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A new screening strategy for varices by liver and spleen stiffness measurement (LSSM) in cirrhotic patients: a randomized controlled trial

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Background and Aims: Variceal bleeding is a common and life-threatening complication in patients with liver cirrhosis. Screening with upper endoscopy is recommended but is uncomfortable to patients. Non-invasive assessment with transient elastography for liver/spleen stiffness measurement (LSM and SSM) is accurate in detecting varices. We aimed to test the hypothesis that a new screening strategy for varices guided by LSM and SSM results (LSSM-guided) is non-inferior to universal endoscopic screening in detecting clinically significant varices in patients with cirrhosis.

Methods: This was a non-inferiority, open-label, randomized controlled trial in two hospitals in Hong Kong. Adult patients with known chronic liver diseases, radiological evidence of liver cirrhosis and compensated liver function. The primary outcome was clinically significant varix diagnosed with upper endoscopy. Patients randomized to LSSM arm would first undergo transient elastography examination; those with high LSM (≥12.5 kPa) or SSM (≥41.3 kPa) results would then proceed to upper endoscopy examination for varix screening. On the other hand, patients randomized into control arm would directly undergo upper endoscopy examination.

Results: Between October 2013 and June 2016, 548 patients were randomized to LSM arm (n = 274) and conventional arm (n = 274) which formed the intention-to-test (ITT) population. Patients in both study arms were predominantly middle-aged men with hepatitis B-related cirrhosis. Around 30% of patients had splenomegaly. Among 264 patients who attended transient elastography examinations, LSM and SSM value was 14.0 ± 9.6 kPa and 37.5 ± 20.7 kPa respectively. In the ITT analysis, 11/274 participants in the LSSM arm (4.0%) and 16/274 in the conventional arm (5.8%) were found to have clinically significant varices. The difference between two groups was 1.8% (90% CI, -4.9% to 1.2%, P <0.001). 51/274 participants in the LSSM arm (18.6%) and 67/274 in the conventional arm (24.5%) were found to have any varices (P =0.12). Hypoalbuminemia, splenomegaly and high SSM but not LSM were independently associated with clinically significant varices.

Conclusions: LSSM-guided screening strategy is non-inferior to the convention approach to detect clinically significant varices. This approach should be recommended to patients with liver cirrhosis (ClinicalTrials.gov: NCT02024347).
French validation cohort: 43 NAFLD patients underwent FibroScan and LB (all read by the same pathologists) in a single liver centre in France. American validation cohort: Patients referred for a routine colon cancer screening in a single American center were enrolled. They were screened for evidence of NAFLD using FibroScan, LiverMultiScan (magnetic resonance imaging proton density fat fraction (PDFF), liver inflammation and fibrosis (LIF) score) and magnetic resonance elastography (MRE). Patients with PDFF ≥5% or LIF ≥2 or LSM ≥7 kPa on FibroScan or ≥3kPa on MRE were recommended a LB, which were all read by a single expert pathologist.

**Results:** Derivation cohort: 144 patients with a median BMI of 32.9 [IQR=6.9] kg/m² and age of 54 [21] years. 58% were male and 58% had NASH. French cohort: 43 patients with a BMI of 30.0 [8.0] kg/m² and age of 53 [22] years. 67% were male and 84% had NASH. American cohort: 443 patients were screened. 154 (35%) patients fulfilled the criteria and underwent a LB. They had a BMI of 32.6 [6.1] kg/m² and age of 57 [10] years. 64% were male and 16% of had NASH. Performance of the NASH score is presented in the Table below.

**Conclusions:** A novel score based a single FibroScan examination (LSM & CAP) has shown a good diagnostic performance for NASH in the derivation cohort. When applied to the external validation cohorts the score shows excellent sensitivity and acceptable specificity.

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**Oral Presentation #3 (PS 120)**

**Parallel session: Non-invasive assessment of liver disease**

**Date & Time:** Saturday 22, 2017- 08h30→08h45, Elicium 1

**Non-invasive assessment of liver disease**

**Reliability criteria for the diagnosis of fatty liver using Controlled Attenuation Parameter by Transient Elastography – A multicentre study of 754 patients**

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**Background and Aims:** Controlled Attenuation Parameter (CAP) by transient elastography can be performed together with liver stiffness measurement (LSM) and is often used to diagnose fatty liver. Unlike LSM, however, factors affecting the accuracy of CAP have not been determined. We aim to define the reliability criteria of CAP.

**Methods:** CAP was measured within 1 month prior to liver biopsy in consecutive patients at 3 centres in Europe and Hong Kong. The primary outcome was the diagnosis of fatty liver, defined as steatosis involving ≥5% of hepatocytes.

**Results:** We recruited 754 patients (derivation cohort, n = 340; validation cohort, n = 414; mean age 52; 55% male; 46% non-alcoholic fatty liver disease; 20% chronic hepatitis C; 13% chronic hepatitis B; 71% had ≥5% steatosis). Overall, the area under the receiver-operating characteristics curve (AUROC) for CAP to diagnose fatty liver was 0.85 (95% CI 0.82-0.88). The interquartile range (IQR) of CAP had negative correlation with CAP (r = -0.32, P <0.001), suggesting the IQR-to-median ratio of CAP would be an inappropriate reliability parameter (Figure). In the derivation cohort, the IQR of CAP was the only parameter associated with the accuracy of CAP (AUROC 0.86, 0.89 and 0.76 in patients with IQR of CAP <20, 20-39, and ≥40 dB/m, respectively). Likewise, the AUROC of CAP was 0.90 and 0.77 in patients with IQR of CAP <40 and ≥40 dB/m, respectively (P = 0.004). The corresponding sensitivities in detecting fatty liver were 94.2% and 75.0%. The superior performance of CAP in patients with IQR of CAP <40 dB/m was consistently shown in subgroups by age, gender, body mass index (BMI), and aetiologies. In contrast, the AUROC of CAP was unaffected in patients with BMI ≥30 kg/m², alanine aminotransferase ≥300 IU/L and bilirubin ≥50 µmol/L.

**Conclusions:** The diagnosis of fatty liver by CAP is more reliable when the IQR of CAP is below 40 dB/m. Traditional factors affecting the performance of LSM have little impact on the reliability of CAP.

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**Oral Presentation #4 (PS 123)**

**Parallel session: Non-invasive assessment of liver disease**

**Date & Time:** Saturday 22, 2017- 09h15→09h30, Elicium 1

**Non-invasive assessment of liver disease**

**Validation of the Baveno VI elastography criteria for the definition of compensated advanced chronic liver disease: an individual patient meta-analysis**

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**Background and Aims:** The Baveno VI consensus recommendations propose the use of liver stiffness (LS) by transient elastography (TE) as a tool for suspected compensated advanced chronic liver disease (cACLD): a LS <10 KPa in the absence of other clinical signs rules out and a LS >15 KPa is highly suggestive of cACLD. We aimed to validate these criteria in an individual patient meta-analysis.

**Methods:** We included patients from eight centres (Bordeaux n = 1335, Cluj n = 1180, Palermo n = 808, Angers n = 518, Firenze n = 334, Royal Free n = 303, Athens n = 154, Beaujon n = 75) who had a liver biopsy and TE within 6 months. We only included patients with well-compensated liver disease and a diagnosis of chronic hepatitis B (CHB), chronic hepatitis C (CHC) or non-alcoholic fatty liver disease (NAFLD). METAVIR was used as the staging system for fibrosis and cACLD was defined as a fibrosis stage of ≥F3. The interquartile range/median ratio (IQR/M) was used for the assessment of TE reliability as previously published: "very reliable" (IQR/M ≤0.10), "reliable" (0.10 < IQR/M ≤0.30), or IQR/M >0.30 with LS median <7.1 KPa), and "poorly reliable" (IQR/M >0.30 with LS median ≥7.1 KPa).

**Results:** There were 4707 patients evaluated; in 247 (5.2%), TE was not technically possible and 267 (5.7%) had a poorly reliable measurement, therefore 4198 were considered for the analysis. Mean age was 49.8 ± 12.7, BMI 26.7 ± 4.9 kg/m².
52.8% were males and the majority had CHC (n = 2609, 62%) followed by NAFLD (n = 894, 21.2%) and CHB (n = 695, 16.6%). Fibrosis distribution was: F0 433 (10.3%), F1 1320 (31.4%), F2 1227 (29.2%), F3 689 (16.4%), F4 529 (12.6%). A LS<10 kPa had an 86.8% specificity for ruling out cACLDD and a LS≥15 kPa had a 96.8% sensitivity for ruling in cACLDD. Use of the dual cut-off would result at 671 (16%) patients being classified as indeterminate and would require a further diagnostic test.

**Conclusions:** Liver stiffness by TE at a cut-off of ≥15 has an excellent sensitivity for ruling in cACLDD, while a cut-off of <10 has a moderate specificity for ruling out cACLDD and should be interpreted in the clinical context of each individual case.

**Oral Presentation #5 (LBO 05)**

**Late breaker session**

**Date & Time:** Saturday 22, 2017- 17h00→17h15, Hall 5

**Controlled Attenuation Parameter as an additional tool for the non-invasive prediction of first clinical decompensation in compensated advanced chronic liver disease**

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**Background and Aims:** In compensated advanced chronic liver disease (cACLDD) liver stiffness (LS) ≥21 kPa predicts portal hypertension and onset of first clinical decompensation. Since obesity is an additional negative prognostic factor, Controlled Attenuation Parameter (CAP), which provides quantitative data related to liver fat content, might be an objective tool to improve risk stratification obtained by LS alone in cACLDD.

**Methods:** Consecutive patients with cACLDD (LS ≥10 kPa; Baveno criteria) with available CAP observed between 09/2013-09/2015 and with a minimum 6 months follow-up were included. Patients with previous or ongoing liver decompensation, vascular liver diseases, HCC outside Milano criteria, LS with IQR/M >0.30 or AST >300 IU/ml were excluded. First clinical decompensation, death and OLT were identified on follow-up. Steatosis was excluded by CAP <220 dB/m in 68.4%.

**Results:** We included 193 fully compensated ACLDD patients with a mean follow-up of 19 months (males 65%; viral etiology 58%; Child score 5.4 ± 0.8; platelets 164 ± 64 G/L; LS 21.1 ± 14.1 kPa; LS ≥21 kPa in 33.2%; CAP 255 ± 62 dB/m; CAP ≥220 dB/m in 68.4%). 18 patients developed first decompensation and 7 died. Patients who decompensated on follow-up had higher LS (33.6 ± 19.2 vs. 19.8 ± 13.0, p <0.001) and tended to have higher CAP (275 ± 46 vs. 252 ± 63, p = 0.07), lower platelets (134 ± 74 vs. 167 ± 74, p = 0.07) and worse liver function (Child score: 5.7 ± 1.2 vs. 5.4 ± 0.8, p = 0.13) vs. patients remaining compensated. BMI was similar in the two groups (27.2 ± 5.1 vs. 27.3 ± 4.6, NS).

Decompensation occurred in one (clinically obese) patient with CAP <220 dB/m and in 17 patients with CAP ≥220 (1.6 v. 12.9%; p = 0.013) (Figure).

LS was strongly associated with risk of decompensation (p <0.001), which occurred respectively in 3.8%, 6.7% and 18.9% of patients with <13.6 kPa, 13.6-21 kPa and LS ≥21 kPa (K-W test p = 0.006). None of patients with LS ≥21 kPa and CAP <220 (n = 15) developed decompensation vs. 12/49 (24.5%) with LS ≥21 kPa and CAP ≥220 (p = 0.03). On Cox regression, LS and CAP ≥220 were independently associated with clinical decompensation.

**Conclusions:** Liver stiffness and presence of steatosis by CAP are independently associated with clinical decompensation in compensated ACLDD. CAP allows further refining the non-invasive risk stratification obtained by LS, and is of particular interest in patients with LS ≥21 kPa.

**Poster 1 (LBP-530)**

**Late breaker posters**

**Date & Time:** Thursday 20 April 08h00→Saturday 22 April, 2017 18h00

**Degree of liver fibrosis regression predicted by transient elastography after cure of chronic hepatitis C with direct acting antivirals is overestimated but confirmed by liver biopsy**

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**Background and Aims:** We have previously shown that the majority of patients (60/100) with advanced fibrosis or cirrhosis demonstrated improvement of Fibroscan (TE) scores by at least 1 stage after a median follow-up of 2.5 years (range: 0.5-14 years, IQR: 1-3.5 years) following SVR achieved by DAA therapy (Crissien-Martinez AM, et al. AASLD 2015). Since that time, others have confirmed this finding (Chan J, et al. IDWeek 2016). A smaller study evaluating post-transplant patients achieving SVR with DAAs showed no reversal of cirrhosis by biopsy in 7 patients who had significant improvement by TE, although they did have reversal of sinusoidal fibrosis (Donato M, et al. AASLD 2016). Data matching TE and liver biopsy after SVR are in general lacking.

**Methods:** Patients were consented and followed by prospective and retrospective TE and clinical data collection at 6 month intervals, for up to 7 years. Patients who achieved reversal based on TE and who had a baseline liver biopsy were offered a repeat liver biopsy to confirm the TE findings. Of the 100 patients who were eligible for analysis with at least 1 TE...
measurement of fibrosis, 10 had a baseline liver biopsy and a subsequent liver biopsy after demonstration of reversal by TE.

**Results:** Mean age was 60.7 years, 6/10 male and 9/10 non-Hispanic white of the 65/100 subjects who had cirrhosis at baseline, 36 (55%) demonstrated improvement by TE, with a median time to improvement (MTI) of 2.8 years (IQR 1.0-3.5). Of the 35/100 subjects who had advanced fibrosis, 24 (69%) demonstrated an MTI of 2.0 years (IQR 1.2-2.5). Liver biopsies in 10 patients confirmed reversal of fibrosis found by TE in both groups but to a significantly lesser degree than predicted by TE. 4/9 patients with TE <9.5 kPa still had F3 or F4 on biopsy. The MTI by biopsy was 4.75 years vs. the average MTI of 2.5 years by TE. There were major reductions in sinusoidal fibrosis noted in 7/10 patients. APRI and FIB4 showed significant reductions in 7/10 and 5/10 patients respectively.

**Conclusions:** Although the majority of our subjects with advanced fibrosis or cirrhosis demonstrated improvement by TE scores after a median follow-up of 2.5 years, matched liver biopsies in a subset of these patients indicates the reversal is overstated by TE and is slower than predicted. Early reductions in sinusoidal fibrosis may explain this discordance. It remains unclear how long patients with cirrhosis will require monitoring after SVR achieved by DAA therapy.

**Poster 2 (LBP-533)**

**Late breaker posters**

Date & Time: Thursday April 20, 2017 08h00 – 18h00

**Prospective prevalence study of adult NAFLD/NASH utilizing multi-modality imaging compared with liver biopsy**

Stephen A. Harrison,1,2 Katharine K. Roberts,3, Angelo H. Paredes,4 Christopher Lisanti,5 Ryan Schwope,5 Katherine M. Cebe,4 Jennifer M. Aldridge Whitehead,6,3 Valérie Paradis,7 Pierre Bedossa,3, James K. Aden6

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**Background and Aims:** This is an ongoing prospective study with the following aims: 1) assess the prevalence and severity of NAFLD/NASH in San Antonio; 2) to evaluate the diagnostic performance of FibroScan-(FS) and magnetic resonance imaging (MRI)-based techniques in predicting the degree of hepatic steatosis, inflammation and fibrosis compared to liver biopsy (LB).

