FibroTest/FibroMax Scientific Publications

Key Publications for 2019

EASL 2019

Nonalcoholic steatohepatitis (NASH)

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 steatohepatitis (NashTest 2) using a simplified histological definition* permitting to identify more cases of NASH than the standard histological NASH-CRN definition (Eur J Gastroenterol Hepatol. 2018).

For this purpose, a total of 1,081 metabolic liver disease (MLD) patients were included from the FibroFrance Project (USA- ClinicalTrials.gov number, NCT01927133) and the FLIP European Consortium (http://www.flip-fp7.eu/). The new NashTest 2 does not include BMI and fasting glucose to avoid variability in obese and type2 diabetic (T2D) patients. The NashTest 2 performances [AUROC (95%IC)] were high (0.77 and 0.81), in both training and control groups, respectively, with higher performances than NAFLD fibrosis score, BARD, FIB-4 and ActiTest. Significant MLD (A2 or F2 as per NashTest 2 combination with FibroTest) was strongly associated with type 2 diabetes, when applied to larger populations (US and French cohorts).

In conclusion, the new NashTest 2 enables a quantitative assessment of NASH in subjects with MLD risk. Important fact, this new diagnosis of NASH **(NashTest 2) does not require BMI nor glucose any longer**.

** The new definition of MLD no longer requires the presence of steatosis and the presence of both lobular inflammation and ballooning and enables 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)*

POYNARD 2018

NashTest 2

NASH-FibroTest

Metabolic Steatohepatitis

SteatoTest 2 : a new quantitative test for the diagnosis of steatosis

The diagnostic performance of a simplified blood test (SteatoTest-2) for the prediction of liver steatosis.

Poynard T, Peta V, Munteanu M, Charlotte F, Ngo Y, Ngo A, Perazzo H, Deckmyn O, Pais R, Mathurin P, Myers R, Loomba R, Ratziu V; FLIP consortium, the FibroFrance-CPAM group, the FibroFrance-Obese group, and the Selonsertib group. Eur J Gastroenterol Hepatol. 2019;31:393-402.

European guidelines of EASL-EASD-EASO (J Hepatol 2016) recommend serum biomarkers able to detect more than 5% steatosis (NASH-CRN histological classification) such as the SteatoTest.

The aim of the present study was the construction of a new SteatoTest 2, non-inferior to the reference first-generation SteatoTest but not requiring BMI or bilirubin as these two components can increase test variability (Gilbert syndrome, hemolysis or fluctuations in weight in obese patients).

Five different subsets of patients (n=2,997) with biopsies were evaluated for test construction and validation, and four other to assess the prevalence of steatosis in target populations with increasing risks of steatosis (n=141,842). One of the strength of the study was the inclusion of a wide spectrum of patients from severe NASH to controls without histological steatosis (n=158) or without risk of steatosis such as selected blood donors (n=207) and healthy volunteers (2,562).

The performances of the SteatoTest 2 in the different cohorts were all non-inferior to the reference test ($P<0.001$) with an AUROC (95%CI) = 0.822 (0.810-0.824) in the overall population including controls.

In conclusion, SteatoTest-2 is simpler and non-inferior to the first-generation SteatoTest for the diagnosis of steatosis≥5% and for a better applicability.

POYNARD 2018

SteatoTest 2

NASH-FibroTest

Metabolic Steatohepatitis

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BIO Predictive

Prognostic validation of FibroTest in patients with NAFLD

Long term prognostic value of the FibroTest in patients with non-alcoholic-fatty-liver disease, compared to chronic hepatitis C, B, and alcoholic liver disease.

