FibroTest Scientific Publications
Key Publications for 2015

Bonnard 2015
FibroTest
APRI
Fib-4
HCV
Genotype 4

Comparison of liver biopsy and noninvasive techniques for liver fibrosis assessment in patients infected with HCV-genotype 4 in Egypt.

Bonnard P, Elsharkawy A, Zalata K, et al.J

Viral Hepat. 2015 ;22:245-53.

FibroTest along with non-patented markers, APRI and Fib-4, and transient elastography (TE) was revalidated agains biopsy in monoinfected 312 HCV –genotype 4 Egyptian patients. For FibroTest, AUROC (Obuchowski method) was reported 0.76 (0.69–0.82) and no influence of schistosomiasis was noticed. The diagnostic value per protocole was comparable to TE, but for a signifinactly higher applicability. Because of epidemic context of HCV authors focused on Fib-4 interest while TE was juged less applicable in this population with high BMI and FibroTest measurements may not routinely performed in Egypt. However we are reluctant to not standardized (i.e. platelets) analyses and to markers based on transaminases more subject to variability with cytolysis and necro-inflammatory activity.

Zelber-Sagi 2015
FibroTest
SteatoTest
NAFLD
Coffee

FibroTest and SteatoTest for the evaluation of cofee consumption effects

Coffee consumption and nonalcoholic fatty liver onset: a prospective study in the general population.

Zelber-Sagi S, Salomone F, Webb M. et al. Transl Res. 2015 Mar;165(3):428-36.

In this cross-sectional study in a sample of the general population, authors evaluated the association between coffee consumption and fatty liver onset in the general population. Fatty liver was diagnosed with abdominal ultrasound (US) and SteatoTest (FibroMax), whereas FibroTest was used to assess fibrosis degree. High coffee consumption was associated with a lower proportion of clinically significant fibrosis F2 Metavir (FibroTest higher than 0.48): 9% vs 16%, P<.05. High coffee consumption is not able to counteract steatogenesis as per SteatoTest and liver US, whereas was associated with lower odds for significant fibrosis as per FibroTest {OR=0.49, 95%CI(0.25–0.97); P<.05}, the more important determinant of clinical outcomes in NAFLD.

Haseltine 2015
FibroTest
HCV
after SVR
APRI
Fib-4

Non-invasive followup with Fibrotest after SVR

Successful treatment with telaprevir-based regimens for chronic hepatitis C results in significant improvements to serum markers of liver fibrosis.

Haseltine EL1, Penney MS, George S, Kieffer TL. J Viral Hepat. 2015.

Authors performed a retrospective analysis of data generated from one Phase 2 and two Phase 3 telaprevir clinical studies (PROVE3, ADVANCE, REALIZE). N=1208 patients had repeated biomarker tests, FibroTest, APRI, FIB-4 and Forns' Score before and after HCV treatment (at 24 weeks). Consistent with previous studies, patients who attained SVR exhibited significant improvements in scores from each of these tests after treatment. Overall FibroTest improvement in SVR was more modest (i.e. fibrosis regression of less than a Metavir stage) suggesting a more realistic approach as FibroTest not being related to necroiflammatory imporovement as ALT is not included in its algorithm, contrary to APRI and Fib-4.

Bio Predictive

Pais 2015
FibroMax
HBV

Epidemiology of steatosis according to FibroMax in chronic hepatitis B (CHB)

Prevalence of steatosis and insulin resistance in patients with chronic hepatitis B compared with chronic hepatitis C and non-alcoholic fatty liver disease.

Pais R, Rusu E, Zilisteanu D et al. Eur J Intern Med. 2015;26:30-6.

The authors proposed to compare the prevalence and determinants of steatosis (FibroMax) and insulin resistance (IR) in CHB compared to CHC and pure NAFLD. Patients with CHB (N=110), CHC (N=111) and NAFLD (N=136) were evaluated by biomarkers of steatosis (SteatoTest>0.38 as a surrogate for steatosis >5%), IR (HOMA-IR) and fibrosis (FibroTest>0.48 as a surrogate for significant fibrosis, >=F2). The lowest degree of IR (mean Homa 2.3), of steatosis >5% (21%) and of fibrosis >=F2 (10%) was in CHB. CHB patients with steatosis had higher BMI (29 vs. 24 kg/m2), waist circumference (96 vs. 84cm) and HOMA-IR (3.9 vs. 1.8) than those without steatosis. However, metabolic risk factors and HOMA-IR were not associated with significant fibrosis as in CHC.