**Methods:** Patients referred for a routine colon cancer screening with no prior history of liver disease or alcohol abuse offered participation in the study. Screening for NAFLD using 5 modalities was performed. 2 FibroScan® (FS) modalities: liver stiffness measurement (FS-LSM) and Controlled Attenuation Parameter (FS-CAP) and 3 MRI-based imaging-based modalities: MR elastography (MRE-LSM), proton density fat fraction (MRI-PDFF) and liver inflammation fibrosis score (LMS-LIF, Liver Multiscan®). Patients with FS-LSM ≥7 kPa, MRE-LSM ≥3 kPa, PDFF ≥5%, or LIF ≥2 were proposed a LB. LB were assessed by two expert pathologists in a double-blind manner with consensus, using the NASH CRN scoring system. The FLIP algorithm was also utilized to assess degree of disease activity. Diagnostic performance was assessed using area under receiver operating curve (AUROC).

**Results:** To date, 673 patients have been screened, of which 176 underwent LB. All imaging modalities performed in 449 patients. 328 patients (73%) had a normal liver (289 with normal imaging and 39 with normal LB). 63 (14%) and 58 (13%) patients had biopsy-confirmed NAFLD and NASH respectively. The prevalence of NAFLD and NASH was therefore 27% and 13%, respectively. Sex, BMI, ethnicity, diabetes status, hypertension status and lifestyle factors all were significantly linked to the normal/NAFL/NASH status. 160 patients were fully assessed (imaging modalities and LB): 24% were S0, 36% S1, 24% S2 and 16% S3. Respective AUROCs for FS-CAP and MRI-PDFF were for S ≥1: 0.80 [0.73; 0.88] and 0.93 [0.88; 0.98], for S ≥2: 0.82 [0.75; 0.88] and 0.96 [0.93; 0.99] and for S ≥3: 0.76 [0.68; 0.85] and 0.94 [0.89; 0.98]. 59% were F0, 28% F1, 9% F2 and 4% F3/F4. Respective AUROCs for FS-LSM, and MRE-LSM were for F ≥2: 0.81 [0.73; 0.89], 0.83 [0.73; 0.92].

**Conclusions:** Using several novel FS or MRI-based imaging markers, this study confirms the high prevalence of NAFLD and NASH among adults in south Texas. FS-CAP and MRI-PDFF are very good imaging modalities to non-invasively assess liver fat and FS-LSM/MRE are very good imaging modalities to non-invasively assess fibrosis in NAFLD.
Results: In all patients undergoing variceal ligation, LS increased immediately and significantly from a mean 40.3 ± 19.0 to 56.1 ± 21.5 kPa. In patients undergoing TIPS placement, LS decreased significantly from 53.1 ± 16.6 to 43.8 ± 17.3 kPa and the decreasing LS was significantly correlated with portal pressure (r=0.558). In the retrospective cohort, varices growing in size over a mean time interval of 4.3 ± 3 months were highly associated (r=0.638) with a significant decrease in LS values from a mean of 54.9 ± 23.5 to 47.9 ± 23.8 kPa while no changes of laboratory parameters were observed. Likewise, portal pressure and LS increased significantly after ligation of isolated liver lobes in the animal model from 8.6 ± 0.4 to 10.4 ± 0.5 mmHg and from 4.1 ± 0.5 to 8.9 ± 1.5 kPa, respectively. Of note, no changes of arterial or central venous pressure were observed.

Conclusions: Rapid changes of portal pressure is a strong modulator of LS both in healthy and diseased organs. Thus, LS measurements after variceal ligation or TIPS placement cannot be interpreted in terms of disease progression or regression. Finally, in patients with stable cirrhosis, a sudden decrease of LS may be indicative for new collateral formation.

Poster 4 (THU-034)
Cirrhosis and its complications: Clinical aspects
Date & Time: Thursday April 20, 2017 – 8h00-18h00

Systematic review with meta-analysis: liver stiffness and platelet count to identify patients with compensated liver disease at low risk of variceal bleeding
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Background and Aims: The 2015 Baveno VI guidelines recommend against performing upper gastrointestinal endoscopy in patients with compensated cirrhosis who have a liver stiffness <20 kPa and a platelet count >150’000/mm³ because of a low prevalence of varices at risk of bleeding in this population.

Aim: Synthesize the available evidence on the usefulness of the combined use of liver stiffness and platelet count to identify patients without esophageal varices.

Methods: Meta-analysis of trials evaluating the usefulness of a given cut-off for liver stiffness and platelet count to rule out the presence of esophageal varices.

Results: Fifteen studies were included. There were 997 patients with low liver stiffness and normal platelet count and 2'367 patients with either high liver stiffness or low platelet count. All studies excepting 5 used the Baveno VI criteria. Compared to patients with either high liver stiffness or low platelet count, those with low liver stiffness and normal platelet count had a lower risk of varices (OR=0.23, 95% CI=0.17-0.32, p<0.001) with moderate heterogeneity between studies (I²=52%). They also had a lower risk of varices at risk of bleeding (OR=0.22, 95% CI=0.13-0.39, p<0.001) with low heterogeneity between studies (I²=21%). In the sensitivity analyses excluding studies that did not use a liver stiffness cut-off of 20 kPa or a platelet cut-off of 150’000/mm³, the pooled estimate rate for varices at risk of bleeding was 0.031 (95% CI=0.017-0.055) with no heterogeneity between studies (p=0.5, I²=0%). In the subgroup analysis including only published studies, the pooled estimate rate for varices at risk of bleeding was 0.025 (95% CI=0.012-0.052) for patients with low liver stiffness and normal platelet count, with no heterogeneity between studies (p=0.8, I²=0%).

Conclusions: Patients with low liver stiffness and normal platelet count have a lower risk of varices than those with either high liver stiffness or low platelet count. Varices at risk of bleeding are found in no more than 4% of patients when liver stiffness is <20 kPa and platelet count is normal.

Poster 5 (THU-143)
Viral hepatitis: Hepatitis A, B, D, E - Clinical (except therapy)
Date & Time: Thursday April 20, 2017 – 8h00-18h00

Nucleos(t)ide analogue decreased liver stiffness of e-antigen negative chronic hepatitis B (CHB) patients over a 10-year interval
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Background and Aims: Fibrosis progression is observed in many patients with CHB despite hepatitis B e antigen seroconversion (ESC). Non-invasive assessment of liver fibrosis via transient elastography (TE) has been well validated. There is a lack of data on the factors associated with liver fibrosis change using TE on a long term basis. We aim to study the change in liver stiffness measurement (LSM) in e-antigen negative patients over a 10-year period.

Methods: From December 2014 to October 2016, we recruited Asian CHB patients who had undergone ESC, either spontaneous or treatment-induced, and had regular follow-up at the Department of Medicine, Queen Mary Hospital, Hong Kong. All recruited e-antigen negative patients had prior valid LSM between 2005-2006. LSM was performed by Fibroscan (Echosens, Paris, France). Following the EASL-ALEH recommendations, liver fibrosis was defined as LSM >9 kPa (in patients with normal alanine aminotransferase,ALT) or >12 kPa (with ALT 1-5 times upper limit of normal,ULN). Liver cirrhosis was defined as LSM >12 kPa (with normal ALT) or >13.5 kPa (with ALT 1-5 times ULN).

Results: 421 patients (mean age of ESC 35.2 ± 9.2 years; mean age at repeating LSM:51.2 ± 9.0 years; 55.6% male) were recruited. 332 (78.7%) of them had spontaneous ESC. 225 (53.5%) were treated with nucleos(t)ide analogue therapy before (n = 89) or after ESC (n = 136) for a mean duration of 5.4 years (± 6.3 years). Only 6 (1.4%) achieved hepatitis B surface antigen seroclearance. 62.7% of them had undetectable DNA (n = 264). Compared to baseline, the median LSM showed significant reduction (5.1 kPa; IQR 4.2 kPa-6.6 kPa vs. 6.1 kPa; IQR: 4.9 kPa-8.3 kPa; P <0.001).The proportion of patients with significant fibrosis and cirrhosis also showed significant reduction from 9.2% & 10.2% respectively to 4.3% & 4.5%, respectively (P <0.01 for both groups). A total of 69.2% showed interval decrease in LSM (mean change:-2.9 kPa). Lower body weight, waist circumference, hip circumference, diastolic blood pressure, ALT and AST were associated with decrease in LSM.Moreover, usage of antiviral therapy and undetectable serum HBV DNA were also associated with decrease in LSM. Multivariate analysis showed antiviral therapy to be the only factor associated with decrease in LSM (OR:1.997, CI:1.161-3.434, P = 0.012).
Conclusions: LSM of e-antigen negative CHB patients showed significant interval change upon follow-up of 10 years. Reduction in the proportion of patients with significant fibrosis and cirrhosis was observed. Nucleos (t)ide analogue therapy significantly reduced LSM.

Results:

- Mean basal TE was 5.6±1.6 kPa and at 3 years 5.8±1.8 kPa (p=0.24). TE value increased in 63 (1.3±1.1 kPa) and those without change or increase (n=69), there were no differences in any of the analyzed variables.

- Comparing patients with an increase ≥1 kPa with those with no change or decrease (n=60), the former had higher AST levels (27.8±8.9 vs. 22.7±6.9; p=0.054), without differences in the rest of the variables. TE value was ≤6.5 kPa in 73% in the initial study and in 76% in the second one. Comparing patients with TE ≤6.5 and >6.5 in the second TE, the former had higher basal levels of HBsAg (3.4±1.0 vs. 2.9±1.0 log10 IU/ml; p=0.03), higher levels of basal HBV-DNA (2795±3731 vs. 836±1862 IU/ml; p=0.00) and of highest HBV-DNA during the follow-up (8669±13467 vs. 3295±5902; p=0.03), while those with TE >6.5 had higher AST levels (29.9±9.1 vs. 23.8±9.1; p=0.027) and BMI (27.9±5.4 vs. 25.5±5.3; p=0.038). Diabetes was more frequent among those with TE >6.5 kPa (10% vs. 2.1%; p=0.09), as was steatosis (36% vs. 20%; p=0.08). There were no differences in sex, age, basal ALT, highest ALT, platelets or as was steatosis (36% vs. 20%; p=0.08).

Poster 7 (THU-207)

**Viral hepatitis: Hepatitis C - Clinical (except therapy)***

Date & Time: Thursday April 20, 2017 – 8h00-18h00

**Characterization of liver fibrosis stage and regression in chronic hepatitis C infected patients after achieving sustained virologic response using direct-acting antivirals as demonstrated by elastography**

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**Background and Aims:** Cirrhosis due to HCV infection has been associated with increased risk for hepatocellular carcinoma. The aim of our study was to assess changes in liver Transient Elastography (TE) and fibrosis-4 (FIB-4) score in patients with chronic hepatitis C (CHC) in a large cohort of patients and in a subcohort who achieved sustained viral response (SVR).

**Methods:** Our cohort included approximately 1,200 patients with chronic liver disease. In our cohort, approximately 500 had liver biopsies. Retrospective prospective study included 60 patients with CHC and a baseline liver biopsy who achieved SVR after treatment with DAA regimens and had a pretreatment TE study and at least one follow up TE measurement at 24 weeks or later post end of treatment response (EOTR). The estimated stage of liver fibrosis based on TE was categorized as F0-F2 (~9.4 kPa), or F3 (9.5 – 12.4 kPa), or F4/cirrhotics (~12.5 kPa).

**Results:** Approximately 1,200 patients were successfully assessed by fibroscan and comparisons made with clinical parameters of liver disease. The median baseline TE for the entire cohort was 11.9 Kpa (range 3.8 to 65.2) and at follow up, TE decreased to 7.35 Kpa (range 2.9 to 34.8) with a median change in TE of -3.4 Kpa (range -35.3 to +1, p=7.355e-11). Follow up median TE done in the cirrhotic population after treatment was 7.35 Kpa (range 2.9 to 34.8) with a median change in TE of -3.4 Kpa (range -35.3 to +1, p=7.355e-11).
median time of 39 weeks post EOTR decreased to 11.7 Kpa and FIB4 was 2.3. The median change of TE in cirrhotic patients was -6.5 kpa (range -35.3 to +1, p=1.043e-7) and for FIB4 was -1.97 (range -17.47 to -0.33, p=1.49e-8). Non-cirrhotic patients (TE<12.4) comprised 55% of the entire cohort and their median change of TE was -2.4 Kpa (range -6.4 to 0.7, p=1.539e-6) and FIB4 was -0.68 (range -2.8 to 0.41, p=2.987e-6). 48% of the entire cohort down-staged their liver fibrosis as determined by TE. In a multiple logistic regression analysis for factors associated with down-staging in liver fibrosis, we found that patients who were treatment naïve were more likely to improve their fibrosis stage (OR 5.73, p=0.033).

Conclusions: Liver fibrosis stage, as determined by TE, improved after achieving SVR with DAA treatments in most patients. The significant drop in TE measurement post SVR was also correlated with a significant drop in FIB4. Although cirrhotic patients had a more significant drop in their median TE when compared to non-cirrhotic patients, they had a lower probability of improving their fibrosis stage.

Poster 8 (THU-209)

Viral hepatitis: Hepatitis C - Clinical (therapy)

Date & Time: Thursday April 20, 2017 – 8h00-18h00

In hepatitis C virus-related advanced fibrosis and cirrhosis, early decline of liver stiffness following antiviral therapy with daas is related to decline in liver inflammation

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Background and Aims: Decline in Liver Stiffness (LS) as measured by transient elastography (TE) has been described in most patients following HCV therapy with direct-acting antiviral agents (DAAs). In patients with advanced fibrosis or cirrhosis (METAVIR F3-F4), substantial early post-treatment declines in LS have been observed at a time point when a significant regression of fibrosis is not yet expected. This study examines the influence of pre-treatment liver inflammation and its decline post-treatment on the early decline of LS following DAA therapy.

Methods: In six centers, HCV patients who received their first all-oral DAA therapy and had at least one LS measure pre-and post-treatment were retrospectively identified and included if pre-treatment LS ≥9.5 kPa. Patients with ascites or liver cancer were excluded. ALT levels were used as a surrogate of liver inflammation.

Results: Among 185 eligible patients, 60 (32%) were classified based on pre-treatment baseline (BL) LS as F3 (LS = 9.5-12.4 kPa), and 125 (68%) as F4 cirrhosis (LS ≥12.5 kPa), among whom 64 (35%) had low LS (12.5-19.9 kPa, F4a), 36 (20%) had intermediate LS (20.0-29.9 kPa, F4b), and 25 (13%) had high LS (≥30.0 kPa, F4c). With each increasing LS category (F3-F4a-F4b-F4c), there was a significant increase in BL esophageal varices (0-3-36-56%, respectively) and BL thrombocytopenia <100,000 /mm3 (5.3-33-40%). Median time between BL and post-treatment (PT) LS measures was 10.3 months (IQR, 7.7 – 14.4 months). Mean absolute decline of PT vs. BL LS increased with each LS category (2.9-6.7-7.11-18 kPa, p <0.001), but the mean percent decline was not different (17-29-31-26%, p = 0.89). There was a significant correlation between the log10 decline of PT/BL ALT level and log10 decline of PT/BL LS; R = 0.21, p = 0.005. The rate of patients with a decline to PT LS <9.5 kPa was 73-47-11-0% (p <0.001) with a rate of 27% (34/125) among F4 patients. In these F4 patients, LS decline to <9.5 kPa was associated with absence of BL esophageal varices (0% vs. 32% in patients with PT LS ≥9.5 kPa, p = 0.001), lower rate of BL thrombocytopenia <100,000 /mm3 (3% vs. 30%, p = 0.001), and of BL APRI <1.0 (60% vs. 26%, p = 0.001).