Munteanu M, Pais R, Peta V, et al., for the FibroFrance Group. Aliment Pharmacol Ther 2018 (in press)

FibroTest (FibroSure in USA) validated for the diagnosis of the stages of fibrosis in NAFLD (Aliment Pharmacol Ther 2016) had demonstrated a significant prognostic value for the overall survival and to predict cardiovascular events in patients with type-2 diabetes (T2D) or dyslipidemias. (Aliment Pharmacol Ther 2014). Therefore, since 2016, FibroTest has been integrated in the diagnostic strategy to assess disease severity in the presence of suspected NAFLD and metabolic risk factors. (EASL-EASD-EASO guidelines J Hepatol 2016)

The present study proposed to validate FibroTest for the 10-years prediction of liver-related mortality in the prospective NAFLD FibroFrance-cohort from a tertiary center (Pitié-Salpêtrière Hospital, Paris)*. The comparator was it's performance in chronic hepatitis C (CHC), the most validated population.

A total of 7,082 pts were included: 1,079 NAFLD, 3,449 CHC, 2,051 CHB and 503 ALD with a median (range) follow-up of 6.0 years (0.1-19.3). FibroTest significantly predicted overall survivals all in chronic liver diseases with similar performance in NAFLD as in CHC.

FibroTest significantly predicted survival without liver-related death (LRD) in NAFLD patients

The prognostic value of FibroTest for the survival without LRD was validated for the first time in NAFLD patients and was even higher than in patients with CHC [AUROC (95%CI)]: 0.941 (0.905-0.978) and 0.875 (0.849-0.901; P=0.01), respectively.

FibroTest could stratify the risk of death in NAFLD cirrhosis

The present study demonstrated the FibroTest ability to stratify NAFLD cirrhosis in 3 classes with increased probabilities of death: F4.1 (non-complicated cirrhosis; scores >0.74-0.85), F4.2 (oesophageal varices risk; scores >0.85-0.95) and F4.3; severe complications risk, scores >0.95-1.00): 0.90 (0.80-0.99), 0.96 (0.88-1.00), and 0.67 (0.43-0.91) (Logrank=8.1; P=0.018).

In conclusion, this study conducted on a large sample size of patients with long-term follow-up, has demonstrated that FibroTest has a high predictive value for the liver-related mortality in patients with NAFLD.

*ClinicalTrials.gov number;NCT01927133

Editorial: Prognostic validation of FibroTest

Editorial: FibroTest to predict liver-related mortality in NAFLD. Should this change the diagnostic algorithm in NAFLD?

Bush AM, Torres DM. Editorial: Aliment Pharmacol Ther. 2018;48:1319-1320.

The editorial review of the previous study (Munteanu et al. APT 2018) underlined that these results suggested that FibroTest due to the high prognostic value, could be considered at least as second line after a cheaper screening tool to eliminate those at low risk from further immediate evaluation.

FibroTest may then be useful to identify NAFLD risk patients who should be considered for biopsy, clinical treatment trials, or maximal lifestyle interventions. Other biomarker panels such as ELF or the ProC3 tests have not been compared head-to-head with transient elastography or FibroTest, the most validated noninvasive prognostic tools.

Authors concluded that accuracy, cost, and ease of administration will all be important in determining the future NAFLD risk stratification tool of choice from the current options.

MUNTEANU 2018

NashTest 2
FibroTest
NASH-FibroTest

Metabolic
Steatohepatitis

BUSH 2018

Editorial

NAFLD

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BIO Predictive

Simplified definition for metabolic liver diseases

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 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)]. Patients were from the FibroFrance project (USA-NCT01927133) and from the FLIP consortium (http://www.flip-fp7.eu/).

The impact of definitions variability on the prevalence of NASH (evaluated by FibroMax tests) was studied for the following clinical situations: 1/ less 5% steatosis for NASH; 2/ no steatosis requirement for NASH; and 3/ severe NASH based on the SAF-activity grade at least A2. 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 only and not requiring >5% steatosis, has a lowest risk of false-positives and false-negatives.

Improvement of quantitative NashTest 2 and SteatoTest and after bariatric surgery in morbidly obese

Circulating Endocannabinoids Are Reduced Following Baiartric Surgery and Associated with Improved Metabolic Homeostasis in Humans.

Azar S, Sherf-Dagan S, Nemirovski A, et al. Obes Surg. 2018. doi: 10.1007/s11695-018-3517-0.

