2012
FibroTest
Survival

Tuesday, Nov. 13
Poster 1733

Long term survival of liver fibrosis after virological cure (SVR) in patients with chronic hepatitis C (CHC): The avenue of the scars?

Thierry Poynard et al. Pitié-salpêtrière hospital, Paris, France

Aim. CHC is both a virologic and a fibrotic disease and complications can occur in SVR pts with residual fibrosis. Due to the burden of repeated biopsies, no study has been done on the long-term outcome of fibrosis after SVR in a large population. FibroTest (FT) has been validated as a biomarker of fibrosis progression (J Hepatol 2012) and of mortality (Gastroenterology 2011). The aim was to estimate the impact of SVR on the 10-year survival of fibrosis (SOFT) using repeated centralized interpretable FT and liver stiffness measurements (LSM) by FibroScan.

Methods. In a prospective CHC cohort, the date of entry was the date of first FT. The main endpoint was a significant decrease of fibrosis, defined as FT decrease of at least 0.20, equivalent to 1 METAVIR stage. SOFT was estimated with the Kaplan-Meier method. The impact of SVR was estimated by logrank test and by Cox model including fibrosis risk factors: Alcohol, BMI, HIV, duration of treatment and the fibrosis progression rate (FPR) from birth to first FT.

Results. 902 pts were included: mean age 49.9yr, women 41%, genotype 1 69%, Caucasian 71%, BMI >30kg/m2 5%, alcohol consumption >30g/d 5%, HIV coinfection 25%. Mean (range) number of FT was 4.1 (2-9), over 4.1yr (1-14), and 2.9 (2-5) LSM over 3.0yr (1-7). Baseline fibrosis was F2F3F4 METAVIR in 44.5% (401/902) including 151 (16.7%) F4, and an FPR of 0.33. SVR was obtained in 178 (19.7%) pts and PCR was still positive in 724 (80.3%) pts (non-SVR). The overall SOFT was 94% (95%CI 92-96%, 332 pts still at risk) and 82% (95%CI 76-88%; 48 at risk) at 5yrs and 10yrs respectively. A fibrosis decrease was observed in 54 pts, almost all of them (51/54;94%) were F2F3F4. In these 401 pts, SVR (n=102) vs non-SVR (n=299), the SOFT were not different at 5yrs (83%;73-93% vs 90%;85-95%) but significant at 10yrs (46%;27-64% vs 76%;66-86% P=0.01). The only factor associated with SOFT in univariate/multivariate analysis was the persistence of detectable HCV RNA (Hazard Ratio;95%CI;Pvalue) /(Risk Ratio/95%CI/Pvalue) = (0.52;0.29-0.94;0.02)/(0.46;0.25-0.84/0.01). HIV, BMI, alcohol consumption, gender, ethnicity, genotypes and previous FPR were not significantly associated. For LSM, followup was shorter and no difference was observed at 5yrs: survival of LSM>=7.1 55% in SVR vs 57% in non-SVR (P=0.60). One case of hepatocellular carcinoma and one cholangiocarcinoma occurred in pts still F4 and F3.

Conclusion. In CHC pts who had previously developed significant fibrosis, viral cure was not associated with fibrosis regression in 46 % of cases, 10 years later. Careful follow-up should be done to detect liver cancer and anti-fibrotic drugs are needed.

BioPredictive S.A.
40 rue du Bac
75007 PARIS
Tel : +33 1 45 44 30 64

BioPredictive

2012
FibroTest
Cirrhosis

Monday, Nov. 12
Poster 1167

Validation of 4-stage cirrhosis classification in patients diagnosed at an early-stage

Marika Rudler et al. Pitié-salpêtrière hospital, Paris, France

Background: Pts with compensated cirrhosis have better prognosis than those with decompensated liver disease. A recent revised 4-stage cirrhosis classification has been proposed (2 sub-stages within compensated cirrhosis: stage 1/2: without/with varices) and 2 sub-stages within decompensated cirrhosis (stage 3: with ascites; stage 4: with hepatic encephalopathy (HE) or jaundice or variceal bleeding (VB)), depicting probabilities of outcome for each sub-stage. With the widespread of non-invasive methods for the detection of fibrosis progression, we hypothesize that cirrhosis is diagnosed at an earlier stage. We therefore aimed to validate prospectively the 4-stage classification, in a cohort of consecutive asymptomatic pts newly diagnosed with cirrhosis by non-invasive methods.