Conclusions: In HCV patients with F3-F4 fibrosis, PT decline of LS is correlated to PT decline in ALT level. Over 25% of F4 patients had PT LS <9.5 kPa. These patients may not have had BL cirrhosis with a significant proportion of their BL LS stemming from liver inflammation, or PT LS may need to be redefined to account for resolved inflammation.

Poster 9 (THU-243)

Viral hepatitis: Hepatitis C - Clinical (therapy)

Date & Time: Thursday April 20, 2017 – 8h00-18h00

Liver stiffness and portal hypertension predict failure to DAA treatment in a real-life cohort of hepatitis C virus -infected patients treated with recommended regimens

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Background and Aims: Treatment of chronic hepatitis C (HCV) has dramatically improved with the introduction of interferon-free regimens. Unfortunately, a small fraction of patients fails to reach a sustained virological response even with direct-acting antiviral agents (DAA). In this setting little is known about the risk factors associated with treatment failure.

Methods: Among 369 consecutive HCV-infected patients who started an optimal (according to the 2016 EASL guidelines) DAA treatment at our Unit, we included 253 who achieved at least a 12-week follow up after treatment completion. The study cohort included mainly males (n = 154, 60.8%), with cirrhosis (n = 168, 66.4%), of whom 25.6% (47/183) showed clinically significant portal hypertension, as evidenced by esophageal varices at upper GI endoscopy. Most patients (n = 152, 60.1%) were infected with genotype 1, 51 (20.1%) with genotype 2, 30 (11.8%) and 20 (8%) with genotype 3 and 4, respectively. Patients underwent treatment with sofosbuvir (n = 50, 20.1%), sofosbuvir/ledipasvir (n = 34, 13.3%), sofosbuvir/daclatasvir (n = 26, 10.3%), sofosbuvir/daclatasvir (n = 26, 10.3%), sofosbuvir/ledipasvir (n = 80, 31.5%), ombitasvir/paritaprevir/ritonavir with (n = 56, 22.1%) or without (n = 7, 2.7%) dasabuvir. Data were processed by intention-to-treat (ITT) with univariate and multivariate analyses. The study population included 229 patients who...
achieved SVR-12 (90.5%) and 24 (9.5%) who failed for any reason: virological relapse (n = 9), death (n = 10) or drop-out (n = 5).

**Results:** At univariate analysis, cirrhosis (p = 0.005), presence of medium/large esophageal varices (p = 0.0001), a higher liver stiffness (p = 0.00007), previous HCC (p = 0.002), diabetes (p = 0.006), viral genotype 2 (p = 0.02), low platelet count (p = 0.02), low total cholesterol level (p = 0.001), INR prolongation (p = 0.02) and a higher MELD score (p = 0.000001) were all significantly associated with treatment failure. DAA failure was unrelated to HCV viral load (p = 0.16) and treatment schedule (p = 0.25). At stepwise multivariable logistic regression, only liver stiffness and the presence of medium or large esophageal varices confirmed the capability to significantly predict treatment failure (p = 0.02, p = 0.02 and p = 0.01 respectively), with an area under the ROC curve of 0.93.

**Conclusions:** In a real-life setting, around 10% of patients with HCV-related liver disease fails after DAA treatment. Failure is strongly and independently associated with the presence of high liver stiffness and clinically significant portal hypertension.

**Poster 10 (THU-283)**

**Viral hepatitis: Hepatitis C - Clinical (therapy)**

Date & Time: Thursday April 20, 2017 – 8h00-18h00

**Changes in liver stiffness assessment in chronic hepatitis C patients treated with direct-acting antivirals: monocentric experience between 2015 and 2016**

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**Background and Aims:** Chronic hepatitis C (CHC) remains a major cause of liver-associated mortality due to decompensated cirrhosis and risk of hepatocellular carcinoma development, especially in HIV-HCV-coinfected patients. The approval of directly acting antivirals (DAAs)-based regimens now ensures HCV eradication in up to 90-95% of CHC patients, with expected subsequent liver fibrosis improvement. Long-term effects on histologic liver improvement after DAAs treatment are still under examination. The aim of this analysis was to evaluate changes of liver stiffness (LS) measurement in CHC o HIV-HCV-patients treated with different DAAs regimens in a “real life” setting.

**Methods:** Between March 2015 and May 2016, 80 consecutive CHC patients treated with DAAs at our Infectious Diseases Outpatient Clinic were included. Baseline characteristics, safety data, on treatment HCV-RNA at week 2, week 4, week 8 and monthly thereafter and sustained virological response at 12 and 24 weeks (SVR12 and SVR24) after end of treatment (EOT) were assessed. Non invasive LS measurement with transient elastography (TE) was performed using a FibroScan instrument (Echosens, France) in all patients at baseline (BL) and 12, 24 and 48 weeks after EOT when possible.

**Results:** The median age of the patients was 54 years (range 28-72), 44 (55%) were males, 27 (34%) were HIV-HCV-positive and, according to Child-Pugh score assessment and LS measurement, 48 patients (60%) had compensated cirrhosis. All the patients achieved SVR12 and SVR24. In CHC patients the median LS value decreased from 20,5 kPa at BL (53 patients) to 12,5 KPa at SVR12 (49 patients) to 12 kPa at SVR24 (20 patients) with a further unchanged value of 12 kPa at SVR48 (5 patients). In 27 HIV-HCV-patients the median LS value decreased from 11,4 kPa at BL to 8,9 kPa at SVR12.

**Conclusions:** In our cohort of CHC and HIV-HCV-patients a remarkable decrease in LS measurement with non invasive TE assessment after successful treatment with DAAs was observed, especially in cirrhotic patients. In accordance with the results of recent although to date few experiences LS reduction occurred nearly completely in the first 12-24 weeks after EOT and then remained almost unchanged or showed only minor decrease during further follow-up LS assessments. It has to be elucidated with long term evaluation in a larger cohort of patients if the observed LS measurement reduction is due to real fibrosis regression or alternatively to the improvement of chronic liver necroinflammation.

**Poster 11 (THU-354)**

**Fatty liver disease: Clinical aspects**

Date & Time: Thursday April 20, 2017 – 8h00-18h00

**Performance of the Fibroscan and other noninvasive scales for detecting hepatic fibrosis in patients with nonalcoholic fatty liver disease**

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**Background and Aims:** To determine the diagnostic performance of a non-invasive test such as FibroScan in detecting hepatic fibrosis in patients with nonalcoholic fatty liver disease. To explore possible improvements in the predictions by incorporating other scales for detecting hepatic fibrosis. To determine the diagnostic performance of a non-invasive test such as FibroScan in detecting hepatic fibrosis in patients with nonalcoholic fatty liver disease. To explore possible improvements in the predictions by incorporating other scales for detecting hepatic fibrosis.

**Methods:** We prospectively studied 78 adult patients diagnosed with nonalcoholic fatty liver disease (NAFLD) through liver biopsy. The histological findings were classified according to the FLIP (fatty liver inhibition of progression) Pathology Consortium algorithm based on the SAF score (Steatosis, Activity, Fibrosis). We determined the diagnostic performance of FibroScan and the various indices (BARD, APRI, NAFLD) by calculating the ROC area under the curve (ROCA). We selected the best cutoff that would maximize the sensitivity and specificity, according to Youden’s index. By employing a logistic regression model, we assessed the independent contribution of other fibrosis scales to the FibroScan results.

**Results:** Most of the patients were women (60.3%), and the mean age was 54.2 years (SD, 10.7 years). Fibrosis was detected in 43 cases (55.1%), more than half of which (69.8%)
had a fibrosis grade greater than or equal to 2. The FibroScan showed greater diagnostic performance with an M probe (ROCa 0.78; 95% CI 0.65–0.91) than with an XL probe (ROCa 0.60; 95% CI 0.31–0.88). However, both probes were equivalent when the valid measurements were selected (M probe: ROCa 0.78; XL probe ROCa 0.83). FibroScan ROCa (95% CI) 0.819 (0.699–0.940) Cutoff 8.5. IBARD 0.673 (0.521–0.825) 2. APRI 0.817 (0.699–0.934) 0.45. NAFLD 0.668 (0.512–0.824) 0.36. In general, the FibroScan had the greater discriminating capacity in detecting hepatic fibrosis. The combination of FibroScan, APRI and NAFLD in a multivariate model increased the discriminative capacity with an ROCa of 0.922 (95% CI 0.849–0.995).

Conclusions: Once the validity of the measurements was determined, we were able to conclude that the FibroScan is a test with high diagnostic performance in detecting hepatic fibrosis. The incorporation of the APRI and NAFLD scales to the FibroScan results could significantly improve the capacity for detecting fibrosis.

**Post 12 (THU-366)**

**Fatty liver disease: Clinical aspects**

Date & Time: Thursday April 20, 2017 – 8h00-18h00

The combination of Fibroscan with blood markers in the Fibrometer VCTE significantly reduces the use of liver biopsy for the assessment of advanced fibrosis in non-alcoholic fatty liver disease

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**Background and Aims:** Fibroscan and FibroMeter accurately diagnose advanced liver fibrosis in non-alcoholic fatty liver disease (NAFLD) (J Hepatol 2016). However, they have a grey zone where the diagnosis remains undetermined. As already shown in chronic hepatitis C, we aimed to evaluate if combining fibrosis tests reduces this grey zone and thus the need for liver biopsy in NAFLD.

**Methods:** 723 biopsy-proven NAFLD patients with Fibroscan (FS) and blood tests were included. Blood tests evaluated were: NAFLD Fibrosis Score (NFS), Fibrometer VCTE (FM\(^{VCTE}\)), FibroMeter\(^{VCTE}\) (FM\(^{VCTE}\); a combination of Fibroscan with the blood markers of FM\(^{VCTE}\) in a single formula). The primary diagnostic target was advanced fibrosis as defined by NASH CRN fibrosis stage F≥3.

**Results:** Liver stiffness measurement with the FS M probe (FS\(_{M}\)) failed with no valid measurement in 105 patients. The per-protocol analysis performed in the 618 remaining patients showed that FM\(^{VCTE}\) had a significantly higher AUROC (0.861 ± 0.015, p <0.009) than NFS (0.725 ± 0.020), FM\(^{VCTE}\) (0.772 ± 0.020) and FS\(_{A}\) (0.831 ± 0.016). The rate of patients included in the grey zone between the 90% sensitivity and 95% specificity thresholds was the lowest with the FM\(^{VCTE}\) (35.8%, p <0.030 vs other tests). Six test combinations were evaluated: SAFE (Sebastiani, Hepatology 2009), Bordeaux algorithm (BA, Castera J Hepatol 2010), NFS-FS\(_{A}\) (Petta, Liver Int 2015), FM\(^{VCTE}\), FM\(^{VCTE}\) first then FM\(^{VCTE}\) (FS\(_{A}\)-FM\(^{VCTE}\)). Diagnostic accuracy and rate of liver biopsy were, respectively: 90.8%/73.8%, 88.0%/43.7%, 96.1%/67.2%, 92.6%/35.8%, 89.6%/28.3%, 89.5%/28.0%, FM\(^{VCTE}\)-FM\(^{VCTE}\) and FS\(_{A}\) -FM\(^{VCTE}\) provided thus the lowest rate of liver biopsy (p <0.001 vs. others) with a high diagnostic accuracy around 90%. The FS XL probe (FS\(_{XL}\)) was available in a subset of 371 patients. An intention-to-diagnose analysis was performed in this subgroup by using FS\(_{XL}\) in case of FS\(_{A}\) failure (n = 67) and liver biopsy in case of FS\(_{XL}\) failure (n = 7). Diagnostic accuracy and rate of liver biopsy of the six tests combinations (SAFE, BA, NFS-FS\(_{A}\), FM\(^{VCTE}\), FM\(^{VCTE}\)-FM\(^{VCTE}\), FS\(_{A}\) -FM\(^{VCTE}\)) were, respectively: 89.5%/71.2%, 86.8%/42.9%, 95.1%/67.9%, 89.5%/35.0%, 86.5%/28.0%, 87.3%/27.2%.

**Conclusions:** The synchronous combination of Fibroscan with biomarkers in the FibroMeter\(^{VCTE}\) improves the non-invasive diagnosis of advanced fibrosis in NAFLD. In clinical practice, the sequential use of fibrosis tests (first: Fibroscan or FibroMeter\(^{VCTE}\), then, if necessary: FibroMeter\(^{VCTE}\)) significantly reduce the need for liver biopsy.

**Post 13 (THU-422)**

**Genetic and pediatric liver diseases**

Date & Time: Thursday April 20, 2017 – 8h00-18h00

**Fontan-associated liver disease: diagnosis by elastography and laparoscopic liver biopsy**

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**Background and Aims:** Patients with a Fontan circulation tend to develop liver fibrosis, liver cirrhosis and even hepatocellular carcinoma. Assessment of fibrosis in Fontan associated liver disease (FALD) is needed to facilitate the disease progression. Our aim was to evaluate the non-invasive diagnostic performance of Vibration-Controlled Transient Elastography (VCTE) in patients who had undergone Fontan operations.

**Methods:** All participants provided written informed consent, and the study protocols were approved by the institutional ethics committee. A total of 60 patients with Fontan circulation undergoing cardiac catheterization with or without laparoscopic liver biopsy were enrolled in this study, and all patients underwent liver stiffness measurement by VCTE. Moreover, we measured hemodynamic data and serum markers related to fibrosis, and examined hepatic and splenic blood flow with duplex Doppler ultrasonography.

**Results:** Median age was 24 years (range 9-35). Median time since Fontan procedure was 15 years (range 5.0–31.5). Mean liver stiffness measurement by VCTE was 20.8±9.6 kPa. Univariate regression analysis using liver stiffness value as a continuous outcome variable shows significant correlations with time since Fontan procedure (P = 0.001) and pulmonary vascular resistance (P = 0.04). We compared the liver stiffness value between less than and more than 15 years after the Fontan procedure. Liver stiffness was significantly higher in patients who underwent surgery more than 15 years prior (P = 0.011). The patients who underwent laparoscopic liver biopsy were asymptomatic, and their liver function tests were within normal limits. However, laparoscopy showed nodular cirrhosis, lymphoma.
vesicles, and white icing sugar-like plaques on the surface of the liver in all patients who underwent laparoscopic liver biopsy. Therefore, these patients were diagnosed with liver cirrhosis secondary to FALD. No severe complication (e.g., bleeding) was found after laparoscopic liver biopsy.

**Conclusions:** To the best of our knowledge, this is the first report of FALD diagnosis by laparoscopic liver biopsy. The present study shows that patients who undergo the Fontan procedure are at increased risk of developing liver fibrosis and liver cirrhosis. VCTE may be a useful screening tool for FALD.

### Poster 14 (THU-475)

**Non-invasive assessment of liver disease**

**Date & Time:** Thursday April 20, 2017 – 8h00-18h00

**The Non-Alcoholic Fatty Liver Disease liver fat score is associated with liver disease mortality in the United States population**

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**Background and Aims:** Fatty liver disease is common in the United States and worldwide with a global prevalence of 20% to 30%. It can progress to chronic liver disease and cirrhosis which was the 12th leading cause of death in the United States in 2014. The non-alcoholic fatty liver disease (NAFLD) liver fat score (LFS) was derived in a Finnish population and includes alanine aminotransferase (ALT), aspartate aminotransferase (AST), diabetes, metabolic syndrome, and fasting insulin (Kotronen, Gastroenterol, 2009; 137:865). The hepatic steatosis index (HSI) was derived in a Korean population and includes ALT, AST, diabetes, sex, and BMI (Lee, Dig Liver Dis, 2010; 42:503). We examined whether these two potential markers of liver health were associated with increased overall and cause-specific mortality in a U.S. population-based survey with up to 23 years of linked-mortality data.

