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ORAL AND POSTED COMMUNICATIONS

**49th Annual Meeting of the European Association
for the Study of Liver
April 9→13, 2014
London, United Kingdom**



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Postgraduate Course

Session title: Chronic viral hepatitis
Place: ICC Auditorium
Date & Time: April 9– 12:40→13:00

Non-invasive tests are on a par?

Speaker: Mireen Friedrich-Rust
Dpt of Internal Medicine 1, J.W. Goethe University Hospital, Frankfurt, Germany

Postgraduate Course

Session title: Translational aspects (advanced liver fibrosis – new classification, imaging, therapeutic targeting)
Place: ICC Capital Hall
Date & Time: April 10– 10:30→12:00

Non Invasive diagnostic and prognostics

Speaker: Massimo Pinzani
Royal Free Hospital, London, United Kingdom

Oral Presentation 1

FM

Session title: Non invasive
Place: Capital Suite 7-8-9
Date & Time: April 11– 16:00→16:15

Prognostic models for mortality using the successive values of non-invasive fibrosis tests in patients with chronic liver disease

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Background and aims: As the liver fibrosis progression is highly related to prognosis, we aimed to build a model for predicting mortality that takes into account the multiple liver fibrosis assessments done at various time points during the clinical monitoring of chronic liver disease.

Methods: 1,565 patients with various causes of chronic liver disease, included in a prospective cohort from 2005 to 2009, with available data for FibroScan, APRI, FIB-4, Hepascore, FibroMeter^{2G}. Date and cause of death were checked using the national death registry. Time-fixed (using only baseline variables) and time-dependent Cox models were built in a random set of 783 patients. The prognostic performance of each model was evaluated by the Harrell's C-index in the other half of the population.

Results: On 1st January 2011, the median follow-up was 2.8 years (from 0.003 to 5.98), the non-invasive tests were carried out from 1 to 8 times. 263 patients died, 116 deaths were liver-related. Multivariate models to predict all-cause mortality included age, sex, Fibroscan, FibroMeter^{2G}: C-index was 0.834 [0.805-0.863] for time-fixed model, 0.837 [0.808-0.866] for time-dependent model. Prognostic models for liver-related mortality were also based on age, sex, and Fibroscan, FibroMeter^{2G}: 0.867 [0.830-0.904] for time-fixed model, 0.879 [0.845- 0.914] for time-dependent model.

Conclusions: Using time-varying covariates only slightly improves prediction for liver-related mortality in this study, but the usefulness of updating values of liver fibrosis tests should be assessed for a more long-term prognosis. Combination of elastometry and blood test provides excellent prognostication.

Oral Presentation 2

Session title: Non invasive
Place: Capital Suite 7-8-9
Date & Time: April 11– 16:15→16:30

Prospective comparison of liver and spleen stiffness and composite scores, using supersonic-shear-imaging or

transient elastography, for detecting clinically significant portal hypertension in patients with cirrhosis

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Background and aims: Liver (LS) and spleen stiffness (SS) measurements, using transient elastography (TE), as well as composite scores (LSPS and PH risk score) have been proposed for the non-invasive evaluation of clinically significant portal hypertension (CSPH) but their use in patients with advanced cirrhosis may be hampered by limited TE applicability and insufficient accuracy. Supersonic-shear-imaging (SSI) is a novel promising technique, challenging TE but its ability to detect CSPH has never been evaluated.

Aims: To compare prospectively in patients with cirrhosis: 1) the applicability of SSI and TE; 2) the accuracy of LS, SS, LSPS and PH risk score, using SSI and TE, for detecting CSPH (HVPG≥10 mm Hg) and esophageal varices.

Methods: 79 consecutive cirrhotic patients (median age 59; Child A (30%), B (25%), C (45%); median HVPG 17 mm Hg; ascites 70%) who underwent SSI and TE at the time of HVPG were studied.

Results: The applicability of SSI was significantly better than that of TE for both LS and SS (97% and 97%, vs. 44% and 42%, respectively; p< 0.001). LS >24.6 kPa, using SSI had 81% sensitivity, 88% specificity and 82% diagnostic accuracy for CSPH. LS (AUROC 0.87) and PH risk score (0.82), using SSI, performed significantly better for CSPH than SS (0.64) (p=0.003 and p=0.02, respectively). Neither LS, SS, LSPS or PH risk score (by SSI or TE) differed between patients with / without esophageal varices.

Conclusions: In patients with cirrhosis, liver stiffness, using Supersonic-Shear-Imaging has the highest applicability and diagnostic performance for clinically significant portal hypertension.

Oral Presentation 3

Session title: Non invasive
Place: Capital Suite 7-8-9
Date & Time: April 11– 16:30→16:45

Prothrombotic genetic risk factors are associated with liver stiffness in the general population: results from the Rotterdam study

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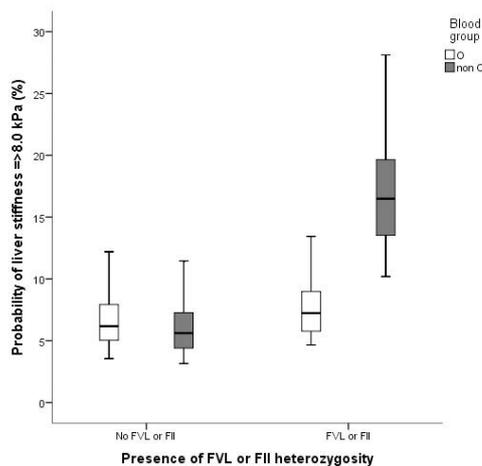
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Background and aims: The coagulation system is known to be involved in fibrogenesis. We aimed to study whether well-known genetic risk factors of thrombophilia - factor V Leiden (FVL), prothrombin G20210A (FII) and blood group non-O - increase the risk of liver fibrosis in the general population.

Methods: This research is part of the Rotterdam Study, a large population-based cohort of subjects aged ≥55 years. In all participants, we measured liver stiffness (LS) using transient elastography (FibroScan®). Blood group and the presence of FVL and/or FII heterozygosity were determined by genotyping and imputation.

Results: Reliable LS measurements and genetic data were obtained from 1059 participants (74.2±5.6 years; 50.2% male). Median LS was 5.1 kPa (IQR 4.1-6.3), 101 subjects (9.5%) had LS≥8.0 kPa (clinically relevant fibrosis). FVL was present in 50 participants (4.7%) and FII heterozygosity in 20 (1.9%). Presence of FVL or FII was significantly associated with LS≥8.0 kPa (OR 2.1, 95%CI 1.1-4.1, p=0.019). This association was independent of age, sex and ALT in multivariable analysis (OR 2.1, 95%CI 1.1-4.1, p=0.029). Presence of FVL or FII in individuals with blood group non-0 resulted in a probability of 16.7% of having LS≥8.0 kPa versus 6.8% in blood group 0 (p=0.15, see Figure 1).

Conclusions: FVL and FII heterozygosity are associated with a two-fold increased risk of clinically relevant fibrosis. Presence of FVL or FII increased this risk mainly in individuals with blood group non-0. These findings suggest that FVL, FII and blood group non-0 may play a role in liver fibrogenesis in the general population.



Oral Presentation 4

Session title: Non invasive
Place: Capital Suite 7-8-9
Date & Time: April 11– 17:30→17:45

Non-invasive diagnosis of liver fibrosis by FibroScan in patients with alcoholic liver disease: a meta-analysis with individual data

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Background and aims: The non-invasive diagnosis of alcoholic liver fibrosis by FibroScan remains debated. Specific liver stiffness cut off for F4 stage, and impact of transaminases or alcoholic hepatitis are unresolved issues.

Methods: Eight published studies were included, with 801 patients having a liver biopsy (4 stage fibrosis F1 to F4) and a FibroScan evaluation : Amiens(n=103), Bondy(n=147), Erasme(n=123), Bordeaux(n=59), Saint-Luc(n=100), Heidelberg(n=80), Bucheon-Seoul(n=45) and Angers(n=144).

A two stage random effect meta-analysis with individual data was performed.

Results: F≥2 Prevalence was 83% (range:67-98%) (heterogeneity p< 0.0001). With best sensitivity and specificity balance, Cut off F≥2 was 7.43±1.7kPa, AUROC 0.88[95%CI:0.85-0.94], sensitivity0.82[0.78-0.86], specificity0.79[0.74-0.85], PPV0.87[0.81-0.93], NPV0.70[0.62-0.78], accuracy0.78[0.72-0.84], LH+3.70[2.86-4.54], LH-0.12[0.15-0.28]. F4 Prevalence was 43% (26-85%) (heterogeneity p< 0.0001). Cut off F4 was 19±2.4kPa, AUROC 0.91[0.87-0.95], sensitivity0.83[0.78-0.88], specificity0.82[0.78-0.86], PPV0.77[0.68-0.87], NPV0.83[0.75-0.92], accuracy0.83[0.80-0.87], LH+4.3[3.07-5.53], LH-0.30[0.11-0.49]. To assess transaminase impact, whole population was divided into tertile (ASAT < 41; ≥41 and ≤78.5; >78.5 UI/L). Cut offs were respectively 9.78kPa [95%:12.6-17.8], 9.67[7.9-11.4], 11.37[10.1-12.6] for F≥2 (p=ns); and 15.2[12.6-17.8], 20[16.4-23.6], 21.5[18-25] for F4 (p< 0.05). In patients without or with histological alcoholic hepatitis features, cut offs were respectively 10.3[9.5-11.1], 11.6[7.1-16.1] for F≥2 (p=0.57), and 17.7[15.1-19.3], 29.7[22.6-36.8] for F4 (p=0.0015). Finally whole population was divided into tertile according to bilirubine (10.26< ; ≥10.26 and ≤19.38; >19.38 umol/L). Cut offs were respectively 8.34 kPa [7.57-9.29], 9.83[8.72-10.94], 13.36[11.6-15.1] for F≥2 (p< 0.05); and 12.16[10.5-13.8], 17.52[15.2-19.8], 26.37[23.-29.5] for F4 (p< 0.05).