Methods: From 2006, we included all asymptomatic pts referred to our unit of Hepatology for chronic hepatopathy who met the following criteria: (1) discovery of cirrhosis, defined as concordant and interpretable FibroScan≥12.5 kPa and FibroTest≥0.74; (2) no hepatocellular carcinoma (HCC) at 1st ultrasound exam. Endpoints were: (1) 2-year transition from one stage to another; (2) outcome probabilities according to clinical stages.

Results: 181 pts with compensated cirrhosis were included (male gender=71.5%, age=56.0±11.8 yrs, Child-Pugh A=100%, FibroTest=0.87±0.07, Fibroscan=22.0 (95%IC: 20.0-25.7) kPa). Cirrhosis was related to hepatitis C in 61.3%, hepatitis C and HIV in 13.3 %, alcohol and virus C in 6.1%, alcohol in 8.3%, hepatitis B in 3.9%, and NASH/other causes in 7.1% patients. At time of diagnosis, distribution of stages was as follows: stage 1: 152 pts (84.0%), stage 2: 29 pts (16.0%), stage 3 and stage 4: 0%. At 2-year, transition from stage 1 to stage 2 occurred in 12/72 (16.7%) pts with available endoscopy. Transition from stage 1 to stage 3 occurred in 2/152 (1.3%) pts, transition from stage 2 to stage 3 occurred in 1/29 (3.4%) pts; transition to stage 4 occurred in 1 pt who was stage 1 at inclusion (0.7%). At 2-year, no death was recorded. Mean follow-up was 40.6 ±20.2 months. 16/181 (8.8%) pts developed HCC during follow-up, without any difference in stage 1 or 2 cirrhosis at diagnosis (p=0.73). Aetiology of cirrhosis was considered as treated in 37 pts (21 HCV-sustained responders, 6 HBV pts with negative viral load under analogues, 10 weaned from alcohol). None of those pts progressed to stage 3 or 4.

Conclusion: Transition from one stage to another is far lower than previously described when the diagnosis of cirrhosis is made at an early stage with non-invasive methods. Specific treatment of cirrhosis cause is the best way to prevent complications.

2012
FibroTest
Tenofovir impact

Saturday, Nov. 10
Poster 449

Longitudinal changes in liver fibrosis as assessed by fibrotest during up to 3 years in patients with chronic hepatitis B virus (HBV) infection receiving tenofovir DF after failure to other antiviral treatment

Florian van Bömmel1 et al. University Hospital Leipzig, Germany.

Background: TDF is a strong inhibitor of HBV replication and recently it has been demonstrated that the majority of treatment-naïve patients achieves a histologic regression of liver fibrosis during five years of treatment. However, this association has not yet been shown for patients receiving TDF monotherapy after failure to other nucleos(t)ide analogues. We have studied longitudinal changes in liver fibrosis in these patients using Fibrotest (FT, Biopredictive, France), a non-invasive fibrosis tests validated for the assessment of liver fibrosis in patients with HBV infections.

Methods: FT was performed in 171 frozen serum samples from 57 patients (means of age 48±15[range,18- 75] years, BMI 35±3 [18-35], HBV DNA 7.6±6.7 [2.8-8.8] log10 copies/mL, HBsAg 3.6±0.6 [2.3-4.6] IU/mL, 40 HBeAg positive, 36 (62%) HBV genotype D) representing baseline and treatment years 2 or 3. Baseline results of FT were compared to HBV DNA and HBsAg levels, HBV genotype, BMI and patient's age by multivariate analysis.

