Screening general population

Harris 2017
FibroTest
Elastography
Histology
Screening Review

FibroTest for the screening of unknown liver diseases in the general population

Prevalence of clinically significant liver disease within the general population, as defined by non-invasive markers of liver fibrosis: a systematic review.

Authors proposed to review 19 studies of fibrosis screening, among which 11 used non-invasive tests. Only TE and FibroTest were compared with histological endpoints. The prevalence of advanced liver fibrosis and cirrhosis in the general population (GP) were 0.9–2.0% and 0.1–1.7%, respectively; even higher prevalences (0–27.9% and 2.4–4.0%, respectively) than in the GP were reported in targeted populations with risk factors of liver disease, such as non-alcoholic fatty liver disease, hazardous alcohol use, or type 2 diabetes. FibroTest was considered as the most validated for liver fibrosis screening and to consistently detect otherwise unrecognized liver disease in GP (Poynard et al. 2010, Zelber-Sagi et al 2012 and Grattagliano et al. 2013).

Authors concluded that only the use of validated specific markers like FibroTest can consistently detect disease that would have otherwise been missed by current referral pathways based on abnormal liver function tests.

Ginès 2016
FibroTest, Elastography, Screening Review

Review of the screening studies with FibroTest and TE

Screening for liver fibrosis in the general population: a call for action.

Authors alert about the lack of strategies for detection of liver fibrosis at early stages, while liver cirrhosis is one of the main causes of death and disability worldwide. The authors review the screening studies in the general population, using noninvasive methods, FibroTest or TE. Authors reminded the screening done using FibroTest on 7463 French subjects over 40 years or more that revealed a prevalence of unknown advanced fibrosis of 2.8% and of unknown cirrhosis of 0.3%. Most of the cases from the general population with previously unknown fibrosis were associated with non-alcoholic fatty liver disease. The prevalence of increased liver stiffness as per TE was about 17% suggesting a possible overestimation of fibrosis by TE mainly due to the presence of steatosis (see Poynard authors' reply below).

Authors concluded that these data suggest that programs of screening for liver fibrosis in the general population should be assessed.

Find all the general and scientific informations regarding our non-invasive tests on our website :
https://biopredictive.com
Poynard 2017
FibroTest Screening Letter

FibroTest more accurate for screening early fibrosis stages
Screening studies of transient elastography and FibroTest in the general population.
Authors wrote this letter to Gines et al. to stress several points. First, is that a prospective screening with FibroTest in 696 type 2 diabetes patients was missing from the review. Two direct head-to-head comparisons of non-invasive tests already exist and there is a higher prevalence of significant fibrosis presumed by TE than by FibroTest. These differences could be related to a lower performance of TE than FibroTest as a fibrosis marker of early fibrosis stages. Authors suggest that screening studies in very low-risk patients such as blood donors and healthy volunteers, may improve detection of false positive and therefore the appropriate cutoffs for screening.

Metabolic Liver Diseases

FibroMax = FibroTest + ActiTest + SteatoTest + NashTest + AshTest

FibroMax is a liver panel used in the diagnosis and the follow-up of liver fibrosis, steatosis, and inflammations with a blood sample and is done at a local laboratory:
- FibroTest: estimates the liver fibrosis
- ActiTest: estimates the necroinflammatory activity
- SteatoTest: estimates the liver steatosis
- NashTest: estimates the non-alcoholic steatohepatitis
- AshTest: estimates the alcoholic steatohepatitis

Bauer 2017
FibroMax Psoriasis Awareness

Screening for NAFLD with FibroMax in patients with psoriasis
Noninvasive Testing for Nonalcoholic Steatohepatitis and Hepatic Fibrosis in Patients With Psoriasis Receiving Long-term Methotrexate Sodium Therapy.