**Methods:** We studied 8,978 fasted viral hepatitis negative adult participants in the third U.S. National Health and Nutrition Examination Survey (NHANES), 1988-1994. Intermediate and high steatosis probabilities were dichotomized based on published cut-offs. Participants were passively followed for mortality, as identified by death certificate underlying or contributing cause diagnoses, by linkage to National Death Index records through 2011. Hazard rate ratios (HR) for mortality were calculated using Cox proportional hazards regression to adjust for common mortality risk factors.

**Results:** The prevalence of intermediate and high steatosis probability using the LFS as a marker was 28.9% and 7.4%, respectively. During follow-up, there were 2,729 deaths from all causes and 89 with liver disease, including primary liver cancer. In age-adjusted analyses, liver disease mortality was increased with an intermediate (HR, 3.2; 95% confidence interval [CI], 1.3-7.4) or high (HR, 9.4; 95% CI, 4.1-21.6) LFS. With multivariate adjustment, the risk was further increased (Figure). In contrast, a higher HSI was not associated with increased liver disease mortality (Figure). There was no association of a higher LFS or HSI with all-cause or cardiovascular disease mortality in multivariate-adjusted analyses.

**Conclusions:** In the U.S. population, a higher steatosis probability using the LFS, but not the HSI, was associated with increased liver disease mortality. Neither score was associated with other mortality outcomes. The performance of liver fat scores may vary among diverse populations.

### Poster 15 (THU-477)

**Non-invasive assessment of liver disease**

**Date & Time:** Thursday April 20, 2017 – 8h00-18h00

**Magnetic Resonance Elastography vs. Transient Elastography in detection of fibrosis and noninvasive measurement of steatosis in patients with biopsy-proven nonalcoholic fatty liver disease**


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**Background and Aims:** Magnetic Resonance Elastography (MRE) techniques and ultrasound-based Transient Elastography (TE) can be used in noninvasive diagnosis of fibrosis and steatosis in patients with nonalcoholic fatty liver disease (NAFLD). We performed a prospective study to compare the performance of Magnetic Resonance Elastography (MRE) vs. TE for in diagnosis of fibrosis, and MRI-based proton density fat fraction (MRI-PDFF) analysis vs. TE-based controlled attenuation parameter (CAP) for diagnosis of steatosis in patients undergoing biopsy to assess NAFLD.

**Methods:** We performed a cross-sectional study of 104 consecutive adults (56.7% female) who underwent MRE, MRI-PDFF, TE, and liver biopsy assessment (using the Nonalcoholic Steatohepatitis Clinical Research Network Histologic Scoring System) from October 2011 through May 2016 at a tertiary medical center. The primary outcomes were fibrosis and steatosis. Secondary outcomes included dichotomized stages of fibrosis and NASH vs. no NASH. Receiver operating characteristic (ROC) curve analyses were used to compare performances of MRE vs. TE in diagnosis of fibrosis (stages 1–4 vs 0) and MRI-PDFF vs. CAP for diagnosis of steatosis (grades 1–3 vs. 0) with respect to findings from liver biopsy assessment.

**Results:** MRE detected any fibrosis (stage 1 or more) with an area under the ROC (AUROC) of 0.82 (95% CI, 0.74–0.91),
which was significantly higher than that of TE (AUROC, 0.67; 95% CI, 0.56–0.78). MRI-PDF detected any steatosis with an AUROC of 0.99 (95% CI, 0.98–1.00), which was significantly higher than that of CAP (AUROC, 0.85; 95% CI, 0.75–0.96). MRE detected fibrosis of stages 2, 3, or 4 with AUROC values of 0.89 (95% CI, 0.83–0.96), 0.87 (95% CI, 0.78–0.96), and 0.87 (95% CI, 0.71–1.00); TE detected fibrosis of stages 2, 3, or 4 with AUROC values of 0.86 (95% CI, 0.77–0.95), 0.80 (95% CI, 0.67–0.93), and 0.69 (95% CI, 0.45–0.94). MRI-PDF identified steatosis grades 2 or 3 with AUROC values of 0.90 (95% CI, 0.82–0.97) and 0.92 (95% CI, 0.84–0.99); CAP identified steatosis grades 2 or 3 with AUROC values of 0.70 (95% CI, 0.58–0.82) and 0.73 (95% CI, 0.58–0.89).

Conclusions: In a prospective, cross-sectional study of more than 100 patients, we found MRE to be more accurate than TE in identification of liver fibrosis (stage 1 or more), using biopsy assessment as the standard. MRI-PDF is more accurate than CAP in detecting all grades of steatosis in patients with NAFLD.

**Poster 16 (THU-479)**

Non-invasive assessment of liver disease

Date & Time: Thursday April 20, 2017 – 8h00-18h00

Screening for nonalcoholic fatty liver disease by Transient Elastography with Controlled Attenuation Parameter in unselected patients with inflammatory bowel disease

Chiara Saroli Palumbo1, Sophie Restellini2, Che-Yung Chao3, Achuthan Aruljothy4, Talat Bessissow5, Giada Sebastiani3

Background and Aims: Nonalcoholic fatty liver disease (NAFLD) is the most frequent liver disease in Western countries. Patients with inflammatory bowel disease (IBD) are at risk for NAFLD due to chronic inflammation, hepatotoxic drugs, and alteration of gut microbiota. However, prospective data in unselected patients by means of validated and accurate diagnostic methods are lacking.

Methods: We prospectively investigated prevalence and risk factors of NAFLD and liver fibrosis by Transient Elastography (TE) with associated controlled attenuation parameter (CAP) in unselected IBD patients free of liver disease as part of a routine screening program. Hepatic steatosis (involving >10% of hepatocytes) was defined as CAP ≥238 dB/m. Significant liver fibrosis and cirrhosis (stage 2 and 4 out of 4, respectively) were defined as TE measurement ≥8 and ≥13 kPa. Active IBD was defined as partial Mayo score ≥3 and Harvey Bradshaw Index ≥5 for ulcerative colitis and Crohn’s disease, respectively. Predictors of NAFLD and significant liver fibrosis were determined by logistic regression analysis.

Results: 326 patients (mean age 42.8±15.5, 48.8% male) were included; 66% had Crohn’s disease, and 32% had active disease at time of recruitment. Prevalence of NAFLD, significant liver fibrosis and cirrhosis was 39.6%, 9.5% and 1.5%, respectively. Main predictors of NAFLD were older age and being overweight (see Table). Significant liver fibrosis was independently predicted by IBD duration, being overweight and dyslipidemic.

Table. Multivariate analysis of predictors of NAFLD and fibrosis

Conclusions: NAFLD diagnosed by TE with CAP is a major comorbidity in unselected IBD patients without known liver disease. These patients may also have significant liver fibrosis and cirrhosis, likely suggesting the coexistence of non-alcoholic steatohepatitis. Non-invasive screening strategies can help early diagnosis and initiation of interventions in this population, including weight loss, and treatment of metabolic comorbidities.

**Poster 17 (THU-480)**

Non-invasive assessment of liver disease

Date & Time: Thursday April 20, 2017 – 8h00-18h00

Liver stiffness based model predicts portal hypertension, esophageal varices and hepatocellular carcinoma in Caucasian patients with hepatitis B virus-related cirrhosis responsive to antiviral therapy

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Gastro-Hepatology, AOU Città della salute e della scienza di Torino, Torino, Italy

Background and Aims: In HBV-related cirrhosis the antiviral therapy reduces but does not eliminate the risk of HCC. Endoscopic monitoring of EV remains controversial in responsive patients. LSPS (LS value X spleen diameter/platelet count) has been correlated with PH, EV and risk of HCC. We assessed the prognostic role of LSPS in predicting these goals in cirrhotics responsive to long term antiviral therapy with NUC(s).

Methods: A longitudinal study was performed in 121 cirrhotics treated for a median of 8 years (median age 54, M/F 100/21). HBeAg/antiHBe 5/116, no HCV, HIV or HDV coinfection and responsive to antiviral therapy who underwent HVPG (hepatic venous pressure gradient) and LS measurement. Sixty-one patients (50.4%) had clinical PH (cPH) (US, EV, ascites and/or LS >11 kPa and/or plts <100,000) at baseline.

Results: LSPS ≤0.62 and <1.4 identified all patients without PH measured by HVPG (>6 mmHg, NPV = 100%) and without EV (NPV 93.7%), respectively. After antiviral therapy LSPS ≤0.62 was detected in 51.3% of patients (16.4% and 76.6% of subjects with and without clinical PH at baseline). Median LS decreased from 16.1 to 9.5 KPa. The reduction was significantly higher in patients with LS <11 kPa at baseline (p <0.0001). HCC developed in 26 patients (21.5%, 2.6% year) with a higher incidence in patients with LSPS >0.62 after antiviral therapy (36% vs. 7%, 7.1% vs. 0.75% year, p <0.001) but no difference was detected in lamivudine-exposed patients. On univariate analysis patients with HCC had a higher LS and LSPS after therapy and cPH baseline (p <0.001). On multivariate analysis LSPS post-therapy and cPH baseline were the only independent predictors of HCC after adjusting for ALT, duration and type of therapy, age, LS, platelets count and hepatic steatosis. Quantitative HBsAg load was not significantly different in patients with or without cPH. LSPS >0.62 and HCC.

Conclusions: LSPS is useful to identify patients with PH and EV, avoiding endoscopy. LSPS ≤0.62 baseline or induced by antiviral therapy is associated with a lower risk of HCC. In patients responsive to antiviral therapy this goal is obtainable in about 75% of the subjects without cPH baseline and in less than
20% of the others. The fibrotic burden rather than HBV variants seems to be relevant in the oncogenic mechanism. These results support early antiviral treatment of HBV-related liver disease in order to maintain or induce LSPS ≤0.62 and the use of the score to define the HCC risk and the individual endoscopic surveillance in treated patients.

**Poster 18 (THU-482)**

Non-invasive assessment of liver disease

Date & Time: Thursday April 20, 2017 – 8h00-18h00

Acoustic Radiation Force Impulse elastography combined with ultrasound spleen platelets portal vein Doppler score in variceal screening: Improved performance compared with baveno VI criteria for avoidance of endoscopy in cirrhotics

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2) Radiology, Central midlesex hospital, London North West hospitals NHS trust, London, United Kingdom

**Background and Aims:** Liver stiffness measurements (LSM) alone have insufficient predictive value for portal hypertension. The Baveno VI criteria proposed the use of Transient Elastography (TE) and platelet thresholds to reduce endoscopic screening for varices (EVs) in compensated cirrhosis (cACLD). However, detailed validation of this approach is limited. ARFI has the advantage of simultaneous US assessment of the portal circulation. A high predictive value for a 10 point SPVD score (Spleen Platelets portal Vein Doppler) was previously shown for the detection of EVs in unselected cirrhotics. Our aim was to validate the Baveno VI criteria using ARFI and to compare performance with SPVD score.

**Methods:** From 1512 consecutive LSM+US examinations between 2010 and 2014, patients were identified a) with LSM >1.5 m/s (equivalent to TE >10 KPa), b) who were Child Pugh ≤7 and fulfilled Baveno VI criteria for cACLD, and c) who had OGD within 12 months of ARFI. SPVD was scored from US reports and platelets. EVs were classified as clinically significant or small according to Baveno VI. An ARFI threshold of <2.8 m/s was chosen as equivalent to TE <20 KPa, and SPVD score of <2. Predictive performance of cut offs for both ARFI/Platelets and ARFI/SPVD were compared.

**Results:** One hundred and twenty four patients fulfilled study criteria (median age 59, 62% male). Aetiologies were viral in 19%, ALD 34%, NAFLD 14% and other 33%. Forty seven (38%) had EVs, of which 33 (70%) were clinically significant. Median LSM and platelets were 2.56m/s and 163, respectively. Predictive data for significant EVs using a) Baveno VI equivalent by ARFI; b) ARFI+SPVD; and c) SPVD alone were: sensitivity 82/100/94 (p = 0.03), specificity 47/53/66 (p <0.005), NPV 88/100/97 (p = 0.03), overall accuracy 56/61/73% (p <0.001), respectively. ARFI+SPVD correctly identified all significant EVs, SPVD alone missed 2(4%), whereas Baveno VI missed 6(13%, p <0.05). SPVD alone achieved 27 correctly “saved” screening endoscopy (22% of total) due to its higher specificity, whereas Baveno VI and ARFI/SPVD failed to achieve savings.

**Conclusions:** This study confirms reasonable NPV for clinically significant EVs using equivalent Baveno VI criteria with ARFI instead of TE. However, the SPVD score showed significantly higher negative and overall predictive values, either combined with ARFI or alone. Although further validation is needed centres using ARFI, or similar LSM techniques, should consider substituting LSM+SPVD in preference to Baveno VI for EV screening prior to endoscopy.

**Poster 19 (THU-484)**

Non-invasive assessment of liver disease

Date & Time: Thursday April 20, 2017 – 8h00-18h00

ElastPQ shear-wave elastography compared to Fibroscan Transient Elastography for fibrosis staging in patients with NAFLD

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**UCL Institute for Liver and Digestive Health, Royal Free Hospital and UCL, London, United Kingdom**

**Background and Aims:** Shear Wave Elastography with ElastPQ (EastPQ SWE) is a recently introduced elastography-based technique for non-invasive fibrosis assessment. We compared ElastPQ SWE to elastography evaluation by 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 liver biopsies.

**Methods:** Anthropometric parameters (weight, height, BMI and waist circumference (WC) were measured and routine bloods with a lipid profile were done. Transient Elastography (TE) with Fibroscan (Echosens) and SWE with ElastPQ (Philips) were carried out in all patients. Liver biopsies were considered valid if done within 1 year from elastography.

**Results:** We enrolled 218 consecutive patients with NAFLD, mean age 56±13 years, 59.2% males, 41.7% with diabetes, 56% arterial hypertension, 78% hyperlipidaemia. ElastPQ SWE showed a good correlation with F-TE (Spearman’s = 0.688, p <0.0001), which was better for mild and moderate stages of fibrosis. A ≥2 kPa difference between F-TE and ElastPQ SWE was observed in 38 patients. On the univariate analysis, predictors of such a difference were BMI (p = 0.014), WC (p = 0.036) and F-TE stiffness (p <0.0001). On the multivariate analysis, independent predictors was a F-TE ≥10 kPa (OR 4.151, 95% CI 1.835-9.392, p = 0.001), while BMI was marginally associated (OR 1.063, 95% CI, p = 0.058). In the subgroup of 60 patients with available liver biopsies, the distribution of fibrosis was as follow: F0 = 8 (13%), F1 = 24 (40%), F2 =15 (25%), F3 = 7 (12%) and F4 = 11 (18.3%) biopsies. The optimal cut-off values of ElastPQ SWE for individual stages of fibrosis were lower than those of F-TE. ElastPQ showed better sensitivity and specificity compared to F-TE for F≥3 and F4 (Table 1).

**Conclusions:** ElastPQ and F-TE showed a good correlation, mainly for low values of liver stiffness, in patients with NAFLD. The optimal cut-off values of ElastPQ are lower than those of F-TE for individual stages of fibrosis. ElastPQ has a better sensitivity and specificity than F-TE in staging advanced liver fibrosis and cirrhosis but this needs to be confirmed in larger cohorts.

