4, hyaluronic acid, transient elastography etc. and (c) self-declared healthy subjects [n = 30]. Data were analyzed using R (v 2.3.2) and Orange (v 3.4.1) software. Data reduction to 3 principal components (PCs) explained 97.8% of total variance. Data was further classified by k-nearest neighbor’s (k-NN) algorithm, a non-parametric machine learning algorithm for classification.

**Results:** In patients with NAFLD cirrhosis, eNose was able to accurately classify with 100% sensitivity (p < 0.001, cross-validation verification [CVV] 96%) from healthy subjects, independent of age and gender. Sensor 1, Sensor 2, Sensor 3 and Sensor 4 identified NAFLD cirrhosis patients with AUC 0.96 (standard error = 0.043; p < 0.001), 0.89 (standard error = 0.046; p < 0.001), 0.98 (standard error = 0.016; p < 0.001) and 0.96 (standard error = 0.022; p < 0.001) respectively. eNose was able to differentiate between healthy from; non-cirrhotic NAFLD (p < 0.001, CVV 96.8%) and NAFLD cirrhotic (p < 0.001, CVV 95.1%). However, it could not differentiate non-cirrhotics from cirrhotic in NAFLD (p = 0.88). 60 participants (30 healthy and 30 NAFLD cirrhotic) were analyzed using a leave-one-out CVV for creating training sets and validation sets. This method, designed to reflect the generalization property of the k-nearest neighbor’s classifier, scored a classification rate of 96%.

**Conclusion:** Our study demonstrates the ability of eNose to accurately distinguish NAFLD from healthy individuals. Thus, eNose technology can provide rapid, non-invasive point-of-care screening to risk stratify patients, which can reduce the burden of liver biopsy.

**FRI-434**

**A study of breath metabolome in Non-alcoholic fatty liver disease**

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**Background:** Human breath contains numerous volatile compounds which reflect metabolic activity. Electronic nose (eNose) technology can rapidly detect these volatile metabolites to provide breath prints non-invasively. Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome. We hypothesized breath prints obtained from eNose could distinguish healthy individuals from those with NAFLD.

**Method:** The study was prospective single-center cohort study (ClinicalTrials.gov: NCT02950610) with training cohort and onega against all (leave-one-out) cross validation verification (CVV). eNose (SpiroNose) is a custom-made device made up of five-sensor arrays each containing four sensors, previously validated in respiratory and liver disease [1, 2]. eNose on exhaled breath was performed on well characterised NAFLD patients; (a) NAFLD Child’s A cirrhosis (n = 30; n = 4, liver biopsy; n = 20, endoscopic features of portal hypertension; n = 6, radiological features), (b) NAFLD non-cirrhosis (n = 30; n = 8, liver biopsy; n = 22, non-invasive markers e.g. NAFLD fibrosis score, Fib4, hyaluronic acid, transient elastography etc. and (c) self-declared healthy subjects [n = 30]. Data were analyzed using R (v 2.3.2) and Orange (v 3.4.1) software. Data reduction to 3 principal components (PCs) explained 97.8% of total variance. Data was further classified by k-nearest neighbor’s (k-NN) algorithm, a non-parametric machine learning algorithm for classification.

**Results:** In patients with NAFLD cirrhosis, eNose was able to accurately classify with 100% sensitivity (p < 0.001, cross-validation verification [CVV] 96%) from healthy subjects, independent of age and gender. Sensor 1, Sensor 2, Sensor 3 and Sensor 4 identified NAFLD cirrhosis patients with AUC 0.96 (standard error = 0.043; p < 0.001), 0.89 (standard error = 0.046; p < 0.001), 0.98 (standard error = 0.016; p < 0.001) and 0.96 (standard error = 0.022; p < 0.001) respectively. eNose was able to differentiate between healthy from; non-cirrhotic NAFLD (p < 0.001, CVV 96.8%) and NAFLD cirrhotic (p < 0.001, CVV 95.1%). However, it could not differentiate non-cirrhotics from cirrhotic in NAFLD (p = 0.88). 60 participants (30 healthy and 30 NAFLD cirrhotic) were analyzed using a leave-one-out CVV for creating training sets and validation sets. This method, designed to reflect the generalization property of the k-nearest neighbor’s classifier, scored a classification rate of 96%.

**Conclusion:** Our study demonstrates the ability of eNose to accurately distinguish NAFLD from healthy individuals. Thus, eNose technology can provide rapid, non-invasive point-of-care screening to risk stratify patients, which can reduce the burden of liver biopsy.
Background and Aims: Breath-omics is gaining popularity as a method for non-invasive measure of biomarkers for various diseases. Breath metabolome is a multitude of volatile organic compounds (VOCs) reflecting pathological metabolic processes. The purpose of this study was to compare breath VOCs in patients with non-alcoholic fatty liver disease (NAFLD) and healthy controls.

Method: Breath samples were collected from well characterized NAFLD patients; a) NAFLD Child’s A cirrhotics (n = 15; n = 14, endoscopic features of portal hypertension; n = 1, radiological feature), b) NAFLD non-cirrhosis [n = 14; n = 3, liver biopsy; n = 11, elevated transient elastography and fibrosis scores and c) self-declared healthy subjects [n = 15]. Exhaled breath collection and breath condensate analysis has been previously well described [1]. VOCs were identified using mass spectrometry analysis; comprising of abundant and trace compounds. Compounds based on the mass spectra and a peak appearing at a retention time that was consistent in all samples. The mass spectra of each compound were matched in the chromatogram and further identified using AMDIS® software. The peak areas of the compounds were collected from extracted ion chromatograms of the most dominant parent ion of the compound and the peak automatically integrated using Xcalibur®. All compound peak areas were normalised by internal standard (d8-toluen). The peak areas of the compounds were normalised by internal standard (d8-toluen), which was added to all samples when it was analysed. Data were analysed by non-parametric ANOVA (Kruskal–Wallis) and Dunns post-hoc. Receiver Operating Characteristic (ROC) curves were used to determine the diagnostic accuracy of the volatiles compound.

Results: Body mass index adjusted exhaled breath levels of acetone, dimethyl sulphide, d-limonene, acetophenone and alfaterpine were significantly higher (p < 0.001, p < 0.01, p = 0.005, p < 0.001, p = 0.001, p < 0.001) in patients with NAFLD cirrhosis than that seen with healthy subjects. D-limonene is found to provide the most discriminatory power for NAFLD cirrhosis, AUROC = 0.91 (95% CI 0.79, 1.0; standard error 0.06) (Figure 1). Additionally, breath acetone and dlimonene concentrations can differentiate NAFLD non-cirrhosis from NAFLD cirrhosis (p < 0.001 and p < 0.05). Breath acetone level can distinguish between NAFLD non-cirrhotic and NAFLD cirrhotic; AUROC = 0.88 (standard error 0.07) and achieves a sensitivity of 90% with a specificity of 70% (Figure 2).

Conclusion: Breath VOCs have a promising future as biomarkers for a non-invasive diagnostic and prognostic tool in the management of NAFLD. D-limonene and acetone can identify NAFLD non-cirrhosis from NAFLD cirrhosis with confidence. Future validation of our finding to external cohort is needed.
Magnetic Resonance Elastography versus Transient Elastography in detection of fibrosis in nonalcoholic fatty liver disease: A systematic review and meta-analysis of individual participant date


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Background and Aims: Magnetic resonance elastography (MRE) and transient elastography (TE) are noninvasive imaging techniques used to diagnose liver fibrosis in patients with nonalcoholic fatty liver disease (NAFLD). Previous studies comparing the efficacy of MRE versus TE have been single-center studies. Therefore, we aimed to perform a meta-analysis of individual participant data from published studies to compare the diagnostic performance of MRE versus TE for the staging of liver fibrosis in NAFLD using liver biopsy as the gold standard.

Method: A computer-aided systemic literature search of multiple databases from January 1, 2005 to September 05, 2017 identified 3 studies (Imajo et al. Gastroenterology 2016, Park et al. Gastroenterology 2017, Chen et al. Radiology 2017) with MRE and TE assessment for the detection of liver fibrosis in patients with NAFLD, using liver biopsy as a reference. Data for 318 participants, including baseline characteristics, histologic fibrosis stage, MRE, and TE measurements, were collected by contacting the study authors and of those, data from 230 participants with MRE, reliable TE measurement and liver biopsy availability were included in the analysis using a pre-specified meta-analysis protocol. Through pooled analysis, the cluster-adjusted area under the curve (AUROC) of MRE and TE was calculated for the detection of each stage of fibrosis, and AUROC comparisons between MRE and VCTE were performed using the Delong test.

Results: The pooled analysis included 230 participants with biopsy proven NAFLD with mean (± sd) age and BMI of 52.2 (± 13.9) years and 31.9 (± 7.5) kg/m2, respectively. The distribution of stage 0, 1, 2, 3 and 4 fibrosis was 31.7%, 27.8%, 15.7%, 13.9%, and 10.9%, respectively. The AUROC (95% CI) of TE versus MRE for the detection of fibrosis stages ≥1 was 0.82 (0.78–0.86) vs. 0.87 (0.82–0.91), p < 0.05, fibrosis stage ≥ 2 was 0.87 (0.82–0.91) vs. 0.92 (0.88–0.96), p < 0.05, fibrosis stage ≥ 3 was 0.84 (0.78–0.90) vs. 0.93 (0.89–0.96), p < 0.001, and fibrosis stage ≥ 4 was vs.0.84 (0.73–0.94) vs. 0.94 (0.89–0.99), p < 0.01, respectively.

Conclusion: In this pooled analysis of data from individual participants with NAFLD in 3 independent studies, MRE demonstrated a higher diagnostic accuracy than TE for the detection of individual stages of fibrosis using liver biopsy as a reference. Both MRE and TE have a role in the detection of fibrosis in NAFLD depending upon the desirability for accuracy.
Background and Aims: CAP is a quantitative, ultrasound-based measure of hepatic steatosis. Our objectives were to assess the: (1) correlation between CAP and MRI-estimated proton density fat fraction (PDFF), and (2) responsiveness of CAP to change in a clinical trial of subjects with NASH.

Method: CAP (FibroScan; Echosens, France) and MRI-PDFF were measured at baseline (BL) and Week 12 (W12) in a Phase 2, multicenter trial of NASH subjects treated with the acetyl-CoA carboxylase (ACC) inhibitor GS-0976 20 mg, GS-0976 5 mg, or placebo orally once daily for 12 weeks. MRI-PDFF was read centrally and CAP was performed locally where available. A ≥30% relative reduction in MRI-PDFF between BL and W12 was considered clinically significant. Spearman correlations (ρ) were used to evaluate associations between CAP and MRI-PDFF, and changes in MRI-PDFF and CAP by treatment arm were evaluated using Wilcoxon rank-sum and Fisher exact tests.

Results: The majority of subjects were female (65%) and diabetic (60%); median BL MRI-PDFF (n = 126) and CAP (n = 69) were 14.37% (IQR 11.07, 18.98) and 329 dB/m (298, 359), respectively. 52% (72/138) of all CAP measurements were obtained using the FibroScan M probe. Among demographic and BL clinical parameters, CAP was correlated with body mass index (ρ = 0.32, p = 0.008), waist circumference (ρ = 0.31, p = 0.010), and fasting serum glucose (ρ = 0.24, p = 0.046). CAP and MRI-PDFF were significantly correlated at BL (ρ = 0.29, p = 0.016) and W12 (ρ = 0.32, p = 0.009). However, absolute (ρ = 0.22, p = 0.094) and relative changes (ρ = 0.21, p = 0.096) in CAP and MRI-PDFF between BL and W12 were not significantly correlated. In subjects treated with GS-0976 20 mg daily, a 28.9% median relative reduction in MRI-PDFF was observed between BL and W12 (p = 0.002 vs. placebo). A 13.0% reduction in the 5 mg group was not statistically different from placebo (Figure). Relative reductions in CAP were smaller and did not differ significantly between treatment groups (Figure). Relative reductions ≥30% in MRI-PDFF in the GS-0976 20 mg, GS-0976 5 mg, and placebo groups were observed in 48%, 23%, and 15% of subjects (p = 0.004 vs. GS-0976 20 mg; p = 0.43 vs. GS-0976 5 mg), respectively. Relative CAP reductions ≥30% were observed in 10%, 0%, and 7.7% of subjects, respectively (both p > 0.05 vs. placebo). The median relative change in CAP in 23 MRI-PDFF responders was −7.5% (IQR −14.8, 1.8) compared with −3.0% (−10.8, 9.9) among non-38 responders (p = 0.23).