The aim of the study was to evaluate if the FibroMax panel (NASH FibroSure) can be used for patients with psoriasis to aid in determining for the initiation of methotrexate (MTX) therapy and to monitor for the development of MTX-induced hepatotoxic effects. Among patients that underwent FibroMax testing prior to starting MTX therapy, 27.5% had elevated fibrosis scores as per FibroTest and 78.3% had elevated steatosis scores as per SteatoTest. Among patients who underwent testing during MTX therapy, the cumulative MTX dose was associated with higher hepatic fibrosis as per FibroTest score in women. Authors concluded that FibroMax panel could be used to monitor changes in fibrosis in patients with psoriasis receiving MTX.

SAF score is the new simplified histologic classification for the main liver lesions (steatosis, activity, and fibrosis) in NAFLD risk patients.

SAF ready

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Find all the general and scientific informations regarding our non-invasive tests on our website:
https://biopredictive.com
Viglino 2017
FibroMax
SteatoTest
NashTest
FibroTest
COPD
NAFLD

Screening for NAFLD with FibroMax in chronic obstructive pulmonary disease (COPD)

Nonalcoholic fatty liver disease in chronic obstructive pulmonary disease.


The authors aimed to investigate the relationship between COPD severity and nonalcoholic fatty liver disease (NAFLD) using validated FibroMax panel. The prevalences of steatosis, NASH and fibrosis as per SteatoTest, NashTest and FibroTest were 41.4%, 36.9% and 61.3%, respectively. In multivariate analysis, steatosis and fibrosis as per SteatoTest and FibroTest, respectively, were significantly associated with gender, body mass index (BMI), untreated sleep apnoea and insulin resistance. Only BMI was a risk factor of NASH as per NashTest. The authors concluded that NAFLD is highly prevalent in COPD and biomarkers of liver damage may allow specific lesions to be detected and treated.

Olivares Gazca 2017
FibroMax
NAFLD
Thrombocytopenia
Elastography

Thrombocytopenia of the NAFLD diagnosed with FibroMax.

More on the thrombocytopenia of the nonalcoholic fatty liver disease


Authors are hematologists and proposed to study the cause of mild thrombopenia in a prospective cohort of patients. FibroMax along with transient elastography were used to exclude cirrhosis. After exclusion of other causes of thrombopenia, authors identified by using FibroMax that non-alcoholic fatty liver disease (NAFLD) should be considered as a cause of mild thrombocytopenia that was associated with overweight.

Wiest 2017
FibroMax
Morbid obeses
NAFLD
Shearwave Elastography

FibroMax panel in clinical trial on morbid obese patients

Targeting the gut-liver axis in liver disease.


Authors listed the research clinical trials involving the gut-liver axis that is widely implicated in the pathogenesis of liver diseases. One of the cited studies is that of Cohen-Erza et al. Hepatology 2016 (Abstract) performed on morbidly obese patients with NAFLD and type 2 diabetes who underwent endoscopic duodenal-jejunal bypass liner (Endobarrier) implantation. The implementation of the device led to significant improvements in the patients’ metabolic profile, liver fibrosis stage, liver fat content and steatohepatitis, as evaluated by SteatoTest and NashTest included in the Fibromax panel and by 2D-shearwave elastography.
FibroTest/FibroSure Scientific Publications

Key Publications for 2017

**HIV**

**Steininger 2017**

FibroTest for HIV

Acute Hep C Elastography

Utiliy of FibroTest in HIV-infected men having sex with men (MSM) after acute HCV-infection (AHC)

HIV-positive men who have sex with men are at high risk of development of significant liver fibrosis after an episode of acute hepatitis C.


Acute hepatitis C (AHC) virus infection remains a major health concern in HIV-infected MSM. Authors aimed to study the course of liver fibrosis, using FibroTest and transient elastography (TE), after an episode of AHC. Among 178 patients included, 10.8% had a spontaneous clearance and 70.7% achieved SVR. Three years after the first ACH, 39.4% of patients had significant liver fibrosis (METAVIR >=F2 stage) and 11.6% cirrhosis, mainly associated to age, alcoholism, and nonresponse to ACH therapy. In conclusion, this subgroup at high-risk of significant liver fibrosis could warrant closer monitoring by non-invasive markers and should be considered for early treatment.

