FibroTest/FibroMax Scientific Publications

Key Publications for 2018

EASL 2018

Metabolic Liver Diseases (MLD)

NASH-Test V2 : a new quantitative test for the diagnosis of nonalcoholic steatohepatitis (NASH)

Impact of steatosis and inflammation definitions on the performance of NASH tests.

Poynard T, Munteanu M, Charlotte F, et al. FLIP consortium, the FibroFrance-CPAM group; and the FibroFrance-Obese group. Eur J Gastroenterol Hepatol. 2018;30:384-91.

Authors aimed to construct a new noninvasive quantitative test for the diagnosis of NASH (NIT-NASH) using a simplified histological definition* that permits to identify more cases of NASH than the standard histological NASH-CRN definition (Eur J Gastroenterol Hepatol. 2018). A total of 1,081 metabolic liver disease (MLD) patients were included from the FibroFrance Project (USA-NCT01927133) and the FLIP European Consortium (http://www.flip-fp7.eu/). NIT-NASH does not include BMI and fasting glucose to avoid variability in obese and type2 diabetic (T2D) patients. The performances [AUROC (95%IC)] were high (0.77 and 0.81), in both training and control groups, respectively.

NIT-NASH had higher performances than NAFLD fibrosis score, BARD, FIB-4 and ActiTest.

Significant MLD (A2 or F2 as per NIT-NASH combination with FibroTest) was strongly associated with diabetes when applied in larger populations (US and French cohorts).

In conclusion, the new NIT-NASH enables a quantitative assessment of NASH in subjects with MLD risk. Important fact, this new diagnosis of NASH (NIT-NASH) does not require BMI and glucose any longer.

** The new definition of MLD does not require the presence of steatosis and the presence of both lobular inflammation and ballooning and enable the diagnostic of NASH in patients with steatosis less than 5%, and a grade 2 lobular inflammation without ballooning. (Poynard et al. Eur J Gastroenterol Hepatol. 2018) (see next abstract)*

POYNARD 2018

NASHTest v2
NASH-FibroTest,
Metabolic,
Steatohepatitis

New quantitative test for the diagnosis of nonalcoholic steatohepatitis (NASH)

Diagnostic performance of a new noninvasive test for nonalcoholic steatohepatitis using a simplified histological reference.

Poynard T, Munteanu M, Charlotte F et al; for the FLIP Consortium, the FibroFrance-CPAM Group, the FibroFrance-Obese Group. Eur J Gastroenterol Hepatol. 2018. doi: 10.1097/MEG. 0000000000001064.

Authors proposed to improve the identification of NASH cases by using a SAF-simplified-score, which does not require the presence of steatosis and of both activity features as the standard definition does [NASH-CRN (Kleiner Hepatology 2005)].

The impact of definitions variability on the prevalence of NASH (evaluated by FibroMax) was studied for: 1/ less 5% steatosis for NASH; 2/ no steatosis requirement for NASH; 3/ severe NASH based on the SAF-activity grade at least A2.

Patients were from the FibroFrance project (USA-NCT01927133) and from the FLIP consortium (http://www.flip-fp7.eu/). The present study confirmed that the variability in the estimated performance of NIT-NASHs is related to the diverse histological definitions of NASH.

In conclusion, a simplified definition of NASH, based on activity and not requiring >5% steatosis, had the lowest risk of false-positives/false-negatives.

POYNARD 2018

New definition
NASHTest v2,
NASH-FibroTest,
Metabolic,
Steatohepatitis

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FibroTest and SteatoTest for the NAFLD screening in Type 2 Diabetes

European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO) clinical practice recommendations for the management of non-alcoholic fatty liver disease: evaluation of their application in people with Type 2 diabetes.

Sberna AL, Bouillet B, Rouland A, et al. Diabet Med. 2018;35:368-375.

The study aimed to evaluate the application of the recently proposed recommendations by the European Associations EASL, EASD and EASO for the diagnosis, treatment and follow-up of non-alcoholic fatty liver disease (NAFLD) in n=179 type 2 diabetes (T2D) patients.

According to the guidelines, the following non-invasive tests (NIT) were done for steatosis and fibrosis evaluation: SteatoTest and FibroTest [FibroMax panel, (BioPredictive, France)], proton magnetic resonance spectroscopy (H-MRS), fatty liver index score (FLI) and non-alcoholic fatty liver disease fibrosis score (NFS).

According to H-MRS, 68.7% of participants had steatosis (liver fat content >5.5%) and according to SteatoTest, 78.7% had important steatosis (score >0.57) with 70% concordant results with H-MRS.

FibroTest identified 2.2% T2D having clinically advanced fibrosis (FibroTest >0.57), but normal ALT, AST and GGT.

Non-invasive assessment of non-alcoholic fatty liver disease: Clinical prediction rules and blood-based biomarkers.

Vilar-Gomez E, Chalasani N. J Hepatol. 2018;68:305-15.

Based on the assumption that the diagnostic accuracy can be improved by combining biomarkers, the authors proposed an algorithm using non-invasive tests (NIT) that includes FibroTest, to assess patients with NAFLD risk.