Conclusion: Among NASH subjects in this multi-center trial of GS-0976, measures of hepatic steatosis quantified by CAP and MRI-PDFF were moderately correlated. However, changes in these parameters were not correlated and CAP was less responsive to change than MRI-PDFF. Further validation of CAP is necessary before it can be considered a valid endpoint for use in clinical trials of interventions for NASH.

FRI-455

Liver and pancreatic steatosis in children are both associated with metabolic syndrome but have different influence on insulin sensitivity and glucose metabolism

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Background and Aims: Children with obesity have high risk for ectopic fat accumulation both in liver and pancreas. It is known that liver steatosis can be independent risk factor for metabolic complications. We still don’t have proved data about existence of independent association between metabolic complications and pancreatic fat. Aim of our study was to compare influence of liver and pancreatic steatosis on metabolic complications in children by estimation of the ultrasound attenuation.

Method: We examined 114 children aged 7–17 years, 67 with obesity, 48 without obesity. Anthropometry, lipid spectrum and insulin level with calculation HOMA1-IR and HOMA2-IR indices, oral glucose tolerance tests were assessed using standard techniques. Pancreatic and liver steatosis were diagnosed by ultrasound study (US). Alsew estimated liver controlled attenuation parameter (CAP) with usage Fibroscan 502 Touch (France) and pancreatic ultrasound attenuation coefficient (UAC) with usage UltimapAxPexpert® (Radmir, Ukraine).

Results: The prevalence of liver steatosis evaluated by ultrasound was 27.3%, pancreatic steatosis – 56.1%. CAP level positively correlated with degree of liver steatosis according to US (r = 0.59, p < 0.05), also UAC positively correlated with degree of pancreatic steatosis according to US (r = 0.46, p < 0.05). We found association between CAP and UAC in whole group and nonobese subcohorts. The CAP (233 [193.0; 263.0] dB/m2) and UAC (2.58 [2.31; 2.75] dB/ms2) were elevated in subjects with obesity. We found association between UAC and body mass index-standard deviation score (BMI-SDS) in whole group (r = 0.42, p < 0.05) and obesity subcohort (r = 0.44, p < 0.05), while no association between CAP and BMI-SDS was found in whole group neither in subcohorts. CAP correlated to fasting glucose level, fasting insulin level, HOMA1-IR and β-cell function (β) (according to HOMA2-IR) in simple regression: UAC negatively correlated with glucose level 60 min after load in obese subcohort (r = −0.40, p < 0.05) and insulin sensitivity (%) (according to HOMA2-IR) (r = −0.38, p < 0.05). Both CAP and UAC were associated with components of metabolic syndrome (MetS) such as waist circumference, systolic blood pressure. While CAP additionally correlated with level of TG (r = 0.30, p < 0.05). In nonobese subcohorts both CAP and UAC correlated with LDL and nonHDL level, also UAC negatively correlated with HDL.

Conclusion: In children with obesity, CAP is elevated and associated to MetS, fasting glucose, insulin resistance, beta-cell function, but not to glucose tolerance, or BMI-SDS. While UAC was associated with MetS, BMI-SDS, glucose 60 min after load in oral tolerance test, glucose sensitivity but not to beta-cell function. This study demonstrates that liver and pancreatic steatosis both are associated with MetS but have different influence on glucose metabolism and insulin sensitivity.
Comparison of HepaFat-Scan and controlled attenuation parameter for the estimation of hepatic steatosis in patients with non-alcoholic fatty liver disease using histology as the reference standard

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Background and Aims: We aimed to compare HepaFat-Scan, an MRI-based technology for the measurement of liver fat, with Fibroscan controlled attenuation parameter (CAP) for the estimation of hepatic steatosis in patients with non-alcoholic fatty liver disease (NAFLD).

Method: Consecutive NAFLD patients who underwent liver biopsy at the University of Malaya Medical Centre were enrolled in this study, and had MRI and Fibroscan examinations on the same day. Histopathological examination of liver biopsy specimen was performed by a single expert pathologist who was blinded to clinical data and reported according to Non-alcoholic Steatohepatitis Clinical Research Network scoring system. Area under receiver operating characteristic curve (AUROC) was used to evaluate the diagnostic accuracy of HepaFat-Scan and CAP for the estimation of hepatic steatosis using liver histology as the reference standard.

Results: Data for 72 patients were analyzed (mean age 58.3 ± 9.8 years, males 45.8%, mean body mass index 29.9 ± 4.0 kg/m2, central obesity 95.8%). The distribution of steatosis grades was as follows: S1, 33%; S2, 57% and S3, 10%. The AUROC (95% confidence interval), sensitivity, specificity, positive predictive value and negative predictive value of HepaFat-Scan and CAP for the diagnosis of steatosis grades ≥ S2 and S3 using previously validated cut-offs are shown in Table 1.

Table 1: The AUROC (95% confidence interval), sensitivity, specificity, positive predictive value and negative predictive value of HepaFat-Scan and CAP for the diagnosis of steatosis grades ≥ S2 and S3 using previously validated cut-offs.

<table>
<thead>
<tr>
<th>Grade</th>
<th>HepaFat-Scan</th>
<th>Controlled attenuation parameter</th>
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<tbody>
<tr>
<td></td>
<td>AUROC (95% confidence interval)</td>
<td>AUROC (95% confidence interval)</td>
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<tr>
<td>S1</td>
<td>0.95 (0.80–0.96)</td>
<td>0.71 (0.58–0.81)</td>
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<tr>
<td>S2</td>
<td>0.85 (0.74–0.93)</td>
<td>0.60 (0.47–0.71)</td>
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<tr>
<td>S3</td>
<td>0.85 (0.74–0.93)</td>
<td>0.60 (0.47–0.71)</td>
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Conclusion: The HepaFat-Scan has higher accuracy for the estimation of hepatic steatosis in NAFLD patients compared with the CAP.

Evaluation of severity of hepatic fibrosis and steatosis in biopsy proven NAFLD patients using MR imaging, transient elastography, and serum biomarker

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Background and Aims: As nonalcoholic fatty liver disease (NAFLD) is becoming a leading cause of chronic liver disease, non-invasive diagnosis of disease severity is urgently needed. For the diagnosis of liver fibrosis, transient elastography (TE) has acceptable accuracy in viral related liver disease. But in patients with severe steatosis, TE has shortage. Aim of our study was plan to analyze hepatic fibrosis, steatosis, and inflammation in patients with biopsy-proven NAFLD using MR imaging, TE, and serum biomarkers.

Method: This is a multicenter prospective study of patients with biopsy-proven NAFLD. The patients were underwent liver biopsy, MRI and TE 6 months before enrollment. MRI examination included mDIXON, MR spectroscopy (MRS), and MR elastography (MRE). TE measured liver stiffness and controlled attenuation parameter (CAP). Twenty serum biomarkers were analyzed using the Luminex Multiplex Assay.

Results: 46 patients with biopsy-proven NAFLD patients were enrolled from October 2016 to May 2017. Mean age and BMI were 51.2 ± 12.8 years and 27.6 ± 7.5 kg/m2, respectively. Female was dominant (30, 63.4%) and other co-morbidities were diabetes (n = 18, 38.3%), hypertension (n = 16, 34.0%) and dyslipidemia (n = 15, 31.9%). For diagnosis of advanced fibrosis (stage 3–4), the AUROC of MRE tended to be superior (0.88; 95% CI, 0.74–0.97) compared with TE (0.85; 95% CI, 0.72–0.95) (p = 0.532). For diagnosis of severe steatosis (stage 2–3), CAP (0.69; 95% CI, 0.51–0.83) showed lower AUROC compared with mDIXON (0.83; 95% CI, 0.67–0.93; p = 0.35) and MRS (0.83; 95% CI, 0.67–0.93; p = 0.109), respectively. In serum biomarker analysis, increased resistin had a significant association with severe steatosis (stage 2–3) compared to mild steatosis (stage 0–1) (OR = 1.36; 95% CI, 1.01–1.83; p = 0.04). Total PAI-1 showed tendency of association with presence of NASH (OR = 1.063; 95% CI, 1.01–1.8; p = 0.04). Increased IFN-γ was associated with severe inflammation (stage 2–3) compared to mild inflammation (stage 0–1) (OR = 1.36; 95% CI, 1.01–1.83; p = 0.04). Total PAI-1 showed tendency of association with presence of NASH (OR = 1.063; 95% CI, 0.99–1.14; p = 0.07).

Conclusion: In our preliminary results, MRI (mDIXON, MRS and MRE) tended to identify more severe steatosis and fibrosis compared to TE in patients with biopsy-proven NAFLD. Serum IFN-γ was significantly associated with inflammation and serum resistin was also associated with steatosis. Non-invasive modalities using MRI and serum biomarker could be potential tools for diagnosis and classification of disease severity in patients with NAFLD.

Screening for liver fibrosis using transient elastography by fibroscan and fibrotest in type 2 diabetic patient

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Background and Aims: Patients with type 2 diabetes (T2D) are at risk for non-alcoholic fatty liver disease (NAFLD) leading to advanced fibrosis, cirrhosis, and liver cancer. We examined the efficacy of a screening strategy with noninvasive fibrosis biomarkers, FibroTest and FibroMax (FT, BioPredictive, France) and transient elastography (TE,
Fibroscan, Echosens, France) in patients with T2D without previous history of liver disease.

Method: We prospectively studied 104 patients without a history of liver disease seen for T2DM. The biomarker data were obtained, and patients with presumed advanced fibrosis were re-investigated by a hepatologist using, if necessary, ultrasonography, endoscopy, or liver biopsy in order to confirm fibrosis.

Results: 104 patients were included, mean age 56.4 ± 9.5yrs. (range of 29–82), 60.6% females, mean (range) BMI 33.3 ± 5.1(22–47), 72.1% (> = 30 kg/m²). According to the FibroTest biomarkers, advanced fibrosis was diagnosed in 44 out of 104 patients (42%), while the TE biomarkers confirmed the diagnosis in 45% of cases (47/104). Among of 104 patients advanced fibrosis was confirmed in 42 subjects (40%), liver cirrhosis - in 11 patients (10.6%), including 2 cases of esophageal varices, 9 cases of splenomegaly and thrombocytopenia. According to SteatoTest 66% patients had advanced steatosis (cutoff score > = 0.76) and 39.8% according to CAP (dB/m), cutoff score = 30.0. In patients who were 50 years or older, the prevalence of confirmed advanced FibroTest diagnosed F4 in 10 subjects (10.4%). The comparative analysis between these results and those of the TE showed discordance in 21 cases (20.2%). The TE performed false positive diagnosis in 9 cases, while FTonly in 3. At the same time, FT registered 1 case of false negative result, while TE indicated it in 4 patients. Among 44 patients with advanced fibrosis (F2-F4) according to FT normal ALT level was in 29.6% cases (p-value = 0.58267) and 45.5% (p-value = 0.00034) had normal GGT.

Conclusion: Noninvasive fibrosis biomarkers, FT and TE, might be used for the detection of advanced fibrosis in patients with T2DM. ALT and GGT are not a reliable markers to detect fibrosis.

FRI-474

Body mass index influences Controlled Attenuation Parameter (CAP) values measured with Fibroscan® M probe. When should we evaluate steatosis with the XL probe?


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Background and Aims: The FibroScan® XL probe quantifies liver fibrosis in obese patients. Anthropometric variables should be taken into account to choose the appropriate probe. Controlled Attenuation Parameter (CAP) quantifies the degree of steatosis. Recently, CAP determination has been incorporated into the XL probe but there are no studies comparing CAP values between both probes (M and XL) in obese patients. The aim of the study was to evaluate the correlation of CAP values with M and XL probe, in patients with BMI ≥28 kg/m².

Method: Non-randomized prospective study, evaluating all patients with chronic liver disease and BMI ≥28 kg/m² from April to October 2017. The measurements with the FibroScan® M and XL probe were performed the same day and by the same explorer. Clinical, anthropometric, analytical and elastographic data have been analyzed.