<table>
<thead>
<tr>
<th>ElastPQ</th>
<th>F-TE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut-off (kPa)</td>
<td>Sensitivity %</td>
</tr>
<tr>
<td>F2</td>
<td>6.8</td>
</tr>
<tr>
<td>F3</td>
<td>9.3</td>
</tr>
<tr>
<td>F4</td>
<td>11.5</td>
</tr>
</tbody>
</table>
Non-invasive assessment of liver disease

Date & Time: Thursday April 20, 2017 – 8:00-18:00

Normal values of liver stiffness as measured by Transient Elastography: pooled individual participant data meta-analysis from 26 studies and 14,883 participants


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Background and Aims: Transient Elastography (TE) is a noninvasive technique that measures liver stiffness (LSM) as a surrogate for the severity of liver fibrosis. We aim to define, for the first time, LSM ranges in healthy and susceptible cohorts and identify parameters that influence hepatic stiffness through a pooled IPD meta-analysis.

Methods: We identified 2284 abstracts. Two independent reviewers examined all entries, and 127 abstracts were extracted. A total of 26 cohorts were available. We defined susceptibility by the presence of either diabetes, hypertension, or dyslipidemia. Data was divided into four groups (Figure). A one-stage random effects meta-analysis was conducted based on two-level mixed-effects linear regression models after adjusting for steatosis on ultrasound (US), gender, BMI, diabetes, blood pressure and dyslipidemia. We evaluated the robustness of our findings by conducting two-stage meta-analysis.

Results: 14,883 individuals were analyzed. Predictive mean LSM was established for all groups (Fig. 1). In multivariate analysis, steatosis on US, male gender, BMI, diabetes and systolic blood pressure during exam were significantly associated with increase in LSM, while diastolic blood pressure was significantly associated with decrease in LSM (Table). Dyslipidemia, age, and the country of origin did not affect LSM. Sensitivity analyses suggested that the findings across studies were similar (I² = 0%) and the pooled effect sizes were similar to the main analyses.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Coef</th>
<th>SE</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.05</td>
<td>0.01</td>
<td>0.03-0.07</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.15</td>
<td>0.02</td>
<td>0.11-0.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>-0.02</td>
<td>0.01</td>
<td>-0.04-0.00</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* represents the change in LSM associated with the presence of each covariate.

Conclusions: We established a cutoff for LSM <5 kPa to be the normal limit in non-obese and non-susceptible people. We demonstrate that steatosis on US, in otherwise normal subjects increases LSM. In addition, gender and certain metabolic characteristics significantly influence LSM. Blood pressure at time exam is a dynamic factor that also affects it. These parameters should be accounted for when interpreting any transient elastography test result.
Since a recent liver biopsy was not available for most patients, TE was used as a surrogate of histological fibrosis, adopting the cutoffs validated in PBC (7.1, 10.7 and 16.9 kPa for fibrosis stages ≥F1, ≥F2, ≥F3, and = F4, respectively). AUROC curves were obtained in order to define optimal cutoffs for pSWE.

Results: Three (6%) male, mean age 57 (± 13) years, 38 (81%) AMA+ve, 3 (6%) autoimmune-overlap, 9 (18%) with signs of portal hypertension (PH). TE and pSWE correlated significantly (p < 0.0001). LS obtained with both the techniques correlated with radiological evidence of cirrhosis, PH, inflammation, cholestasis, APRI, FIB-4, Fibroindex, GUCI and King’s score (p < 0.0001), Lok index (p < 0.01) but not with AST/ALT and MELD score. AUROCs (95% CI) for pSWE were 0.91 (0.80 – 1.0), 0.91 (0.80 – 1.0), 0.97 (0.92 – 1) for fibrosis stage ≥1, ≥2, ≥3, respectively. Optimal cutoff values were 6.5 (90% sensitivity, 88% specificity), 8.8 (93% sensitivity, 93% specificity), 13.5 (100% sensitivity, 97% specificity) for mild, moderate and severe fibrosis/cirrhosis, respectively.

Conclusions: In our cohort of PBC patients, pSWE strongly correlated with TE and the currently used scores of liver fibrosis. These preliminary data suggest that pSWE is an accurate non-invasive tool for staging liver stiffness in PBC, showing an optimal sensitivity and specificity in detecting significant fibrosis with a cutoff of 13.5 kPa.

Poster 22 (THU-497)
Non-invasive assessment of liver disease
Date & Time: Thursday April 20, 2017 – 8h00-18h00

Diagnostic accuracy of magnetic resonance elastography with liver fibrosis assessment in chronic viral hepatitis patients
Hana Park, Yun Bin Lee, Joo Ho Lee, Mi Na Kim, Young Eun Chon, Yeon Jung Ha, Seong Gyuhwang, Kyu Sung Rim
Internal Medicine, CHA Bundang Medical Center, CHA University, Gastroenterology, CHA Bundang Medical Center, CHA University, Seongnam-si, Korea, South

Background and Aims: Magnetic resonance elastography (MRE) and Transient Elastography (TE) are emerging noninvasive methods as alternatives to liver biopsy. The diagnostic accuracy of TE was reported as reliable for cirrhosis, but controversial for significant fibrosis. The aim of this study was to determine the clinical performances of MRE for assessment of liver fibrosis in patients with chronic viral hepatitis.

Methods: One hundred and three patients with chronic viral hepatitis (HBV 78, HCV 25) underwent liver biopsy at CHA Bundang Medical Center in Korea between May 2012 and January 2015. We evaluated MRE and TE in comparison with the Metavir scoring system for assessing the severity of liver fibrosis. Liver stiffness measured by MRE showed reliable correlation with the liver fibrosis stage as confirmed by liver biopsy (r = 0.729, p < 0.001). The diagnostic accuracy was assessed by analysis of the area under the receiver operator characteristics curve (AUROC).

Results: The diagnostic performance of MRE was better (The AUROC of MRE, 0.88 for F1, 0.88 for F2, 0.89 for F3 and 0.93 for F4) than that of TE (The AUROC of MRE, 0.80 for F1, 0.83 for F2, 0.86 for F3 and 0.90 for F4). In contrast with TE, MRE could distinguish significant fibrosis from mild fibrosis. A cut-off value of > 4.23 kPa discriminates significant fibrosis from mild fibrosis with sensitivity of 80%, specificity of 81% (p < 0.001).

Conclusions: MRE is a reliable noninvasive method for identifying significant fibrosis and cirrhosis in patient with chronic viral hepatitis. It has better diagnostic performance than TE for the diagnosis of significant fibrosis and cirrhosis.
Poster 24 (FRI-016)
Cirrhosis and its complications: Clinical aspects
Date & Time: Friday April 21, 2017 – 8h00-18h00

Performance of FibroScan® to detect large esophageal varices in chronic liver diseases is improved by a novel spleen-dedicated examination
Horia Stefanescu1, Paul Cales2, Mirella Fraquelli3, Nathalie Ganne-Carrie4, Matteo Rosselli5, Victor de Ledinghen6, Davide Festi7
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2) Hepato-Gastroenterology Department, University Hospital, Angers, France
3) Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy
4) Hepato-Gastroenterology Department, APHP Hôpital Jean Verdier, Université Paris 13, Inserm UMR 1162, Bondy, France
5) University College of London, Institute for liver and Digestive Health, Royal Free Hospital, UK
6) Hepato-Gastroenterology Department, Haut Leveque Hospital, Pessac, France
7) Department of Medical and Surgical Sciences, University of Bologna, Italy

Background and Aims: Esophageal varices (EV) represent one of the most severe complications of cirrhosis with a prevalence of 50 to 60% among cirrhotic patients. International guidelines therefore recommend that all cirrhotic patients should be screened for the presence of EV. The main objective of this study was to introduce a new spleen-dedicated FibroScan® examination and to compare its performances with those of the standard FibroScan® and other biomarkers to detect significant EV (SEV) (grade 2 and 3).

Methods: We studied 199 patients with chronic liver diseases due to HCV, HBV or alcohol. Liver stiffness (LS) and spleen stiffness (SS) were assessed using Vibration Controlled Transient Elastography (FibroScan®, Echosens Paris, France). SS was assessed 1) using acquisition settings dedicated to the spleen and especially designed by Echosens for this study 2) using a standard commercial FibroScan®. The results of these two SS measurements are respectively noted SS-New and SS-Ref. The 199 patients underwent upper GI-endoscopy for assessment of EV grade within 3 months before SS measurement. Four subgroups of patients were studied: i) Subgroup 1: 162 patients with at least 8 valid SS-New and SS-Ref (20% SEV); ii) Subgroup 2: 87 patients with at least 8 valid SS-New and HVPG performed within 3 months of SS-New (32% SEV); iii) Subgroup 3: 160 patients with at least 8 valid SS-New and valid LS according to Boursier criteria (18% SEV) and iv) Subgroup 4: 140 patients with at least 8 valid SS-New and Lok score assessment (23% SEV).

Results: In subgroup 1, better performance was obtained for the detection of SEV with SS-New (AUC=0.78) than with SS-Ref (AUC=0.71) (Delong test, p=0.05). In subgroup 2, a significant correlation was found between SS-New and HVPG (Spearman ρ = 0.59, p<0.001). AUC for SEV was higher for SS-New (0.83) than for HVPG (0.77) but not significantly different (Delong test). A non-inferiority test showed that SS-New was not inferior to HVPG (p < 0.05). In subgroup 3, SS-New obtained the best performance for SEV (AUC=0.80) and was significantly better than LS (AUC = 0.60) (Delong test, p<0.001). In subgroup 4, Lok score and SS-New both obtained AUCs of 0.72 for predicting SEV (Delong test not significant).

Conclusions: This study suggests that the novel spleen-dedicated FibroScan® examination achieves better performances than the standard FibroScan® for the detection of SEV. This new examination seems to be promising to replace HVPG measurement with at least the same performances.

Poster 25 (FRI-146)
Viral hepatitis: Hepatitis A, B, D, E - Clinical (except therapy)
Date & Time: Friday April 21, 2017 – 8h00-18h00

Liver transient elastography (Fibroscan®): performance for the absolute mortality and clinical disease progression risk evaluation in chronic hepatitis C
Fatima Serejo1, Clídenia Baldaia2, Marianna Vasconcelos3, Joana Freitas2, JoséVelosa1
1) Gastroenterology, Hospital de Santa Maria, 2) Genetics and Endocrinology, Lisbon Medical School, Lisbon, Portugal

Background and Aims: Liver fibrosis is an established surrogate marker for mortality. Scores for mortality and disease progression were previously described.

Aims: To analyze the performance of hepatic Transient Elastography (TE) for the evaluation of the risk mortality and disease progression in HCV mono infected patients (pts).

Methods: Retrospective analysis of 340 HCV pts, 192 males, G1-69.8%, G3-19.3%, G4-11.9%. All patients performed TE (Fibroscan®): Cutoff values for fibrosis were 5.43 kPa for F2 (PPV 0.96, NPV 0.25); 8.18 kPa for F2 (PPV 0.82, NPV 0.97); 12.0 kPa for F4 (PPV 0.93, NPV 0.73). TE values were also adjusted using the formula: (1 / [1+e (- 3.46+0.34xTE+0.006xAST+0.008xALT-0.538x+0.155xthriglicerides+0.0319xplatelets)]). Absolute risk score mortality (Rm) and disease progression (Rc) were calculated and stratified according to Van der Meer (Low Rm <87.1 and Rc < -91.9, Intermediate Rm 87.1-221.2 and Rc 91.9-61, High Rm >221.2 and Rc >61 (Gut. 2014, May 9). Risk scores were related with TE using the cut-offs: 8 kPa for F2 3 and 12 kPa for F4. Statistical analysis performed by SPSS23 (significance p<=0.05).

Results: Rm-Low 52.9%; Intermediate 33.2%; High 14.1%. Rc -Low 77%, Intermediate 1% and High 22%. Patients with intermediate/high Rm and TE ≤8 kPa were 34.6 % vs > 8 kPa 66.7%. Patients intermediate/high Rc and TE ≤8 kPa were 12.5% vs > 8 kPa in 40.2%. Table shows Rm and Rc for patients with advance fibrosis and with cirrhosis defined by adjusted and non-adjusted TE values. Non-significant differences between adjusted and non-adjusted were observed.

Conclusions: Even in the absence of cirrhosis, HCV patients with liver stiffness higher than 8 kPa predicts a higher absolute mortality rate and disease progression risk. These particular patients show a poor clinical outcome, so they need close monitoring and treatment decision should not be delayed.
**Background and Aims:** Despite the benefit of lifestyle changes, there is no standard treatment for Fibrotic nonalcoholic steatohepatitis (NASH). However, the concept of reversibility of liver fibrosis and cirrhosis with various natural biologically active compounds and antioxidant micro-nutrients is not new. Viusid (Catalysis Laboratory, Madrid, Spain) is a nutritional supplement that contains such molecules (activated glycyrrhizic acid, ascorbic acid, folic acid and zinc) with powerful antioxidant, immunomodulatory and anti-fibrotic activities. Evidences showed that Viusid inhibits oxidative stress, lipid per-oxidation (MDA) and several pro-inflammatory cytokines (TNF-alpha, IL-1 & IL-6) involved in fibrogenesis process. Moreover, previous human trials demonstrated the antifibrotic benefits of Viusid against different types of hepatitis including NASH and chronic hepatitis C. The aim of this study was to compare effectiveness of Viusid and vitamin E in reducing steatosis and liver fibrosis in patients with fibrotic NASH.

**Methods:** 52 patients diagnosed with nondiabetic and noncirrhotic NASH on liver fibroscan were divided into 2 groups randomly and given Viusid 3 sachets daily to 25 patients or vitamin E 800 IU daily to 27 patients along with a hypocaloric diet and exercise for 3 months.

**Results:** The mean age was 46.2 ± 8.5 years old (range 28-62); 34 men and 18 women. At baseline, there was no significant difference between two groups with respect to mean steatosis, fibrosis and ALT levels. After 3 months treatment with Viusid, as compared with vitamin E, was associated with a significant reduction of both mean steatosis score [from S2-S3 (CAP: 286 ± 16.3 dB/m) to S0-S1 (CAP: 208 ± 18.5 dB/m) in Viusid group vs. from S2-S3 (CAP: 278 ± 14.4 dB/m) to S1-S2 (CAP: 253 ± 12.1 dB/m) in vitamin E group (p <0.00001)] and fibrosis score [from F1-F2 (E: 6.8 ± 0.5 kPa) to F0-F1 (E: 5.1 ± 0.7 kPa) in Viusid group vs. from F1-F2 (E: 6.9 ± 0.5 kPa) to F1-F2 (E: 6.5 ± 0.4 kPa) in vitamin E group (p <0.00001)]. Similarly, the mean alanine transaminase (ALT) levels also significantly decreased from 114 ± 25.9 U/L to 43 ± 9.1 U/L in Viusid group compared to from 105 ± 15.5 U/L to 55 ± 11.7 U/L in vitamin E group (p = 0.00007).

**Conclusions:** Viusid was superior to vitamin E in reducing steatosis & fibrosis score in nondiabetic and noncirrhotic NASH patients. However, further large scale trial is needed to better assess the value of Viusid for fibrotic NASH management.

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**Poster 27 (FRI-342)**

**Fatty liver disease: Clinical aspects**

Date & Time: Friday April 21, 2017 – 8h00-18h00

The diagnostic accuracy of Vibration ControlledTransient Elastography for cirrhosis in subjects with nonalcoholic fatty liver disease

Mohammad S. Siddiqui, Raj Vuppulanchi, Mark Van Natta, Danielle Brandman, James T. Tonascia, Naga Chalasani, Michael S. Middleton, Arun J. Sanyal and NASH-CRN

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**Background and Aims:** There is a major unmet need to develop non-invasive methods to identify development of cirrhosis in subjects with nonalcoholic steatohepatitis (NASH) that can be deployed at point of care. Vibration-Controlled Transient Elastography (VCTE) measures liver stiffness which is related to fibrosis. While VCTE has been approved as a measure of liver stiffness, it has not yet been extensively validated for the diagnosis of cirrhosis. AIM: To evaluate the diagnostic accuracy of VCTE for cirrhosis in patients with nonalcoholic fatty liver disease (NAFLD).