The present study, based n=65 morbidly obese patients, aimed to investigate the changes in the circulating levels of endocannabinoid (eCBs) system, key factors in obesity, at 1 year following sleeve gastrectomy surgery, in relation with liver biomarkers estimating steatosis (SteatoTest), fibrosis (FibroTest) and steatohepatitis (NashTest-2 quantitative score).

One year after bariatric surgery, a significant improvement was observed in SteatoTest (0.55 vs 0.25, $p<0.001$) and in NashTest-2 quantitative scores (0.41 vs 0.32, $p<0.001$).

At one year after surgery, arachidonic acid (AA) serum changes were found to be positively associated with SteatoTest changes (0.452, $p<0.05$), stronger than the associations with other factors as serum ALT levels, fat-free mass and waist circumference. In the same way, the 2-arachidonoylglycerol (2-AG) delta change was positively correlated with SteatoTest score (0.266, $p<0.05$) and also with circulating triglyceride and total cholesterol levels.

These results suggest that eCB changes (AA and 2-AG) at 1 year after bariatric surgery are correlated with clinical and liver benefits and with a significant regression of both steatosis and inflammation as per SteatoTest and NashTest-2 quantitative scores, respectively.

POYNARD 2018

Methodology
NashTest 2

AZAR 2018

NASH-FibroTest
NashTest 2
SteatoTest
FibroTest

Obesity

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BIO Predictive

Independent review of noninvasive diagnosis of NAFLD inclusing FibroMax tests

Noninvasive Assessment of Liver Disease in Patients With Nonalcoholic Fatty Liver Disease.

Castera L, Friedrich-Rust M, Loomba R. Gastroenterology. 2019 Jan 18. pii: S0016-5085(19)30051-4.

Authors proposed to summarize the current state of the noninvasive assessment of liver disease in NAFLD, to provide an expert synthesis of how these noninvasive tools could be utilized in clinical practice.

Nonalcoholic fatty liver disease (NAFLD) is estimated to afflict approximately 1 billion individuals worldwide. Thus, according to authors of this review, the key issues in NAFLD risk patients are the differentiation of NASH from simple steatosis and identification of advanced hepatic fibrosis without having to resort to liver biopsy.

Authors acknowledged that FibroTest (FibroMax panel, BioPredictive) was largely validated din NAFLD and NASH patients with different degree of risk and is actually recommended along with other proprietary tests. They stressed that the use of patented serum biomarkers (FibroTest, Fibrometer, or ELF) could be considered in patients with intermediate risk according to local availability. Nevertheless, authors suggested an algorithm for risk stratification of patients with suspected NAFLD taking into account FIB4 and NAFLD fibrosis score (NFS) for a primary care setting. Despite the free availability of FIB4 and NFS, their choice is questionable as they are not specific to fibrosis and have lower accuracies than patented biomarkers.

SteatoTest (from the FibroMax panel, BioPredictive) has being validated independently for the use of NAFLD as well as other markers of steatosis (Fatty Liver Index, NAFLD Liver Fat Score, lipid accumulation product and Hepatic Steatosis Index). Their individual diagnostic performances seem difficult to compare, as they have been validated against different standards (biopsy, ultrasonography or MRS) and very few of them were compared directly. Nevertheless, European guidelines recommend using ultrasonography as first-choice imaging in adults at risk for NAFLD. Nevertheless MRI-PDFF seems to be the noninvasive gold standard for liver fat quantification but this technique is expensive and not available in routine.

NashTest (FibroMax panel, BioPredictive) was extensively validated by the developer, in 494 obese patients (French cohort) with a low prevalence of NASH (17.2%), the diagnostic performance (AUROC) being good 0.84. Authors criticize the highly selected population (morbidly obese) and conclude that none of the currently available serum marker was able to differentiate NASH from simple steatosis and combining different approaches could improve accuracy. One limitation of the present review was no to take into account the recently released new quantitative NashTest 2 (BioPredictive).

FibroTest and SteatoTest identified NASH in Type 2 Diabetes without elevated liver enzymes

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;35:368-75.