Results: At baseline and year 2 and year 3, FT scores showed a mean of 0.39± (range, 0.05-0.99), 0.37± (0.6-0.95) and 0.41± (0.5-0.82), respectively (p=n.s.). The translation into Metavir scores F0, F0-F1, F1, F1-F2, F2, F3 and F4 for the same time points resulted in 15, 7, 7, 13, 4, 4 and 7 patients at baseline, 15, 6, 5, 8, 4, 2, 2, and 4 patients at year 2 (11 missing) and 15, 5, 4, 6, 2, 6, 1 and 5 patient at year 3 (13 missing). Higher Metavir scores at baseline were associated with HBV DNA levels > 6 log10 copies/mL, age > 50 years and HBV genotype D at baseline (p<0.001). Between baseline and year 2 or 3, F3 and F4 fibrosis remained unchanged in 5 patients, improved in 4 and worsened in 2 patients fro F3 to F4. Additionally, F1 and F2 fibrosis increased to F3 or F4 in 3 patients. Persistence or progression of fibrosis was associated with male gender (100%), age > 45 years at treatment initiation (p=0.006), and HBsAg levels < 3.5 log10 IU/mL at month 12 of treatment. All patients with fibrosis progression had a BMI > 26.

Conclusion: In some of these difficult-to-treat patients a regression in fibrosis was present during TDF treatment, however in less than reported in treatment-naïve patients. An age > 45 years, elevated BMI and lower HBsAg levels at 12 months of treatment were risk factors for persistence or progression of fibrosis. Non-invasive fibrosis tests can be a useful tool to assess fibrosis during NUC treatment, however they need to be investigated in larger studies.

BioPredictive S.A.
40 rue du Bac
75007 PARIS
Tel : +33 1 45 44 30 64

BioPredictive

FibroTest/FibroSure Scientific Publications

Posters for AASLD 2012

2012
FibroTest
Entecavir impact

Saturday, Nov. 10
Poster 450

Impact of entecavir (ETV) on liver fibrosis and activity as assessed by the non-invasive methods of FibroTest–ActiTest (FT-AT) and liver stiffness measurements (LSM) in patients with chronic hepatitis B (CHB)

Fabien Zoulim et al. Hospices Civiles de Lyon, Lyon, France.

Background. A meta-analysis of longitudinal studies in patients (pts) with chronic hepatitis B (CHB, n=772) demonstrated that the treatment impact on the fibrosis progression rate was similar when using FT or liver biopsy (LB). The same was observed for LSM, although with possible overestimation of fibrosis regression due to LSM variability related to necroinflammatory activity (NIA) (AVT 2010). Both FT and LSM received EASL guidelines recomandations in CHB (J Hepatol 2012). Aim: To prospectively evaluate the histological impact of approved ETV treatment (0.5 mg per day) using non-invasive methods, i.e. FT, AT and LSM. **Methods**. 133 CHB monoinfected, NUC-naive pts without comorbidity were pre-included in 19 centers in France. Several data were recorded at baseline (M0) and every six months (M6, M12) the 1st year and at the end of the 2nd year of treatment: viral load (VL), FT-AT, LSM and LB at M0 only according to the center's routine practice. VR being defined as undetectable HBVDNA<20 IU/ml and <9 IU/ml Statistics included Bonferroni Multiple Comparison Tests.
Results. 116 pts without missing data were included;. Repeated measures ANOVA showed a significant regression between M0,M6 and M12 mean(se) of significant NIA as per AT: M0 0.55(0.03) vs M6 0.27(0.03, P<0.0001), and M12 0.24(0.03, P=0.0001 vs M0). The same was true for AF as per FT: M0 0.68(0.02) vs M6 0.50(0.02, P=0.001) vs M12 0.52(0.02, P=0.007). No difference between M0 and M6 fibrosis as estimated in pts with repeated App-LSM [M0 8.2(0.9) vs M6 7.2(1.1,P=0.50) vs M12 6.1(0.39, p=0.62) kPa], including AF pts [10.4(1.3) vs 8.5(1.5,P=0.35)kPa], excepted for M12 in AF pts . 3(0.61,P=0.03 vs M0)kPa]. 20/34(59%) pts with presumed A1A2A3 M0 were A0 at M6. 8/24(33%) pts with presumed M0 AF, were F0F1 at M6. Decreases of FT and AT were observed both in pts with and without VR: 15.4% vs 50% (p=0.17) and 70% vs. 43% (p=0.16), respectively.
Conclusion. After 6 months of ETV treatment, AF and NIA as presumed by FT and AT were significantly reduced, regardless of the VR.