Results: 386 patients with BMI ≥ 28 and chronic liver disease were evaluated (37% with hepatitis C, 31% non-alcoholic fatty liver disease, 14% Hepatitis B, 18% others). Patients (n = 89) evaluated by a nonexperienced explorer (<500 TE) or those without both probes (n = 116) were excluded. Thus, 181 patients assessed with both probes by an experienced explorer were included. The median (range) age was 57 (27–93), 61% were men and 52% diabetic, 37% had a BMI between 28–30, 50% between 30 and 35 and 13% a BMI ≥35. The skin-capsule distance (SCD) according to the BMI category was 18 (13–24) mm, 20 (11–25) mm and 22 (15–25) mm, respectively. The CAP correlation with both probes was p = 0.78 (p < 0.001). There were no differences between the median CAP (dB/m) values with M (275) and XL (277) probes (p = ns). However, CAP values were significantly lower with M probe (278) compared to XL probe (287) (p = 0.014) in patients with BMI ≥ 35 kg/m², probably due to a lower distribution of fat in the cortical area of the liver.

Conclusion: Controlled Attenuation Parameter (CAP) shows a good correlation between the FibroScan® M and XL probes. However, in patients with a BMI ≥35 kg/m² values with M probe underestimate the degree of steatosis, making necessary to evaluate these patients with the XL probe.

FRI-475

The easy Liver Fibrosis Test (eLIFT) avoids unnecessary specialized evaluations of liver fibrosis in NAFLD and ALD patients

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD) are risk factors for cirrhosis and liver related complications. Therefore, all NAFLD and ALD patients should theoretically undergo a non-invasive evaluation of liver fibrosis. However, the best non-invasive tests of liver fibrosis are limited by their cost and/or poor accessibility. Moreover, NAFLD and ALD patients represent a very large population, with most of them having no/mild fibrosis which would induce a majority of “unnecessary” specialized evaluations of liver fibrosis. The easy Liver Fibrosis Test (eLIFT) is a very simple fibrosis test including common parameters (age, sex, GGT, AST, platelets, prothrombin time). It has been developed to identify patients at-risk of advanced liver fibrosis who require further specialized evaluation. We aimed to evaluate whether the eLIFT helps to appropriately avoid unnecessary specialized evaluations of liver fibrosis in NAFLD and ALD patients.

Method: NAFLD and/or ALD patients referred for the first time to our centre for a non-invasive evaluation of liver fibrosis between October 2014 and March 2017 were included. Patients with other causes of chronic liver disease were excluded. FibroMeterVCTE (FMVCTE) which includes in a single formula the Fibroscan result and the parameters of the FibroMeterVIRUS, was considered as the reference for the noninvasive evaluation of liver fibrosis (best non-invasive test in a recent large series of 1946 patients, J Hepatol 2017). As previously published, eLIFT ≥8 identified patients at-risk of advanced fibrosis.

Results: 543 patients were included: 260 NAFLD, 185 ALD and 98 NAFLD + ALD. FMVCTE diagnosis was no/mild fibrosis in 55.2% of patients, advanced fibrosis in 33.1%, undetermined in 11.6%. 247/543 patients (45.5%) had eLIFT <8. Among patients with eLIFT <8, 207/247 (83.8%) had no/mild fibrosis according to FMVCTE. Among the 40 remaining patients, FMVCTE diagnosis was advanced fibrosis in 17 and undetermined in 23. 155 NAFLD patients had eLIFT <8 and 124 of them (80.0%) had no/mild fibrosis according to FMVCTE, 59 of the 66 ALD patients with eLIFT <8 (89.4%) had no/mild fibrosis according to FMVCTE, and 24 of the 26 NAFLD + ALD patients (92.3%).

Conclusion: Used as first-line test in NAFLD and ALD, the eLIFT avoids unnecessary specialized non-invasive evaluations of liver fibrosis in half of the patients referred to a tertiary centre.

FRI-476

Feasibility and utility of controlled attenuation parameter and transient elastography in the assessment of nonalcoholic fatty liver disease severity in children

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Background and Aims: Estimating the severity of liver steatosis by controlled attenuation parameter (CAP) and liver fibrosis by transient elastography (TE) using the Fibroscan™TM machine provides a noninvasive method to establish the presence of nonalcoholic fatty liver disease (NAFLD) and assess its severity. Although the use of CAP/TE is becoming routine practice in adults, limited data exist in children with suspected NAFLD. The aim of this study was to assess the feasibility and utility of measuring CAP/TE by Fibroscan™TM in a cohort of children with suspected NAFLD referred to a community gastroenterology clinic.

Method: All children seen at our clinic from May to October 2017 with suspected NAFLD (elevated ALT or fatty infiltration on ultrasonography) who had CAP/TE measured were included. Fibroscan™TM was performed by an experienced operator. Standard criteria for having valid measurements were applied (IQR < 30% with ≥70% success rate). The severity of steatosis was evaluated by CAP: <225 db/m no steatosis, 225–250 mild, 250–300 moderate, and >300 severe. The severity of liver stiffness/fibrosis was evaluated by TE: <7 kPa no significant fibrosis, 7–10 kPa mild or moderate, >10 kPa advanced. Clinical and laboratory parameters were collected. Chi-square test was used for statistical comparison between mild-to-moderate and severe steatosis; and presence or absence of significant fibrosis. Crude and adjusted logistic regression models were used to determine associations between patients’ characteristics and CAP/TE.

Results: 44 children with suspected NAFLD were referred in the specified time period. Mean age (± SD) was 14.0 years (± 3.5). Majority were males (77%), obese (95%), and Hispanic (89%). All patients (44/44) had successful Fibroscan™TM measurements but the adult probe (XL) needed to be used in 21/44 (48%) of our patients and the regular M probe was used for the rest. All patients had CAP > 225 indicating steatosis and 50% of female and 80% of male patients had severe steatosis with CAP > 300 (Figure). On multivariable analysis, the presence of elevated AST (>48 U/L) was associated with a 9.6-fold increase in the presence of severe steatosis (p = 0.04), whereas the presence of positive smooth muscle antibody (SMA) was significantly protective. Evidence of fibrosis based on TE was present in 43% of children and 17% of male subjects had TE > 10 kPa indicating the potential for having advanced fibrosis. Factors associated with significant fibrosis included the presence of prediabetes, hypertension, hemoglobin level, and serum bilirubin (p < 0.05 for all).

Conclusion: CAP/TE provides a reliable way to confirm the diagnosis of NAFLD and assess its severity in children. Larger pediatric studies that assess the correlation with liver histology and disease progression are urgently needed.

Background and Aims: The controlled attenuation parameter (CAP) has shown a good correlation with the intrahepatic fat amount in cross-sectional studies. However, there is no study on whether the change of CAP scores can also show good correlation in a longitudinal setting. Therefore, we investigated the correlation between CAP and magnetic resonance imaging-estimated proton density fat fraction (MR PDFF) through serial examination in a longitudinal setting.

Method: Sixty-five patients with nonalcoholic fatty liver disease were evaluated with MR PDFF and transient elastography including CAP at baseline and 3 months later.

Results: CAP and MR PDFF at baseline showed a strong correlation in assessing hepatic steatosis (r = 0.66, p < 0.001). After treatment, the correlation between the change in CAP after treatment and the intrahepatic fat change (%) on MR PDFF was not satisfactory (r = 0.37, p = 0.005) in the longitudinal setting. The optimal cutoff value of the change in CAP for discriminating an improvement or an aggravation in intrahepatic fat percentage (>1% change in MR PDFF) was selected as 38 dB/m (area under the receiver operating characteristic curve = 0.559). For CAP changes >38 dB/m, the predictive value was 14/16 (87.5%), whereas for changes <38 dB/m, the predictive value was 12/41 (29.3%). Thereby, the accuracy of the method using the change in CAP was only 26/57 (46%). In addition, Cohen’s kappa values was not significant (κ = 0.11, p = 0.186).

Conclusion: Careful interpretation of the steatosis change based on the CAP score is needed when the absolute change value <38 dB/m in a longitudinal setting.

Background and Aims: Elevated de novo lipogenesis (DNL) contributes to the pathogenesis of NASH. Acetyl-CoA carboxylase (ACC) catalyzes the first and rate-limiting step in DNL. Here, we describe the efficacy, safety, and pharmacodynamic effects of GS-0976, a liver-targeted inhibitor of ACC, in subjects with compensated cirrhosis due to NASH.

Method: In a proof-of-concept study, 10 subjects with suspected compensated cirrhosis (Child-Turcotte-Pugh [CTP]-A) due to NASH (defined by any one of biopsy, liver stiffness by magnetic resonance elastography [MRE] ≥4.67 kPa or transient elastography ≥14.0 kPa, or Fibrotest ≥0.75) received GS-0976 20 mg orally once daily for 12 weeks.
weeks. Centrally-readmagnetic resonance imaging-protondensity fat fraction (MRI-PDDF) and MRE, and serum markers of fibrosis were measured at baseline (BL), Week 4 (W4), and Week 12 (W12). For DNL determination, heavy water (2H2O, 35 mL) was administered three times daily for one-week cycles prior to baseline, W4, and W12. Deuterium incorporation into palmitate was measured in fasting plasma samples by GC/MS, and mass isotopomer distribution analysis was used to calculate hepatic DNL and its inhibition by GS-0976.

**Results:** Compared to BL, statistically significant reductions in hepatic PDDF (median: 9.2 vs. 4.6%; \( p = 0.004 \)) and serum ALT (46 vs. 32U/l; \( p = 0.008 \)) were observed. Decreases in PDDF were significant in W4. A \( >30\% \) relative decline was seen in 5 subjects at W4 (50%) and 7 subjects (70%) at W12. No significant changes in MRE-stiffness or serum fibrosis markers were observed. Decreases in PDDF correlated with changes in ALT, ELF score, and PIII-NP. GS-0976 was well-tolerated; no subjects prematurely discontinued study medication. Median (IQR) fasting triglycerides increased from 147 mg/dl (105, 231) at BL to 159 mg/dl (142, 248) at W12 (\( p = 0.008 \)), but other lipid parameters were unchanged. One subject had asymptomatic Grade 3 hypertriglyceridemia and responded to fibrate therapy. Data regarding the impact of GS-0976 on fasting hepatic DNL are pending.

**Conclusion:** In a proof-of-concept study, 12-week therapy with the liver-targeted, oral ACC inhibitor GS-0976 in subjects with compensated cirrhosis due to NASH was safe and associated with significant improvements in hepatic steatosis and serum ALT.

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**Role of alpha-1 antitrypsin genotypes in the progression of adult liver disease**


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**Background and Aims:** Alpha-1 antitrypsin deficiency (A1AD) is an autosomal codominant disease associated with an increased risk of liver and lung disease in adults. The association between liver disease and homozygosity for the mutant Z allele (PiZZ) is well-established, however, the contribution of other genotypes to the pathogenesis of adult liver disease is unclear. We aimed to assess the prevalence of liver fibrosis in different A1AD genotypes, including rare variants.

**Method:** Multicenter cross-sectional case-control study, including adult A1AD patients treated in pneumology departments of four Portuguese academic and one non-academic centers. Data pertaining pulmonary function and imaging were retrospectively collected. Clinical, biochemical, and liver stiffness (LS) measured by transient elastography (TE, Fibroscan) data were prospectively collected at time of enrollment. Significant liver fibrosis was defined by LS values ≥17.0 kPa. Patients with concomitant liver diseases were excluded. Controls were recruited within a prospective epidemiological study in the general adult population.

**Results:** 142 cases and 200 controls were included. Our study comprised 47 PiZZ, as well as 76 PiM heterozygotes (38 MZ, 34 SZ, 3 MheerenZ, 1 ZQ0s), 10 PiS (5 SS, 5 MS), and 9 PiMmalton or (1 MZ, 1 S). We found a significant decrease in the prevalence of liver fibrosis in A1AD patients compared to controls. Further studies are needed to validate these findings.
Figure 1: Liver fibrosis by alpha-1 antitrypsin deficiency genetic group.