Conclusions: This meta-analysis showed higher liver stiffness cut-off for diagnosis of alcoholic cirrhosis. Transaminase and alcoholic hepatitis impact significantly higher cut-off, but only for F4 stage. Bilirubin impact both F≥2 and F4 cut-offs diagnosis.

Oral Presentation 5

Session title: Non invasive
Place: Capital Suite 7-8-9
Date & Time: April 11– 17:45→18:00

Liver stiffness assessed by FibroScan is a major prognostic factor in primary sclerosing cholangitis

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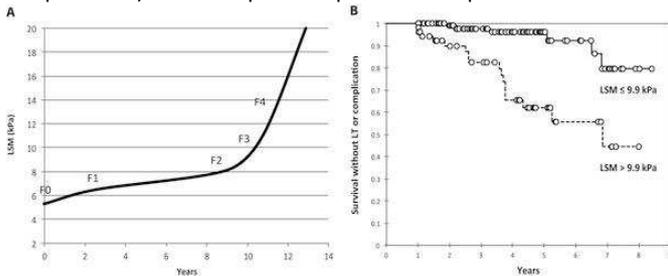
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Background and aims: We previously showed that liver stiffness measurement (LSM) assessed by vibration-controlled transient elastography (FibroScan, Echosens) is a reliable marker of severe liver fibrosis in primary sclerosing cholangitis (PSC). The aim of the present study was to assess the prognostic value of LSM in PSC.

Methods: All the patients included met the following criteria: diagnosis of PSC based on typical radiologic and/or histological features; absence of severe complications at entry; at least one reliable LSM available; a minimum follow-up of 1 year after last LSM. The progression rates of LSM were estimated using a mixed linear model. Clinical outcomes were defined by death, liver transplantation, cirrhotic complications, or cholangiocarcinoma.

Results: A total of 168 patients (64% male; mean age 39 years) were included. The average follow-up was 3.9 years (range, 1.0-8.4 years). 142 (85%) patients had more than one LSM. The mean number of LSM per patient was 3.5 (range, 1-12). The progression rates estimated from fibrosis stages F0, F1, F2, F3, and F4 were 0.47±0.45 kPa/year (p=ns), 0.25±0.67 kPa/year (p=ns), 1.64±0.78 kPa/year (p=0.0368), 3.40±0.89 kPa/year (p=0.0002), and 4.37±0.76 kPa/year (p< 0.0001), respectively, indicating a significant exponential progression in LSM from F2 (figure, A). Compared to classical prognostic factors, baseline LSM > 9.9 kPa (HR=6.4; p<

0.0001; figure, B) and increase in LSM > 2.5 kPa/year (HR=5.8; p=0.0004) were independent predictors of poor outcomes.



Conclusions: In PSC, liver stiffness assessed by FibroScan increases significantly and exponentially over time. LSM and its progression rate are two major prognostic factors of PSC.

Poster # P1322

Session title: Late Breaker Posters
Place: Poster Exhibition
Date & Time: April 10– 9:00→18:00

Real-time shear-wave elastography (SWE,Aixplorer™) performances in chronic hepatitis C (CHC) patients compared to liver stiffness measurement (LSM,FibroScan™) and fibrotest™ with liver biopsy (LB) as reference

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Background and aims: Liver fibrosis is a predictor of disease progression and treatment response in CHC. SWE is a new three-dimensional elastography for fibrosis evaluation. The purpose of this study is to evaluate SWE accuracy compared to that of LSM and Fibrotest with liver biopsy as reference.

Methods: Consecutive CHC-patients had undergone LB scoring METAVIR (from F0 no-fibrosis to F4-cirrhosis) and SWE (Super-Sonic Imagine S.A.), LSM M-probe (Echosens) and Fibrotest (BioPredictive), within the period not exceeding 12-weeks from LB-date. Three SWE-measurements were performed in the 5th,6th and 7th liver segments by a radiologist. Statistical analysis used standard-AUROC and Obuchowski-method.

Results: 99 CHC-patients were assessed and 93 included with four not missing applicable fibrosis-estimators. Main characteristics: 63%males, age 38yrs(21-63); fibrosis stages prevalences(n): F0F1-65.6%(61), F2F3-24.7%(23), F4-9.7%(9) and 37.9%(35) important necroinflammatory activity. 5th liver segment SWE-measurements was used for analysis as there was no difference with those in the 6th,7th segment or their mean. Standard-AUROC(95%CI) for SWE, LSM and Fibrotest were, respectively: advanced fibrosis (F2F3F4) 0.899(0.789-0.954;p=NS vsLSM and vsFibrotest), 0.942(0.860-0.977;p=0.02 vsFibrotest) and 0.840(0.724-0.910); for cirrhosis 0.971(0.912-0.990;p=NS vsLSM and vsFibrotest), 0.979(0.929-0.994;p=0.03 vsFibrotest), 0.867(0.705-0.943). Overall accuracies [AUROC(SE)] by Obuchowski method were: for SWE 0.917(0.015;p=0.37 vsLSM and p=0.14 vsFibrotest), LSM 0.903(0.016) and Fibrotest 0.867(0.020). Sensitivity analyses performed in 53 patients with LB sample length >=10mm found no differences between AUROC neither for F2F3F4 nor for cirrhosis (all p=NS).

Conclusions: SWE had similar performances to those of LSM and Fibrotest for advanced fibrosis and cirrhosis. One SWE-measurement had accuracy not different of the mean of three liver segments SWE-measurements

Poster # P515

Session title: Cirrhosis & its complications: clinical aspects
Place: Poster Exhibition
Date & Time: April 11– 9:00→18:00

Non-invasive prediction of clinically significant portal hypertension using transient elastography and spleen diameter/platelet count ratio in b-viral and alcohol cirrhosis: external validation study

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- 6- Department Internal Medicine, Kangwon University School of Medicine, Chuncheon, Republic of Korea

Background and aims: We externally validated LS and two proposed index; LSPS (LSM × spleen diameter / platelet count), PH risk score (-5.953 + 0.188 X LS + 1.583 X sex (1: male; 0: female) + 26.705 X spleen diameter/platelet count ratio) for cirrhosis.

Methods: For 81 HBV and 288 alcohol-related cirrhosis, LS and HVPG were performed and we analyzed the correlation between LS, LSPS, PH risk score and HVPG. CSPH defined as HVPG ≥ 10 mmHg.

Results: In HBV, the mean HVPG and LS were 14.0 ± 6.0 mmHg and 33.0 ± 20.8kPa. LS (r2=0.466, P< 0.001), LSPS (r2=0.430, P< 0.001) and PH risk score (r2=0.490, P< 0.001) showed significant linear correlation with HVPG. The AUROC of index for the prediction of CSPH were 0.857, 0.879 and 0.873. The sensitivity and specificity of LS were 83.6 % and 70.0% with a cut-off value 16.7kPa for CSPH. In alcohol, the mean HVPG and LS were 13.4 ± 5.5 mmHg and 38.3 ± 22.2kPa. LS (r2=0.374, P< 0.001), LSPS (r2=0.2350, P< 0.001) and PH risk score (r2=0.395, P< 0.001) showed significant linear correlation with HVPG. The AUROC of index for the prediction of CSPH were 0.857, 0.859 and 0.867 respectively. The sensitivity and specificity of LS were 85.0 % and 70.9% with a cut-off value 22.9kPa for CSPH.

Conclusions: In the non-invasive prediction of CSPH in HBV and alcohol related cirrhosis, LS, LSPS, PH risk score all showed good predictive value. The correlations with HVPG were better in HBV related cirrhosis than alcohol related cirrhosis.

Poster # P521

Session title: Cirrhosis & its complications: clinical aspects
Place: Poster Exhibition
Date & Time: April 11– 9:00→18:00

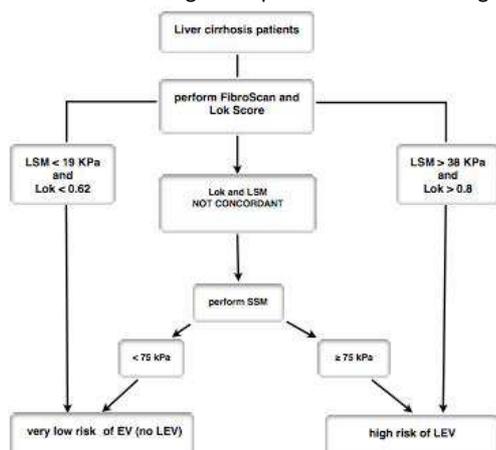
Proposal for a new, stepwise algorithm combining liver and spleen stiffness and Lok score for diagnosis of large esophageal varices in patients with liver cirrhosis

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Background and aims: Noninvasive assessment of liver cirrhosis (LC) patients for diagnosing esophageal varices (EV) is becoming of great importance. Liver stiffness measurement (LSM), spleen size, platelets count and serological scores such as Lok score - used alone or in combination, has been proved to correlate well with EVs. Spleen stiffness measurement (SSM) has also been showed to predict with good accuracy large EV (LEV), especially if a new calculation algorithm is used, which permits recordings up-to

150kPa. Therefore, we propose a new, stepwise sero-elastographic algorithm (figure1) for assessment of LEVs in LC patients. Our aim was to evaluate the diagnostic performance of this algorithm.