**Matta 2016**

FibroTest for HIV/HCV

Review of FibroTest performances in HCV-HIV and HBV-HIV

Use of Non-invasive Testing to Stage Liver Fibrosis in Patients with HIV.


Authors reviewed and listed the studies that supported the use of FibroTest in HIV co-infected patients. FibroTest performances (AUROC) for advanced fibrosis in HIV-HCV co-infection were as follows (Number of patients, Author-Year): 0.856 (N=130, Myers 2003), 0.81 (N=272, Cacoub-2008), 0.778 (N=444, Cales-2010), 0.85 (N=116, Castera-2014), 0.75 (N=101, Schmid-2015) and 0.84 for cirrhosis (N=101, Schmid-2015). FibroTest performances for advanced fibrosis in HIV-HBV co-infection for advanced fibrosis/cirrhosis were: 0.77 / 0.87 (N=108, Bottero-2008) and 0.86 / 0.93 (N=59 Miaihes-2011), respectively. Authors concluded that non-invasive test should be considered in HIV co-infected patients to evaluate fibrosis in conjunction with other clinical, laboratory, and imaging data.

**Piroth 2017**

FibroTest for HIV/HCV

FibroTest used in HIV/HCV-co-infected

Efficacy and safety of direct-acting antiviral regimens in HIV/HCV-co-infected patients


Authors evaluated the efficacy and safety of all-oral DAA-based regimens in HIV/HCV-co-infected patients enrolled in the French nationwide ANRS CO13 HEPAVIH observational cohort. A total of 323 patients (median age 53 years) were included. Cirrhosis diagnosis was based on liver biopsy, liver stiffness >12.5 kPa, FibroTest >0.75 or on physical and biological signs of end-stage liver disease. The SVR rate at 12 weeks after treatment cessation was 93.5% overall. The all-oral DAA regimens were well tolerated and most common adverse effects were fatigue and digestive disorders.
Boyd 2017
FibroTest
HIV/HBV

Liver Fibrosis Regression assessed using FibroTest during tenofovir-containing ART

Liver fibrosis regression and progression during controlled hepatitis B virus infection among HIV-HBV patients treated with tenofovir disoproxil fumarate in France: a prospective cohort study.


The aim of this study was to evaluate the dynamic of liver fibrosis as per FibroTest, at baseline and every six to twelve months, in n=167 TDF-treated HIV-HBV co-infected patients followed-up (FU) sixty months (IQR = 36-93). Among patients with baseline F3-F4 fibrosis (28.1%), 14.9% regressed to F0-F2 at last FU-visit. Among patients with F0-F2-baseline fibrosis (71.9%), 16.7% progressed to F3-F4 at last FU-visit. Fibrosis progression was not associated with virus-related factors, but with male gender, older age, lower nadir CD4+ cell count, higher fasting glycaemia and anaemia at TDF-initiation. Authors stressed the importance of continuous fibrosis monitoring as part of routine care in this patient group.

Taibi 2017
FibroTest
Coopscore
Hepascore
HIV/HBV

FibroTest versus other biomarkers in HIV-HBV co-infected

Diagnostic accuracy of the Coopscore© to predict liver fibrosis in human immunodeficiency virus/hepatitis B virus co-infection.