**Methods:** Adult patients with NAFLD who had a VCTE within 1 year of a liver biopsy or who had a prior biopsy demonstrating cirrhosis was available for review were enrolled prospectively. VCTE was performed using a standardized protocol across 8 clinical centers. The liver histology was read by the Pathology committee of the NASH CRN using predefined diagnostic criteria. The sensitivity, specificity and predictive values of VCTE for cirrhosis were measured.

**Results:** A total of 282 patients with NAFLD (# cirrhosis = 61) who met inclusion criteria who had a successful VCTE were enrolled. The subjects were mainly female (69%) and Caucasian (81%) with a mean age of 53 years. The mean (S.D.) liver enzymes were: AST: 48 (34), ALT: 61 (43), Alk phos: 83(30) U/L. The mean total bilirubin was 0.7 (0.6) mg/dl and INR was 1.05 (0.17). The median BMI was 34(6) kg/m². The median time from liver biopsy was 53 days. 60% of subjects had definite NASH and mean NAS was 4.3 (1.8). The cross-validated AUROC for assessment of fibrosis with specificity fixed at 90% were: stage 0 vs. 1-4: 0.74, stage 0-1 vs. 2-4: 0.81, stage 0-2 vs. 3-4: 0.83, Stage 0-3 vs. 4: 0.85 (95% CI 0.79-0.91). When only those who had a liver biopsy within the previous year were included the AUROC (threshold liver stiffness: 15.5 kPa) for differentiating stage 4 vs 0-3 with specificity fixed at 0.9 was 0.93 (95% CI: 0.86-0.99). The sensitivity was 0.76 and yielded a positive and negative predictive value of 0.37 and 0.98 respectively.

**Conclusions:** Using rigorous standards of performance and assessment (specificity fixed at 0.9), VCTE was able to identify those with cirrhosis with AUROC from 0.85-0.93. 90-98% of patients without cirrhosis had a liver stiffness measurement below 15.5 kPa. VCTE can therefore be used to exclude cirrhosis with high accuracy. There is now a need for additional algorithms to be developed to enhance the positive predictive value of VCTE for the diagnosis of cirrhosis.

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**Poster 26 (FRI-341)**

**Fatty liver disease: Clinical aspects**

Date & Time: Friday April 21, 2017 – 8h00-18h00

An open-label randomized clinical study to compare the effects of a nutritional supplement versus vitamin E on fibroscan score in nonalcoholic steatohepatitis patients

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**Background and Aims:** Despite the benefit of lifestyle changes, there is no standard treatment for Fibrotic nonalcoholic steatohepatitis (NASH). However, the concept of reversibility of liver fibrosis and cirrhosis with various natural biologically active compounds and antioxidant micro-nutrients is not new. Viusid (Catalysis Laboratory, Madrid, Spain) is a nutritional supplement that contains such molecules (activated glycyrrhizic acid, ascorbic acid, folic acid and zinc) with powerful antioxidant, immunomodulatory and anti-fibrotic activities. Evidences showed that Viusid inhibits oxidative stress, lipid per-oxidation (MDA) and several pro-inflammatory cytokines (TNF-alpha, IL-1 & IL-6) involved in fibrogenesis process. Moreover, previous human trials demonstrated the antifibrotic benefits of Viusid against different types of hepatitis including NASH and chronic hepatitis C. The aim of this study was to compare effectiveness of Viusid and vitamin E in reducing steatosis and liver fibrosis in patients with fibrotic NASH.

**Methods:** 52 patients diagnosed with nondiabetic and noncirrhotic NASH on liver fibroscan were divided into 2 groups randomly and given Viusid 3 sachets daily to 25 patients or vitamin E 800 IU daily to 27 patients along with a hypocaloric diet and exercise for 3 months.

**Results:** The mean age was 46.2 ± 8.5 years old (range 28-62); 34 men and 18 women. At baseline, there was no significant difference between two groups with respect to mean steatosis, fibrosis and ALT levels. After 3 months treatment with Viusid, as compared with vitamin E, was associated with a significant reduction of both mean steatosis score [from S2-S3 (CAP: 286 ± 16.3 dB/m) to S0-S1 (CAP: 208 ± 18.5 dB/m) in Viusid group vs. from S2-S3 (CAP: 278 ± 14.4 dB/m) to S1-S2 (CAP: 253 ± 12.1 dB/m) in vitamin E group (p <0.00001)] and fibrosis score [from F1-F2 (E: 6.8 ± 0.5 kPa) to F0-F1 (E: 5.1 ± 0.7 kPa) in Viusid group vs. from F1-F2 (E: 6.9 ± 0.5 kPa) to F1-F2 (E: 6.5 ± 0.4 kPa) in vitamin E group (p <0.00001)]. Similarly, the mean alanine transaminase (ALT) levels also significantly decreased from 114 ± 25.9 U/L to 43 ± 9.1 U/L in Viusid group compared to from 105 ± 15.5 U/L to 55 ± 11.7 U/L in vitamin E group (p = 0.00007).

**Conclusions:** Viusid was superior to vitamin E in reducing steatosis & fibrosis score in nondiabetic and noncirrhotic NASH patients. However, further large scale trial is needed to better assess the value of Viusid for fibrotic NASH management.
Poster 28 (FRI-343)
Fatty liver disease: Clinical aspects
Date & Time: Friday April 21, 2017 – 8h00-18h00
Effect of a probiotic on fatty liver index and liver stiffness in NAFLD patients: randomized clinical trial
Nazarii Kobylia1, Natalia Bosak1, Tetyana Falalayeveya2, Tetyana Beregova2, Petro Bodnar3

Background and Aims: Probiotics have beneficial effect on nonalcoholic fatty liver disease (NAFLD) in animal models. Despite a large number of animal data, randomized placebo-controlled trials (RCT) in NAFLD are still lacking in humans. We performed a double-blind single center RCT of alive multistrain probiotic vs. placebo in type 2 diabetes patient with NAFLD detected on ultrasonography (US).

Methods: A total of 58 patients met the criteria for inclusion. They were randomly assigned to receive multiprobiotic “Symbiter” (concentrated biomass of 14 probiotic bacteria genera Bifidobacterium, Lactobacillus, Lactococcus, Propionibacterium) or placebo for 8-weeks administered as a sachet formulation in double-blind treatment. The primary main outcomes were the change in fatty liver index (FLI) and liver stiffness (LS) measured by Shear Wave Elastography (SWE). FLI a validated prediction score for hepatic steatosis severity designed Bedogni et al. Secondary outcomes were the changes in transaminases activity, serum lipids and cytokines (TNF-α, IL-1β, IL-6, INF-γ) levels. ANCOVA was used to assess the difference between groups.

Results: In probiotic group FLI significantly decreased from 84.33 ± 2.23 to 78.73 ± 2.58 (p <0.001) and but remained static in the placebo group (82.57 ± 2.45 to 81.6 ± 2.36; p = 0.367). In both interventional groups slight insignificant reduction of LS measured by SWE were detected. Therefore, LS from baseline in probiotic group (7.16 ± 0.2 to 7.66 ± 0.22; p = 0.052) decreased more pronounced as compared to placebo group (7.28 ± 0.22 to 7.14 ± 0.26; p = 0.396). Analysis of secondary outcomes showed that probiotic reduced level of serum aspartate aminotransferase (AST) - 14.8%, p <0.001; gamma-glutamyl transpeptidase (GGT) - 20.4%, p = 0.001; and triglycerides (TG) on 22.5%, p = 0.001. From markers of chronic systemic inflammatory state only TNF-α (14.5 %, p <0.001) and IL-6 (28.1 %, p = 0.001) changes significantly after treatment with probiotics.

Conclusions: Probiotic therapies can reduce liver fat, aminotransferases activity, TG, TNF-α and IL-6 in NAFLD patients. Modulation of the gut microbiota represents a new treatment for NAFLD and should be tested in larger studies.

Poster 29 (FRI-491)
Liver transplantation / surgery: Clinical aspects
Date & Time: Friday April 21, 2017 – 8h00-18h00
Prospective comparison of Coefficient Attenuation Parameter and ultrasound for grading graft steatosis in a large real-life cohort of liver-transplant patients
Christiane Stern1, Claire Francoz2, Audrey Payance1, Pierre Emmanuel Rautot1, Maxime Ronot2, Valerie Paradis3, Pierre Bedossa4, François Durand1, Valérie Vilgrain1, Laurent Castéra1
1) Hepatology department, 2) Radiology department, 3) Pathology department, Hopital Beaujon, Clichy, France

Background and Aims: The Controlled Attenuation Parameter (CAP), a novel non-invasive technique using transient elastography, has shown good accuracy for detecting and grading steatosis in patients with chronic viral hepatitits or NAFLD. However, the accuracy of CAP for grading graft steatosis after liver transplantation (LT) is unknown. The aim of this prospective study was to compare the diagnostic performance of CAP and liver ultrasonography (US) in LT patients, taking liver biopsy (LB) as reference.

Methods: 102 consecutive LT patients undergoing LB, either systematically at 1-year post-LT or because of liver tests abnormalities, were enrolled from January 2014 to May 2016 at our institution. CAP and US measurements were performed the day of LB. Steatosis was graded on LB as: no/minimal steatosis (S0: <10%), mild steatosis (S1: 10-33%), moderate steatosis (S2: 34-66%) and severe steatosis (S3: >66%). Steatosis was graded semi-quantitatively on US, by an expert radiologist, as: absent, mild, moderate and severe. Accuracies of CAP and US for grading S≤1 and S≥2 were evaluated by calculating sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values, as well as the percentage of correctly classified patients.

Results: A total of 91 patients were analyzed (3 were excluded due to LB <10 mm and 8 of the remaining 99 (8%) because of CAP failure). Baseline characteristics were: mean age 53 ± 1 yrs; male 73%; mean BMI 24.6 ± 0.6 kg/m2; LB median size 20 mm. Steatosis grades and fibrosis stages on LB were: S0: 76%, S1 19%, S2 2%, S3 3%; and F0 65%, F1 24%, F2 6%, F3 5%. Median CAP was 220 dB/m (range 100-376). Steatosis was detected on US in 31% of patients (9% classified as S ≥2). Comparisons of performance of US and CAP for grading S≥1 and S≥2 are shown in the table. Overall, 73% of patients were correctly classified with US vs. 53% with CAP for S ≥1 (p = 0.005), whereas 90% of patients were correctly classified with US vs. 83% with CAP for S ≥2 (p = NS). Combining US and CAP did not increase diagnostic performance.

Conclusions: In this large cohort of liver-transplant patients, CAP and liver US have acceptable diagnostic performance, better at ruling out than ruling in graft steatosis. US in expert hands performed better than CAP for detecting any grade of steatosis.

Poster 30 (SAT-300)
Fatty liver disease: Clinical aspects
Date & Time: Saturday April 22, 2017 – 8h00-18h00
The severity of steatosis does not influence liver stiffness measurements in patients with non-alcoholic fatty liver disease
Roberta Forlano1,2, James Maurice1,2, Benjamin Mullish1, Napat Angkathunyakul3, Eliezer Goldin1,2, Gaetano Serviddio4, Michael Yee4, Nikolas Giannakeas5, Alexandros T. Tzallas5, Markos G. Tsipouras6, Shahid Khan1,2, Simon Taylor-Robinson1, Robert D Goldin2,3, Mark Thursz2, Pinelopi Manousou1
1) Department of Hepatology, Imperial College, London, United Kingdom 2) Centro Universitario per Ricerca e la cura delle Epatopatie, Università degli Studi di Foggia, Foggia, Italy 3) Department for Cellular Pathology 4) Department of Endocrinology, Imperial College, London, United Kingdom
Background and Aims: Non-invasive characterization of hepatic steatosis and fibrosis based on Fibroscan elastography and controlled attenuation parameter (CAP) is used widely for the diagnosis and follow up of patients with NAFLD. However, to date, the validation of non invasive markers is based in semi- quantitative scoring of steatosis and fibrosis in liver biopsies. The aim of this study was to assess whether the degree of steatosis as determined by CAP and the degree of fibrosis by liver stiffness measurements correlate with the fat and collagen quantitation respectively in liver biopsies of patients with NAFLD.

Methods: 80 consecutive patients with biopsy confirmed NAFLD and transient elastography with CAP score within 3 months of the biopsy date were prospectively evaluated. Twenty liver biopsies with steatosis<5% were used as controls. Biopsies were digitized at 2x magnification and then analysed by our automated software, which processes the images in two stages: Machine learning clustering and Morphological Image Processing. Fat and fibrosis quantitation were expressed as percentages of the relative areas of fat and collagen respectively and of tissue.

Results: Correlation between CAP score and fat% was statistically significant (p =0.002, Rho=0.45) only in identifying fat but not distinguishing between stages of steatosis. Regression analysis revealed an R2=0.206 (figure 1a). The AUROC for identifying fat>5% was 0.82(p=0.001, 95%CI=0.71-0.92) with the best cutoff at 250dB/m (95% sens, 60% specificity). Correlation between liver stiffness and fibrosis quantitation (%) was statistically significant (p <0.001, Rho=0.802) with an R2 of 0.679 (figure 1b).

When our cohort was split to those with fat% ≤10% and >10% in the liver biopsies there was no difference between liver stiffness and fibrosis quantitation in Pearson’s correlation: Rho=0.883 and Rho=0.843 respectively (figure 2).

Conclusions: Liver stiffness is a reliable noninvasive tool for estimating the severity of fibrosis in NAFLD. The presence of severe steatosis evaluated by fat quantitation in liver biopsies did not influence liver stiffness measurements.

Poster 31 (SAT-467)

Non-invasive assessment of liver disease

Prevalence of fatty liver and fibrosis in patients with type 2 diabetes mellitus and previously undetected liver disease as assessed by transient elastography and ultrasound

Ivica Grgurevic1, Tomislav Bokun1, Sanda Mustapić2, Vladimir Matic3, Dario Rahelic2, Tomas Matic2, Nermin Salkić3, Velimir Bozikov2, Marko Banić2, Milan Kujundžić1
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3) Department of gastroenterology and hepatology, University hospital Tuzla, Bosnia and Herzegovina

Background and Aims: To assess the prevalence of fatty liver and significant liver fibrosis in patients with type 2 diabetes mellitus type (T2DM) and previously unknown liver disease.

Methods: Patients with T2DM from outpatient diabetes clinic without known liver disease were prospectively included in the study. All patients underwent liver stiffness (LSM in kPa) and controlled attenuation parameter (CAP in dB/m) measurements by transient elastography (FibroScan® 502 Touch, Echosens, FR) in order to quantify severity of liver fibrosis (LSM<7.9 kPa for F<2 and >9.6kPa for F≥3; Wong et al. Hepatology 2010) and steatosis respectively. Steatosis grade was semiquantitatively (S0-S3) assessed by conventional ultrasound (US) as well. Anthropometric and relevant biochemical parameters were recorded, and FIB-4 score was calculated for each patient.