Methods: 150 consecutive LC patients (56.7% males, mean age 55.28y) were included. All patients underwent LSM, SSM (up to 150kPa). Lok-score was calculated based on common biological tests. EVs were quantified by endoscopy (EV grade 2 and 3 were considered as large). The algorithm was applied and the LEVs were predicted. The performance was tested for absolute concordance.

Results: 63 patients had LEV (16 gr3 EV and 47 gr2 EV) while 54 had gr1 EV and 33 had no EV. LSM was higher in patients with LEV (38.10 vs 43.03 kPa, p=0.1). SSM was also higher in LEV patients (66 vs 83.2 kPa, p=0.01). LEV predicted by algorithm correlated weakly with endoscopy-assessed LEV (r=0.296;p=0.0001) showing, however, an average absolute interclass agreement (ICC=0.494;p=0.0001).

Conclusions: The above stepwise algorithm, combining LSM, Lok Score and extended (up to 150kPa) SSM might represent a promising noninvasive method for LEV diagnosis in cirrhotic patients, but needs further validation.

Poster # P533

Session title: Cirrhosis & its complications: clinical aspects

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Transient elastography can predict hepatic decompensation in patients with chronic hepatitis C

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Background and aims: Liver cirrhosis is a dynamic progressive process leading to multiple complications and death in patients with chronic liver disease. Transient elastography (TE) is a new, highly accurate noninvasive technique, which enables to evaluate hepatic fibrosis to detect advanced fibrosis and cirrhosis.

The aim of this study was to evaluate the accuracy of TE in predicting hepatic decompensation in patients with chronic hepatitis C (CHC).

Methods: A total of 450 patients with CHC who attended outpatient clinics of National Liver Institute, Egypt for evaluation for antiviral therapy were recruited in the study. Regular follow-ups for two years to detect the development of hepatic decompensation (variceal bleeding, ascites or hepatic encephalopathy) were done. Liver stiffness measurement (LSM) by TE was done initially and at the end of follow up period.

Results: During follow-up (median, 24 months), hepatic decompensation developed in 30 patients. The mean value of the initial LSM was 27.5±8.66 vs 9.29±6.67 in decompensated patients and patients who did not develop decompensation respectively (p value < 0.005). After 2 years LSM increased in decompensated patients while it decreased in other patients (34.78±9.33 vs

8.58±5.44 respectively, p value < 0.005). The areas under the receiver operating characteristic curve of the initial LSM in predicting the development of hepatic decompensation was 0.95 (CI: 0.92-0.97). On multivariate analysis, LSM was identified as independent predictors of hepatic decompensation [HR, 1.09 (0.94-1.28)].

Conclusions: LSM using TE can accurately predict the development of hepatic decompensation in patients with CHC.

Poster # P699

Session title: Viral hepatitis: Hepatitis A, B, D E - Clinical (except therapy)

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Predictors of hepatic steatosis in a prospective study of European untreated hepatitis B surface antigen (HBsAg) carriers: evaluation by Controlled Attenuation Parameter (CAP)

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Background and aims: Little is known about the relevance of hepatic steatosis in HBsAg carriers in the European population. Recently, a novel controlled attenuation parameter (CAP) has been designed for ultrasound-based noninvasive assessment of steatosis. The aim of the present study was to prospectively perform CAP measurement to investigate predictors of steatosis in a cohort of European untreated HBsAg carriers.

Methods: 123 HBsAg carriers who were part of a multicentric prospective cohort were referred to liver stiffness measurement simultaneously with CAP. Elevated ALT levels (ALT>ULN) were detected in 14/123 patients, whereas 8/123 had elevated GGT values (GGT>ULN). Steatosis was categorized by using the following cut-offs: grade 0:< 222 dB/m, grade 1:222-232 dB/m, grade 2:233-289 dB/m, grade 3:>289 dB/m. Biochemical, virological and metabolic factors were compared.

Results: In 16 patients CAP-measurement failed due to obesity. In the remaining 107 HBsAg carriers CAP detected grade 0 in 36, grade 1 in 13, grade 2 in 38, and grade 3 steatosis in 20 patients. Higher BMI, lower HDL (p< 0.002) and higher age (p< 0.004) were associated with steatosis. In the subgroup of patients with elevated liver enzymes, 9/13 (ALT>ULN) and 7/8 (GGT>ULN) had documented steatosis by CAP. Taking into account only patients with HBV-DNA< 1000U/ml, 6/7 (ALT>ULN) and 5/5 (GGT>ULN) had increased CAP.

Conclusions: Steatosis was mainly associated with metabolic factors in our cohort of HBsAg carriers, whereas virological parameters and fibrosis stage had no influence. In the subgroup of patients with HBV-DNA< 1000U/ml, steatosis and metabolic determinants, but not viral factors, were correlated with elevated liver enzymes.

Poster # P727

FM

Session title: Viral hepatitis: Hepatitis C - Clinical (except therapy)

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Validation and comparison of six non-invasive scores for the diagnosis of liver fibrosis in children with chronic hepatitis C

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Background and aims: To assess the diagnostic performance of 6 non-invasive fibrosis scores, not validated before in children with chronic HCV infection.

Methods: Fibrometer, Hepascore, Forns score, Fibroindex, FIB-4 and APRI were assessed in Fifty two children with HCV, using liver

histology as reference standard. The primary end-point was the area under characteristic curves (AUROC) for the detection of significant fibrosis by METAVIR classification.

Results: 13% of studied children had significant fibrosis. Hepasscore has poor performance (AUROC 0.638), the remaining studied scores have good diagnostic accuracies (AUROCs ranged from 0.921 for APRI to 0.825 for Fibro index). ALL cores showed excellent negative predictive value (NPV > 95%) to exclude significant fibrosis, while none of the scores present with a positive predictive value (PPV) good enough (>90%) to reliably predict significant fibrosis in HCV studied children. In multiple stepwise logistic regression including the five scores, APRI and Fibrometer (AUROCs 0.921 and 0.857 respectively) were the only scores independently associated to significant fibrosis.

Our results strongly suggest that exclusion of significant fibrosis can be made with more than 95% certainty when APRI is lower than 0.68 or Fibrometer is lower than 2.94. By contrast, significant fibrosis cannot be predicted with the same certainty.

Conclusions: We suggest to perform APRI in all children, those classified by APRI as non significant fibrosis did not need further evaluation due to high NPV. However, children showing significant fibrosis by APRI had to undergo liver biopsy. With this algorithms we obtained 93% accuracy in exclusion of significant fibrosis and saved around 80% of liver biopsy.

Poster # P751

Session title: Viral hepatitis: Hepatitis C - Clinical (except therapy)

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Distinct values of liver stiffness predicts progression to advanced liver fibrosis in HIV-infected patients with chronic hepatitis C

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Background and aims: The use of DAA is restricted by some governments to patients with advanced liver fibrosis in order to save costs. However, response rates are lower in patients with advanced liver fibrosis.

Methods: All HCV/HIV-coinfected patients with Metavir F0-F2 (liver stiffness < 9.6 kPa by elastometry), and with a follow-up >3 years were identified at our institution. Liver fibrosis progression (LFP) was defined as a change to Metavir F3-F4 estimates.

Results: A total of 344 HIV/HCV-coinfected patients with baseline F0-F2 were identified. Hepatitis C therapy was given to 205, of whom 94 (44.8%) achieved SVR. Significant differences between groups included a lower proportion of genotypes 1-4 vs 2-3 (52% vs 90% p < 0.001) and higher IL28B-CC vs non-CC (63% vs 25%, p < 0.001) among SVR patients. After 53 months mean follow-up, LFP occurred in 5.4% SVR, 25.7% non-SVR and 18% not-treated patients (p = 0.005 SVR vs others). In multivariate analysis, only achievement of SVR independently prevented from LFP (OR 0.47 [IC95% 0.24-0.9] p = 0.001). When comparing 25 not-treated patients that experienced LFP with 115 that did not, only greater baseline liver fibrosis elastometry values predicted LFP in multivariate analysis (OR 1.84 [IC95% 1.03-3.3] p = 0.03). The best cut-off discriminating for LFP (ROC curve) in not-treated patients was baseline 6.35 kPa (PPV: 80% & NPV: 65%; p < 0.001).

Conclusions: In HIV/HCV-coinfected patients with baseline null-mild liver fibrosis (F0-F2), LFP occurred in 18% within a mean of 4.5 years. Fibrosis progression was significantly greater in those with >6.35 kPa, which therefore should also be candidates for new DAA-based therapies.

Poster # P799

Session title: Fatty Liver Disease: Clinical

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Affects of steatosis on liver stiffness values measured by transient elastography in patients with chronic hepatitis B

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Background and aims: To investigate the impact of steatosis on liver stiffness (LS) detected by transient elastography (Fibroscan) in patients with chronic hepatitis B (CHB).

Methods: 303 cases of CHB who underwent liver pathology and Fibroscan were retrospectively analysed. Biochemical parameters were collected. LS values in same degree of liver fibrosis with and without steatosis and in the same stage of liver fibrosis combined with different degrees of steatosis were compared using ANOVA. Cut-off values were obtained by Receiver Operating Characteristic (ROC curve) analysis.