Authors assessed comparatively the performances of FibroTest, Coopscore (CS) and 3 other blood biomarkers – Hepascore (HS), Zeng score (ZS), Fibrometer (FM) in 97 patients HIV-HBV co-infected. Histological fibrosis staging (METAVIR) was the reference. For predicting significant fibrosis (Metavir >=F2), FibroTest performance (AUROC) was 0.778, significantly greater than HS, ZS, FM and similar to the CS performances. To predict severe fibrosis (F3) or cirrhosis (F4) all scores had similar performances to CS. This study revalidated once more, the excellent performance of FibroTest for fibrosis staging among HIV-HBV co-infected patients.
HBV

Parikh 2017
FibroTest HBV Review

Review article on fibrosis assessment for chronic hepatitis B

Fibrosis assessment in patients with chronic hepatitis B virus (HBV) infection.

It was admitted that the detection and quantification of liver fibrosis is a key factor for chronic hepatitis B management and prognostication. Authors stressed that non-invasive algorithms can reliably stage liver disease and are now incorporated into International guidelines for HBV management. Authors reminded that in a meta-analysis of 71 studies, APRI had lower performance than FIB-4, transient elastography (TE) and FibroTest in both HBV and HCV patients. FibroTest was identified to rule out cirrhosis as per recent meta-analysis. (Houot et al. Aliment Pharmacol Ther 2016)

Alcoholic Liver Disease

Voican 2017
FibroTest Elastography Alcohol

New FibroTest validation in excessive drinkers

Transient elastography alone and in combination with FibroTest® for the diagnosis of hepatic fibrosis in alcoholic liver disease.

This multicenter prospective study aimed to evaluate whether the combination between FibroTest and liver stiffness measurements (LSM) by transient elastography adds diagnostic value relative to LSM alone for the liver fibrosis assessment in patients with excessive alcohol intake. Two hundred seventeen heavy drinkers underwent liver biopsy, LSM by TE, FibroTest and other biomarkers. LSM had limits as it was significantly correlated not only with fibrosis stage but also with steatosis grade. Moreover, LSM values were also significantly higher in patients with alcoholic hepatitis. For LSM, Fibrotest and combination LSM-Fibrotest, the Obuchowski performances for the diagnosis of fibrosis were 0.94, 0.92 and 0.95, respectively. The performance of LSM was similar with that of Fibrotest. The combination LSM- FibroTest did not improve the performance of FibroTest alone.
Crisan 2017
FibroMax
HCV
IP-10

FibroMax panel correlations with IP-10 in HCV patients
Interferon-Gamma-inducible protein-10 in chronic hepatitis C: Correlations with insulin resistance, histological features & sustained virological response.
The aim of this study on HCV patients was to evaluate the role of serum IP-10 levels on sustained virological response (SVR) and the associations with insulin resistance (IR), liver histology and surrogate liver disease markers from the FibroMax panel. IP-10 was significantly associated with fibrosis stage as per FibroTest, activity degree as per ActiTest, significant steatosis as per SteatoTest and IR in patients with chronic HCV infection.

Natarajan 2017
FibroTest
HCV
Prognosis

FibroTest used to identify cirrhosis in chronic hepatitis C
Role of Non-hepatic Medical Comorbidity and Functional Limitations in Predicting Mortality in Patients with HCV.
Authors proposed to determine the effect of comorbidities and functional status on survival in a cohort of 1,052 HCV chronic carriers. The functional status was assessed as per Schonberg Index (SI) based on age, gender, and medical comorbidities. Comorbidities and functional limitations as per SI predicted higher mortality in patients with HCV, independently of cirrhosis. Baseline cirrhosis as per FibroTest had the highest hazard ratio for mortality in HCV patients, higher than congestive heart failure or alcohol ingestion suggesting that FibroTest is a real marker of severity of the disease. Comorbidities as per SI should be taken also into account for predicting mortality.