Perazzo 2014
FibroMax
Prognosis
Metabolic

Prognostic value of liver fibrosis and steatosis biomarkers in type-2 diabetes and dyslipidaemia.

Perazzo H, Munteanu M, Ngo Y, Lebray P, Seurat N, Rutka F, Couteau M, Jacqueminet S, Giral P, Monneret D, Imbert-Bismut F, Ratziu V, Hartemann-Huertier A, Housset C, Poynard T; the FLIP Consortium.

Aliment Pharmacol Ther. 2014 Sep 3. doi: 10.1111/apt.12946

A study carried out in 2312 patients with type-2 diabetes and / or dyslipidemia followed for 12 years assessed the prognostic value of non-invasive biomarkers (FibroMax panel) of liver fibrosis (FibroTest) and steatosis (SteatoTest) in patients with type diabetes 2 and / or dyslipidemia. The presence of advanced fibrosis or severe steatosis was associated with an increased risk of overall mortality. In addition, a presence of an advanced liver fibrosis at baseline but also the progression to advanced liver fibrosis during follow-up, were both predictors of cardiovascular events in patients with type 2 diabetes.

Poynard 2014
FibroTest
Cirrhosis severity
HCV

Staging chronic hepatitis C in 7 categories using fibrosis biomarker (FibroTest™) and transient elastography (FibroScan®).

Poynard T, et al

J Hepatol. 2014;60:706-14.

The aim of the study was to extend the validation of FibroTest and transient elastography (TE) by Fibroscan as markers of severity of cirrhosis, defined by the following critical steps: cirrhosis without complications (F4.1 = FibroTest score 0.75-0.84), occurrence of esophageal varices (F4.2 = FibroTest score 0.85-0.94) and severe complications (F4.3 = FibroTest score 0.95-1.00): primary liver cancer, bleeding from varices or decompensation (ascites, encephalopathy, or jaundice). Individual data updates to 3927 patients, including 1046 with cirrhosis without complications at baseline were collected from three prospective cohort studies ("EPIC," "Paris," and "Bordeaux"). Among patients without varices at baseline, the incidence of varices at 5 years was 4% with a significant predictive value for FibroTest (AUROC 0.77, p <0.001). At 10 years, the FibroTest was predictive of serious complications, including hepatocellular carcinoma (AUROC 0.84 p <0.0001). Similarly to FibroTest, transient elastography was predictive of serious complications (p <0.0001) but with a lesser applicability. The authors conclude that the increase in FibroTest scores was associated with the occurrence of serious complications, including all hepatocellular carcinoma, liver failure, and bleeding of esophageal varices but also associated with the development of esophageal varices.

Poynard 2014
FibroTest
HBV
Cirrhosis Severity

Staging chronic hepatitis B into seven categories, defining inactive carriers and assessing treatment impact using a fibrosis biomarker (FibroTest®) and elastography (FibroScan®).

Poynard T, Vergniol J, Ngo Y, Foucher J, Thibault V, Munteanu M, Merrouche W, Lebray P, Rudler M, Deckmyn O, Perazzo H, Thabut D, Ratziu V, de Ledinghen V; FibroFrance Study Group and the Bordeaux HBV Study Group.

J Hepatol. 2014 Jul 10. pii: S0168-8278(14)00457-7.

According to the model validated in chronic hepatitis C, this study validated FibroTest and the transient elastography (TE) as severity markers of cirrhosis (F4), defined by the following critical steps: uncomplicated cirrhosis (F4.1), occurrence of esophageal varices (F4.2) and severe complications (from F4.3): primary liver cancer, bleeding from varices or decompensation (ascites, encephalopathy or jaundice). After 10 years of follow-up of 1312 patients pooled from two prospective cohorts ("Paris" and "Bordeaux") with no history of complications, the incidence was 1.7% F4.2 and 3.7% F4.3 including hepatocellular carcinoma (HCC). FibroTest and TE were predictive for F4.2 and F4.3 and can identify cirrhosis patients with high morbidity. In addition, the combination of normal FibroTest-ActiTest better identified the low progression of fibrosis and inactive HBV carriers, compared with their standard definition based on ALT.