**Conclusion:** Akin to PiZZ, PiZ heterozygosity is associated with liver fibrosis development. Moreover, our results suggest that rare A1AD variants may also promote liver fibrogenesis. Routine laboratory tests are not predictive of significant liver fibrosis, highlighting the need for non-invasive methods such as TE in patients with A1AD.

SAT-039

**Alpha1-antitrypsin augmentation therapy is associated with an improvement in liver-related parameters in patients with severe alpha1-antitrypsin-deficiency**

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**Background and Aims:** Severe alpha1-antitrypsin deficiency (‘PiZZ’ genotype) constitutes one of the most common genetic disorders, and its lethality is due to the associated lung and liver disease. While alpha1-antitrypsin (AAT) augmentation therapy inhibits the progression of PiZZ-related lung affection, liver transplantation constitutes the only cure for PiZZ-related chronic liver failure. Since AAT augmentation decreases the production of toxic PiZ in vitro, we evaluated its impact on liver-related parameters in PiZZ carriers.

**Method:** Overall, 364 adult PiZZ carriers without known liver disease underwent a systematic clinical and laboratory work-up to exclude hepatic comorbidities and to assess pulmonary symptoms.

Liver fibrosis was non-invasively quantified by liver stiffness measurement (LSM) using transient elastography. Liver-related parameters were compared in PiZZ carriers with (221) and without (143) AAT augmentation therapy. Results were adjusted for age, sex, BMI, and diabetes mellitus.

**Results:** Quantitative measures are expressed as mean with standard deviation or as relative frequency (%). Abbreviations: BMI, body mass index; AAT, alpha1-antitrypsin; CAT, chronic obstructive pulmonary disease assessment test; ULN, upper limit of normal (sex-specific); APRI, AST to platelet ratio index; FIB-4, Fibrosis-4 score. PiZZ carriers receiving AAT augmentation therapy were older and presented with more advanced lung disease, as demonstrated by higher CAT (COPD assessment test) values and a more frequent need for long-term oxygen treatment. In contrast, they displayed lower serum AST and GGT activities, lower liver stiffness, APRI and Fb4 values (surrogate markers of liver fibrosis) as well as higher platelet counts (marker of portal hypertension). Multivariate analysis confirmed the association of AAT augmentation with improved liver-related parameters.

SAT-049

**Mild iron overload in homozygous carriers of the alpha1-antitrypsin PiZ variant is not a major driver of liver fibrogenesis**

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**Background and Aims:** Carrier of the common alpha1-antitrypsin (AAT) “PiZ” variant predisposes to liver fibrosis progression, but the disease-promoting factors remain largely unknown. Therefore, we studied the extent of iron overload in patients with homozygous carriage of the PiZ variant (“PiZZ”) and the impact of mild iron overload on PiZ-overexpressing transgenic mice (PiZ mice).
Method: 297 PiZZ carriers and 196 subjects without an AAT mutation (non-carrier), all without known liver disease, underwent a thorough clinical and laboratory workup including measurement of serum iron, ferritin, and transferrin. FibroScan determined liver fibrosis via liver stiffness measurement (LSM) and liver steatosis via controlled attenuation parameter (CAP), respectively. Datawere adjusted for age, sex, BMI, diabetes mellitus and alcohol consumption where appropriate. PiZ mice were crossed with HFE-knockout mice (HFE-KO) and evaluated at the age of 3 and 18 months by quantitative RT-PCR, immunoblotting and histological/immunological staining. Results: Serum parameters of iron metabolism were mostly within the normal range in PiZZ carriers. However, compared to non-carriers, PiZZ carriers had lower transferrin levels (261 vs. 280 mg/dl), but displayed higher ferritin saturation (30% vs. 26%) and ferritin levels (212 vs. 145 ng/ml; all p < 0.001). PiZZ subjects with LSM≥ 7.1 kPa, indicating significant fibrosis, had higher ferritin levels than individuals with LSM < 7.1 kPa (325 vs.177 ng/mp, p < 0.001). Likewise, PiZZ carriers with CAP ≥ 280 dB/m, suggesting severe steatosis, had higher ferritin levels than subjects with CAP < 280 dB/m (270 vs. 182 ng/ml, p = 0.002). HFE-KO and double transgenic (DTg) mice displayed similar extent of iron overload. Moreover, loss of HFE did not modify the amount of PiZ expression and accumulation in the liver. 18 months old PiZ and DTg mice showed a comparable amount of fibrosis in Sirius red staining and the hydroxyproline assay.

Conclusion: Using a large PiZZ patient cohort, we demonstrated that PiZZ accumulation does not typically lead to a clinically relevant iron overload. Studies in PiZ mice revealed that a minor iron overload is well tolerated and does not promote progression of liver fibrosis.

SAT-063
Evaluation of the new criteria in the diagnosis of cystic fibrosis liver disease

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Background and Aims: In cystic fibrosis (CF), liver disease (CFLD) is the third leading cause of mortality. As liver biopsy has been considered as inconsistent in diagnosis of CFLD, a combination of noninvasive modalities additional to liver histology, including physical examination, biochemical and imaging were utilized in the conventional Debray criteria [DC]. More recently, noninvasive biomarkers have been applied and were included in the Newcriteria (NC) (Koh C et al., Hepatology 2017;66:591–601). In current studywe aimed to evaluate the NC for the diagnosis of CFLD.

Method: Longitudinal data were collected from a cohort of genetically confirmed CF patients. CFLD was diagnosed by both DC and NC. According to NC, CFLD was present if there was radiologic or histologic evidence of cirrhosis or diffuse liver disease or a positive finding in at least two of the four categories including liver function tests, imaging, transient elastography (>6.8 kPa) or other noninvasive liver fibrosis biomarkers (AST/ALT ratio (AAR), ≥1, FIB-4 index ≥3.25, APRI > 0.50).

Results: 62 patients with CF, [56.5% male, median age at diagnosis 6.00 (2.25–33.00) months, age at enrollment 25 (22–31) years], were prospectively followed up for 33 (28–36) months. 16 (25.8%) patients met the classical DC for CFLD. No difference in demographics, INR, AAR and FIB4 were observed in patients with CFLD vs those without according to DC. However, AST (P = 0.012), ALT (P = 0.045), ALP (P = 0.022), g-GT (P = 0.026), liver stiffness (P = 0.03) and APRI (P = 0.032) were higher in CFLD vs no CFLD patients. According to NC, 26 (41.9%) had CFLD. No difference in age at diagnosis and enrollment, sex, genotypes and duration of follow-up were shown between CFLD and no CFLD. However, AST (p = 0.001), ALP (p = 0.002), g-GT (p = 0.002), INR (p = 0.023), liver stiffness (p < 0.001), AAR (p = 0.035), FIB4 (p < 0.001) and APRI (p = 0.001) were higher in CFLD vs no CFLD patients. 13 (50%) of patients who were classified as CFLD according to the NC had evidence of diffuse liver disease/cirrhosis in imaging and all of them had at least one additional parameter. From the 13 (50%) patients with no evidence of diffuse liver disease, 38.4%, 30.8% and 30.8% had 2, 3 and 4 of the four sets of parameters, respectively, classifying them as CFLD.

Conclusion: The New criteria are able to identify 16.1% more CFLD patients compared to historical ones. The multiple non invasive biomarkers incorporating in New criteria may enhance the ability to detect CFLD.

SAT-065
Transient elastography as a screening method for chronic liver disease in apparently healthy population. Results from de ETHON cohort


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Background and Aims: Transient elastography (TE) has been very useful for the diagnosis of chronic liver diseases. The aim of this study was to evaluate the use of TE in apparently healthy population and to determine the factors associated with the presence of significant fibrosis (SF) and advanced fibrosis (AF).

Method: Epidemiological, cross-sectional, population based multicenter (Santander, Madrid, Valencia) study from the ETHON cohort. The participants were selected through a random and representative sample by means of sampling by two-stage conglomerates with stratification according to socioeconomic status, rural/urban area and age, being representative of the general population. TE, an epidemiological questionnaire, laboratory test and anthropometric measurements were obtained in the same day.

Results: Between 2015 and 2017, 12519 subjects were included, in 1079 (8.6%) no reliable TE results were obtained. Data of 11440 subjects were analyzed. 53.8% of subjects aged 50–79 years, 58.1% women. 16.3% presented strict criteria for metabolic syndrome (MS) (NCEP ATP-III), 1.3% with anti-HCV+, 0.8% HBsAg+, 7.3% reported harmful alcohol consumption. 7.4% had SF (TE > 7 ≤ 12.6 KPa) and 1.6% had AF (TE > 12.6 KPa). 66.1% of patients with SF and 41.1% of patients with AF had normal liver function tests. In 48.8% of the subjects with SF Controlled Attenuation Parameter (CAP) values were suggestive of severe steatosis (S2 > 280 dB/m) OR 3.3 (1.9–5.7) (p < 0.001) and in 60% of the subjects with AF CAP values were suggestive of severe steatosis (S2 > 280 dB/m) OR 3.3 (1.9–5.7) (p < 0.001). In the multivariate analysis, factors independently related to the presence of SF were: age OR 1.5 (1.3–1.7) (p = 0.001), male sex OR 1.7 (1.5–2.0) (p < 0.001), the MS OR 1.8 (1.5–2.1) (p < 0.001), anti-HCV+ OR 1.9 (1.3–3.0) (p = 0.02) and HBsAg+ OR 2.5 (1.4–4.4) (p = 0.002). In AF, age OR 1.5 (1.3–1.7) (p < 0.001), male sex OR 1.7 (1.5–1.9) (p < 0.001) and the MS OR 1.8 (1.5–2.1) (p < 0.001) were independently related to its presence.

Conclusion: A high percentage of the apparently healthy population showed SF. The independent predictors of its presence were age, male sex, MS, antiHCV+ and HBsAg+. On the other hand, a non-negligible percentage of the apparently healthy population had AF. Age, male sex and MS were the independent factors of its presence. TE
is a useful tool for screening chronic liver disease in healthy population, even with normal liver function tests.

**SAT-066**

Prognostic value of 2D-shear wave elastography for staging cirrhosis in chronic liver diseases in two severity classes according to liver-related complications

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**Background and Aims:** In chronic liver disease (CLD), FibroTest (FT, BioPredictive), and transient elastography (TE-M probe, Echosens), are associated with increased overall and liver-related mortality and morbidity. Moreover, FT and TE-M were validated as markers of occurrence of cirrhosis without complications (F4.1), oesophageal varices (EV) grade 2 or more (F4.2), and severe complications (SC) (F4.3) – EV rupture, encephalopathy, ascites and hepatocellular carcinoma (HCC) (J Hepatol 2010). The aim of this study was to extend the validation of elastography by 2D-shear wave elastography (2D-SWE), as a prognostic marker of occurrence of cirrhosis without complications (F4.1) versus cirrhosis with EV and SC (F4.2–F4.3).

**Method:** 3,853 patients (pts) with CLD were pre-included prospectively from Jan-2012 to Dec-2013. 3627 pts had 2D-SWE, and excluding minimal stiffness <0.2 kPa. Cirrhosis was defined by FibroTest (95% CI) without EV/SC were: 78.8% (69.4–88.2) in the group F4.1; 89.9% (84.3–95.5) in F4.2 (12.5 kPa ≥ 2DSWE < 20 kPa, p = 0.025 vs F4.2); and 94.5% (91.4–97.6) in the group without cirrhosis (F4.3). All pts underwent LSM during follow-up. 15 pts underwent LSM after alloHCT when a liver event was suspected. Pts with definite diagnosis of liver-related outcome. Selected symptomatic patients underwent LSM during follow-up.

**Results:** Of 120 screened patients, 105 fulfilled the inclusion criteria: 40% female, median age 59 (range 18–74) years. Indications for alloHCT comprised acute leukemia/ myelodysplastic syndrome/ lymphoma and other in 50/29/21% of cases. Conditioning regimens were non-myeloablative in 56 pts, reduced intensity in 22 pts and myeloablative in 27 pts. 22 pts had a 10/10 HLA-matched related donor, 62 a matched unrelated donor (UD) and 21 a mismatched UD. 32 (30%) pts developed severe complications and 9 of these died during follow-up. 15 pts (40% female, age 59 (39–68) years) developed liver-related complications: n

**Conclusion:** Liver biomarkers, such as 2D-SWE, have prognostic values in patients with CLD for predicting varices and severe complications in cirrhotic patients. Previously validated FT and TE predictions of varices and severe complications were comparable and both were superior to 2D-SWE.