This study aimed to evaluate the application of the recently proposed European EASL-EASD-EASO NAFLD-guidelines (J Hepatol 2015) in n=179 type-2 diabetic (T2D) patients.

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

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

FibroTest identified clinically advanced fibrosis (FibroTest >0.57) in 2.2% T2D patients having normal liver enzymes (ALT, AST and GGT), so otherwise not detected.

CASTERA 2018

Review

FibroMax

NAFLD

SBERNA 2018

SteatoTest
FibroTest

T2D
Obesity

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BIO Predictive

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.

FibroTest used to study the potential antifibrotic effect of antiplatelet agents.

Use of Antiplatelet Agents Is Inversely Associated With Liver Fibrosis in Patients With Cardiovascular Disease.

Schwarzkopf K, Bojunga J, Rüschenbaum S, Martinez Y, Mücke MM, Seeger F, Schoelzel F, Zeuzem S, Friedrich-Rust M, Lange CM. Hepatol Commun. 2018;2:1601-9.

The authors explored the relationship between the use of antiplatelet agents and liver fibrosis in a prospective cohort study of patients undergoing coronary angiography at the University Hospital Frankfurt.

N= 337 (67%) were on antiplatelet therapy at the time of s inclusion and assessment for liver fibrosis by transient elastography (TE) and FibroTest. 48% patients were receiving acetyl salicylic acid, 8% patients were receiving monotherapy with a P2Y12 receptor antagonist (clopidogrel, prasugrel, or ticagrelor), and 44% patients antiplatelet agents of both classes. In univariate linear regression analyses, the use of antiplatelet agents was also inversely associated with FibroTest values (beta, –0.38; SD beta, 0.15; P = 0.02). This association remained significant after adjustment for age, sex, AST levels, and presence of diabetes. Furthermore, there was a significant correlation between platelet counts and PDGF-β serum concentration (rho, 0.33; P < 0.0001), and between FibroTest score and PDGF-β/platelet ratio (p=0.048).

Authors concluded that the use of antiplatelet agents might have a protective role against the occurrence of liver fibrosis as presumed by surrogate markers (TE, FibroTest) and to the necessity to explore more the potential of antiplatelet agents as antifibrotic therapy.

NASH Fibrosis screening using FibroMax in subjects with ultrasound steatosis

Non-invasive diagnosis of steatosis, inflammatory changes and liver fibrosis in patients with non-alcoholic fatty liver diseases. Pilot study.

Ciećko-Michalska I, Szczepanek M, Wierzbicka-Tutka I, Zahradnik-Bilska J, Mach T. Arch Med Sci Atheroscler Dis. 2018 Dec 28;3:e179-e183.

A recent Polish study performed in a small number of patients (n=36) evaluated noninvasively the presence of steatosis, activity and fibrosis patients with NAFLD (fatty liver in abdominal ultrasound examination), using non-invasive tests from FibroMax panel: SteatoTest, ActiTest and FibroTest.

Despite equal prevalence of steatosis and activity in men and women according to surrogate markers, SteatoTest and ActiTest, in the male group versus female group, the prevalence of presumed severe fibrosis (F3 stage) was higher, 21 vs 12%. The study indicated a high percentage of patients with presumed hepatic fibrosis as per FibroTest referred to an outpatient clinic with ultrasound fatty liver and normal or abnormal liver enzymes.

Authors stressed the importance of non-invasive screening for liver fibrosis using specific tests such FibroMax in subjects having ultrasound steatosis and independently of liver enzymes level. Early detection of liver disease may improve the prognosis of these patients.

VILAR-GOMEZ 2018

FibroTest
NAFLD
NASH

SCHWARZKOPF 2018

FibroTest

Cardiovascular Disease

Antiplatelet agents

CIEĆKO-MICHALSKA 2018

SteatoTest
FibroTest
ActiTest

NAFLD

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BIO Predictive

Hepatocellular carcinoma (HCC)

LCR2 and LCR2, two multi-analyte blood tests to assess liver cancer risk including in non-cirrhotics

LCR2 and LCR2, two multi-analyte blood tests to assess liver cancer risk in patients without or with cirrhosis.