Park 2014
FibroTest
HBV
Prognostic

Prognostic value of the combined use of transient elastography and FibroTest in patients with hepatitis B.

Park MS, Kim SU, Kim BK, Park JY, Kim DY, Ahn SH, Shin SH, Kang W, Moon C, Han KH.

Liver Int. 2014 Sep 2. doi: 10.1111/liv.12678.

An independent study evaluates the prognostic value of the combination of FibroTest and the transient elastography by Fibroscan to predict hepatic events in 151 patients with chronic hepatitis B. Authors concluded that the combination FibroTest-Elastography significantly predicted the development of liver complications but with only a slight additional advantage compared to FibroTest alone.

Xu XY 2014
FibroTest
HBV
Meta-Analysis

The effectiveness of noninvasive biomarkers to predict hepatitis B-related significant fibrosis and cirrhosis: a systematic review and meta-analysis of diagnostic test accuracy.

Xu XY, Kong H, Song RX, Zhai YH, Wu XF, Ai WS, Liu HB.

PLoS One. 2014 Jun 25;9(6):e100182.

This is a conducted systematic review of published literature on PubMed, EMBASE and Cochrane (30 studies) to compare the diagnostic performance and accuracy (QUADAS survey) in chronic hepatitis B (HCB) for the three biomarkers : APRI, FIB-4, and FibroTest. Standard AUROCs for APRI, FIB-4, and FibroTest were for fibrosis 0.77, 0.75, and 0.84 and for cirrhosis 0.75, 0.87, and 0.90, respectively. Age and etiology affected the diagnostic performance of APRI but not that of FibroTest. The authors concluded that the Fibrotest had excellent diagnostic accuracy for identifying fibrosis and cirrhosis associated with chronic hepatitis B, while the FIB-4 had only modest benefits.

Salkic 2014
FibroTest
HBV
Meta-analysis

FibroTest/Fibrosure for significant liver fibrosis and cirrhosis in chronic hepatitis B: a meta-analysis.

Salkic NN, Jovanovic P, Hauser G, Brcic M.

Am J Gastroenterol. 2014 Jun;109(6):796-809.

A systematic review of studies with FibroTest vs biopsy in chronic hepatitis B (CHB) was made recently by Salkic et al. using MEDLINE and EMBASE searches with a total of 16 identified studies (N = 2494) and 13 studies (N = 1754) included in the meta-analysis of heterogeneity for advanced fibrosis and cirrhosis, respectively. The AUROCs (95% CI) for significant fibrosis and cirrhosis were excellent, 0.84 (0.78-0.88) and 0.87 (0.85-0.90), respectively, including all CHB studies. Although the meta-analysis presents some limitations related to the lack of individual data, it re-validates FibroTest in CHB.

Pan 2014
HBV
Tenofovir Follow-up

Efficacy and safety of tenofovir disoproxil fumarate in asian-americans with chronic hepatitis B in community settings.

Pan CQ et al.

PLoS One. 2014;9:e89789

The study was conducted in adult Asian American patients with chronic hepatitis B (CHB), prospectively enrolled and treated with tenofovir 300 mg once daily and for 48 weeks. The impact of Tenofovir treatment on fibrosis was assessed by repeated FibroTest at baseline and at week 48 (W48). 90 patients were included, 60% were HBeAg-positive at baseline and, at W48, 82 % had undetectable HBV DNA and normal ALT in 66%. The percentage of patients with FibroTest score F0 (no fibrosis) has increased from 48% to 51%, and the percentage of F4 (cirrhosis) decreased from 4% to 1%. Two patients had F3 at baseline and F2 at W48. The 4 patients with F4 (cirrhosis) fibrosis at baseline have regressed at W48 (3 F3 and one F2) No patient had worsening of cirrhosis during the study. Once again, this longitudinal study highlights the usefulness of FibroTest for longitudinal monitoring of CHB patients undergoing long-term treatment.