**SAT-070**

Liver stiffness measurement predicts short-term liver related morbidity of allogeneic hematopoietic stem cell transplantation

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**Background and Aims:** Allogeneic hematopoietic stem cell transplantation (alloHCT) is the treatment of choice for various forms of leukemia and lymphoma. Unfortunately, the intended graft-versus-host effect is frequently accompanied by potentially severe side effects of the conditioning regimen and the graft-versus-host disease (GVHD). Especially sinusoidal obstruction syndrome (SOS), druginduced liver injury (DILI) and liver GvHD contribute to early morbidity and mortality of alloHCT. Liver stiffness measurement (LSM) may potentially help to predict these liver-related complications.

**Method:** For this monocentric prospective study patients (pts) scheduled for alloHCT underwent LSM with point shear-wave elastography (pSWE) and transient elastography (TE) before start of the conditioning therapy. Pts were followed up for 100 days after alloHCT and classified according to liver-related outcome. Selected symptomatic patients underwent LSM during follow-up.

**Results:** Of 120 screened patients, 105 fulfilled the inclusion criteria: 40% female, median age 74 (range 18–74) years, body mass index 24.6 ± 4.6 kg/m². Indications for alloHCT comprised acute leukemia/ myelodysplastic syndrome/ lymphoma and other in 50/29/21% of cases. Conditioning regimens were non-myeloablative in 56 pts, reduced intensity in 22 pts and myeloablative in 27 pts. 22 pts had a 10/10 HLA-matched related donor, 62 a matched unrelated donor (UD) and 21 a mismatched UD. 32 (30%) pts developed severe complications and 9 of these died during follow-up. 15 pts (40% female, age 59 (39–68) years) developed liver-related complications: n

**Conclusion:** Liver biomarkers, such as 2D-SWE, have prognostic values in patients with CLD for predicting varices and severe complications in cirrhotic patients. Previously validated FT and TE predictions of varices and severe complications were comparable and both were superior to 2D-SWE.

Figure 1: (abstract: SAT-066): Survival Curves according to 2D-SWE classes of liver disease severity
LSM can be useful to diagnose liver complications after alloHCT.

Liver stiffness measurement by 2D SWE from General Electric is similar with Transient Elastography in clinical disease the occurrence of clinical significant portal hypertension (CSPH).

The aim of the study is to test if 2D-elastography from General Electric (2DSWE. GE) is a new method developed to assess liver fibrosis. The discriminative ability of CAP for any grade of steatosis and S2-S3 steatosis was studied using the area under receiving operating characteristic curves (AUROC).

On liver biopsy, steatosis was found in 69.4% (S1 = 33.9%, S2 19.4%, S3 16.1%), and S2-S3 was almost exclusively seen in patients with NAFLD/NASH or metabolic syndrome + alcohol or viral disease (43 of 44). CAP was accurate in identifying any steatosis (AUROC 0.827; 95%CI 0.746–0.908, p < 0.0001), and S2-S3 steatosis (0.864; 95%CI 0.796–0.93, p < 0.0001). Restricting the analysis to the 73 patients with bridging fibrosis/cirrhosis on histology, 55 (75%) had steatosis (S2-S3 in 27). In this subgroup CAP performance for any degree of steatosis and S2-S3 steatosis was 0.766 (0.631–0.900), p = 0.001 and 0.828 (0.727–0.930), p < 0.001 respectively. CAP performed worse in patients with CAP IQR ≥ 40 dB/m (any steatosis: AUROC 0.675 vs. 0.781 in patients with CAP IQR < 40 dB/m; steatosis S2-S3: AUROC 0.675 vs. 0.799).

Conclusion: Steatosis is very frequent in patients with histologically confirmed advanced fibrosis and cirrhosis and clinical features of metabolic syndrome. CAP discriminative ability in this specific population is fair for steatosis and good for steatosis S2-S3. CAP
SAT-074

Usefulness of liver stiffness measurement by transient elastography for predicting complications in patients with alcoholic liver disease


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Background and Aims: Measurement of liver stiffness by transient elastography (TE) has shown to be useful to predict the risk of developing cirrhosis complications (CC) in patients with viral liver cirrhosis, but there are no data in patients with alcoholic liver cirrhosis (ALC). Aim: To know the ability of TE to predict the development of CC in patients with ALC.

Method: 276 patients with Child class A/B ALC, without hepatocellular carcinoma (HCC) and without decompensation at the time of inclusion were enrolled, all of them with a valid TE measurement (Fibroscan®), and clinical-demographic variables recorded at inclusion, were analyzed. 82% male sex, mean age 56.5 ± 8.4 years, 93% Child A, 80% had esophageal varices and 63.4% had had at least one previous episode of CC. Patients were followed prospectively with clinical, analytical and ultrasound controls, and CC during the followup were registered. For statistical analysis, the usual methods were used.

Results: During a mean follow-up of 29.2 ± 17.3 months, 73 patients developed CC (29 ascites, 17 variceal bleeding, 14 encephalopathy and 13 HCC) with a 4-year cumulative probability of 37.2%. The diagnostic accuracy of TE to predict the development of CC showed an AUC of 0.675 (0.607–0.743). TE value of 25 kPa allowed to distinguish two groups with different risk of developing CC: ≤25 and >25 with a mean annual incidence of 4.5% and 15.5% and a 2-year cumulative probability of 11.6% and 27.8% respectively (p < 0.001). Other variables that were associated in the univariate analysis with the risk of developing CC were: male sex (p = 0.04), esophageal varices (p = 0.04), platelet count < 130 x 10^3/mm3 (p = 0.003), Child B (p < 0.001), AST > ULN (p = 0.040) and GGT > ULN (p = 0.053). On the contrary, age (p = 0.94) previous CC (p = 0.20) or ALT > ULN (p = 0.50) were not associated with the development of CC. In multivariate analysis, variables independently associated with the development of CC were male sex (OR: 2.30; 95% CI: 1.04 to 5.09; p = 0.039), Child B (OR:2.91; 95% CI:1.42–5.97, p = 0.003) and FS > 25 kPa (OR:2.72, 95% CI:1.41–5.24, p = 0.003).

Conclusion: Measurement of liver stiffness using elastography is useful to predict the risk of developing complications in patients with alcoholic liver cirrhosis. A value of 25 kPa allows to distinguish two groups of patients with different risk. In patients with compensated alcoholic cirrhosis, the history of previous decompensation does not influence the development of future complications.

SAT-077

Predictions from a very hard liver: The role of liver stiffness in alcoholic hepatitis

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Background and Aims: Liver stiffness measurement (LSM), especially assessed by transient elastography (TE), is not considered a useful tool for the management of alcoholic hepatitis (AH) patients, because it is difficult to perform and is not reliable due to severe inflammation. However, LSM is considered a very good prognostic tool in advanced liver disease. Recently, real-time bi-dimensional shearwave elastography (2D-SWE) became available, offering significant advantages for examination. On the other hand, in patients with severe AH (SAH) a robust predictor of mortality is still lacking. The aim of this study was to evaluate whether LSMing TE and 2D- SWE could predict mortality in AH patients.

Method: Consecutive patients with AH were included and liver function and severity of AH (Maddrey score (MDF)) was assessed at admission. Whenever possible and accepted by the patient, liver biopsy was performed to confirm the diagnosis. Patients with either SAH confirmed at biopsy, or with MDF ≥ 32 were treated with Prednisone, in the absence of contraindications. LSM by TE (Fibroscan, EchoSens, France) and by 2D-SWE (Aixplorer, SuperSonic Imagine, France) was also performed at baseline and after 7 days of therapy. Overall mortality was assessed during follow-up.

Results: 118 patients (80% males, mean age 52.5 years) were included. 76 (64.4%) patients underwent LB and 67 (56.8%) received Prednisone. 90 (76.2%) patients had MDF ≥ 32. 40 (33.9%) patients died during the mean follow up of 17.4 months. TE could be performed in 70/90 of patients (77.8% applicability), while 2D-SWE in 59/64 patients (92.2% applicability). LSM was significantly higher in patients with MDF ≥ 32, irrespective of the technique, but no significant differences was observed in LSMin patients who survived compared with those who died. However, baseline LSM values ≥64.5 kPa (by TE) and ≥17.3 kPa (by 2D-SWE) predicted mortality with moderate accuracy (AUC of 0.688 [95%CI: 0.545-0.831] for TE and 0.713 [95%CI: 0.548–0.869]). A decrease in LSM after 7 days of therapy by 10% (by TE) or by 8% (by 2D-SWE) appears to be predict survival: AUC for ΔLSM of 0.712 [95% CI: 0.420–0.905] for TE and 0.745 [95% CI: 0.490–0.901].

Conclusion: LSM by 2D-SWE has a better applicability in AH compared with TE. Baseline LSM, irrespective of technique is higher in more severe patients, but there is no or limited value in predicting mortality. However, a decrease of 8–10% in LSM by 2d-SWE/TE could predict overall survival. This work was supported by the a national grant (PN-II-RR-TE-2014–4-0356).

SAT-081

Correlation between controlled attenuation parameter assessed with Fibroscan and steatosis percent objectively quantified from the entire liver biopsy specimen using a computer analysis tool: Preliminary results

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Background and Aims: Usual ultrasonography is a useful method in diffuse liver disease (DLD) patients, but it cannot always differentiate steatosis from fibrosis. Liver biopsy (LB) has traditionally been considered the reference method for the steatosis and fibrosis evaluation, but its accuracy has also been questioned in relation to intra- and inter-observer variability that may lead to over- or understaging or grading. Therefore, discovering more precise analysis of the LB specimens, rather than the subjective histological diagnosis, was desirable for the future development of noninvasive liver assessment tools, like transient elastography (TE) which measures liver stiffness (LS) for fibrosis prediction, respectively controlled attenuation
Non-invasive estimation of hepatic fibrosis and steatosis: comparison of 2D shear-wave elastography and acoustic structure quantification with transient elastography and controlled attenuation parameter

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Background and Aims: Transient elastography (TE) combined with controlled attenuation parameter (CAP) represents the reference standard for non-invasive assessment of hepatic fibrosis and steatosis. Although liver stiffness measurement (LSM) with TE is fast and easy to learn, its application is limited by the intercostal approach, patients’ anthropometry, and requirement of a dedicated device. 2D shear-wave elastography (2D-SWE) techniques provide potential alternatives for LSM, but do not give information on steatosis. Recently, acoustic structure quantification (ASQ) has been proposed as an ultrasound based option for steatosis quantification. The aim of this study was the comparison of TE and CAP with 2D-SWE and ASQ.

Method: Patients with chronic liver diseases prospectively underwent LSM with TE (Fibroscan, M or XL probe) and CAP subsequently followed by 2D-SWE (Toshiba Medical Systems) and liver parenchyma speckle analysis by ASQ (focal disturbance ratio/DF ratio). Exclusion criteria comprised invalid or unreliable TE, elevated aminotransferase levels >5x upper limit of normal, ascites and focal liver lesions. Fibrosis and steatosis were classified according to established TE and CAP cut-offs. Diagnostic performance of 2D-SWE and ASQ was analyzed using receiver operating characteristics curves (ROC).

Results: 200 patients were included in the analysis (49% female, median age 54 years, body mass index 26 [IQR: 24–29] kg/m², 30/25/9/36% NAFLD/viral/autoimmune/other). LSM with 2D-SWE and TE showed a good correlation (r = 0.775 95%CI [0.712; 0.825]). Exclusion criteria comprised invalid or unreliable TE, elevated aminotransferase levels >5x upper limit of normal, ascites and focal liver lesions. Fibrosis and steatosis were classified according to established TE and CAP cut-offs. Diagnostic performance of 2D-SWE and ASQ was analyzed using receiver operating characteristics curves (ROC).