Results: 273 cases were included when excluding BMI > 28 kg/m² and ALT > 200 U/L. Steatosis was present in 75 (31.6%) cases, steatosis was absent in 162 (68.4%) cases. In fibrosis stage of F1, F2, F3 and F4, combining with steatosis and without steatosis has no significant affects on LS values (LS were 5.3±1.4 vs 5.9±1.9, 9.5±4.2 vs 8.7±3.0, 18.4±7.5 vs 15.0±6.6, 21.4±7.5 vs 27.6±5.9 kPa, respectively) (p > 0.05). While in the degree of F2, LS values in patients combined with moderate steatosis (S2) were higher than those in patients without steatosis (S0) (P < 0.05) and with mild steatosis (S1) (P < 0.05) (LS values were 11.28±5.54, 8.68±2.95, 8.12±2.44 kPa, respectively). Cutoff values of F2S0, F2S1 and F2S2 were 6.9, 7.9, 8.8 kPa, respectively.

Conclusions: Combining with steatosis has slight affects on LS values in patients of CHB with different degree of liver fibrosis; In patients with fibrosis stage of F2, LS values in those combined with moderate steatosis (S2) were higher than those without steatosis and with mild steatosis.

Poster # P805

Session title: Fatty Liver Disease: Clinical

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Non-invasive characterization of post-transplant fatty liver disease reveals high prevalence of graft injury in association with metabolic syndrome, recipient PNPLA3 genotype and alcoholic liver cirrhosis

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Background and aims: Hepatic steatosis contributes to liver graft injury and impaired long-term outcome, but data on the prevalence of post-transplant fatty liver disease (FLD) are limited. We therefore performed a comprehensive non-invasive evaluation of post-transplant FLD and associated risk factors.

Methods: 204 liver transplant recipients (n=102 non-alcoholic etiology, non-ALC; n=102 alcoholic liver disease, ALC; 42% female; age median/range 57.8/19.1-79.9 years; time since transplantation 66/2-242 months) underwent transient elastography (TE), Controlled Attenuation Parameter (CAP), ultrasound, and NAFLD fibrosis score

assessment. Recipient DNA samples were genotyped for PNPLA3 (rs738409), and IL28B (rs8099917,rs12979860) polymorphisms.

Results: Valid elastography results and genotyping were available in 157 and 196 cases, respectively. 43% of patients were overweight and 20% obese. 74/204 displayed increased hepatic echogenicity at ultrasound, in 71/157 and 37/157 CAP indicated steatosis (>245dB/m) and advanced steatosis (>300 dB/m), respectively. PNPLA3 non-CC genotype was associated with increased CAP (257/100-400 vs. 222/100-354 dB/m, $p=0.032$), higher liver stiffness (TE 6.4/2.6-74 vs. 5.5/2.4-53 kPa, $p=0.005$), and diabetes mellitus frequency (39% vs. 22%, $p=0.013$). IL28B rs12979860 non-CC genotype was associated with higher BMI and TE values, while no association was observed for rs8099917.

ALC patients had higher diabetes mellitus (41% vs. 25%, $p=0.017$) and PNPLA3 non-CC prevalences (73% vs. 47%, $p=0.005$), and higher BMI values (28.2±4.6 vs. 25.6±4.4 kg/m², $p<0.001$). Median liver stiffness ($p=0.022$), CAP ($p=0.001$) and NAFLD score ($p<0.001$) were elevated in the ALC cohort.

Conclusions: Modern ultrasound assessment frequently detects post-transplant FLD, which is associated with components of the metabolic syndrome and recipient PNPLA3 non-CC genotype, especially in ALC patients.

Poster # P809

Session title: Fatty Liver Disease: Clinical

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Patients with T2DM accompanying severe degree of NAFLD assessed by Controlled Attenuation Parameter using FibroScan

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Background and aims: The high prevalence of hepatic steatosis in diabetic population is well known. However, the severity of hepatic steatosis in diabetic population compared to that of normal or prediabetic population has not yet been assessed, and whether there is a difference in the degree of steatosis between these groups is not known.

Methods: Subjects who underwent laboratory tests for T2DM and CAP using FibroScan® as a regular health check-up were enrolled. CAP value 250dB/m was selected as a cutoff for presence of steatosis, and CAP value 300dB/m for moderate to severe steatosis. Biomarkers related to T2DM included fasting glucose, fasting insulin, C-peptide, HbA1c, glycoalbumin, HOMA-IR, HOMA-β, and hs-CRP.

Results: Among 340 study participants (T2DM, $n=66$; pre-diabetes, $n=202$; normal glucose tolerance, $n=72$), the proportion of subjects with steatosis increased according to the glucose tolerance status (31.9% in normal glucose tolerance; 47.0% in pre-diabetes; 57.6% in T2DM). The median CAP value was significantly higher in patients with T2DM (265dB/m) compared to those with pre-diabetes (245dB/m) or normal glucose tolerance (231dB/m) (all $P<0.05$). Logistic regression analysis showed that subjects with moderate to severe steatosis had a 2.1-fold higher risk of having T2DM compared to those without steatosis ($P=0.02$; OR=2.4; 95% CI=1.1-4.9), and positive correlations between the CAP value with HOMA-IR ($p=0.407$) and C-peptide ($p=0.402$) were clearly demonstrated.

Conclusions: This study has found that hepatic steatosis is not only a risk factor of diabetes, but that diabetes itself is associated with more severe degree of steatosis. The increasing severity of hepatic steatosis in diabetic subjects may be due to insulin resistance.

Poster # P828

Session title: Fatty Liver Disease: Clinical

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

The common PNPLA3 variant is associated with hepatic steatosis quantified by Controlled Attenuation Parameter and determines the fate of patients with chronic liver diseases

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Background and aims: The common variant p.I148M of the PNPLA3 gene encoding the enzyme adiponutrin represents a genetic driver of severe hepatic phenotypes (Anstee/Day Nat Rev Gastroenterol Hepatol 2013). Here we present the results in patients with chronic liver diseases (CLD) who were referred to our center between 2010 and 2013 for genotyping of PNPLA3 as a part of their diagnostic work-up.

Methods: The PNPLA3 SNP rs738409G>C (p.I148M) was genotyped by Taqman assays in 234 patients with CLD (133 men; 180 with non-viral liver diseases; 14 - 77 years). Liver steatosis was measured non-invasively using controlled attenuation parameter (CAP™) in a subgroup of 97 patients. The control cohort consisted of 279 healthy individuals (114 men; 32 - 98 years).

Results: The PNPLA3 variant increased the odds of presenting with severe liver phenotypes that eventually lead to referral and informed consent for genotyping (common OR = 1.72, $P=0.001$). Median CAP [dB/m] levels differed significantly (ANOVA $P=0.0025$) between carriers of the genotypes [II] ($n=46$), [IM] ($n=40$) and [MM] ($n=11$) and were 246.0, 277.0 and 320.0, respectively. Carriers of the prosteatotic [M] allele had higher ($P=0.0043$) median CAP levels as compared to the [II] individuals.

Conclusions: This is the first study showing an association between hepatic steatosis quantified using CAP and the PNPLA3 variant across various liver diseases. Our results provide evidence that patients with the PNPLA3 risk variant develop more severe liver diseases, supporting the concept of PNPLA3-associated steatohepatitis (PASH; Semin Liver Dis 2013).

Poster # P835

Session title: Fatty Liver Disease: Clinical

Place: Poster Exhibition

Date & Time: April 11– 9:00→18:00

Liver steatosis assessment with CAP at 3.5 Mhz using FibroScan M and XL probe

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Background and aims: Controlled Attenuation Parameter (CAP) measures liver ultrasound attenuation at 3.5 MHz using FibroScan (FS). Currently available on the M probe to quantify steatosis, the aim of this work was to implement the measurement of CAP on the XL probe (dedicated to overweighted patients) and validate its diagnosis performance.

Methods: 180 consecutive patients (21% NAFLD, 25% VHC, 14% VHB, and 40% other - BMI=25±11kg/m², age=51±15years, 53% male) with histological assessment of steatosis within 7 days of FS (liver biopsy≥15 mm, double-blind reading) were enrolled. Steatosis was graded and distributed as follows: S0: steatosis≤10% (63%), S1: 11~33% (11%), S2: 34~66% (10%), S3: ≥67% (16%). Spearman correlation coefficient (SCC), intra-class correlation coefficient (ICC), Area under Receiver Operating Characteristic curve (AUROC) and

Delong-test for comparison of AUROC were used to analyse the data.

Results: SCC of CAP with histological steatosis was 0.65 and 0.64 for XL and M probes respectively. The AUROCs (area under ROC curve) of CAP at 3.5 MHz versus histological steatosis (Table 1) were not significantly different when measured by either the M or the XL probe and cut-off maximizing the Youden index for the M probe had similar performance for CAP measured with XL probe.

Conclusions: Measurement of CAP at 3.5 MHz is feasible in with the FS XL probe and therefore in overweighted patients for whom steatosis is more prevalent. This work confirms that the diagnosis accuracy of CAP for steatosis assessment is equivalent when using either the M or the XL probe.

| Steatosis | | M Probe | XL Probe |
|------------------------|-------------|---------------|---------------|
| ≥ 11 % (n=66 - 37%) | AUC ± SD | 0.832 ± 0.034 | 0.836 ± 0.033 |
| | Cut-off | 267 dB/m | |
| | Sensitivity | 68.2 | 66.7 |
| | Specificity | 86.0 | 89.5 |
| ≥ 34 % (n=47 - 26%) | AUC ± SD | 0.895 ± 0.032 | 0.900 ± 0.031 |
| | Cut-off | 272 dB/m | |
| | Sensitivity | 82.9 | 82.9 |
| | Specificity | 87.9 | 87.2 |
| ≥ 67 % (n=29 - 16%) | AUC ± SD | 0.945 ± 0.017 | 0.949 ± 0.019 |
| | Cut-off | 290 dB/m | |
| | Sensitivity | 86.2 | 89.7 |
| | Specificity | 84.7 | 86.8 |

[Table 1]

Poster # P888

Session title: Liver Transplantation/Surgery: Clinical

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Usefulness of Elf, IP10, FibroScan and their combinations in the early prediction of severe hepatitis C recurrence after liver transplantation

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Background and aims: Early identification of severe hepatitis C recurrence after liver transplantation (LT) may help to indicate antiviral therapy before the disease is too advanced. We evaluated the performance of ELF, IP10 and transient elastography (FibroScan) 6 months after LT to predict severe recurrence.