Poynard, T, Peta, V, Deckmyn, O, et al; for the HECAM-FibroFrance Group. Aliment Pharmacol Ther. 2019; 49:308-320.

Editorial: simplifying screening for primary liver cancer - do the LCR1 and LCR2 tests hold the key? Authors' reply. Poynard T, Deckmyn O, Housset C; HECAM-FibroFrance Group. Aliment Pharmacol Ther. 2019 Mar;49(5):613-614.

Authors aimed: 1/ to construct and validate two sequential tests for early prediction of primary liver cancer (PLC) in patients without cirrhosis; 2/ to improve the performance of the standard surveillance protocol [imaging with or without alphafetoprotein (AFP)], limited to patients with cirrhosis; and 3/ to estimate the risk of PLC using the new sequential tests in 3 external populations with increasing risk.

The study was a retrospective analysis in prospectively collected specimens from an ongoing tertiary center cohort (FibroFrance). Two tests were designed an very early sensitive high-risk test (LCR1) to predict PLC at 10 years and a second test with increased specificity (LCR2) to predict PLC at 5 years. LCR1 components were hepatoprotective proteins (apolipoprotein A1, haptoglobin) with known risk factors [(gender, age, gammaglutamyltranspeptidase (GGT)], and a marker of fibrosis [alpha2-macroglobulin (A2M); LCR2 combined the same components as LCR1 with AFP.

A total of 9892 patients (85.9% without cirrhosis) were included after exclusion of contemporaneous PLC, and followed up for 5.9 years [IQR: 4.3-9.4].

LCR1 time-dependent prognostic AUROCs (95%IC) were not different in construction and validation randomised subsets: 0.874 (0.838-0.910) (N=4944, 113 PLC) and 0.815 (0.769- 0.862) (N=4948, 108 PLC), respectively, p =NS.

The LCR1 prognostic performance at 5 years in non-cirrhotic patients was particularly high in both construction and validation randomized subsets, 0.788 (0.705-0.870) (N=4220, 30 PLC) and 0.779 (0.712-0.846) (N=4277, 54 PLC), p =NS.

LCR2 time-dependent prognostic AUROCs (95%IC) were not different in construction randomised subset: 0.902 (0.860-0.945) (N=2015, 54 PLC) and 0.828 (0.771-0.886) (N=2038, 43 PLC), respectively, p =NS.

For incident PLC (occurring after 1 year of follow-up), LCR2 had higher performances than AFP alone 0.870 (0.834-0.905) versus 0.718 (0.664-0.772), p<0.001. Results were similar in both cirrhotic (N=755, 71 cancers) and non-cirrhotic (N=3298, 26 cancers), all p<0.001.

For contemporaneous PLC (occurring before 1 year of follow-up), once again the performances of LCR2 were superior to AFP: 0.905 (0.875-0.928) vs 0.796 (0.741-0.840), p<0.001.

Efficiency of the sequential algorithm "F4-or-LCR1-High-then-LCR2"

Among 2027 patients with high-LCR1 then high-LCR2, 167 cancers (113 with cirrhosis, 54 without cirrhosis) were detected, that is 12 patients needed to screen one cancer. The negative predictive value (NPV) was 99.5% in the 2026 not screened patients (11 cancers without cirrhosis), higher than the standard surveillance, which detected 113 cancers in 755 patients screened, that is seven patients needed to screen one but with a lower NPV 98.0% in 3298 not screened patients (42 cancers without cirrhosis).

In conclusion, LCR1 and LCR2, had significant prognostic performances including in non-cirrhotic. LCR1 permitted a very early stratification of primary liver cancer in non-cirrhotic. LCR2 had better prognostic performances than AFP in both cirrhotic and non cirrhotic patients with higher efficacy than the standard surveillance for a slightly higher number of patients needed to screen.

POYNARD 2018

LCR1/LCR2

Liver Cancer Stratification Test

HCC

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BIO Predictive

Review: FibroTest, ELF, elastography in excessive drinkers

Non-invasive diagnosis and biomarkers in alcohol-related liver disease.