Conclusion: 2D-SWE shows an excellent agreement with TE and can be used for non-invasive fibrosis classification. ASQ correlates well with the reference standard CAP and provides an alternative for classification of steatosis. The combination of 2D-SWE and ASQ incorporated in a conventional ultrasound device could facilitate patient care.
Method: 109 patients underwent same-day liver biopsy, and measurement of liver fibrosis. Liver biopsy yielded insufficient tissue in 9 patients. Statistical analysis was conducted in 100 patients. Liver fibrosis and necroinflammatory activity were evaluated histologically using METAVIR score. 10 measurements in the left lobe, 10 in the right lobe were taken with EPIQ7TM and VTQ and the median value obtained. The median of ten measurements was obtained with TE. Statistical analyses were performed using SPSS 24. Histological staging was correlated with median values and Spearman correlation calculated (p < 0.05).

Results: 100 consecutive patients with chronic liver disease were enrolled [mean age: 48.41 years, 41 female; 59 male]. 46 patients had non-alcoholic fatty liver disease, 22 patients had chronic hepatitis B and the remainder were of various aetiologies. Spearman correlation with METAVIR score was higher with EPIQ7TM and Fibroscan™ (EPIQ7TM 0.568; TE 0.627; V2Q 0.429). Mean value for EPIQ7TM in the left lobes were higher to those obtained from the right lobe of the liver (Right 8.16 kPa; Left 8.87 kPa) but this was not statistically significant (p = 0.338). Areas under the Curve (AUC) were: TE 0.835; EPIQ7TM 0.785; V2Q 0.91 for less severe fibrosis (F < 2; n = 52); TE 0.826; EPIQ7TM 0.817; V2Q 0.712 for significant fibrosis (F 2 < F < 4; n = 32); TE 0.865; EPIQ7TM 0.820; V2Q 0.792 for cirrhosis (F4, n = 16). Bland Altman plots showed agreement between values obtained with TE and EPIQ7TM with lower value measured by EPIQ7TM. The mean optimal cut-off for significant fibrosis F2/F3 (n = 32) was 8.45 kPa for TE (sensitivity (se) 0.76, specificity (sp) 0.78); 7.52 kPa (se 0.79, sp 0.76) for EPIQ7TM and 9.3 kPa (se 0.76, sp 0.75) for VTQ. The mean optimal cut-off for cirrhosis F = 4 were 11.85 kPa for TE (se 0.79, sp 0.72); 9.01 kPa (se 0.70; sp 0.70) for EPIQ7TM and 13.35 kPa (se 0.73; sp 0.79) for VTQ.

Conclusions: TE and EPIQ7TM correlate well with histological scores of liver fibrosis and perform better than VTQ.

SAT-096

Overestimation and underestimation of liver fibrosis stage classification assessed by transient elastography and twodimensional shear wave ultrasound

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Background and Aims: The accuracy of detailed fibrosis stage classification assessed with transient elastography (fibroscan) was only 65% and, what is more, significant discrepancy rate (≥ 2 fibrosis stage) reached up to 13%. Several causative factors such as age, elevated liver enzyme, body mass index (BMI), skin to liver distance (SLD) are considered to contribute to this discrepancy, but there are few authentic evidences of what really works. In this study, we compared the discordance of fibrosis stage classification between fibroscan and two-dimensional shearwave ultrasound (2D-SWE) and looked for which variables are related with it.

Method: Patients who had a valid measurement and an adequate liver biopsy specimen were 291. The fibrosis stage classifications derived from the cumulated cut-offs calculated for different fibrosis stage by fibroscan aswell as 2D-SWE. The discrepancy score took into account the size of error between fibrosis stage (Metavir) and fibrosis stage classification (fibroscan, 2D-SWE). This score was defined as follows: 0 for correct classification, then 1, 2 or 3 as per the discrepancy of fibrosis stage classification assessed with transient elastography (fibroscan) was only 65% and, what is more, significant discrepancy rate (≥ 2 fibrosis stage) reached up to 13%. Several causative factors such as age, elevated liver enzyme, body mass index (BMI), skin to liver distance (SLD) are considered to contribute to this discrepancy, but there are few authentic evidences of what really works. In this study, we compared the discordance of fibrosis stage classification between fibroscan and two-dimensional shearwave ultrasound (2D-SWE) and looked for which variables are related with it.

Method: Patients who had a valid measurement and an adequate liver biopsy specimen were 291. The fibrosis stage classifications derived from the cumulated cut-offs calculated for different fibrosis stage by fibroscan aswell as 2D-SWE. The discrepancy score took into account the size of error between fibrosis stage (Metavir) and fibrosis stage classification (fibroscan, 2D-SWE). This score was defined as follows: 0 for correct classification, then 1, 2 or 3 as per the misclassification in fibrosis stages.

Results: Patients were male predominant (54.0%), their mean age was 48.9 ± 13.5 years old. Liver fibrosis stage consisted of F0 (13.4%), F1 (22.0%), F2 (24.1%), F3 (16.8%) and F4 (23.7%). The optimal cut-off for each fibrosis stage observed by fibroscans was 6.9 (PF2), 7.9 (PF3), 10.4 (F4) and 6.7 (PF2), 7.1 (PF3), 10.0 (F4) by 2D-SWE. Accurate assessment of fibrosis stage classification by discrepancy score showed that the proportion of underestimation and overestimation was 19.6%, 22.0% in fibroscan, and 21.0%, 17.9% in 2D-SWE. The discrepancy score of fibroscan was higher than that of 2D-SWE (p = 0.032). In multivariate analysis, viral liver disease, shorter SLD, older prothrombin time were associated with underestimation in bothfibroscan and 2D-SWE. Longer SLD and higher AST level significantly increased overestimation in fibroscan and, in 2D-SWE along with age. When a skin to liver distance is over 2.5 cm, 80.0% (12/15) of fibroscan and 46.7% (7/15) of 2D-SWE were overestimated.
SAT-100
Which is the chance for type 2 diabetes patients to develop severe liver disease?

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Background and Aims: The aim of the study was to assess the severity of liver fibrosis and steatosis in a cohort of type II diabetic patients, using non-invasive methods: Transient Elastography (TE) and Controlled Attenuation Parameter (CAP) and see what happen after the controlled attenuation parameter adjustment algorithm is apply.

Method: The study included 464 type II diabetic patients, who were prospectively randomized (every first 6 patients who were referred to the Metabolic Disease Outpatient Clinic on a consultation day), evaluated in the same session by means of TE and CAP (Elastoscan EchoSens) to assess both liver fibrosis and steatosis. Reliable liver stiffness measurements (LSM) were defined as the median value of 10 LSM with an IQR/median <30%. A cut-off value of 10.5 kPa was used to define clinically relevant fibrosis (F ≥ 3). For differentiation between stages of steatosis we used the following cut-off values [2]: S2 (mild)-255 dB/m, S3 (severe)-290dB/m, than we corrected the CAP values according to the presence of diabetes (we deducted 4.4dB/m for each BMI < 25 kg/m² and according to the degree of obesity (we deducted 10dB/m) and according to the degree of obesity (we deducted 4.4dB/m for each BMI > 25 kg/m² added 4.4 dB/m for each BMI < 25 kg/m²).

Results: Out of 464 diabetics screened we excluded those with associated viral hepatitis, those with an AUDIT-C score ≥8 and those with unreliable LSM. The final analysis included 424 subjects (55.6% women, 44.4% men, mean age 60.8 ± 9.3; BMI = 31.7 ± 6 kg/m²) with reliable LSM. Patients with obesity grade I were 61.5%, with obesity grade II 29.1% and 9.4% with obesity grade III (IMC ≥ 40kg/m²). Mild, moderate and severe steatosis by means of CAP was found in 20.3%, 17.1% and 66.9% cases respectively. After the correction we found moderate steatosis in 12.2% cases and severe steatosis in 59.1% cases.

We found no difference in mild and moderate steatosis after the algorithm was apply, p = 0.23, but we found significant statistical differences regarding the severe steatosis, (66.9% vs 59.1%, p = 0.02).

Clinically relevant fibrosis was detected by means of TE (LSM ≥ 10.5 kPa) in 12.4% (54/424) of subjects.

Conclusion: In our group, 79.3% of diabetic patients had moderate and severe steatosis by CAP, 66.9% had severe steatosis, but after applying the controlled attenuation parameter adjustment algorithm we had a significantly decrease (59.1%). Regarding the liver fibrosis, we found that 12.4% of them had severe fibrosis (TE ≥ 10.5 kPa), suggesting the need for their systematical assessment.

SAT-102
The impact of inflammation grade of liver histology on the improvement of liver stiffness assessed by transient elastography

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Background and Aims: Transient elastography (TE; Fibroscan) is now almost indispensable tool to estimate liver fibrosis. Although many clinical factors are known as confounding factors of liver stiffness (LS), there is no knowledge of who will achieve an improvement of liver stiffness if they have a similar liver fibrosis stage. The aim of this study is to see whether baseline hepatic inflammation may affect accurate LS measurement and which factors are associated with improvement of LS in Fibroscan.

Method: This retrospective study included consecutive 678 patients who underwent baseline liver biopsy and sequential LS assessment from 2006 to 2016 at 6 tertiary hospitals in Korea. Liver fibrosis and inflammation were graded on the basis of standard guideline proposed by the Korean Study Group for the Pathology of Digestive Diseases. LS measurement was performed at baseline and 1, 3, 5 years. Improvement of LS was defined as decreased LS value compared with baseline. Logistic regression was used to evaluate factors associated with improvement of LS in Fibroscan.

Results: Mean age of the patients was 47.12 ± 12.25 years and 48.5% were male. Six hundred two patients had viral hepatitis (419 HBV; 183 HCV), 76 non-viral hepatitis. Fibrosis stages 0, 1, 2, 3 and 4 were identified in 13 (1.9%), 96 (14.2%), 132 (19.5%), 186 (27.4%) and 251 (37.0%) patients, inflammation grade 0, 1, 2 and 3 were in 28 (4.1%), 278 (41.4%), 279 (41.2%) and 93 (13.7%), respectively. Baseline inflammation grade was correlated with baseline LSM value, and showed linear correlation with ∆LSM. In addition, as the grade of inflammation increased, the higher percentage of patients showed improvement of LSM. A multivariate analysis showed that higher degree of hepatic inflammation was an independent good predictor for LS improvement (adjusted hazard ratio, 3.33; 95% confidence interval, 1.20–9.26; p = 0.021) after adjustment for fibrosis stage, platelet count, total bilirubin and alanine aminotransferase level. The association of LSM and hepatic inflammation was more significant in viral hepatitis compared with non-viral etiology.

Conclusion: Baseline hepatic inflammation has significant impact on LS value and improvement of LSM, and should be considered as one of the confounding factors of measuring liver stiffness using Fibroscan.

SAT-195
Assessing Baveno VI criteria with a new point-shear wave elastography technique: The BAVElastPQ study


Background and Aims: To date no study has explored the potential role of ElastPQ, a novel point-SWE technique, in the assessment of clinically significant portal hypertension. The aim of our study was to determine a liver stiffness (LS) cut-off value measured by ElastPQ and/or laboratory parameters that could help identify those patients who can safely avoid screening endoscopy, similarly to the recently proposed Baveno VI criteria which recommends a LS value <20 kPa measured by transient elastography in combination to a platelet count >150,000/μl.

Method: Data was collected on 1432 patients who underwent ElastPQ measurement from January 2013 to January 2016 in our
Department. Inclusion criteria were a LS value of ≥7 kPa (to reasonably rule-in all patients with advanced fibrosis and cirrhosis) and an upper gastrointestinal endoscopy within 12 months, with a diagnosis of compensated chronic liver disease. Exclusion criteria were history of decompensated liver disease, evidence of portospleno-mesenteric vein thrombosis and non-cirrhotic portal hypertension. Varices were graded as low risk (grade <2) or high risk (grade ≥2).

**Results:** The study included 195 patients (120[61%] HCV, and 171 [88%] Child-Pugh A). Varices were present in 35% cases, with 10% prevalence of high risk varices. According to ROC curve analysis LS measurement and platelet count were evaluated as predictors of high risk varices. Overall 75/195 (38%) met the “BAVElastPQ” criteria (that is, LS <12 kPa and platelet count >150,000/μl). Within this group 11/64 (17%) had any grade of varices and only 1/74 (1%) had high risk varices. The BAVElastPQ criteria gave sensitivity of 0.95, specificity of 0.42, positive predictive value of 0.15 and negative predictive value of 0.99. The AUROC for LS and platelet count was 0.80 and 0.76, respectively.