Methods: Seventy-five HCV-infected LT recipients were included. Severe recurrence was defined as the presence of F≥2 and/or HVPG≥6 mmHg 12 months after LT. Elastography and serum levels of IP10 and ELF score were evaluated 6 months post-LT.

Results: In thirty patients (40%) with severe recurrence at 12 months, IP10, ELF and elastography 6 months after LT were significantly higher than in patients with mild recurrence (p< 0.001 for ELF and FibroScan; p=0.006 for IP10). AUROCs of ELF, FibroScan and IP10 6 months after LT to predict severe recurrence were, respectively, 0.805, 0.776 and 0.688. Negative (NPV) and positive (PPV) predictive values were 85% and 68% for ELF, 83% and 61% for FibroScan and 73% and 53% for IP10. The combination of ELF with FibroScan in cases where they agreed (61%), yielded NPV and PPV of 96% and 77%. The combination of Fibroscan and IP10 agreed in 60% of patients and yielded NPV and PPV of 87% and 71%.

Conclusions: Noninvasive methods are able to early predict severe hepatitis C recurrence with moderate accuracy. Among the methods evaluated, ELF and FibroScan were more accurate than

IP10, and their combination was particularly reliable to predict a benign evolution of the recurrence

Poster # P1005

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Transient elastography based cirrhosis score significantly improving efficiency of compensated hepatitis B cirrhosis detection

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Background and aims: Transient elastography (TE) is a well-established method for detecting hepatitis B related cirrhosis (HBRC), but was criticized that significant necro-inflammation directly increase liver stiffness and lead to incorrect diagnosis, and more than 20% of patients with CHB were still involved in grey zone and left undiagnosed. Present study tries to improve the performance of TE in detecting HBRC by integrating ultrasound and routine blood tests.

Methods: A total of 170 compensated patients with chronic hepatitis B and larger biopsies samples (at least 20mm length) were analyzed following liver biopsies, transient elastography, ultrasound and routine blood tests.

Results: An algorithm named as Transient Elastography Based Cirrhosis Score (TEBaCS) consisting of liver stiffness, serum albumin, platelet count, coagulation index of International Normalized Ratio (INR) and ultrasonic images of hepatic vessel and liver parenchyma detected HBRC with the area under the receiver operating characteristics curve 0.940 (95% CI 0.896-0.984), which was superior to that of TE alone (0.907, 95% CI 0.855-0.960). With TEBaCS 4, 50 (29.4%) patients were classified as cirrhosis and 120 (70.6%) patients were discriminated as non-cirrhosis with sensitivity 0.881, negative likelihood ratio 0.13, negative predictive value 95.8%, specificity 0.898, positive likelihood ratio 8.7 and positive predictive value 74%. With TEBaCS, all patients could be determined as cirrhosis or non-cirrhosis and obviating liver biopsies, which was significantly superior to TE alone (81.8%).

Conclusions: By integrating TE, ultrasonic images of liver, serum albumin, platelet count and INR, liver biopsies may be completely substituted by TEBaCS for detecting compensated HBRC.

Poster # P1009

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

The histological or ultrasonographic detection of steatosis affects the performance of liver stiffness measurement for fibrosis assessment in patients with chronic Hcv genotype 1 infection

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Background and aims: In Chronic Hepatitis C (CHC), the influence of steatosis on liver stiffness measurement (LSM) is still debated. We assessed the impact of steatosis and its ultrasonographic sign - i.e. Bright Liver Echo Pattern (BLEP) - on LSM values and on Transient Elastography (TE) accuracy for the diagnosis of liver fibrosis, in a cohort of consecutive biopsy-proven patients with Genotype 1 (G1) CHC.

Methods: Consecutive G1 CHC patients (n=618), assessed by demographic, biochemical, metabolic, ultrasonographic and

histological features, were included. TE was assessed using the standard M probe.

Results: Male gender ($p=0.04$), steatosis as continuous variable ($p < 0.001$), severity of necroinflammation ($p=0.02$) and stage of fibrosis ($p < 0.001$) were associated with LSM by multivariate linear regression analysis. Among patients within the same fibrosis stages (F0-F2 and F3-F4; F0-F3 and F4), mean LSM values, expressed in kPa, were significantly higher in subjects with moderate-severe steatosis ($\geq 20\%$) compared with those without, as well as in patients with BLEP on ultrasonography (US) compared with those without. Furthermore, in subjects without severe fibrosis (F0-F2) and without cirrhosis (F0-F3), a higher rate of false-positive LSM results was observed in patients with steatosis $\geq 20\%$ (F0-F2: 35.3% vs. 17.9%; F0-F3: 38.9% vs. 16.6%) and in patients with BLEP on US (F0-F2: 28.0% vs. 18.3%; F0-F3: 29.7% vs. 17.8%) compared with their counterparts.

Conclusions: In patients with G1 CHC, the presence of moderate-severe steatosis, detected by histology or by US, should always be taken into account in order to avoid overestimations of liver fibrosis assessed by LSM.

Poster # P1010

Session title: Non-invasive Markers of Liver Fibrosis
Place: Poster Exhibition
Date & Time: April 12– 9:00→18:00

Liver stiffness in HCV and ALD: fibrosis-related cut-off values depend on degree and location of inflammation

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Background and aims: Liver stiffness (LS) can be drastically elevated during liver inflammation making it difficult to separate fibrosis- from inflammation-induced LS. We here performed a multicenter study both on a portal-tract pronounced (hepatitis C virus infection; HCV) and a predominantly lobular disease (alcoholic liver disease; ALD). The major aim was, first, to learn whether portal and lobular inflammation differently translate into LS elevation and, second, to calculate adapted cut-off values for concomitant inflammation.

Methods: 452 patients with ALD and 1393 patients with HCV were enrolled from five centers (Heidelberg, Paris, Hannover, Düsseldorf, Cluj Napoca). All patients had histological-proven fibrosis stage F0-F4 (METAVIR or Kleiner), LS (Fibroscan) measurement and lab tests.

Results: Among the routine laboratory parameters for liver damage, GOT correlated best with LS ($r=0.54$, $P < 10E-90$) both for HCV and ALD. Therefore, we next calculated the area under the receiver operating curves (AUROC) as a function of GOT levels. Interestingly, cut-off values determined at optimal sensitivity and specificity (Youden index) were almost identical for F0, F3 and F4 in the absence of elevated transaminases (HCV: 5.1, 9.0 and 11.9 kPa, ALD: 4.9, 8.1 and 10.5 kPa). These cut-off values increased exponentially as a function of GOT levels. The impact of GOT on LS was higher in lobular-pronounced inflammation (ALD) and at higher fibrosis stages. Consideration of GOT improved AUROCs for both diseases.

Conclusions: We propose novel GOT-adapted cut-off values namely for HCV were short interventions such as alcohol detoxication are not applicable.

Poster # P1011

Session title: Non-invasive Markers of Liver Fibrosis
Place: Poster Exhibition
Date & Time: April 12– 9:00→18:00

Acoustic Radiation Force Impulse-Imaging in comparison to transient elastography for non-invasive assessment of liver fibrosis in chronic hepatitis C: a prospective international multicenter study

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Background and aims: Acoustic Radiation Force Impulse (ARFI)-Imaging (Siemens Acuson S2000) is an ultrasound-based elastography method which is integrated in a conventional ultrasound machine enabling the exact localisation of measurement site. It might present an alternative method to transient elastography (TE, FibroScan®, Echosens) for the non-invasive assessment of liver fibrosis. The aim of the present prospective international controlled multicenter study was to directly compare ARFI and TE for the assessment of liver fibrosis in patients with chronic hepatitis C using liver biopsy as reference method.

Methods: ARFI-imaging involves the mechanical excitation of tissue resulting in shear-wave propagation which is tracked using ultrasonic, correlation-based methods and is recorded in m/s. 253 patients with chronic hepatitis C were prospectively included in the present study and received ARFI-imaging, TE and blood tests. Liver histology was staged by a central pathologist and used as reference method. In addition, 24 patients with liver cirrhosis confirmed by imaging methods were included

Results: Finally, 247 patients could be included in the intention to diagnose analysis and 182 patients in the per protocol analysis. ARFI imaging and TE correlated significantly with histological fibrosis stage. The diagnostic accuracy expressed as areas under ROC curves for ARFI-imaging and TE are shown in Table 1. No significant difference was found between TE and ARFI in the per protocol analysis for the diagnosis of $F \geq 2$ ($p=0.15$), $F \geq 3$ ($p=0.11$) and $F=4$ ($p=0.19$).

Conclusions: ARFI-imaging and TE are comparable methods for non-invasive staging of liver fibrosis in patients with chronic hepatitis C.