J Hepatol. Moreno C, Mueller S, Szabo G. 2019;70:273-283.

A recent publication proposed to review currently available non-invasive diagnosis and biomarkers in alcohol-related liver disease (ALD). Authors stressed that Enhanced Liver Fibrosis (ELF) and FibroTest (FT) are the most commonly used blood-based assessment tools for liver fibrosis in ALD.

FibroTest had a higher specificity compared to ELF for both fibrosis (80% vs 73%) and cirrhosis (91% vs 71%), respectively. One study was also found ELF to be cost effective for liver fibrosis assessment in patients with ALD, but there is no cost-effectiveness study for FibroTest in ALD.

A study by Thiele et al. (see below) found that ELF and FibroTest had comparable diagnostic accuracy in patients with ALD with AUROCs of 0.92 for ELF and AUROC of 0.90 for FibroTest. This prospective study concluded that advanced fibrosis can be ruled out in patients with ALD based on an ELF <10.5 or an FibroTest value below 0.58. Comparison of the performance of the different biological tests suggests that ELF and FibroTest are better than APRI (aspartate aminotransferase [AST] to platelet ratio index) or FIB4.

Authors proposed a combination of serum-based fibrosis tests with non-invasive imaging as a practical algorithm in patients with excessive alcohol consumption including serum biomarkers as ELF and FibroTest in ALD patients having liver stiffness failure or not-applicable measurement.

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.

MORENO 2019

Review

FibroTest
ELF
TE

Alcohol

THIELE 2018

FibroTest
ELF
TE
2D-SWE

Alcohol

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AshTest to rule-out alcoholic steatohepatitis (ASH) in a proof-of – concept metabolomics study

What's in Metabolomics for Alcoholic Liver Disease?

Suciu AM, Crisan DA, Procopet BD, Radu CI, Socaciu C, Tantau MV, Stefanescu HO, Grigorescu M. J Gastrointestin Liver Dis. 2018;27:51-58.

The aim of this proof-of-concept study was to identify and further characterize the potential metabolomic biomarkers for the diagnosis, staging and severity assessment of alcoholic liver disease (ALD). The study included 30 patients with alcoholic liver diseases and 10 controls and the prevalence of cirrhosis was 57% and 75% of cirrhotic had an AshTest score ≥ 0.18. The study revealed the usefulness of surrogate marker of alcoholic hepatitis, AshTest, in the context of a lack of biopsy-proven alcoholic liver disease.

SUCIU 2018

AshTest

Alcohol

HIV

FibroMax for detecting steatohepatitis (NASH) in HIV-Monoinfected patients

Diagnostic Accuracy of Noninvasive Markers of Steatosis, NASH, and Liver Fibrosis in HIV-Monoinfected Individuals at Risk of Nonalcoholic Fatty Liver Disease (NAFLD): Results From the ECHAM Study.

Lemoine M, Assoumou L, De Wit S, et al.; ANRS-ECHAM Group. J Acquir Immune Defic Syndr. 2019;80:e86-e94

Noninvasive tests of steatosis, nonalcoholic steatohepatitis (NASH), and fibrosis have been poorly assessed in antiretroviral therapy–controlled HIV-monoinfected individuals that are at high risk of NAFLD.

Using liver biopsy (LB) as a reference, authors assessed the performances of the following noninvasive methods: MRI proton-density-fat-fraction (MRI-PDFF), elastograhy by FibroScan (TE) /controlled attenuation parameter (CAP), and of biochemical tests including FibroMax, APRI, FIB4 and nonalcoholic fatty liver disease–fibrosis score (NFS). All participants had persistently elevated transaminases and/or metabolic syndrome, and/or lipodystrophy and LB was indicated if suspected significant fibrosis (FibroScan ≥7.1 kPa and/or FibroTest ≥0.49). A total of 49 among the 140 patients with suspected significant fibrosis had had a LB with the following characteristics: steatosis 76%, NASH activity 47%, and fibrosis in 63% patients [F2: 7 (14%); F3: 6 (12%); and F4: 2 (4%)].