**Conclusion:** The BAVElastPQ criteria correctly identified 99% of patients without high risk varices. By applying such criteria we could have potentially avoided 38% surveillance endoscopies in our cohort.

**SAT-206**

**Addition of simvastatin to standard treatment is safe, effective and improves quality of life in patients with decompensated cirrhosis**

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**Background and Aims:** Simvastatin (SVT) has shown to increase survival in cirrhotic patients with variceal bleeding. However, decompensated cirrhosis actually is a contraindication for statin therapy because risks are largely unknown. We aimed to assess the safety of SVT added to standard therapy in patients with decompensated cirrhosis.

**Method:** In this open, uncontrolled, ambispective trial we analyzed patients with decompensated cirrhosis associated with different complications, a year before and during 12 months of standard treatment plus SVT 20 mg once a day for 2 weeks, and later 40 mg. The primary endpoint was SVT safety. The secondary endpoints were SVT efficacy and quality of life as measured by the Short-Form 36 (SF-36) questionnaire.

**Results:** Baseline parameters: 30 patients were included, aged 57 ± 10 years, male 67%. Etiology: alcohol 60%. MELD 12.3 ± 3.3. D’Amico’s stages 3: 3%, 4: 47% and 5: 50%. Decompensated cirrhosis due to ascites 90%, variceal bleeding 27%, jaundice 27% and hepatic encephalopathy 17%. SVT safety: Related adverse events were myalgia 23%; myalgia plus creatine kinase increase 13%; new onset diabetes 3%; digestive symptoms 63% and headache 13%; liver injury none. SVT dose reduction by muscle symptoms 27%. No patient developed serious adverse events related to SVT or discontinued it for any reason. SVT efficacy: Survival rate: 90%. Patients with cirrhosis complications in the previous year 97% and during the trial 33%, p < 0.001. Hospitalizations for decompensated cirrhosis in the previous year 77% and during the trial 27%, p < 0.001. Child-Pugh score improved from baseline 7.3 ± 1.3 to the end of the trial 6.7 ± 1.7, p = 0.04. Child-Pugh class also improved from baseline/to the end of the trial: A 20%/53%, B 73%/40%, p = 0.01, and C 7%/77%. Liver fibrosis evaluated by transient elastography did not change from baseline (31 ± 16 kPa) to the end of the trial (30 ± 13 kPa). Quality of life: All dimensions and component summaries improved at month 12 compared to baseline. The differences in physical function, role physical, body pain and general health dimensions, and in the physical component summary were statistically significant, p < 0.05.

**Conclusion:** Addition of SVT to standard treatment of patients with decompensated cirrhosis was safe. It was proved effective through clinical assessments although it did not improve liver fibrosis. A better quality of life was observed.

**SAT-218**

**Validation of the banovo criteria for endoscopic surveillance of varices in cholestatic diseases**

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**Background and Aims:** The Banovo VI and AASLD 2016 guidelines recommend the use of non-invasive diagnostic tools (mainly transient elastography-TE) in the identification of patients with compensated advanced chronic liver disease (cACLD) in whom upper endoscopy (UE) screening for varices can be safely avoided, especially in those who require treatment (VNT: large varices or small varices with high-risk stigmata). These recommendations are a liver stiffness measurement (LSM) by TE <20 kPa and a platelet count >150,000/ mm³. Later, the expanded Banovo VI criteria (a LSM <25 kPa and a platelet count >110000/mm³) have suggested a significant increase in UE saved, without increasing the risk of undetected VNT. This tool has not been investigated in patients with cholestatic liver diseases. The aim of this study was to evaluate the performance of Banovo VI criteria in a group of patients with primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) with cACLD.

**Method:** This was a retrospective-prospective cross-sectional study including patients with PBC or PSC assessed with UE between 2009 and 2017 and with paired LSM within one year of the UE. During the study period, criteria to perform an UE were the presence of cACLD as assessed by a LSM ≥10 kPa. Patients with previous complication (ascites, variceal bleeding, hepatic encephalopathy), being on primary prophylaxis for variceal bleeding, HCC diagnosis and liver transplant were excluded from the analysis.

**Results:** Of 194 patients diagnosed with PBC, 29 were excluded. In 17 of the 165 patients included TE was not performed and 39 of the remaining 148 had a TE ≥10 kPa. UE was performed in 34 of the 39 patients with cACLD; 11 (32%) had varices and 2 (6%) were VNT. 20 of these 34 patients were within the Banovo VI criteria and 5 varices were detected, none with VNT. In addition, 24 of the 34 patients were within the expanded Banovo VI and again no VNT were missed. Regarding PSC, 23 patients were included and in 4 of them it was not possible to perform TE. 13 of the remaining 19 patients had a TE ≥10 kPa. UE was not performed in 1 patient. In this group, 4/12 (33%) had varices and 2/12 (17%) were VNT. None of de 4 and 7 patients within the Banovo VI and expanded criteria, respectively, presented VNT.

**Conclusion:** The original and expanded Banovo VI criteria are valid for avoiding endoscopy screening in cACLD due to cholestatic diseases.

**SAT-222**

**Assessment of portal hypertension evolution in hepatitis C virus cirrhosis patients with baseline large oesophageal varices after sustained virological response**


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**Background and Aims:** There’s scarce information on evolution of portal hypertension after sustained virological response (SVR). Furthermore, current guidelines do not address how to manage large...
oesophageal varices in HCV-cirrhosis after SVR. Therefore, data are needed on their evolution as well as their non-hemodynamic evaluation.

**Method:** Single-centre, prospective study. Patients were included if: 1) HCV cirrhosis with baseline large oesophageal varices; 2) SVR after direct-acting antivirals (DAA). Hepatic venous pressure gradient (HVPG) was performed. On the same day, upper gastrointestinal endoscopy (UGE), and liver stiffness measuring with transient elastography (TE; Fibroscan, Echosens, France) and bidimensional shear-wave elastography (2D-SWE; Aplio 500, Toshiba, Japan) were also performed. Betablockers were stopped 5 days before.

**Results:** 30 patients were included (male 56%, median age 66 years, Child-Pugh A/B 73%/27%, median MELD 10 [7–14], overweight 76%, median TE before DAA 27.3 kPa, median time from end of DAA treatment to GPVH 67 weeks [30–171]). GPVH was <12 mmHg (bleeding threshold; BT) in 12/30 (40%) and <10 mmHg (clinical significant portal hypertension; CSPH) in 6/30 (20%). UGE showed regression of varices in 21/26 (81%; 4 patients refused). Feasibility rates for TE and 2D-SWE were 93% (28/30) and 100% (30/30), respectively. Correlation of UGE, TE, and 2D-SWE with HVPG is shown in Table 1 (per protocol).

**Conclusion:** After >1 year of SVR in patients with baseline large oesophageal varices, portal hypertension evolved below the BT in 40% and below the CSPH in 20%. In this situation, there’s a weak correlation between endoscopic variceal size and HVPG. TE and 2D-SWE perform well and similarly to detect CSPH; results are poorer for BT.

SAT-224

**The impact of hepatic steatosis on portal hypertension B**


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**Background and Aims:** Studies in animal models suggested an effect of hepatic steatosis on portal pressure, since diet-induced hepatic steatosis has been shown to promote liver sinusoidal endothelial dysfunction and increase intrahepatic resistance. Thus, we aimed to evaluate the effect of hepatic steatosis on portal pressure in patients with chronic liver disease.

**Method:** Patients who underwent paired hepatic venous pressure gradient (HVPG) and controlled attenuation parameter (CAP®; FibroScan®, Echosense, France) measurements between 01/2014 and 12/2016 were included in this retrospective study.

**Results:** In total, 243 patients with valid HVPG and transient elastography (TE)-based CAP®-measurements were identified. The majority of patients (n = 194, 79.8%) had cirrhosis, as according to published disease-specific cut-offs, and 72.8% had clinically significant portal hypertension (CSPH; HVPG ≥10 mmHg). The most common etiologies of liver disease were virus hepatitis (n = 116, 47.7%) and alcohol abuse (n = 72, 29.6%). Any hepatic steatosis (S1/2/3; CAP®-value ≥248 dB/m) was present in n = 101 (41.6%). Overall, HVPG was comparable between patients with and without hepatic steatosis (14 [2–34] vs. 17 [3–41] mmHg; p = 0.612). Apart from BMI (Pearson’s r: 0.136; p = 0.034), no baseline characteristics showed a correlation with CAP®. To control for severity of liver disease, the correlation between CAP® and HVPG was analyzed within HVPG-strata. Neither in patients with subclinical portal hypertension or normal portal pressure (HVPG <10 mmHg; p = 0.383) nor in patients with CSPH (HVPG ≥10; p = 0.495) any correlation between CAP® and HVPG could be found. The subgroup analysis in different etiologies of liver disease also showed no positive correlation between CAP® and HVPG. Interestingly, in patients with F2/3 liver fibrosis as assessed by TE, there was a significant negative correlation between CAP® and HVPG (Pearson’s r: −0.470; p = 0.004). This may be explained by the fact that TE could overestimate liver fibrosis stage in patients with pronounced hepatic steatosis. This negative correlation vanished in patients with cirrhosis (F4; Pearson’s r: −0.096; p = 0.183).

**Conclusion:** Hepatic steatosis does not increase portal pressure. Liver stiffness assessment by TE tends to overestimate liver fibrosis stage in patients with hepatic steatosis.

**Figure:** Correlation of CAP® and HVPG in patients with F2/F3 fibrosis

SAT-224

**Controlled attenuation parameter does not predict hepatic decompensation in patients with advanced chronic liver disease B**


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**Background and Aims:** Transient elastography (TE)-based controlled attenuation parameter (CAP®) is a non-invasive marker of hepatic steatosis. Recently, CAP® has been proposed as a predictor of decompensation in patients with compensated advanced chronic liver disease (cACLD), although there was no association with liverrelated events in another study. Therefore, our aim was to evaluate the prognostic value of CAP® in patients with cACLD and decompensated cirrhosis (DC).

**Method:** 189 patients who underwent simultaneous TE (stiffness ≥10 kPa) and hepatic-venous pressure gradient (HVPG) measurements between 01/2014 and 12/2016 were included in this retrospective analysis based on prospectively collected data. In cACLD patients, hepatic decompensation was defined by newonset of ascites, hepatic encephalopathy, or variceal bleeding. In patients with DC, the following events were considered as (further) hepatic decompensation: requirement of paracentesis, admission for grade III/IV hepatic encephalopathy, variceal (re-)bleeding or liver-related death.

**Results:** For analysis, the study population was stratified into patients with cACLD (without prior hepatic decompensation, n = 86) and patients with DC (n = 103). Hepatic decompensation occurred in 13 (15.1%) cACLD patients and in 33 (32.0%) patients with DC during a mean follow-up of 23.2 and 16.1 months, respectively. CAP® was not predictive of further hepatic decompensation in cACLD patients (per
SAT-277
Validation and modification of Baveno criteria to rule out high-risk varices in patients with compensated cirrhosis
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Background and Aims: Baveno VI criteria defines patients with compensated cirrhosis in whom endoscopy can be avoided as those with a liver stiffness (LSM) by TE <20 kPa and platelet count and >150,000/mm3. The aim was to validate Baveno criteria in our cohort from India and to determine whether alternate parameters not including TE would be equal/more accurate in ruling out high-risk varices (HRV).

Method: Cross-sectional study evaluating patients with liver stiffness >10 kPa who had endoscopy within 6 months of TE evaluation. Factors like Hemoglobin, Platelet, LFT, RFT, INR, etiology, LSM and MELD score were compared between the groups who had HRV and who did not have HRV.

Results: This study included 272 patients who underwent Transient elastography (TE) and upper GI endoscopy from September 2015 to August 2017 at our centre. 168 (61%) patients were male while 104 (38%) patients were female. Most common etiology was HCV (43%) followed by HBV, NASH and ethanol. Out of 192 patients satisfying Baveno criteria (LSM <20 kPa and platelet >150000/mm3), 190 patients did not have HRV. Sensitivity, specificity, Positive predictive value (PPV) and Negative predictive value (NPV) was 98%, 78%, 91% and 97% respectively. (AUC = 0.89). In all patients, among the factors studied, Platelet count, S. Bilirubin, MELD and LSM significantly differed between patients who had HRV and those who did not have HRV.