2012
FibroTest
Cardiovascular
outcome

Friday, Nov. 9
Break Out
Session V: Fatty
Liver
2PM-3PM

FibroTest and Framingham Risk Score: a combination that improves the prediction of cardiovascular events in type-2 diabetic (T2D) patients with metabolic syndrome

Hugo Perazzo et al. Pitié-salpêtrière hospital, Paris, France

Background: Nonalcoholic fatty liver disease(NAFLD) is a frequent disease inTD2patients and seems to be associated with cardiovascular complications(CVC) and liver fibrosis. Framingham Risk Score(FRS) and presence of metabolic syndrome(MS) accurately identifies patients at moderate to high risk of CVC. The prognostic value of FibroTest(FT) has been validated in patients with chronic hepatitis C, B and alcoholic liver disease but not in patients with NAFLD.
Aims: 1)To evaluate the 5 years-prognostic value of FT in T2Dpatients with MS for the survival without CVC.2)To evaluate if the association of FRS and advanced liver fibrosis (AF-METAVIR F≥2) estimated by FT are more predictive than FRS alone for CVC.
Methods: T2D-patients without liver disease history were prospectively followed(2004-2012) for CVC [myocardial infarction, unstable angina, coronary-bypass, ischemic stroke]. MS was defined by the criteria of the NCEP-ATP III. Subjects with FRS>15% were considered as moderate-high risk of CVC.
Results: 423 T2D patients with MS were included[55.7% males, age 60.2 years, BMI(range) 30.1(19-64.4)Kg/m2]. During a median follow-up of 5.3 years, 56(13.2%) patients developed CVC (79 coronary disease and 5 strokes). The survival without CVC (Kaplan Meier mean 95%CI) was: for AF patients for FT 67%(50-84) vs 87%(83-90) in non-AF(Logrank P<0.01) and for FRS 83%(79-88) in moderate-high FRS vs 92%(86-98) in low FRS(P=0.04). In T2D patients with high-moderate FRS the survival without CVC was 66%(48-83) in AF patients vs 85%(81-90) in non-AF (P<0.01). In a multivariate analysis(Cox model) FT remained significant after adjustment on FRS for the prediction of survival without CVC: risk ratio=6.1(95%CI 1.4-26.4; P=0.04).
Conclusion: FibroTest has a significant prognostic value for the 5-years survival without CVC. FT improves the prediction of CVC in moderate to high FRS TD2-patients with metabolic syndrome. Moderate to high FRS without advanced liver fibrosis have the same risk of CVC than low FRS patientsdiagnosis of cirrhosis is made at an early stage with non-invasive methods. Specific treatment of cirrhosis cause is the best way to prevent complications.

Find all the scientific publications of BioPredictive non-invasive tests on the website :

www.biopredictive.com

BioPredictive S.A.
40 rue du Bac
75007 PARIS
Tel : +33 1 45 44 30 64

BioPredictive

FibroTest/FibroSure Scientific Publications

Posters for AASLD 2012

2012
FibroMax
NASH

Monday, Nov. 12
Poster 1534

Validation of FibroMax and NAFLDscore in a cohort of NAFLD Spanish patients

Rocío Gallego-Durán et al. Valme University Hospital, Sevilla, Spain.