Perazzo 2014
APRI
Analytics
ALT

Variability in definitions of transaminase upper limit of the normal impacts the APRI performance as a biomarker of fibrosis in patients with chronic hepatitis C: "APRI c'est fini ?".

Perazzo H et al. & EPIC3 Group.

Clin Res Hepatol Gastroenterol. 2014 Sep;38(4):432-9.

Some noninvasive markers include transaminase ALT or AST (example of APRI). The study proposed to evaluate the impact on fibrosis markers of two transaminase–related limitations: 1) the lab-related variability in the definition of the upper limit of normal AST (AST-ULN) and 2) the risk of overestimation of fibrosis associated with necroinflammatory activity. For this, two control populations were used: N=7521 healthy volunteers and N=393 blood donors and a population of patients (N=1651) with APRI score, FibroTest and biopsy. ULN AST-varied in the control populations from 26 to 49 IU/L, varying the prevalence of advanced fibrosis stages and cirrhosis from 34.7% to 68.5% and from 11.4% to 32.3%, respectively (all p <0.0001). The diagnostic performance of APRI varied significantly, whereas the performance of FibroTest not including transaminasis were stable. In conclusion, AST-LSN variability could lead to erroneous performance of APRI and other tests of fibrosis including transaminase.

Munteanu 2014
FibroTest
Cirrhosis
Elastography

FibroTest has similar accuracy for cirrhosis with TE

FibroTest (FT) has similar accuracy for cirrhosis in 'intention-to-diagnose' which is superior to transient elastography (TE) in chronic hepatitis B.

Munteanu M., Huot M., Ngo Y., Poynard T Liver Int. 2014: 34: 1128–1129. Letter

This is a response letter to Castera L. Liver Int 2014 that proposed to clarify and upgrade fully validated blood test (i.e. FibroTest) compared to TE performances in cirrhosis wrongly considered the most suitable noninvasive marker in cirrhosis. Firstly, blood test like FibroTest are much more applicable (reliable) compared to TE (97% vs. 81% according to Castera et al. Hepatology 2014) with an even higher TE failure rate in cirrhotics with ascites. Authors argued that in a recent meta-analysis the overall FibroTest AUROC for cirrhosis was 0.87 without differences in authorship independency or HIV-coinfection. The AUROC is higher than 0.80 for cirrhosis in "intention-to-diagnose" that was superior to TE. Finally, authors emphasis that an independent 5-years prognostic study showed similar prognostic values for TE and FibroTest, therefore suggesting similar performances for cirrhosis as the prognosis is mainly related to the evolution the patients with severe fibrosis and cirrhosis. They conclude to the non-superiority of TE versus blood marker FibroTest in cirrhostics, with even a more advantageous overall applicability of FibroTest.

Minville 2014
FibroMax
FibroTest
Sleep Apnea

Nonalcoholic fatty liver disease, nocturnal hypoxia, and endothelial function in patients with sleep apnea.

Minville C, Hilleret MN, Tamisier R, Aron-Wisnewsky J, Clement K, Trocme C, Borel JC, Lévy P, Zarski JP, Pépin JL.

The nocturnal hypoxia characteristic of obstructive sleep apnea (OSA) is a potential contributing factor to the development of non-alcoholic fatty liver disease (NAFLD). The panel FibroMax (including SteatoTest, NashTest, and FibroTest) were used to assess noninvasivelly steatosis, steatohepatitis (NASH) and fibrosis cohort 226 patients with OSA. 61.5% of patients had moderate or severe steatosis and the independent factors associated with were : triglycerids levels, insulin resistance and the nocturnal cumulative duration with oxygen saturation <90% (CT90); 38% of subjects had borderline NASH (N1) or NASH (N2) according to NashTest and that was associated with waist circumference, triglycerids, HOMA-IR and the metabolic syndrome ; and 20% of subjects had advanced fibrosis or cirrhosis and age> 50 years, male gender, abnormal blood sugar or diabetes were all factors associated with fibrosis (F1 or more). Relationship between CT90 and hepatic lesions was observed only in the morbidly obese subjects. In conclusion, NAFLD could be a dysfunction in the mechanisms involved in the OSA, and NAFLD and NASH could be easily evaluated by the FibroMax panel in subjects with OSA.

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