The algorithm combines several prediction rules, free biomarkers (e.g. NAFLD fibrosis score, FIB-4 index and BARD score, Pro-C3 tests) and patented biomarkers (e.g. FibroTest, ELF). The algorithm discriminates between the "high risk" patients for fibrosis F3 or more (FibroTest >0.70) in whom to consider a liver biopsy and the "low risk" patients (FibroTest <0.30) to be monitored with repeated NIT every 2 years.

Authors acknowledged that patented markers of fibrosis such as FibroTest are more specific and have higher positive predictive values for detecting advanced fibrosis and adverse outcomes.

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

Nonalcoholic fatty liver disease in chronic obstructive pulmonary disease.

Viglino D, Jullian-Desayes I, Minoves M, Aron-Wisnewsky J, Leroy V, Zarski JP, Tamisier R, Joyeux-Faure M, Pépin JL. Eur Respir J. 2017;49. pii: 1601923.

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.

SBERNA 2018

FibroTest,
SteatoTest,
NAFLD, T2D

VILAR-GOMEZ 2018

FibroTest,
NAFLD,
NASH

VIGLINO 2017

FibroMax
SteatoTest
NashTest
FibroTest
COPD
NAFLD

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Screening general population

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.

Harris R, Harman DJ, Card TR et al. Lancet Gastroenterol Hepatol 2017 Published Online http://dx.doi.org/10.1016/ S2468-1253(16)30205-9

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.

HARRIS 2017

FibroTest
Elastography
Histology
Screening
Review

HIV

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.

Boyd A, Bottero J, Miailhes P, Lascoux-Combe C, Rougier H, Girard PM, Serfaty L, Lacombe K. J Int AIDS Soc. 2017;20:1-12.

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.

BOYD 2017

FibroTest
HBV/HIV

HBV

Review article on fibrosis assessment for chronic hepatitis B

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

Parikh P1, Ryan JD1, Tsochatzis EA1. Ann Transl Med. 2017 Feb;5(3):40.

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)

PARIKH 2017

FibroTest
HBV
Review

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European consensus definition of severe fibrosis using FibroTest in chronic viral hepatitis

Late presentation of chronic viral hepatitis for medical care: a consensus definition.

Mauss S, Pol S, Buti M, Duffell E, et al.; European consensus working group on late presentation for Viral Hepatitis Care. BMC Med. 2017;15:92.

The European Consensus Working Group* has published the following consensus definitions for the advanced and for the late stage liver disease using non-invasive tools for assessing fibrosis caused by chronic hepatitis B and C in patients who had not received prior treatment. :

- Advanced liver disease is defined by a FibroTest score>0.59, APRI score> 1.5, FIB-4> 3.25, transient elastography (TE)> 9.5 kPa or liver biopsy stage METAVIR> = F3.
- Late-stage liver disease was clinically defined by the presence of decompensated cirrhosis and / or hepatocellular carcinoma.

In conclusion, the authors expect the consensus definitions to be an easy-to-use reference for public health authorities and to better assess the clinical situation on a population basis.

** The European Consensus Working Group includes experts in viral hepatitis from the European Association for the Study of the Liver (EASL), experts from the HIV Initiative in Europe and other relevant stakeholders, including patient associations, health-policy makers and surveillance and medical experts.*

MAUSS 2017

FibroTest,
Cutoff,
Hepatitis B,
Hepatitis C

Alcoholic Liver Diseases (ALD)

New validation of FibroTest in excessive drinkers from primary and secondary healthcenters

Transient and 2-dimensional shear-wave elastography provide comparable assessment of alcoholic liver fibrosis and cirrhosis.

Thiele M, Stæhr Madsen B, Fuglsang Hansen J, et al. Gastroenterology 2018 Jan 4. doi: 10.1053/j.gastro.2018.01.005

Authors proposed to compare prospectively the accuracy of the Enhanced Liver Fibrosis test (ELF), FibroTest, liver stiffness measurements by TE and 2D-SWE and 6 other biomarkers in detection of advanced liver fibrosis in patients with excessive dinking recruited in primary (n=128) and secondary (n=161) healthcenters.

Diagnostic accuracy of FibroTest was high (AUROC 0.90) for advanced fibrosis (AF) (Kleiner stage >=F3 using biopsy), comparable to ELF (0.92, p=NS). In intention-to-diagnose analyses, FibroTest has comparable performances to TE and 2D-SWE for AF (all p=NS).

For the primary care patients, FibroTest values below 0.58 had 94% negative predictive values for AF.

The main strengths of study are the analyses in intention-to-diagnose and the inclusion of patients with metabolic syndrome features and ongoing drinking, which reflect real-life situations.

In conclusion, in excessive drinkers from primary and secondary care, FibroTest can ruled out AF (scores below 0.58) with high diagnostic performances.

THIELE 2018

FibroTest,
ELF,
TE,
2D-SWE,
Alcohol

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Improve of FibroTest and AFP in HCV-SVR

Potent viral suppression and improvements in alpha-fetoprotein and measures of fibrosis in Japanese patients receiving a daclatasvir/asunaprevir/beclabuvir fixed-dose combination for the treatment of HCV genotype-1 infection.