Aim: To analyze the usefulness of several available non-invasive methods (FibroMAX® and NAFLD-Fibrosis-score®) in clinical practice in patients diagnosed with NAFLD.

Methods: 49 NAFLD biopsy-proven patients were included (61% male, 39% female, mean age 49±13 years, 53% metabolic syndrome. Liver biopsy was scored according to NAS and Kleiner stage: (15/49) 30% NAS Score<4, (39/49) 79% mild fibrosis (F2-F4)). FibroMax® test was calculate following the instructions of manufacturers analizing sex, age, weight, height, BMI, Alpha-2-Macroglobulin, haptoglobin, apolipoprotein A1, bilirrubin, GGT, ALT, AST, fasting glucose, total cholesterol and triglycerides. The final outputs were FibroTest (mean 0.37±0.27), SteatoTest (mean 0.61±0.21), NashTest (mean 0.50±0.17), NAFLD-Fibrosis-score (mean -2.08+1.53). FibroMax and NAFLD-Fibrosis-score were correlated with histopathological data and these results were analyzed by SPSS 19.0.

Results: Spearman coefficient correlation between fibrosis score by Kleiner and FibroTest was r=0.36, p=0.01, and in NAFLD-Fibrosis-score r=0.335, p=0.03. The AUROC for prediction of advanced fibrosis was 0.89 (95% CI: 0.80-0.99) for Fibrotest and 0.83 (95%CI: 0.63-1.0) for NAFLD-Fibrosis-score. To discriminate significant fibrosis AUROC 0.66 (95%CI: 0.50-0.82) for FibroTest and 0.61 (95%CI: 0.41- 0.82) for NAFLD-Fibrosis-score. One out of 36 (2.7%) patients showed advanced fibrosis and FibroTest<0.58 and 1/25 (4%) showed advanced fibrosis when NAFLD-Fibrosis-score was < -1.455. AUROC for NASH diagnosis using NashTest was 0.70 (95% CI: 0.53-0.87). 8/8 (100%) patients with NashTest=0.75 showed NasScore > 4. SteatoTest showed an AUROC 0.67 (95% CI:0.46-0.89).

Conclusions: Fibrotest® is a reliable and valuable method in order to exclude advanced fibrosis and to confirm NASH in NAFLD patients. FibroTest® is slightly better than NAFLD-Fibrosis-score® predicting advanced fibrosis. Both tests are easy to perform and allow making a regular follow-up in patients with NAFLD.

2012
FibroTest
Elastography

Monday, Nov. 12
Poster 1317

Liver fibrosis evaluation using supersonic shear imaging (SSI, Aixplorer®): diagnostic performance in comparison with FibroTest® (FT) and Fibroscan® (FS)

Elena Luckina1 et al. Pitié-salpêtrière hospital, Paris, France

Background: SSI is a new transient bidimensional elastography with few studies in chronic liver diseases (LD), no assessment of variability factors (VF), and limited comparisons with other validated fibrosis biomarkers (FIB). Methods without a gold standard have been recently validated for assessing FIB performances without liver biopsy (PlosOne 2008, J Hepatol 2012).

Aim: To assess SSI performances for fibrosis diagnosis using the strength of concordance (SofC), with FT and stiffness measured by 2 FS probes (LSM-M and XL).

Methods: 556 patients(pts) were prospectively included: 62%males; 66%Caucasian, 18%Sub-Saharan, 16%other; 32%HCV,23%HBV,9%ALD,19%NAFLD,17%other LD; ascites 9%; age 54yrs; BMI>27kg/m2 38%, 40% significant fibrosis presumed by FT. SSI result was considered unreliable (UnR) if the minimal (Min) was 0 kPa. The SofC between SSI and FT, LSM-M, LSM-XL were estimated by intra-class correlation coefficient (ICC) and the impact of VF by Spearman coefficient (SCC).