Results: Successful TE measurements were obtained in 237/262 patients (complete failure in 10/262 (3.8%), unreliable in 15/262 (5.7%) ) comprising the cohort for subsequent analysis: average age 63.7±11.9 years, 122 (51%) females, BMI 30.5±5.9 kg/m², HbA1c 62.9±17.4 mmol/mol, ALT 29.7±30.3, FIB-4 =1.37±0.8, LSM 7.3±7.4 kPa and CAP 299±62.8 dB/m. Of the included 237 patients 81% had BMI>25 kg/m², 76.4% had liver steatosis by US and 80.6% by CAP (S≥1, CAP≥238 dB/m), advanced fibrosis (F≥3, TE≥9.6 kPa) was detected in 13.9%, whereas in 78.9% patients LSM was <F2 (<7.9 kPa). Patients within the higher BMI category (>30 vs 25-30 vs <25 kg/m²) had significantly worse liver steatosis (by US and CAP: p<0.001 for both), whereas no difference existed in terms of age, gender, LSM, FIB4 and HbA1c values. Patients within higher steatosis grade as defined by US had significantly higher LSM (5.9 kPa for S0, 6.3 kPa for S1, 7.5 kPa for S2, and 8.4 kPa for S3).
Elastogram quality assessment score in vibration controlled transient elastography: diagnostic performance compared to digital morphometric analysis of liver biopsy


Background and Aims: Vibration Controlled Transient Elastography (VCTE) is one of the most valued non-invasive test modalities for liver fibrosis staging in chronic hepatitis C (CHC). However, results are internally validated solely on the basis of variability and success rate and lack reproducible quality indicators. We propose to analyse the graphic representation of shear wave propagation in VCTE – the elastogram – morphologic characteristics in comparison with morphometric results of liver biopsy (LB), thus eliminating observer variability bias.

Methods: Individual VCTE elastograms from CHC patients were analysed and classified according to two morphologic quality criteria: extension of wave propagation in liver tissue (represented by the length of the graphic representation) and shear wave dispersal (represented by the level of parallelism displayed in the elastogram). Then, a score based on these criteria stratified the individual elastogram in 3 classes: class I representing greatest technical quality and class III representing least technical quality. Liver stiffness results of each measurement were compared with quantified collagen contents in LB fragments determined by morphometric digital imaging analysis.

Results: 2,154 individual VCTE liver stiffness measurements were studied (corresponding to 205 patients, with median age of 51 years, 59% male and 43 UI/ml median ALT). Digital morphometric analysis of LB fragments yielded total area of fibrosis consistent with significant fibrosis (SF) in 62% of samples and advanced fibrosis (AF) in 27%. Elastogram quality analysis resulted in 894 class I measurements (41.5%), 780 class II (36.2%) and 480 (22.3%) class III. Compared to digital morphometric histology results, AUROC for SF according to class (I, II and III) was 0.931, 0.889 and 0.814, respectively. For AF, AUROC were 0.963, 0.915 and 0.817 for classes I, II and III, respectively. Spearman correlation testing for all classes and levels of fibrosis demonstrated significant independent association (r = 0.71, p <0.01).

Conclusions: Our study is the first to propose measurable and reproducible quality criteria for interpretation of VCTE and to validate them against objective assessment of LB through digital morphometric imaging analysis. We concluded that performance indicators for VCTE are significantly influenced by quality assessment of individual measurements and considering these criteria in clinical practice may improve accuracy.
Background and Aims: Previous studies demonstrated a close correlation between transient elastography (TE) and liver biopsy, especially in patients with chronic viral hepatitis. However, biopsy restricts the analysis to only a minimal part of the liver parenchyma. Here we investigated the association between TE, serum markers of portal hypertension (sCD163, VCAM-1) and histology of explanted livers in patients with primary sclerosing cholangitis (PSC).

Methods: Prospectively we recruited 30 patients with PSC (12 women, age 35.6 ± 12.2 years) who were transplanted at our centre. TE (Fibroscan) examination and blood sampling was performed during evaluation for liver transplantation (LT); a second blood sample was taken at the time of LT. Explanted livers were assessed according to the recently proposed, extended Laennec staging system, which comprises seven stages of liver fibrosis and measures mean thickness of fibrotic septa (Kim/Park J Hepatol 2012). Liver scarring was also quantified using measurement of collagen contents. Serum markers of portal hypertensions (sCD163 and VCAM1) were measured using ELISA.

Results: In total, 54% of patients presented with cirrhosis on histology. The mean septum thickness was 267.2 ± 137.4 µm and the thickest septum diameter was 458.8 ± 237.0 µm. The mean liver stiffness was 21.4 ± 18.2 kPa, and >50% patients presented with at least 15 kPa. TE showed significant correlations with the stages of fibrosis in explanted livers as assessed with Laennec (and METAVIR) scores (p = 0.001 and p = 0.006, respectively). TE correlated significantly with mean septa diameter (p = 0.022) and with the diameter of thickest septa (p = 0.045) as well as with collagen contents (p<0.001) in explanted livers. Overall, patients with cirrhosis at histology had significantly (p = 0.002) increased mean liver stiffness as compared to non-cirrhotic livers (28.56 ± 19.44 vs. 9.00 ± 3.81 kPa). Finally, liver stiffness correlated with serum markers of portal hypertension, i.e. CD163 and VCAM1, assessed both at the time of inclusion (p = 0.002 and p = 0.028, respectively) and at the time of LT (p = 0.004 and p = 0.031, respectively).

Conclusions: We demonstrate for the first time that in patients with PSC transient elastography correlates with liver fibrosis quantified in explanted livers using the Laennec staging system. Moreover, it correlates with serum surrogate markers of portal hypertension. Hence, we postulate that elastography is a reliable tool for non-invasive monitoring of PSC patients awaiting liver transplantation.

Poster 34 (SAT-477)
Non-invasive assessment of liver disease
Date & Time: Saturday April 22, 2017 – 8h00-18h00
Effect of meal ingestion on liver stiffness and controlled attenuation parameter
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Background and Aims: Despite the increasing use of noninvasive methods for the assessment of liver fibrosis and steatosis, it is not yet clear the effect of fasting and food intake on these parameters. Our aims were to evaluate the effect of food intake on LS (measured by transient elastography) and CAP in patients with different degrees of liver disease and healthy volunteers, and secondarily, to assess possible anthropometric, clinical and biological parameters associated with variations of LS and CAP.

Methods: Prospective single-center study including patients with liver disease and healthy volunteers. LS and CAP were evaluated using FibroScan® (Echosens, Paris, France) before (fasting ≥8h) and 30 minutes after intake of a standardized breakfast. Anthropometry, body composition and the following clinical and biological parameters were determined in all cases: body mass index (BMI), mass of body fat, lean body mass, and percent of body fat, AST, ALT, GGT, alkaline phosphatase, total bilirubin, platelet count, INR, albumin, glucose, and creatinine.

Results: Three (4%) patients with inconclusive LS determination were excluded. Fifty-nine (72%) patients with liver disease (13 (22%) with cirrhosis) and 23 (28%) healthy volunteers were included. LS significantly increased 30 min after food intake (pre-meal 6.1 (IQR: 4.7-9.8) vs. after-meal 6.8 kPa (IQR: 5.5-10.6); p < 0.001). This difference was only significant in patients with chronic liver disease (p = 0.02) and not with healthy volunteers (p = 0.106). An intraindividual analysis showed that 4 (17%) patients with initial LS of 6-10 kPa and 11 (28%) patients with normal initial LS (<6 kPa) had an after-meal LS of >10 kPa and >6 kPa, respectively. By other hand, 2 (11%) patients with initial LS > 10 kPa and 2 (9%) patients with initial LS of 6-10 kPa had an after-meal LS of <10 kPa and <6 kPa, respectively. CAP values did not changed significantly after food intake. Gender, BMI, mass of body fat, lean body mass, and percent of body fat were not related with significant variations of LS and CAP values after meal intake.

Conclusions: Significant variations of LS were observed after ingestion of a standard meal, which may have consequences for patient management. CAP values were not significantly affected by food intake.

Poster 35 (SAT-478)
Non-invasive assessment of liver disease
Date & Time: Saturday April 22, 2017 – 8h00-18h00
Dynamics of liver stiffness and serum IP10 levels among patients with chronic hepatitis C who achieved SVR with DAA treatment
Cristina Rigamonti, Margherita Tran Minh, Rosalba Minisini, Giulia Guaschino, Mario Pirisi
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Background and Aims: It has been reported that liver stiffness measured by transient elastography (TE, FibroScan®) decreases after direct antiviral agents (DAA) treatment in patients with chronic hepatitis C (HCV); whether this reduction reflects mainly reduced inflammation in the liver has not been established. Interferon-gamma inducible protein 10 (IP-10) is reduced in HCV infected livers and correlates with hepatic inflammation. We aimed to verify if changes in liver stiffness before and after DAA treatment are paralleled by changes in IP10.

Methods: This retrospective study included 80 HCV patients (79% cirrhotics) who achieved sustained virological response (SVR) after DAA treatment (start February 2015 - February 2016) and underwent paired TE and IP10 measurements before as well as 24 weeks after treatment with DAA. The predefined limits to consider significant a change were: TE value ≥30% increase/decrease from baseline, IP10 value ≥20% increase/decrease from baseline. IP-10 was measured in serum samples using the enzyme-linked immunosorbent assay (normal value ≤100 pg/ml). Statistical analysis was performed using SPSS 17.
Results: Six patients were excluded for invalid TE after treatment, thus 74 patients were studied (49 males, median age 62 years, 65% HCV genotype 1, 52% with endoscopic signs of portal hypertension at baseline). Before DAA treatment, 72% with TE >13 kPa, median TE 19.1 kPa (range 8.8–75 kPa), 77% had PI0 >100/g/ml, median PI0 216 g/ml (44–1194 g/ml), platelet count 138000/mcl (36000–553000/mcl). After DAA treatment, 42% with TE >13 kPa, median TE 10.9 kPa (range 4.8–75 kPa), 38% with PI0 >100/g/ml, median PI0 74 g/ml (30–315 pg/ml), platelet count 161000/mcl (33000–401000/mcl). TE and PI0 values decreased significantly after DAA treatment (p=0.0001), median change was -39% (range -79 – +32%) for TE and -62% (range -95 – +119%) for PI0. TE decreased in 62%, increased in 1% and was stable in 37% of patients; PI0 decreased in 78%, increased in 6% and was stable in 16% of patients; 50% of patients showed decrease of both TE and PI0. Delta % change of TE and PI0 were significantly correlated (r=0.40, p=0.005). Platelet count did not significantly increase after treatment (median platelet count change +14%, range -35 – +153%).

Conclusions: Decrease of TE after DAA treatment was paralleled by a decrease in serum PI0 levels, suggesting that improvement of liver inflammation may be a major determinant of TE reduction.

Poster 36 (SAT-482)
Non-invasive assessment of liver disease
Date & Time: Saturday April 22, 2017 – 8h00-18h00
Prospective comparison of shear-wave elastography, CAP and conventional ultrasound for non-invasive detection and grading of steatosis
Maxime Ronot1, Pierre-Emmanuel Rautou2, Marco Dioguardi Burgio1, Audrey Payencé1, Pierre Bedossa3, Valérie Paradis1, Claire Francoz2, Ouadia Nekachtali2, François Durand2, Valérie Vilgrain1, Laurent Castera2
1) Radiology 2) Hepatology 3) Pathology, Beaumont University Hospital, Clichy, France

Background and Aims: Although ultrasound (US) remains the most widely used technique for steatosis evaluation, novel elastography techniques including controlled attenuation parameter (CAP) (FibroScan), and more recently quantification of ultrasound beam attenuation (UBA), or speed of sound (SOS) using shear-wave elastography (Aixplorer) have been proposed. We performed a prospective study to compare the performance of these techniques for diagnosing and grading steatosis, taking liver biopsy (LB) as a reference.

Methods: 296 consecutive adults (62% male, mean 50±14 yrs) underwent LB (median 15mm; 9% ≤10 mm). Data of US performed before referral (routine-US, n = 267), US performed just before liver biopsy (expert-US; n=288), CAP (n = 256), UBA (n = 133), and SOS (n = 155) performed at the time of LB were prospectively collected. Finally, 122 patients (67% male, mean 50 ± 14 yrs) underwent all techniques. Steatosis was graded on LB as S0 (<10%), S1 (10-33%), S2 (33-66%) and S3 (>66%).

Results: Most frequent indications for LB were HBV (n = 39), HCV (n = 28), NAFLD (n = 32), post liver transplantation without (n = 30) or with (n = 80) normal liver tests. Steatosis was grade 0, 1, 2 and 3 in 189 (64%), 65 (22%), 28 (9%), and 14 (5%) patients. Areas under the ROC curves (AUROCs) for detection of different grades of steatosis are shown in the Table. For detection of any steatosis, no difference was observed between the techniques. For the identification of S2 or S3, expert-US and CAP showed the highest performance (p <0.01). For detection of S3, CAP outperformed other techniques with 92% of correctly classified. Combining expert-US and CAP (n = 249) correctly classified 191 (77%), 226 (91%) and 242 (97%) for the detection of any grade, S2, and S3 when both parameters were positive. Similar results were observed in the 122 patients undergoing all techniques.

Table 1: AUROC results for the different techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>AUROC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert-US</td>
<td>0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAP</td>
<td>0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>UBA</td>
<td>0.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SOS</td>
<td>0.76</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

US report: a. steatosis vs. no steatosis or not mentioned, b. none vs. mild-severe, c. none-mild vs. moderate-severe, d. none-moderate vs. severe.

Conclusions: Overall, the ability of the novel SWE derived techniques UBA and SOS to detect steatosis is limited and not better than conventional US performed by an expert radiologist. For severe steatosis, CAP performs better than other techniques. Combining conventional US with CAP improves the proportion of well-classified patients.

Poster 37 (SAT-486)
Non-invasive assessment of liver disease
Date & Time: Saturday April 22, 2017 – 8h00-18h00
Attenuation coefficient measurement as novel real time ultrasound alternative to CAP (Fibroscan)
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Background and Aims: The presence of fat droplets in the hepatocytes (micro- or macrovesicular hepatic steatosis) under condition of chronic diffuse liver disease (CDLD) increases the attenuation of ultrasound (US). A group of Ukrainian scientists proposed an original algorithm for real-time US attenuation measurement (attenuation coefficient measurement – ACM – patent UA №2014 111234).

Methods: From total of 3274 patients who underwent to comprehensive abdominal US (2015-2016) in our clinic, 949 have been diagnosed with fatty liver according to Hamaguchi criteria. All these patient we provide Attenuation coefficient measurement (ACM) (dB/cm) measurement on SoneusP7 device (Ultrassign, Ukraine), with a 1–6 MHz convex transducer in the right and left lobes. For diagnostic accuracy assessment (used CT as standard) and comparison with CAP measured by Fibroscan (Echosens, France) we included 142 patients for subanalysis. Evaluation of diagnostic accuracy of ACM performed using ROC-analysis.

Results: Depending on the stage of steatosis according to B-mode median, 25 and 75 quartiles for ACM were as follows: control group 1.57 (1.32-1.85); S1 - 1.86 (1.78 - 2.11); S2 - 2.26 (2.20-2.49) and respectively for S3 - 2.7 (2.40-2.82) dB/cm. ACM value increase parallel the hepatic steatosis progression (p <0.001), which was also accompanied with presence of very strong correlation between these parameters (r = 0.814, p <0.001). In patient with NAFLD the association between maximum value of ACM and duration of T2DM and triglycerides (model 1, multiple correlation coefficient = 0.55; R2 = 0.26; p = 0.004) and ALT (model 2, multiple correlation coefficient = 0.55; R2 = 0.25; p = 0.005) were observed. After adjustment by the duration of T2DM the level of triglycerides (r = 0.44, p = 0.012) and activity of ALT (r = 0.44, p = 0.012)
significantly correlated with ACM. The AUROC of ACM for steatosis diagnosis was 0.925 (95% CI 0.877-0.973). The optimal cutoff point was >2.27 dB/cm, with sensitivity, specificity, PPV and NPV respectively 91.5, 77.3, 84.6 and 83.8%. ACM value also significantly correlated with CAP (r = 0.630, p < 0.001).