Poster # P1017

FM

Session title: Non-invasive Markers of Liver Fibrosis
Place: Poster Exhibition
Date & Time: April 12– 9:00→18:00

Evaluation of the prognostic value of non-invasive liver fibrosis tests to predict mortality by time-dependent ROC curves

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Background and aims: Recent studies showed the prognostic value of some non-invasive liver fibrosis tests to predict survival and complications. In this study, we compared the ability of the liver fibrosis tests to predict mortality using time-dependent ROC curve

analysis for censored survival data and calculating their AUC at several time points.

Methods: 1,450 patients with various chronic liver diseases, FibroScan, APRI, FIB-4, Hepascore, FibroMeter2G and MELD at baseline were included in a prospective cohort from 2005 to 2009. Date and causes of death were obtained from the national registry. Statistical analyses were performed using the R package timeROC. When studying liver-related mortality, other causes of death were considered as competing risks.

Results: Baseline values of all liver fibrosis tests (except APRI) had good prognostic performance: AUC(t)>0.70 to predict all-cause death that occurred between 0 and 5 years, AUC(t) were from 0.80 to 0.90 for liver-related mortality. AUC(t=3) for predicting 3-year overall mortality were: 0.80 (95% CI=[0.76-0.83]) for FibroMeter2G, 0.77 [0.74-0.81] for Hepascore (p< 0.001 vs FibroMeter2G), 0.76 [0.73-0.80] for FibroScan (p< 0.028), 0.76 [0.72-0.79] for FIB4 (p< 0.001) and 0.67 [0.62-0.71] for APRI (p< 0.001). The prognostic performance of FibroMeter2G was also significantly higher than those of MELD for a death prediction over 3 years. For liver-related mortality, FibroMeter2G had higher performance than MELD to predict liver-related death over 2 years, whereas FibroScan and Hepascore were more performant than MELD for prediction ≥ 3 years.

Conclusions: The time-dependent AUC comparisons provide more comprehensive information about the differences in prognostic ability between non-invasive liver fibrosis tests.

Poster # P1019

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Validation and comparison of non-invasive markers of liver fibrosis in west-African patients with chronic hepatitis B living in the Gambia

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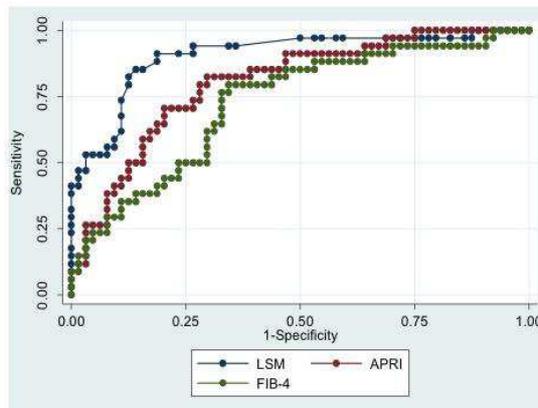
Background and aims: Non-invasive tests of liver fibrosis have been poorly studied in chronic hepatitis B in sub-Saharan Africa. In this study, using liver biopsy as a gold standard, we assessed the diagnostic accuracy of transient elastography (TE), APRI and FIB-4 for evaluating the degree of liver fibrosis in HBV-infected patients enrolled in the PROLIFICA programme in The Gambia.

Methods: Between August 2012 and September 2013, all consecutive patients undergoing liver biopsy had a fasting TE (Fibroscan®) on the same day. Patients with HIV/HCV/HDV coinfections, ascites, liver mass, pregnancy, heart failure, tuberculosis, acute infection and/or invalid liver stiffness measurements (LSM) were excluded from the final analysis; only good quality and concordant pathological results according to two independent blinded pathologists were analysed.

Results: 152 liver biopsies were performed: 18 patients did not fill the inclusion criteria and 26(17%) samples were poor quality or discordant; 108 patients were analysed: male (70%), median age: 35 years (29-39), median LSM: 7.4kPa (6.2-9.6), Metavir Fibrosis: F0-1:66(61%), F2-4:42(39%). For TE, APRI and FIB-4, the AUROC curves were 0.89, 0.80 and 0.73, respectively, for predicting ≥F2; 0.91, 0.79, 0.75 for ≥F3 and 0.98, 0.79 and 0.78 for F4. For TE diagnostic performances were higher compared with those of APRI (P=0.006)

and FIB-4 (P=0.004) with optimal cut-off values at 7.5, 8.3 and 9 kPa for the diagnosis of F2, F3 and F4 respectively.

Conclusions: In West-Africa, TE, APRI and FIB-4 are reliable for detection of fibrosis/cirrhosis in HBV-infected patients, TE having the best performances with slightly different cut-offs compared to Western studies.



Poster # P1022

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Quantification of fibrosis in chronic hepatitis c: performance of transient elastography and Acoustic Radiation Force Impulse using collagen proportionate area as reference

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Background and aims: Liver stiffness, measured by Transient Elastography(TE) or by Acoustic Radiation Force Impulse(ARFI), is proportional to liver fibrosis but also affected by necroinflammation. Since staging of fibrosis is semiquantitative and reported by classes, Collagen Proportionate Area(CPA), a continuous histological variable measuring collagen unaffected by necroinflammation, could correlate more proportionally with TE and ARFI values.

Methods: Ninety-three consecutive patients with chronic hepatitis C(CHC) were evaluated for histological fibrosis(METAVIR score), CPA by Digital Image Analysis(DIA) and liver stiffness by TE and ARFI.

Results: TE was unreliable in six patients (6.4%), while ARFI was feasible in all. By linear regression analysis TE correlated better than ARFI with CPA as a continuous variable(CPA-TE:R2=0.522-p< 0.001; CPA-ARFI:R2=0.454-p< 0.001) and with CPA quartiles(CPAq) (CPAq-TE:R2=0.434-p< 0.001; CPAq-ARFI:R2=0.334 p=0.045). By comparison of ROC curves, the performance of TE in predicting CPA≥10.5%(CPAq 3-4) and CPA>15.4%(CPAq 4) was significantly higher than that of ARFI(AUROC:0.884 vs 0.764;p=0.006 and AUROC:0.863 vs 0.757;p< 0.001 respectively). At univariate analysis age, AST, ALT, GGT, platelets, TE, ARFI and Metavir-grade were related to CPAq3-4. At multivariate logistic regression analysis, only TE(OR:1.67,CI95%:1.13-2.48, p=0.010) was independently related to CPAq3-4. Similarly, AST, ALT, GGT, platelets, TE, ARFI and Metavir-grade were related to CPAq4, but by multivariate analysis only TE(OR:1.39,CI95%:1.01-1.76, p=0.040) was independently associated with CPAq4(>15.4%). The inflammation grade was marginally associated with CPA>15.4%(OR:4.14, CI95%:0.98-17.56, p=0.064).

Conclusions: In patients with CHC, liver stiffness evaluated by TE and ARFI is proportionally related to CPA. TE is slightly more accurate than ARFI for the non-invasive staging of both significant and severe amount of liver fibrosis measured with CPA.

Poster # P1024

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Presence of hepatic steatosis as per non-invasive biomarkers overestimates fibrosis stages based on Liver Stiffness Measurement (LSM) by transient elastography in type-2 diabetic(T2D) patients

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Background and aims: LSM and FibroTest(FT) are validated non-invasive methods to assess liver fibrosis. Necro-inflammatory activity influences LSM overestimating fibrosis. We aimed to evaluate the impact of hepatic steatosis on LSM in T2D patients.

Methods: T2D patients without liver disease that had been screened for fibrosis with FT were reinvestigated using FT and LSM after a 7-year median delay. Patients with minor fibrosis(FT< 0.48;F0F1) at baseline and without progression to advanced fibrosis(AF) on repeated FT were included. Exclusion criteria were the presence of AF by FT(≥0.48;F2F3F4) or activity(ActiTest≥0.17;A1A2A3). Patients staged minor fibrosis by repeated FT but with AF on LSM(≥7.1kPa) at the end of follow-up were considered as supposed LSM overestimation. Severe steatosis(>32% hepatocytes) was defined as SteatoTest≥0.69, Fatty Liver Index(FLI)≥60, Hepatic Steatosis Index(HSI)≥36 or Controlled Attenuated Parameter(CAP)≥283dB/m. LSM applicability was defined as IQR/LSM-ratio< 30%, >60%success rate and ≥10 valid measures.

Results: 102 patients were pre-included[55% male, 62 years, BMI 27.6Kg/m²; ALT 23(10-59), 35% insulin treated]. After exclusion of non-applicable LSM by both M and XL probes (7%), 95 patients were analyzed. Patients with supposed LSM overestimation compared to those without had higher; median[IQR]: BMI 32.0[28.4-43.4] vs. 26.6[24.4-35.3]Kg/m²; waist circumference 109[103-134] vs. 100[93-119]cm; thoracic fold 24.4[19.5-31.5] vs. 18.8[16.5-27]mm; SteatoTest 0.64[0.52-0.84] vs. 0.48[0.32-0.83]; FLI 92[61-99] vs. 60[27-93]; and HSI 46[40-53] vs. 38[34-49],all p< 0.001. In a multivariate analysis[OR(95%CI)], severe steatosis as estimated by SteatoTest [5.2(1.5-22.6);p=0.01], FLI [5.8(1.2-23.6);p=0.03], HSI [6.4(1.2-35.0);p=0.03] or CAP [7.9(1.4-45.0);p=0.02] were associated with supposed LSM overestimation.

Conclusions: The presence of hepatic steatosis in type 2 diabetic patients could overestimate liver fibrosis by liver stiffness measurement.