Results: 410pts had simultaneous SSI, FT and LSM, and among 343pts with all applicable (App) tests, the SSI concordance was 0.22[95%CI (0.12-0.32;P<0.0001)] with FT, 0.42(0.16-0.56;P=0.001) with LSM-M and 0.44(0.23-0.59;P<0.0001) with LSM-XL, without difference between ICC. In 67pts with at least 1 non-App test ICC(95%CI) between SSI and the 3 reference tests were lower vs the 343pts App, but only significantly for SSI vs FT 0.04(-0.21-0.28) vs 0.22(0.12-0.32;P<0.01); SSI/LSM (0.34 vs 0.42;NS), and SSI/XL (0.23 vs 0.44;NS). Among 343pts with App tests it was not expected that ICC was also reduced in 94pts with Min-SSI >0 but <1kPa: in comparison with 249pts with Min-SSI>=1kPa: SSI/FT 0.15(-0.03-0.33) vs 0.26(0.15-0.38;P<0.05), SSI/LSM 0.32(-0.04-0.57) vs 0.49(0.28-0.63;NS), SSI/XL 0.35(-0.02-0.61) vs 0.50(0.35-0.62;NS). Min-SSI was not associated with operator, gender, age, steatosis, activity, cause of LD and ethnicity but associated negatively with cutaneous thickness (CT) (SCC=-0.19;P<0.0001) and BMI (-0.18;P=0.0007). In patients with CT<2mm the ICC SSI/FT was 3 times greater than in CT>=2mm: 0.30(0.18-0.41) vs 0.10(-0.09-0.28;P=0.02). As for LSM-M, SSI was associated with steatosis (SteatoTest) SCC=0.19(P=0.0007) and with activity (ActiTest) SCC=0.18(P=0.0009). However activity did not significantly decrease the concordance with FT: ICC=0.18(0.06-0.29) in A0A1 vs 0.26 in A2A3 (-0.03-0.51;NS); in S0S1 0.24(0.11-0.36) vs 0.20(0-0.39) in S2S3.

Conclusion: SSI is highly correlated with FT, LSM-M and LSM-XL in different LD. VF in SSI must be further analyzed including the impact of CT and BMI. Min-SSI<1kPa could be at risk of false positive/negative for the prediction of fibrosis.

FibroTest/FibroSure Scientific Publications

Posters for AASLD 2012

2012
FibroTest
Best applicability

Monday, Nov. 12
Poster 1377

Applicability criteria of the supersonic shear imaging (SSI) by Aixplorer, compared to the applicability of FibroTest (FT) and liver stiffness measure (LSM) by FibroScan