Akuta N, Toyota J, Karino Y, et al. J Gastroenterol. 2018 Mar 2. doi: 10.1007/s00535-018-1445-3.

The present study assessed the dynamics of hepatic fibrosis with FibroTest and alpha-fetoprotein (AFP) in pre- and post-treatment HCV-genotype 1 patients that achieved SVR in UNITY-3 trial with DAA therapy (daclatasvir/ asunaprevir/ beclabuvir).

A total of 217 patients were included, 46% were aged >65 years and 21% had compensated cirrhosis. Both FibroTest and AFP values improved significantly post-treatment with numerically greater score improvement in cirrhotic patients. FibroTest stage decreased in 44%, remained stable in 50%, and worsened in 6% of patients at SVR.

Improvements in both FibroTest and AFP scores suggest that HCV-SVR may reduce the risk of future liver disease progression and hepatocellular carcinoma, particularly in those with compensated cirrhosis.

FibroTest used to identify cirrhosis in chronic hepatitis C prognosis study

Role of Non-hepatic Medical Comorbidity and Functional Limitations in Predicting Mortality in Patients with HCV.

Natarajan Y, White DL, El-Serag HB, Ramsey D, Richardson P, Kuzniarek J, Shukla R, Tansel A, Kanwal F. Dig Dis Sci. 2017;62:76-83.

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 assesd 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.

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.

Prenner SB1, VanWagner LB2, Flamm SL1, Salem R3, Lewandowski RJ3, Kulik L4. J Hepatol. 2017;66:1173-1181.

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.

AKUTA 2018

FibroTest,
HCV,
HCC

NATARAJAN 2017

FibroTest
HCV
Prognosis

PRENNER 2017

FibroTest
HCV
HCC

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HCV Treatment Prioritization in trials using FibroTest

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

Asselah T, Bourgeois S, Pianko S, et al.. Liver Int. 2018;38:443-450.

ASSELAH 2018
SOFO-VELPA

Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials.

Jacobson IM, Lawitz E, Gane EJ,, et al.. Gastroenterology. 2017;153:113-122.

JACOBSON 2017
SOFO-VELPA-VOXI

Safety and efficacy of daclatasvir-sofosbuvir in HCV genotype 1

Pol S, Bourliere M, Lucier S, et al. J Hepatol. 2017;66:39-47.

POL 2017
SOFO-DACLA

Real-Life Use of 3 Direct-Acting Antiviral Regimen in a Large Cohort of Patients with Genotype-1b HCV Compensated Cirrhosis.

Gheorghe L, Iacob S, Curescu M,et al. J Gastrointestin Liver Dis. 2017;26:275-281.

GHEORGHE 2017
OBV/PTV/r+DSV

Real-world efficacy and safety of ombitasvir, paritaprevir/r+dasabuvir+ribavirin in genotype 1b patients with hepatitis C virus cirrhosis.

Preda CM, Popescu CP, Baicus C, et al A. Liver Int. 2017 . doi: 10.1111/liv.13550.

PREDA 2017
OBV/PTV/r+DSV

Efficacy and safety of paritaprevir/ritonavir, ombitasvir, and dasabuvir with ribavirin for the treatment of HCV genotype 1b compensated cirrhosis in patients aged 70 years or older.

Trifan A, Stanciu C, Gheorghe L, et al. Medicine (Baltimore) 2017; 96: e9271.

TRIFAN 2017
OBT/PTV/r+DSV

Drug Induced Liver Injury (DILI)

DILI-ActiTest a new prognostic biomarker of drug-induced-liver-injury (DILI).

Evidence-based Translation consortium. Serum apolipoprotein A1 and haptoglobin, in patients with suspected drug-induced liver injury (DILI) as biomarkers of recovery.

Peta V, Tse C, Perazzo H, et al; Drug Induced Liver Injury- Groupe Hospitalier Pitié-Salpêtrière; Drug Induced Liver Group of the Injury Safer and Faster PLoS One. 2017;12:e0189436.

The primary objective was to analyze in patients with DILI the prognostic performance of ActiTest and FibroTest proteins apoliprotein-A1 (APOA1), haptoglobin (HAPTO) and alpha-2-macroglobulin (A2M), as predictors of recovery* outcome. N=115 adjucated DILI cases from the European DILI Consortium had at least two samples during 12-weeks follow-up.

APOA1 and HAPTO, both acute phase reactants, have had the strongest negative correlation with DILI during the follow-up.

A new biomarker, DILI-ActiTest [patent pending] combining ApoA1, Hapto, A2M, GGT, age and gender, resulted in a significant prediction of recovery with 67% accuracy and an significant AUROC of 0.72 ($p<0.001$ vs hazard). Further validation of the panel DILI ActiTest should be performed in another group of DILI cases.

** Recovery outcome was defined as an ALT <2x and BILI <2x the upper limit of normal.*

PETA 2017

DILI-ActiTest,
Haptoglobin,
Apolipoproten A1

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