Prenner 2017
FibroTest
HCV
HCC

FibroTest used to identify cirrhosis in chronic hepatitis C with hepatocellular carcinoma (HCC)
Hepatocellular carcinoma (HCC) decreases the chance of successful hepatitis C virus therapy with direct-acting antivirals.
The aim of this study was to assess the efficacy of all-oral-DAA regimens in 421 HCV+ cirrhotic patients who have or had HCC compared to those without HCC. Cirrhosis was defined by one of the following: liver biopsy, transient elastography >12.5 kPa, acoustic radiation force impulse >2.0 m/s, MR-elastography >5 kPa, or FibroTest (FibroSURE) >=0.74. Failure to achieve SVR occurred in 21% of patients with HCC compared to 12% of patients without HCC (p=0.009). Patients with active HCC seemed more likely to fail hepatitis C treatment than patients without HCC.
FibroTest correlations with 25-vitamin D and SVR in HCV cirrhotic patients

25-Vitamin D levels in chronic hepatitis C infection: association with cirrhosis and sustained virologic response.

Backstedt D1, Pedersen M1, Choi M1, Seetharam A1, Ann Gastroenterol. 2017;30:344-348.

Low serum 25-Vitamin D (vit D) levels are associated with advanced fibrosis in chronic hepatitis C infection. The authors aimed to evaluate the prevalence of vit D deficiency in 218 patients and the predictive value of pretreatment levels for a sustained virologic response (SVR). 56.4% patients had cirrhosis as determined by liver biopsy, FibroTest blood test, or imaging. The prevalence of vit D deficiency was significantly higher in cirrhotics (P=0.04) than in non-cirrhotics. However, pretreatment or during therapy supplementation vit D was not associated with an increased rate of SVR.

HCV Treatment Prioritization in trials using FibroTest

Asselah 2017
SOFO-VELPA
Sofosbuvir/Velpatasvir in Patients With Hepatitis C Virus Genotypes 1-6 and Compensated Cirrhosis or Advanced Fibrosis.

Jacobson 2017
SOFO-VELPA-VOXI
Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials.

Pol 2017
SOFO-DACLA
Safety and efficacy of daclatasvir-sofosbuvir in HCV genotype 1

Gheorghe 2017
OBV/PTV/r+DSV
Real-Life Use of 3 Direct-Acting Antiviral Regimen in a Large Cohort of Patients with Genotype-1b HCV Compensated Cirrhosis.

Preda 2017
OBV/PTV/r+DSV
Real-world efficacy and safety of ombitasvir, paritaprevir/ribavirin in genotype 1b patients with hepatitis C virus cirrhosis.
Kucharska 2017

**FibroTest in hemophilia patients**

*Stage of liver fibrosis in patients with congenital bleeding disorders and infected with hepatitis C virus.*


The aim of this study was to determine the utility of FibroTest and of shearwave elastography (2D-SWE by Aixplorer) for the liver fibrosis assessment without liver biopsy in 71 chronically infected HCV carriers with congenital hemophilia. Cirrhosis or significant fibrosis (METAVIR score F4 or >=F2) was observed, respectively, in 18% and 28% of patients using FibroTest and in 3% and 12% using 2D-SWE. Age and the estimated duration of the infection were directly associated with the severity of fibrosis. The authors concluded that both FibroTest and 2D-SWE might properly assess the stage of liver fibrosis in patients with hemophilia, particularly when used together and in relation to other clinical parameters.

Poinsot 2017

**FibroTest in childhood lysosomal acid lipase deficiency (LALD)**

*Childhood/adult-onset lysosomal acid lipase deficiency: A serious metabolic and vascular phenotype beyond liver disease-four new pediatric cases.*


The childhood lysosomal acid lipase deficiency (LALD) is a rare genetic disease and the carriers often present severe fatty liver disease with early cirrhosis. Authors assessed 4 cases of LALD under long-term statin treatment. FibroTest, transient elastography (TE) and liver biopsy assessed liver fibrosis. All 4 cases showed significant liver fibrosis at biopsy (n=2 F3 and one F2); FibroTest results were concordant with TE in 3 from 4 cases. Authors concluded on the importance to evaluate the hepatic and cardiovascular impact in children with LALD.