Elena Luckina1 et al. Pitié-salpêtrière hospital, Paris, France

Introduction. Applicability (App) for non-invasive methods has been studied in large cohorts: for LSM estimated to 84.2% (Castera, Hepatology 2010) and for FT to 98% (Poynard ClinChem 2011).
Aims.1) Evaluate the SSI App in a population of chronic liver diseases 2) Identify the SSI positioning of the acquisition square with the best App. Methods. Patients with concomitant LSM (probes M and XL), SSI and FT were preincluded after excluding failures (FR) and unreliable results (UnR) according to manufacturer recommandations (MR) for LSM and FT and for SSI with minimum 0 KPa and doubtful images. 3 SSI were taken in the right lobe: SSI-Q1 according to MR, 2 other located at 1cm (Q2) and 2cm (Q3) deeper and 1 SSI in the left lobe (QLL).
Results: 556 consecutive patients were included: 344(62%) men, median age 54years(20-89), 32%HCV, 23%HBV, 19%NAFLD, 9% ALD, 17% other causes; 76%Caucasian, 18% sub-Saharan-Africa, 6%Asian; median BMI=25kg/m2(15-52). According to FT and LSM-M or XL, 223(40.1%) and 178(32.4%) had advanced fibrosis and 97(17.4%) and 106(19.3%) cirrhosis, respectively. The median depth of SSI measurement were: Q1 3.5cm, Q2 4.5cm, Q3 5.75cm, QLL 4.25cm; the ultrasound distance between the surface of the skin and the liver capsule (DistSLC) was 1.83cm(0.9 -5.6). FR were 0% for both FT and Q1, LSM-M 6.8%(38/556,p<0.0001 vs FT and Q1), LSM-XL 1.6%(7/448,p=0.03 vs FT and Q1;p<0.0001 vs LSM-M). The UnR were : FT 1.6%(9/556), SSI Q1 2.2%(12/556,p=NS versus FT), LSM-M 5.6%(31/556,p=0.0005 vs FT ;p=0.005 vs Q1), LSM-XL 9.2%(41/448,p<0.0001 vs FT and Q1;p=0.004 vs LSM-M). The App after excluding both FR and UnR were: FT 98.4%, SSI-Q1 97.8%, LSM-M 87.5% (p<0.0001 vs FT and Q1) and LSM-XL 10.7%(48/448,p<0.0001 vs FT and Q1;p=NS vs LSM-M). The App-Q1, Q2 and Q3 were similar (97.8%, 97.7% and 96.4%,all p=NS) and all higher than the App-QLL 67.8%(p <0.0001 vs Q1, Q2 and Q3). The correlations SSI-Q1 with FT and LSM were better in patients with App SSI-Q1 (0.60 and 0.65) compared to non-App (0.32 and 0.30), respectively. In subjects with clinical ascites, the App Q1 was 30/31(96.8%), higher than the App LSM-M 15/31(48.4%,p<0.0001) and the App LSM-XL 18/28(64.3%,p=0.002 vs Q1;p=NS vs LSM-M). In multivariate analysis, the factors associated with the non-App of all SSIs (Q1,Q2,Q3,QLL) were: BMI>27kg/m2 an important activity, ascites (all P<0.0001) and a DistSLC>1.83cm(p=0.001).
Conclusion: The most App SSI is located in the right lobe between 3.5-5.75cm below the skin, providing results in over 96.4% of cases; SSI appears to be interesting in patients with ascites, significantly more App than LSM. BMI, DistSLC, activity and ascites are factors of failure of SSI.

2012
FibroTest
HBV outcome

Monday, Nov. 12
Poster 1321

Non-invasive tests for liver fibrosis and liver stiffness predict 5-year outcomes of patients with chronic hepatitis B

Victor de Ledinghen et al. Hepatology Unit, Hopital Haut-Leveque, Pessac, France

Background and aims: Liver stiffness measurement and non-invasive tests predict overall survival and survival with liver-related death, in chronic hepatitis C. However, in chronic hepatitis B (HBV), we just know that liver stiffness is associated with the risk of hepatocellular carcinoma. We evaluated the 5-year prognostic value of liver stiffness (FibroScan), non-invasive tests of liver fibrosis, and liver biopsy, to predict overall survival and survival with liver-related death, in chronic hepatitis B.

Methods: In a consecutive cohort, we prospectively assessed fibrosis, on the same day, with liver stiffness, FibroTest, APRI, FIB-4, and liver biopsy. We reported death, liver-related death and liver transplantation during a 5-year follow up.

Results: A total of 600 patients (male 64%, mean age 42 years, inactive carriers 36%) with chronic hepatitis B was included. Median follow-up was 49.7 months. At 5 years, 29 patients were dead (13 liver-related deaths) and 4 patients had liver transplantation. Overall survival was 94.1% and survival without liver-related death 96.3%. No liver death was observed in inactive carriers. Survival was significantly decreased in patients diagnosed with severe fibrosis, whatever the non-invasive method used (p<0.0001), or liver biopsy (p=0.02). Patients had their prognosis decreased as liver stiffness and FibroTest increased. The 5-year overall survival was 97.1% in patients with liver stiffness < 9 kPa, and 61.5% in patients with liver stiffness > 20 kPa, and 96.8% for FibroTest ≤0.73, and 49.2% in patients with FibroTest >0.85.