Conclusion: CAP® does not predict the development of (further) hepatic decompensation in patients with cACLD or decompensated cirrhosis, while serum albumin levels and HVPG are of prognostic value.

SAT-499
Impact of duodenal-jejunal bypass liner on non-alcoholic fatty liver disease
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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is strongly linked to obesity and type 2 diabetes mellitus (T2DM). Bariatric surgery induces weight loss, improves T2DM and NAFLD in morbidly obese patients. The endoscopically implanted duodenal-jejunal bypass liner (DJBL) is a less-invasive alternative to bariatric surgery, however data on the influence of NAFLD are limited so far. Thus, we characterized NAFLD after DJBL insertion.

Method: In patients undergoing DJBL treatment for T2DM and/or obesity NAFLD was prospectively characterized by liver stiffness measurement (transient elastography (TE) using M- and XL-probe as appropriate) including controlled attenuation parameter (CAP), and by the enhanced liver function (ELF) score. Alanine-ammonitransferase (ALT), gamma-glutamyltransferase (GGT) and ferritin were used as parameters of hepatic inflammatory activity.

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Background and Aims: There are increasing concerns about Proton Pump Inhibitor (PPI) use in liver cirrhosis. Yet, it is still widely prescribed in this population and sometimes with no indication. However, PPI users are not well defined and there is little data on the cumulative dosage of PPI in the cirrhotic population. This study aims to review the indication, cumulative dosage and duration of PPI use in liver cirrhosis.

Method: Patients admitted to a tertiary hospital with a confirmed diagnosis of liver cirrhosis by histology or transient elastography from January 2016 to June 2017 were identified. Only the following were included: those on follow up with a hepatologist and with complete inpatient records including: Baseline blood tests, previous medical records, medication lists and recent liver imaging. For patients prescribed with PPIs, the indication, dosage and duration were reviewed. We used the cumulative defined daily dose (cDDD) as recommended by the WHO to describe both inpatient and discharge PPI prescriptions and stratified them into 4 groups: cDDD <28 (<1-month use), cDDD 28–56 (1 to 2 months use), cDDD 57–84 (2–3 months use) and cDDD >84 (>3 months use).

Results: A total of 100 patients were included into the study. 32% were female and 68% were male. 46% were Chinese, 35% Malay, 17% Indian and 2% Eurasian. Mean age was 62.6 ± 10.9 years. Hepatitis C was the most common etiology of cirrhosis (25%). 42% of patients were child-pugh B and 41% were child-pugh A. A total of 64 patients were prescribed with PPI of which 37 (57.8%) had unclear or no indication. Of these 64 patients, 42(65.6%) were overprescribed in terms of dose and duration. On discharge, up to 31 (48.4%) were prescribed a cDDD > 3 months of which 16 (51.6%) had unclear or no indication. Interestingly, using logistic regression analysis, those >75 years old (OR= 8.22, (1.24–54.78); p = 0.029) and with history of hepatic encephalopathy (OR= 7.03, (1.11–44.49); p = 0.038) were more likely to be PPI users after adjustment.

Conclusion: A majority of inpatients with liver cirrhosis are on PPIs of which 57.8% had unclear or no indications and 65.6% were overprescribed in terms of dose and duration. This continued even on discharge where 48.4% were prescribed 3 months of PPI and 51.6% had no clear indication. PPI users were also more likely to be older and have hepatic encephalopathy at baseline.
Results: DJBL was inserted in 31 patients and explanted in two cases after <2 weeks due to abdominal discomfort. Thus, 29 patients (59% female, median age 57 years) underwent DJBL treatment for a median period of 12 months (range 6.2–16.7). All of these achieved a significant weight loss (median loss 10%; BMI baseline 39.5 ± 8.6 vs. 35.2 ± 8.2 kg/m² at end of treatment, p < 0.001) and 52% an improvement of T2DM (HbA1c 7.3 ± 1.3 vs. 7.0 ± 12%, p = 0.154). Serial TE/CAP and ELF values between baseline and end of DJBL treatment were available in 23 and 26 patients, respectively. CAP improved from 332 (249–368) to 283 (180–368) dB/m (p = 0.003, Figure), ALT, GGT, and ferritin from 60.3 (31.4–41) to 0.43 (0.18–3.46) μkat/l (p < 0.001), 0.66 (0.22–7.74) to 0.37 (0.11–5.46) μkat/l (p < 0.001), and 147 (18–487) to 61 (9–402) ng/ml (p < 0.001), respectively. The number of patients with ALT, GGT and ferritin values upper the normal limit decreased from 11 to 3, 10 to 3, and 8 to 1.

Conclusion: DJBL is an effective option for endoscopic treatment of obesity and improves hepatic steatosis and inflammatory activity within a short period of time.

SAT-502
Cardiovascular risk factors and fibrosis severity in NAFLD: is there a link?

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Background and Aims: It is well documented that patients with NAFLD have an increased cardiovascular risk due to the presence of metabolic comorbidities. However, it is not clear whether cardiovascular risk is associated with an increased risk of liver disease in patients with NAFLD. Carotid artery intima media thickness (CA IMT) can be used as a predictor of increased cardiovascular risk. Therefore, we evaluated if IMT correlates with fibrosis severity in such patients.

Method: Consecutive patients with NAFLD were included. Transient elastography (TE) with FibroScan (Echosens) was performed in all patients and significant fibrosis was defined as liver stiffness (LS) value ≥ 7.2 kPa. Abdominal fat thicknesses (subcutaneous minimum and maximum (SComm, SComax), pre-peritoneal (PP), peri-renal (PR), visceral (VF) and abdominal fat index (AFI, PP/SComm), epicardial fat thickness (EF), spleen size (SS) and CCA IMT were measured using Affiniti 70G ultrasound (Philips). A right CCA IMT > 75 percentile was considered as significant predictor of cardiovascular disease according to published data.

Results: We enrolled 319 consecutive patients with NAFLD, 56.3% male, mean age 54 ± 13y, BMI 31.7 ± 5.8 kg/m², waist circumference (WC) 107 ± 15 cm, 44% with diabetes, 55.7% hypertension, 81% hyperlipidaemia. In the univariate analysis, a LS value ≥ 7.2 kPa was associated with diabetes, hypertension, right CCA IMT > 75 percentile, age, BMI, WC, VF, SS, cholesterol, platelets, AFI, EF, GGT and ALT. In the multivariate analysis predictors of significant liver fibrosis were diabetes (OR 3.652, 95%CI 1.814–7.354, p = <0.0001), AFI (OR 0.549, 95% CI 0.342–0.881, p = 0.013), SS (OR 1.305, 95% CI 1.080–1.577, p = 0.006) and ALT (OR 1.012, 95% CI 1.004–1.020, p = 0.003). Conversely, predictors of a right CCA IMT > 75 percentile were increasing age (OR 1.096, 95%CI 1.060–1.134, p < 0.0001) and waist circumference (OR 1.034, 95%CI 1.010–1.057, p = 0.005). In the subset of 112 patients with available liver biopsy, the presence of NASH or significant fibrosis was not associated with an increased CCA IMT or epicardial fat.

Conclusion: Significant liver fibrosis is independent of increased cardiovascular risk in patients with NAFLD and is mainly associated with presence of diabetes, increasing ALT and decreasing AFI. Therefore, the progression of liver fibrosis is at least in part due to factors which are independent of the general features conditioning cardiovascular risk in patients with metabolic syndrome. Targeted interventions for components of the metabolic syndrome should be offered to all NAFLD patients irrespective of the severity of the underlying liver disease.

SAT-510
A Comprehensive Assessment of Serial Transient elastography in various Liver disease Etiologies at the Toronto Liver Centre (CASTLE-TLC)

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Background and Aims: Liver disease is a major cause of morbidity and mortality globally, with non-alcoholic fatty liver disease (NAFLD) becoming an major cause for concern, followed by viral hepatitis (HBV & HCV) and alcoholic liver disease (ALD). To understand the burden of liver disease in Ontario, a comprehensive retrospective analysis is currently underway to characterize all liver disease patients at the Toronto Liver Centre (TLC).

Method: 3610 medical charts at the Toronto Liver Centre from Feb. 1995 to Sep. 2017 were reviewed and assessed for: patient demographics, liver disease etiology, liver fibrosis staged by Transient Elastography (TE), liver biopsy, imaging, & blood work, were collected & entered into a standardized form. Patient grouping was organized by primary liver etiology: NAFLD/NASH, HBV, HCV & Other (autoimmune hepatitis, alcoholic liver disease, primary biliary cirrhosis, primary sclerosing cholangitis, etc.). Data on cirrhotic patients (based on TE vs. biopsy vs. ultrasound) was also assessed to determine: sensitivity, specificity, positive predictive value (PPV) & negative predictive value (NPV) for the presence or absence of cirrhosis.

Results: Of the 3610 records analyzed, 2378 had TE results with 85.7% having a Metavir score of F2 & below; only 9% of patients had a Metavir score > F3. Similar results were obtained with biopsy samples: 40/403 (9.9%) patients with biopsy results had a Metavir score > F3. For the entire cohort, only 8.14% of patients had cirrhosis, & only 3.91% of patients had cirrhosis with portal hypertension, 1722 patients had NAFLD/NASH, 585 HBV only, & 580 HCV only; the remainder had viral hepatitis plus another liver condition except NAFLD: 145 had HBV plus other liver disease (20.3%), 125 had HCV plus other liver disease (17.5%), & 20 had HBV/HCV coinfection & other liver disease (2.8%). Cirrhosis was present in 6.6% of patients with HCV, 4.6% in NAFLD/NASH, 2.6% in HBV, and 22.5% in other diseases. Amongst the
cirrhotic group as diagnosed by ultrasound distribution was: HCV (2.4%), HBV (1.0%), & NAFLD/NASH (1.1%). The rate of cirrhosis in patients that were reported to be F4 or greater by TE was: (72.7%) NAFLD/NASH, (62.5%) HBV, & (56.0%) HCV. The sensitivity, specificity, PPV and NPV of F4 in TE to predict cirrhosis in patients with NAFLD/NASH is 72.7%, 98.08%, 62.50% & 98.79% respectively. For HBV patients the values were 62.50%, 98.26%, 41.67% & 99.25% respectively. For HCV patients the values were 56.00%, 93.54%, 45.16% & 95.72%.

*Made possible with financial support from Gilead Sciences Canada.

**Conclusion:** In this initial analysis of data from an ongoing retrospective analysis, the vast majority of patients had levels of liver fibrosis of F2 and below, and fewer than 10% had histology or TE results consistent with cirrhosis. There was a high degree of agreement between the various methods used to assess fibrosis and cirrhosis (TE, biopsy and ultrasound).
United States of America: The FibroScan® system is intended to provide 50Hz shear wave speed measurements and estimates of tissue stiffness as well as 3.5 MHz ultrasound coefficient of attenuation (CAP: Controlled Attenuation Parameter) in internal structures of the body. FibroScan® is indicated for noninvasive measurement in the liver of 50 Hz shear wave speed and estimates of stiffness as well as 3.5 MHz ultrasound coefficient of attenuation (CAP: Controlled Attenuation Parameter). The shear wave speed and stiffness, and CAP may be used as an aid to clinical management of adult patients with liver disease. Shear wave speed and stiffness may be used as an aid to clinical management of pediatric patients with liver disease.

European Union: FibroScan® is a class Ila medical device according to Directive EC/93/42 and is manufactured by Echosens. Assessment of its conformity with the essential requirements of the Directive EC/93/42 is established by the LNE-G-MED (n°0459) - France -. FibroScan® is indicated for the non-invasive measurement of liver stiffness (E) and controlled attenuation parameter (CAP) in humans. It is expressly recommended to carefully read the guidance within the users’ guide and labeling of the device. FibroScan® examination must only be performed by operators certified by the manufacturer or its accredited local representative. The values obtained with FibroScan® must be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical record of the patient. In France, liver stiffness measurement by FibroScan® is reimbursed by national Social Security medical insurance, in some circumstances and under certain conditions: see terms on the ameli.fr website.