Poster # P1025

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Utility of transient elastography and non-invasive fibrosis indices in assessing changes in fibrosis in patients with chronic hepatitis C

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Background and aims: Transient elastography (TE) and serum markers of fibrosis correlate with liver histology in the assessment of

liver fibrosis in patients with HCV. Their utility in prospectively assessing changes in fibrosis is less clear.

To compare the ability of TE and serum indices and scores to assess progress of liver fibrosis in HCV patients.

Methods: 450 consecutive patients with HCV were followed for 2 years. TE and non-invasive tests of fibrosis (AST/ALT ratio, Forns' index, Fibroindex, AST to platelet ratio index (APRI), Fib-4, Göteborg University cirrhosis index (GUCI), Lok index and Fibrosis index (FI)) were significantly correlated to initial biopsy, and were repeated after 24 months.

Results: Patients were 39.2±10.2 years old and 67.3% were males. 269 (59.8%) patients received antiviral therapy, and 151 (56.1%) had sustained virological response (SVR). After 2 years, treated patients had significantly lower TE (-0.94±6.12 kPa vs. 0.95±3.48 kPa, p< .0001), Forns' index (-0.1±1.1 vs. 0.1±0.8, p=.028) and Fibroindex (-0.04±0.4 vs. 0.03±0.3, p=.042). Other non-invasive tests did not show significant change between treated and untreated patients. Responders had decrease in TE (-2.82.8±4.4, p< .0001) and non-invasive tests, (Forns' index: -0.5±0.8, Fibroindex -0.2±0.3, Lok index -2±13.7, FI -0.1±0.5) while in non-responders non-invasive tests and TE increased (TE +1.45 ± 7.09 kPa).

Conclusions: Fibrosis evaluated by TE and serum markers regressed after SVR, and progressed in non-responders. TE and Forns' index could be useful in evaluating progress and change in fibrosis over time, and might be alternatives to serial biopsy.

Poster # P1028

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Non-invasive score system for fibrosis (NISF) in chronic liver disease: a new model combining biochemical, elastographic and ultrasound data

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Background and aims: We elaborated a Non-Invasive Score system for Fibrosis (NISF) for chronic viral hepatitis (CH) and Non-Alcoholic Fatty Liver Disease (NAFLD), comparing its diagnostic performance versus FibroScan.

Methods: One hundred and forty-one patients undergoing liver biopsy were prospectively enrolled (83 CH, 58 NAFLD). Clinical, biochemical, elastographic and ultrasonographic parameters (collected by 2 blind operators), with good inter-observer agreement and correlation to histologic stage, were combined into 2 algorithms to predict fibrosis. Predicted fibrosis stages (3 for CH: F0-1, F2, F3-4 and 2 for NAFLD: F0-1, F2-3-4) were compared to Metavir/Brunt histological score.

Results: The algorithms can be processed by a calculator as mathematical formulas or graphically displayed as nomograms.

CH-NISF includes: bluntness of liver edges, irregularity of left lobe surface, S4 diameter, liver stiffness, platelet count, ALT values. CH-NISF agrees with liver biopsy in 80%, 62.5% and 79% of F0-1, F2 and F3-4 stages, respectively. The diagnostic accuracy for discrimination of F3-4 vs F0-1, F2 vs F0-1 and F3-4 vs F2 is better for CH-NISF (AUROCs of 0.95, 0.83 and 0.92, respectively) compared to Fibroscan alone (AUROCs of 0.92, 0.57 and 0.79, respectively).

NAFLD-NISF includes: liver stiffness, platelet count and AST levels. For discrimination of F0-1 versus F2-3-4 stages, NAFLD-NISF and Fibroscan show similar diagnostic accuracy (0.86 for NAFLD-NISF vs 0.81 for Fibroscan).

Conclusions: CH-NISF can be proposed as an easily-available tool, superior to Fibroscan alone, to predict histologic fibrosis,

especially in intermediate stages. Further evaluations are needed to improve NISF accuracy in NAFLD.

Poster # P1035

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Liver (LS) and Spleen Stiffness (SS) in patients with haemoglobinopathies. Data from Transient Elastography (TE)

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Background and aims: LS measured by TE is a non-invasive predictor of liver fibrosis in chronic liver disease (CLD) and in thalassemic patients. Recent data indicate that also SS is useful in assessing liver disease severity in CLD. Present study aimed at assessing reproducibility and major determinants of LS and SS in patients with haemoglobinopathies.

Methods: 120 patients were enrolled: 30 had thalassemia major (TM), 74 thalassemia intermedia, 8 thalassodrepanocytosis and 8 sickle cell disease. Of them, 114 were assessed for LS and SS (#59; 52%) or LS alone (#55; 48% splenectomised). Controls were 70 healthy volunteers. TE examinations were considered accurate with >10 valid measurements, SR >60% and IQR < 30%. Liver fibrosis was staged by METAVIR in HCV RNA positive patients. Intra-class correlation coefficients and AUROC were used for inter-observer agreement and diagnostic accuracy.

Results: LS and SS resulted highly reproducible (0.98, 95% CI 0.95-1.0 and 0.86, 95% CI 0.80-0.91, respectively). At multivariate analysis, major determinants of LS were ALT and PT ratio ($p < 0.0001$), and for SS splenic volume ($p < 0.0001$). In TM and TI, LS had a good diagnostic power in ruling out severe fibrosis/cirrhosis (AUROC 0.93, sensitivity 100%, specificity 70%, LR+ 4; LR- 0.01) in the subset of patients who underwent liver biopsy.

Conclusions: LS and SS determination by TE are highly reproducible tools in patients with haemoglobinopathies. The two parameters resulted significantly higher in patients than in controls and not influenced by iron overload. LS was highly accurate in excluding severe fibrosis/cirrhosis

Poster # P1036

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Assessment of liver fibrosis in patients with autoimmune liver diseases using ARFI elastography

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Background and aims: Transient elastography (TE) is considered as one of the best non-invasive methods staging liver fibrosis in primary biliary cirrhosis. Only few data are present about the diagnostic accuracy of ARFI elastography in patients with autoimmune liver diseases. Therefore, the aim of our study was to evaluate prospectively the diagnostic accuracy of liver stiffness measured by ARFI elastography in comparison to liver biopsy and TE in patients with autoimmune liver diseases.

Methods: A total of 112 patients with autoimmune hepatitis (AIH, n=62) and primary biliary cirrhosis (PBC, n=50) (82 females, 30 males; mean age 53 ± 14 y) were enrolled in the study. All patients received ARFI elastography. Results were compared with TE and liver biopsies in order to evaluate the diagnostic accuracy.

Results: The diagnostic accuracy of ARFI detecting liver fibrosis \geq F3 and \geq F4 in patients with AIH were 0.85 and 0.98, respectively, in comparison to liver biopsy and 0.93 and 0.96 in comparison to TE with cut off values of 1.34 m/s, 1.56 m/s and 1.47 m/s, 1.56 m/s, respectively. In patients with PBC, the diagnostic accuracy detecting liver fibrosis \geq F3 and \geq F4 were 0.96 and 0.88, respectively, in comparison to liver biopsy and 0.92 and 0.97, respectively, in comparison to TE with cut off values of 1.64 m/s, 2.50 m/s and 1.48 m/s, 2.46 m/s, respectively.

Conclusions: ARFI elastography is able to diagnose advanced liver fibrosis and liver cirrhosis in patients with autoimmune liver diseases with an excellent diagnostic accuracy. However, cut-off values were different from those with viral hepatitis

Poster # P1038

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

New quality criteria for transient elastography can increase the proportion of valid measurements with high accuracy for detection of liver cirrhosis and portal hypertension

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Background and aims: Recently, new quality criteria for transient elastography (TE) measurements have been proposed (Boursier et. al. Hepatology 2013): very reliable: IQR/M < 0.1; reliable: IQR 0.1-0.3, or IQR/M > 0.3 if TE < 7.1kPa; poor reliable: IQR/M > 0.3 if TE > 7.1kPa. We evaluated the diagnostic power and accuracy of TE measurements according to these new quality criteria (accurate=very reliable+reliable) for non-invasive assessment of liver fibrosis (liver biopsy) and portal hypertension (HVPG).

Methods: Patients undergoing TE, HVPG measurement and liver biopsy within 3 months at a tertiary care were retrospectively identified.

Results: Among 278 patients (48.7±13.1years, 74.7%male, 75.7%viral etiology, 57% F3/F4), traditional TE quality criteria identified 71.6% reliable measurements, while new criteria yielded in 83.2% accurate LS measurements (23.1% very reliable, 60.1% reliable). Reliable TE values according to traditional or new criteria were all significantly and similarly strong correlated with fibrosis stage (R=0.648 vs. R=0.636) and HVPG (R=0.836 vs. R=0.846). The accuracy for diagnosing liver cirrhosis (F4, cut-off: 14.5kPa) was 76.5% and 75.0% for traditional and new TE criteria, respectively. The positive (PPV) and negative (NPV) values for new criteria at the 14.5kPa cut-off were 83% and 70%. For predicting HVPG≥10mmHg (cut-off: 16.1kPa), the accuracies were 88.9% and 89.8% using traditional or new criteria, respectively. Both criteria resulted in AUCs for diagnosis of HVPG≥10mmHg of over 0.95 with a PPV and NPV of 76% and 97%, respectively.

Conclusions: Applying new quality criteria for TE measurements significantly increases the number of valid TE measurements without affecting accuracy of TE for diagnosis of liver cirrhosis and portal hypertension.