Conclusion: Non-invasive diagnosis of liver fibrosis, either by liver stiffness measurement or FibroTest, can predict survival in chronic hepatitis B. Thus, these tools may help physicians to early assess prognosis and discuss specific treatments, such as liver transplantation.

Find all the scientific publications of BioPredictive non-invasive tests on the website :

www.biopredictive.com

BioPredictive S.A.
40 rue du Bac
75007 PARIS
Tel : +33 1 45 44 30 64

BioPredictive

2012
FibroTest
Alcohol

Monday, Nov. 12
Poster 1332

Fibroscan (Transient Elastography) is the most reliable non-invasive method for the assessment of severe fibrosis and cirrhosis in alcoholic liver disease.

Michael Fernandez et al. Erasme Hospital, Brussels, Belgium.

BACKGROUND: Fibroscan(FS)has proved invaluable in the non invasive assessment of liver fibrosis in various chronic liver diseases.Surprisingly,no clear consensus with regard to the best cut-offs for the degree of liver fibrosis exists in alcoholic liver disease(ALD),which is common in Western countries.The aims of the study were to compare the liver stiffness (LS) by the FS and different biochemical markers with histological scores of liver fibrosis,and to establish the best LS cut-offs for severe fibrosis(F≥3)and cirrhosis(F4).We also evaluated the influence of high-AST on the reliability of our LS cut-offs.

METHOD: Our retrospective study included 139 compensated ALD patients(≥5 drinks a day in the preceding year),who underwent liver biopsy(Percutaneous in 54 or Transjugular liver biopsy in 85 patients).Fibrosis was staged using Metavir classification.Standard liver imagery,FS,FIBROTEST(FT),Fib-4,APRI and FORNS scores and the simple biochemical markers such as AST and ALT were tested in all patients. Areas under the receiver operating characteristic curves(AUROC)were used to determine the diagnostic accuracy for F≥3 and F4.

RESULTS: Characteristics of the population were the following:68% men,mean age 54±0.86 years,mean porto- systemic gradient 6.8±0.61 mmHg.Distribution of liver fibrosis was as follow:F0:17.3%,F1:6.5%,F2:23%,F3:12.2%and F4:41%.41 of the 139 patients presented with ASH signs at liver biopsy.Mean AST, ALT, GGT and LS, were 78.5±7.03UI/l, 68.2±7.63UI/l,442.14±53.56UI/l and 25±2.03kPa,respectively.Failure rate of FS was of 10%.AUROC(95% confidence interval)for the diagnosis of severe fibrosis(F≥ 3)and cirrhosis(F4)were 0.89(0.83-0.95;p< 0.0001)and 0.94(0.90- 0.97;p<0.0001)respectively, better than the biochemical scores like **FT(0.81 and 0.88)**,APRI(0.67 and 0.75),FIB-4(0.70 and 0.72)and FORNS(0.65 and 0.78).The best cut-off values of LS for predicting F≥3 and F4 were respectively 10.5kPa(Se:91% Sp:67 % with PPV:75% NPV: 87%)and 15.7kPa(Se: 90 % Sp:87% with PPV:82 % NPV:93%).According to these cut-offs, the use of liver biopsy could have been avoided in 80% and 88% of patients. AST presented a significant positive correlation with LS levels(i.e. AST and LS concomitantly increased).However, surprisingly, diagnostic accuracy and cut-offs value were not modified by removing AST>100UI/l conversely to previous studies.Furthermore,FS correlated significantly(r=0 .67;p< 0.0001)with the porto-systemic gradient.

CONCLUSION: Our results suggest that LS is currently the most reliable non-invasive indicator of severe liver fibrosis and cirrhosis in ALD and should be recommended in the initial assessment and follow up of liver fibrosis in our ALD patients.

BioPredictive S.A.
40 rue du Bac
75007 PARIS
Tel : +33 1 45 44 30 64

BioPredictive