Preda 2017

**FibroTest in Fontan-associated liver disease (FALD)**

*Non-invasive Investigations for the Diagnosis of Fontan-Associated Liver Disease in Pediatric and Adult Fontan Patients.*


Authors evaluated the usefulness of FibroTest and transient elastography (TE) for Fontan-associated liver disease (FALD) and compared them to ultrasound (US) and standard laboratory tests (SLT). 27 patients were assessed and 93% and 100% staged F1 or more as per FibroTest and TE, respectively. FibroTest results were suggestive of fibrosis regardless of time post-Fontan diagnosis. TE was significantly correlated with time post-Fontan, but not with US-detected liver abnormalities. Authors concluded that non-invasive markers of liver fibrosis do not appear to provide reliable insight into progression of FALD-related fibrosis and recommended to maintain standard monitoring with SLT and liver US.
Consensus definitions of staging fibrosis using non-invasive tools
Late presentation of chronic viral hepatitis for medical care: a consensus definition.

European consensus working group* released definitions of advanced and late stage liver disease in hepatitis B and C virus infections. Two definitions were agreed upon.

- Advanced liver disease was defined as significant fibrosis assessed by Fibrotest > 0.59, APRI score > 1.5, FIB-4 > 3.25, or transient elastography (TE) > 9.5 kPa
- Late stage liver disease was clinically defined by the presence of decompensated cirrhosis and/or hepatocellular carcinoma.

Authors expect that consensus definitions will be easy-to-use reference for public health authorities and will help to improve epidemiological understanding of viral hepatitis as well as testing policies and strategies.

* The working group included viral hepatitis experts from the European Association for the Study of the Liver (EASL), experts from the HIV in Europe Initiative, and relevant stakeholders including patient advocacy groups, health policy-makers, international health organisations and surveillance experts.

Use of fibrosis algorithms instead of standard liver enzymes
Developing a new algorithm to diagnose advanced liver fibrosis: A lift or a nudge in the right direction?
Adams LA, Sterling RK. J Hepatology 2017.66: 1111–1113

The editorial stressed the importance of the need to change the paradigm of liver disease assessment in the community to include fibrosis algorithms rather than relying on standard liver enzymes. Authors listed the observed diagnostic accuracies for the different combinations of FibroTest as follows (Algorithm, Number of patients, Author-Year): for cirrhosis 80% (APRI->FibroTest; N=332; Boursier 2009), 94% (FibroTest+Fibroscan; N=332; Boursier 2009), 92% (APRI->FibroTest; N=2035; Sebastiani 2009), 89% (APRI->FibroTest; N=302; Castera 2010), 96% (FibroTest+Fibroscan; N=302; Castera 2010), 91% (APRI->FibroTest; N=1013; Sebastiani 2012), 94% (APRI+FibroTest; N=1013; Sebastiani 2012), 89% (APRI->Fibroscan; N=1785; Boursier 2012), 94% (FibroTest+Fibroscan; N=1785; Boursier 2009) and for advanced fibrosis of the different combinations of FibroTest were: 85% (APRI + FiB4 + FibroTest; N=446; Crisan 2012).

Authors suggested that overall accuracy and predictive values of non-invasive makers could be improved if two non-invasive fibrosis assessments are used.
Modelisation of targeted treatment recommendations in chronic hepatitis C
Are targeted treatment recommendations in chronic hepatitis C tailored to diagnostic methods of fibrosis?

The impact of different treatment strategies based on stage of fibrosis (FibroTest, transient elastography and other patented blood markers) was evaluated in three countries (France, Italy and UK), using a mathematical model. This analysis showed that:

i) A prioritization strategy of HCV treatment for patients with advanced disease would decrease the overall impact of treatment on morbidity and mortality; and

ii) A strategy initiating HCV treatment to all (universal therapy) would already show a benefit in reducing 5-year morbidity and mortality.