Poster # P1039

Session title: Non-invasive Markers of Liver Fibrosis

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Applicability (APP) criteria for real-time Shearwave Elastography (RT-SWE) by aixplorer compared to Transient Elastography (TE) by FibroScan and to Fibrotest

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Background and aims: App of non-invasive methods, liver stiffness measurements (LSM) by FibroScan and Fibrotest, are defined after excluding failures and unreliable results.(Castera 2010, Poynard 2010). RT-SWE by Aixplorer is a new 3D-elastography coupled with a B-mode imaging.

To better identify applicability criteria for SWE in terms of positioning and acquisition procedure.

Methods: We used standard-AUROC and the strength of concordance with validated methods, LSM and Fibrotest. Each patient had 3-SWE regions of interest (ROI) studied [right lobe (RL)] with 3 measures within each: central-zone (Q-boxC), zone displayed in blue-color (Q-boxB), and in red-color (Q-boxR).

Results: 189 prospective-patients were pre-included with App-FT; 166(87.8%) had concomitant App-LSM: 57%males, age=53yrs, BMI=25kg/m², ALT=40IU/L; 30% advanced fibrosis (AF) as per Fibrotest. Q-boxC and the mean of three C-measurements correlated with Fibrotest (p< 0.05).Q-boxB correlated with Fibrotest (p< 0.05) unlike to Q-boxR (p=NS). Taking Fibrotest as standard, the best AUROCs were obtained for Q-boxC (0.73) and Q-boxB (0.74), but not different from the mean of 3 Q-boxC(0.71) and Q-boxB (0.69).Using the mean of 3 Q-boxC (-B) does not improve diagnosis provided by Qbox-C(-B) alone (p=NS). SWE with a ratio SD/mean-SWE >60% versus < 60% were less correlated to LSM (Spearman correlation-coefficient=0.11,p=0.55vs0.37, p< 0.0001) and to Fibrotest (SCC=0.14,p=0.46vs0.33, p< 0.001).

Conclusions: A single measurement in the central-zone or blue-zone of the ROI has the best accuracy similar to the mean of 3 measurements. ROI zones displayed in red have to be avoided as they are poorly correlated with validated fibrosis markers. SD should be included among quality criteria for SWE-reliability

Poster # P1094

Session title: Viral Hepatitis: Hepatitis B & D - Clinical (Therapy, New Compounds, Resistance)

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Fibrosis regression in persons treated for HBV utilizing transient elastography (FibroScan)

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Background and aims: Chronic hepatitis B (HBV) may result in significant fibrosis with time and requires continuous evaluation. Transient elastography (FibroScan) is the preferred non-invasive modality. We sought to evaluate if therapy for HBV results in changes in fibrosis level utilizing FibroScan technology, and to report if fibrosis regression is affected by the choice of therapeutic agent.

Methods: Retrospective analysis of patients with chronic hepatitis B undergoing follow-up FibroScans (12 months apart) at a

tertiary care center over a 36-month period. A Mann Whitney U test determined whether there was any statistical significant difference between the initial and follow-up FibroScan results with clinical significant change considered ≥ 2.0 kPa.

Results: 102 (66%) of 154 patients (Mean Age = 49; 60.4% Males) were on HBV treatment, divided in to high potency (entecavir or tenofovir) (n=55) or low potency (lamivudine) (n=47) agents. Individuals on therapy showed a significant improvement in average FibroScan of -1.49 kPa (SD=4.85) compared to individuals not on treatment changing -0.11 kPa (SD=2.185) (p=0.0341).

30.2% of the individuals of the treatment group showed ≥ 2.0 kPa improvement, whereas only 20.0% of the untreated group showed a similar change. Fibrosis change was analyzed by treatment type: 34.4% of the high-potency group, 25.6% of the low-potency group, and 8.4% of the no treatment group showed improvements in Fibroscan readings over 12 months.

Conclusions: Therapy of persons with HBV results in improvement of fibrosis level even in short-term follow-up, and can be effectively evaluated by non-invasive methods including FibroScan.

Poster # P1201

Session title: Viral Hepatitis: Hepatitis C - Clinical (Therapy)

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Utility of serum markers and transient elastography to identify serious adverse effects during antiviral therapy in HCV infected cirrhotic patients. a multicenter study

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Background and aims: Antiviral treatment in HCV-cirrhotic patients can produce serious adverse events (SAEs), especially in patients with a low platelet count (< 100,000/ μ l) and low albumin levels (< 3.5g/dL). The aim of our study was to evaluate the diagnostic efficacy of serum fibrosis markers and transient elastography (TE) to identify SAEs during antiviral treatment.

Methods: From January 2010, 190 HCV-infected patients with a liver stiffness measurement (LSM) >14 kPa were evaluated in 5 reference centers. We included those patients receiving double therapy (DT) (n=73) with Peg-IFN and RBV or triple therapy (TT) (n=117) with boceprevir or telaprevir.

Results: Fifty patients (68%) with DT and ninety-five (81%) with TT developed adverse events (p=0.050) during follow up. Bacterial infections occurred in 4 (5%) patients with DT and in 26 (22%) with TT (p=0.002). Eighteen patients (10%) developed SAEs defined as stop of treatment due to: decease (n=3), decompensation (n=5), bacterial infection (n=7) or hematological side effects (n=3). Multivariate analysis (OR, 95%, p) showed the level of albumin and the HALT-C value as independent predictive variables related to the presence of SAEs. Patients with albumin < 3.5 g/dL and HALT-C >68% developed SAEs in 50% compared to only 5% (p=0.029) of those with albumin >3.5gr/dL and HALT-C < 68%.

Conclusions: HCV antiviral treatment in patients with elastography >14kPa who present hypoalbuminemia < 3.5 g/dL and

a HALT-C value >68% is associated with serious adverse effects in half of cases and should be performed in reference centers.

Poster # P1212

Session title: Viral Hepatitis: Hepatitis C - Clinical (Therapy)

Place: Poster Exhibition

Date & Time: April 12– 9:00→18:00

Use of baseline FibroScan to predict efficacy and safety of treatment for 1143 patients in the Telaprevir early access programme

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Background and aims: This study evaluated the usefulness of Fibroscan for predicting anaemia and SVR in patients with genotype-1 HCV with severe fibrosis (F3) or compensated cirrhosis (F4), treated with telaprevir-based triple therapy.

Methods: Patients were treated with telaprevir, pegylated interferon-alpha and ribavirin (PR) for 12 weeks, followed by PR. For 1143 patients tested by Fibroscan at baseline, multivariate logistic regression was used to correlate baseline Fibroscan scores with anaemia (Hb < 10g/dl) and SVR during the study.

Results: Of the 1143 patients evaluated, the median score (interquartile range) was 11.0kPa (10-12) for the 514 F3 patients and 21kPa (16.3 - 29) for the 629 F4 patients. Overall, 729 patients (63.5%) had baseline scores < 18kPa, 270 (23.6%) between 18-30kPa and 149 (13.0%) >30kPa. Higher Fibroscan score correlated with lower platelets and albumin, and higher alpha-fetoprotein and bilirubin (p< 0.001 for each comparison). Baseline Fibroscan score was predictive of anaemia (Hb< 10 g/dL) in univariate analysis (Odds Ratio=2.15 per 10-fold higher, 95% CI=1.23-4.00, p=0.0079), but not in multivariate analysis: independent predictors were older age, female sex, haemoglobin, weight-based ribavirin dosing and baseline HCV RNA. Baseline Fibroscan was also predictive of SVR in univariate analysis (Odds Ratio=0.15 per 10 fold higher, 95% CI=0.07-0.30, p< 0.001), but not in multivariate analysis: independent predictors were Genotype 1b, alpha fetoprotein and prior null response and cirrhosis.

Conclusions: Higher baseline Fibroscan scores were correlated with higher risks of anaemia and lower chances SVR, in univariate analyses. However there were more accurate predictors of these outcomes identified in multivariate analysis

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Does Liver Stiffness measurement (LS) by Transient Elastography (TE) have a role in evaluation of portal hypertension in children?

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Background and aims: There is a need for non-invasive methods able to predict, with acceptable diagnostic accuracy, the presence and the size of varices and the risk of variceal bleeding. This study was designed to determine if TE can indirectly evaluate portal hypertension in children.

Methods: Forty five patients (mean age 11.4±3.07years) suffering portal hypertension of different etiologies were enrolled. All endoscopies were performed by the same endoscopist. The time interval between endoscopy and TE was less than one month. Both endoscopist and FibroScan operator were blinded to the results.

Results: The median (IQR) LS values in 20(44.4%) patients with history of portal hypertensive bleeding were significantly higher than those without: (58(24.9) vs 28(21.9) kPa, p=0.002). Using ROC curve a cut-off value of 43.25 kPa LS for the prediction of bleeding with 80% sensitivity, 74% specificity, 72.7% PPV and 80% NPV.

For patients without or with grade I esophageal varices (EV) (n=19(42.2%) median (IQR) LS was significantly lower than those with significant EV: (26(9) vs56(24.4) kPa, p< 0.001). A cut-off value of 35.1 kPa LS had 84.6% sensitivity, 78.9% specificity, 84.6% PPV and 79% NPV.

In 11(24.4%) patients without or with mild portal hypertensive gastropathy(PHG) median (IQR) LS was significantly lower than those with severe PHG: (24(6.7) vs50.5(35.5)kPa, p=0.001). A cut-off value of 27.85 kPa LS had 79.4% sensitivity, 81.8% specificity, 93.1% PPV and 56.3% NPV.

Conclusions: TE is a reliable noninvasive method not only for prediction of significant varices and PHG, but more importantly; liability for portal hypertensive bleeding in children.