Conclusions: The ACM as novel real time ultrasound approach can be used for noninvasive hepatic steatosis diagnosis, allows clinicians to follow up disease progression and response to treatment.

**Poster 38 (SAT-487)**

Non-invasive assessment of liver disease

Date & Time: Saturday April 22, 2017 – 8h00-18h00

How to combine blood test and elastography to stage liver fibrosis in chronic hepatitis C?

Paul Cales1, Jérôme Boursier1, Victor de Ledinghen2, Isabelle Hubert1, Frédéric Oberti1

Background and Aims: In chronic hepatitis C, the EASL-ALEH recommends performing transient elastography and a blood test to diagnose significant fibrosis; test concordance confirms diagnosis. Our aim was to validate this rule and evaluate whether combining the blood markers of the blood test and transient elastography (constitutive tests) into a single combined test, as suggested by AASLD-IDSA recommendations, improves accuracy, especially with a new classification metric.

Methods: 1019 patients were included in an exploratory set (HCV, n = 679) or in a validation set (HIV-HCV or HBV, n = 340). Accuracy was mainly evaluated by correct diagnosis rate for severe fibrosis (Metavir F3+F4, primary outcome) by classical test scores (0 to 1) or a fibrosis classification (6 fibrosis class from F0/1 to F4), reflecting Metavir staging, according to a factual method. Accuracy was compared as a function of test concordance.

Results: Score metric; there were no significant difference in accuracy between the blood test (FibroMeter: 75.7%), elastography (Fibroscan: 79.1%) and the combined test (FibroMeterVCTE: 79.4%) (p = 0.066); the score accuracy of each test was significantly (p <0.001) decreased in discordant vs. concordant tests. Classification metric: combined test accuracy (91.7%) was significantly (p <0.001) increased vs. the blood test (84.1%) and elastography (88.2%); accuracy of each constitutive test was significantly (p <0.001) decreased in discordant vs. concordant tests but, importantly, not with combined test: 89.0 vs. 92.7% (p = 0.118). Multivariate analysis for accuracy showed an interaction between concordance and fibrosis level, thus, in the 1% of patients with full classification discordance and severe fibrosis, non-invasive tests were unreliable (accuracy: 44.4%); this compares very favorably with the test discordance rate of 28% indicating liver biopsy. The advantage of combined test classification was confirmed in other diagnostic targets (significant fibrosis, cirrhosis) and in the validation set.

Conclusions: The EASL-ALEH recommendation on test concordance is validated. A test combining blood markers and liver stiffness, provided it is expressed in classification instead of score, improves this rule and validates the AASLD-IDSA combination recommendation. This avoids 99% of liver biopsies and offers precise staging. Finally, combination classification is the most useful diagnostic method. Indeed, test combination offers performance, classification adds precision and both solves most of the test discordancess.

**Poster 39 (SAT-489)**

Non-invasive assessment of liver disease

Date & Time: Saturday April 22, 2017 – 8h00-18h00

Longitudinal changes in liver stiffness by magnetic resonance elastography (MRE), liver fibrosis, and serum markers of fibrosis in a multi-center clinical trial in nonalcoholic steatohepatitis (NASH)

Rohit Loomba1, Eric Litwitz2, Reem Ghalibi3, Magdy Elkhashab4, Stephen Caldwell5, Manal Abdelmalek6, Kris Kowdley7, Ren Xu8, Guang Chen9, Constantine S. Djedjos10, Robert P. Myers11, G. M. Subramanian12, Zachary Goodman9, Michael Charlton10, Claude Sirlin1, Michael S. Middleton1

Background and aims: MRE is a noninvasive imaging technique to estimate liver stiffness. Selonsertib (SEL, formerly GS-4997) is a selective inhibitor of apoptosis signal-regulating kinase 1 (ASK1) being studied for the treatment of NASH. The objectives of this study were to examine correlations between MRE with histologic measures of fibrosis, and to assess associations between changes in these measures in a multi-center clinical trial of SEL in subjects with NASH.

Methods: Centrally-read 2D, 60 Hz MRE was performed at baseline (BL), W12, and W24 in a Phase 2 multi-center clinical trial of 72 subjects with NASH (NAS ≥5 and F2-3 fibrosis) treated with SEL 6 mg or 18 mg orally QD alone or in combination with simtuzumab (SIM, 125 mg SQ weekly) or SIM alone for 24 weeks. For the purposes of this analysis, study groups were combined. Liver biopsies, including morphometric assessment of hepatic collagen content and fibrosis staging according to the NASH Clinical Research Network (CRN) system, liver stiffness by FibroScan, and serum markers of fibrosis were assessed at BL and W24. Fibrosis response was defined as a ≥1-stage reduction in fibrosis and NAS response was defined as a ≥2-point reduction in NAS from BL to W24. Statistical comparisons were made using Kruskal-Wallis tests and Spearman correlations (r).

Results: Liver stiffness by MRE was correlated with fibrosis stage (BL: r=0.29, W24: r=0.55), hepatic collagen content (BL: r=0.15 [p=0.25], W24: r=0.55), liver stiffness by
FibroScan (BL: rs=0.46, W24: rs=0.62), and ELF test (BL: rs=0.26, W24: r=0.44) (all p<0.05 unless noted). At W24, the median percent change in liver stiffness by MRE was greater in subjects with improvement in fibrosis stage (-2.2% vs. 3.3%, p=0.20) or NAS response (-8.6% vs. 2.1%, p=0.08), but these differences were not statistically significant. Relative reductions of liver stiffness by MRE ≥ 15% at W24 were significantly associated with reductions in serum markers of fibrosis, high sensitivity C-reactive protein (hsCRP), and HbA1c (Figure).

Conclusions: Liver stiffness by MRE is significantly correlated with fibrosis measured histologically and by noninvasive means. Reductions in liver stiffness by MRE in subjects treated with SEL are associated with improvements in noninvasive markers of fibrosis and inflammation.

### Poster 40 (SAT-492)
Non-invasive assessment of liver disease

Date & Time: Saturday April 22, 2017 – 8h00-18h00

The assessment of liver fibrosis stage by two-dimensional shear wave ultrasound and Transient Elastography in patients with chronic liver disease

Sang Gyune Kim1, Bora Lee2, Jeong Joowoo3, Young Seok Kim4, Soung Won Jeong5, Jae Young Jang6, Rae Hwan Lee7, Young Don Kim8, Gab Jin Cheon9, Hong Soo Kim10, Boo Sung Kim11

Background and Aims: Several real-time two-dimensional shear wave elastography (2D-SWE) have been developed to assess liver fibrosis with readily use of combining elastography and traditional ultrasound imaging. However, compared with transient elastography (Fibroscan), the diagnostic accuracy and clinical usefulness of these methods were not fully validated. In this study, newly developed 2D-SWE (LOGIQ E9, GE healthcare, UK) was evaluated for predicting liver fibrosis stage and compared with fibroscan.

Methods: Out of 2,144 patients who received 2D-SWE during May 2015 to Nov 2016, one hundred-fourty (6.5%) who failed to get available value of 2D-SWE due to obesity or poor echo window and 207 (9.7%) with high value of AST or ALT were excluded in the analysis. Liver biopsy was performed in 244 patients. 2D-SWE measurement was considered valid when homogenous color pattern in a region of interest of at least 10 mm was shown at 10 different sites. Diagnostic performance was calculated using area under the receiver operating characteristics curve (AUROC).

Results: Patients were male predominant (53.7%), their mean age was 49.1±13.9 years old and most common etiology of liver disease was hepatitis B (34.4%) followed by autoimmune hepatitis (17.6%). Liver fibrosis stage consisted of F0 (14.8%), F1 (20.1%), F2 (23.8%), F3 (15.6%) and F4 (25.8%). Overall, 2D-SWE was well correlated with transient elastography (r = 0.855, P <0.001). 2D-SWE median values (kPa) increased with increasing stage of liver fibrosis [ F0 (5.0 ± 1.0), F1 (5.7 ± 1.2), F2 (6.8 ± 2.0), F3 (8.7 ± 2.1), F4 (12.5 ± 2.9)] (p for trend <0.001). For the diagnosis of liver cirrhosis, AUROCs and optimal cutoff of 2D-SWE were 0.931 (95% confidence interval [CI], 0.905-0.958) and 9.9 kPa which was not significantly different from fibroscan [0.918 (95% CI 0.878-0.957)] (p = 0.186). The sensitivity, specificity, positive predictive value and negative predictive value of 2D-SWE for predicting cirrhosis were 90.2%, 86.5%, 70.7% and 94.8% respectively. For diagnosing significant liver fibrosis (≥F2), AUROCs and optimal cutoff of 2D-SWE were 0.889 (95% CI, 0.849-0.929) and 6.68 kPa.

Conclusions: With good comparability to fibroscan and availability of a conventional ultrasound examination, Two-dimensional SWE is a useful tool for stratifying liver fibrosis stage and diagnosing liver cirrhosis.

### Poster 41 (SAT-496)
Non-invasive assessment of liver disease

Date & Time: Saturday April 22, 2017 – 8h00-18h00

Transient Elastography has limited efficacy for fibrosis assessment in End Stage Renal Disease patients on maintenance haemodialysis with suspected liver disease

Sunil Taneja, Amritangshu Borkakoty, Sahaj Rathi, Ajay Duseja, Radha K. Dhiman, Yogesh Chawla

Background and Aims: Patients with End Stage Renal Disease (ESRD) are at high risk of acquiring chronic viral hepatitis B and C and subsequent liver disease. While noninvasive assessment of liver fibrosis by Transient Elastography has emerged as a reliable tool, its validity in patients with volume overload states like renal failure and heart failure is ambiguous.

Aims: To study the correlation of liver stiffness measurement (LSM) with liver fibrosis on histology, and change in LSM and body impedance parameters before and after hemodialysis (HD) in ESRD patients with suspected liver disease.

Methods: We prospectively enrolled 68 patients of ESRD on maintenance hemodialysis (MHD) with suspected liver disease and compared LSM before and after HD. The change in LSM (DLSM) values were then correlated with the change in body weight and total body water, duration and frequency of HD. 18 patients underwent a liver biopsy, and correlation of LSM with histopathological grade of fibrosis was assessed.

Results: The mean age of the study population was 40 ± 14 yrs. Hepatitis C was the most common cause of liver disease followed by hepatitis B. There was a significant reduction of...
LSM values after HD (18.5 ± 14.9 vs. 11.2 ± 10.1 kPa, P <0.001), with a mean LSM reduction of 7.2 ± 8.2 kPa. The decline in LSM after HD strongly correlated with the LSM at baseline (r = 0.77, P = <0.001). The population was divided in four quartiles based on LSM, which revealed lowest decline in LSM in the first quartile and highest in the last (Q1 1.2 ± 1.3, Q2 3.7 ± 1.5, Q3 6.9 ± 3.5, Q4 17 ± 10.5 kPa) after HD with significant difference between the quartiles. There was no significant correlation between DLSM and change in body weight, total body water, duration and frequency of HD. However, DLSM was higher in patients when total fluid removed was >2.5L with a trend towards significance (8.6 vs. 5.1, P =0.09). Among 18 patients who underwent biopsy, LSM values after HD performed better at detecting significant fibrosis than before HD, with AUROC 0.64 (0.38-0.90) vs. 0.71 (0.46-0.97). A LSM value after HD of 12.2 was 71% sensitive and 74% specific for detection of significant fibrosis (≥F2), while values <9 kPa ruled out significant fibrosis.

Conclusions: The use of Transient elastography to assess liver fibrosis in patients of ESRD on MHD has limited efficacy. LSM values are falsely high in these patients and seems to be influenced by fluid overload status. A cutoff of LSM <9 kPa after hemodialysis may be used to rule out significant fibrosis.

Poster 42 (SAT-499)
Non-invasive assessment of liver disease
Date & Time: Saturday April 22, 2017 - 8h00-18h00
Impact of hepatic steatosis and Controlled Attenuation Parameter (CAP) on accuracy of fibrosis staging using Transient Elastography

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3) R & D Department, Echosens, Paris, France
4) Center for Fatty Liver, Department of Gastroenterology, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai
5) Research Institute of Liver Diseases, Tianjin Second People’s Hospital, Tianjin, China
6) Centre d’Investigation de la Fibrose hépatique, Hôpital Haut-Lévêque, CHU de Bordeaux, Pessac, France
7) Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India
8) Department of Medical Imaging, Iuliu Hatieganu University of Medicine and Pharmacy, Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor", Cluj-Napoca, Romania
9) Division of Gastroenterology and Hepatology, Institute of Gastroenterology and Endocrinology, Hanoi Medical University, Hanoi, Vietnam
10) Department of Medicine, Faculty of Medicine, University of Malaysia, Kuala Lumpur, Malaysia
11) Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, Hong Kong, China
12) Department of Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Medical School University of Pavia, Pavia, Italy
13) Gastroenterology and Hepatology Unit, Gastrointestinal Endoscopy Unit, Department of Medicine, University of Pavia, Pavia, Italy
14) Division of Gastroenterology & Hepat., Opt of Medicine, Univ of Calgary, Alberta, Canada
15) Departments of Gastroenterology and Metabolism, Hiroshima University Hospital, Hiroshima, Japan
16) Department of Internal Medicine, J.W. Goethe-University Hospital, Frankfurt, Germany
17) Department of Internal Medicine, Hôpital Jean Verdier, Bondy,
18) Department of Pathology, Physiology and Imaging, University Paris Diderot, Paris, France

Background and Aims: Non-invasive characterization of chronic liver disease is of utmost importance. Fibrosis is an important prognostic factor often accompanied by steatosis, particularly in NAFLD patients. Transient Elastography (TE) has become the method of choice, however, recent research suggests that steatosis may influence diagnostic TE performance. Controlled attenuation parameter (CAP) added to TE allows simultaneous assessment of steatosis and fibrosis and could be related to TE accuracy.

Methods: This is a secondary analysis of data originally collected for an individual patient data meta-analysis on CAP. Data on aetiology, liver histology, TE and CAP were available from 2735 patients (BMI ≤ 35 kg/m²; TE-biopsy-interval ≤ 30 days) using the Fibroscan® M-probe. The main exclusion criteria for the current analysis were unknown aetiology, unreliable TE measurement and data already used for the same research question. Comparisons of liver stiffness measurements (LSM) employed a t-test after logarithmic transformation. Aetiology specific optimal LSM cut-offs were found with the Youden index in a Receiver Operation Characteristic analysis. The probability of correct fibrosis classification as it depends on CAP-values was estimated with logistic regression and a smoothing spline.

Results: 2194 patients fulfilled the inclusion criteria (37% women, 44±13 years old, BMI 25±4 kg/m², 43% hepatitis B, 40% hepatitis C, 17% NAFLD/NASH). Fibrosis staging was F0=11%, F1=37%, F2=29%, F3=11%, F4=12% and steatosis grading was S0=52%, S1=28%, S2=15%, S3=5%.

In NAFLD/NASH patients without advanced fibrosis (S1 was associated with slightly elevated LSM values compared to cases with lower degrees of steatosis: 13% (95% CI 2-24%, p=0.003) (Figure a). Effects were even smaller and not significant for HBV and HCV. A heterogeneous picture is observed for advanced fibrosis, where steatosis >S1 is associated with elevated LSM only in HCV.

However, the probability of correct fibrosis classification by LSM did not fall with increasing CAP values in all aetiologies, including NAFLD/NASH (Figure b).

Conclusions: Advanced steatosis can impair the accuracy of LSM measurements. However, high CAP values may not be associated with poorer diagnostic performance of LSM in staging fibrosis. This depends on the prevalence in the particular cohort and the natural progression of the underlying disease.
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 IIa 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.