Regarding steatosis, MRI-PDFF, CAP and SteatoTest had the following performances [AUROCs (95%IC)] :0.98 (0.96-1.00), 0.88 (0.76-0.99) and 0.68 (0.51-0.85), respectively.

Regarding fibrosis (≥F2), APRI, FIB-4, FibroScan and FibroTest had the following performances [AUROCs (95%IC)]: 0.86 (0.74-0.98) and 0.81 (0.67-0.95), 0.61 (0.43 to 0.79) and 0.61 (0.44-0.78)].

Regarding NASH activity, alanine aminotransferase ≥36 IU/L and NashTest had the following performances [AUROCs (95%IC)]: 0.83 (0.71-0.94) and 0.60 (0.44-0.76), respectively.

We acknowledged the excellent intention of the authors to evaluate the most validated noninvasive methods in a HIV population. However, we do not agree with their conclusions. There are several major limitations that have to be stressed: the retrospective character of the study, low number of patients, inclusion bias based on the selection of subjects having abnormal liver enzymes and significant fibrosis as per TE and FibroTest. The impact on the results of this selection (exclusion of patients having normal TE/ FibroTest) is reflected in the relatively low AUROCs for both, FibroTest and TE.

LEMOINE 2019

FibroMax

HIV

NASH

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HBV-HIV coinfected

New validation of FibroTest in HIV-HBV

FibroTest and other biomarker assessment in HIV-HBV coinfected patients Diagnostic accuracy of the Coopscore to predict liver fibrosis in human immunodeficiency virus/ hepatitis B virus co-infection.

Taibi L, Boyd A, Bosselut N, et al. Ann Clin Biochem. 2018;55:236-243.

The authors proposed to compare the diagnostic performances of several biomarkers of liver fibrosis: FibroTest, Coopscore (CS) Hepascore (HS), Zeng score (ZS), Fibrometer (FM) and transient elastography (TE) in 97 HBV- HIV co-infected patients.

High standards of methodology were used as the Obuchowski's method was done in addition to standard AUROC and the study performed direct comparison between markers.

- The diagnostic performances for significant fibrosis (METAVIR stages F2-F4), were similar for FibroTest (0.778), CS (0.836) and FM (0.790) and superior to HS (0.727) and ZS (0.746).
- The diagnostic performances for severe fibrosis (F3) or cirrhosis (F4) all scores had similar performances.

In conclusion, this study confirms the diagnostic value of FibroTest in the classification of clinically significant fibrosis in coinfected HIV-HBV patients.

FibroTest to assess fibrosis progression in HIV patients coinfected with HBV genotype G

Hepatitis B virus genotype G and liver fibrosis progression in chronic hepatitis B and human immunodeficiency virus coinfection.

Malagnino V, Bottero J, Miailhes P, Lascoux-Combe C, Girard PM, Zoulim F, Lacombe K, Boyd A. J Med Virol. 2019;91:630-641.

Authors proposed to evaluate fibrosis dynamics (regression/progression) in a prospective cohort (n=158, 89% males, median age 39 years) of HIV-HBV coinfected patients having had FibroTest at baseline and every 6 to 12 months during a median (range) follow-up of 83 months (IQR = 37-97). Regression was defined as a change from F3-F4 to F0-F1-F2 FibroTest stages and progression as a change from F0-F1-F2 to F3-F4 between baseline and end of follow-up.

Among 43 (27.2%) patients with F3-F4 baseline liver fibrosis presumed with FibroTest, 7 (16.2%) regressed to F0-F1-F2 fibrosis at the last follow-up visit. Among the 115 (72.8%) patients with F0-F1-F2 fibrosis at baseline, 19 (16.5%) progressed to F3-F4 fibrosis at the last visit.

In multivariate analysis, fibrosis progression was independently associated with older age (P <0.005), baseline CD4+ cell count less than 350/mm3 (P <0.01), longer antiretroviral therapy duration (P <0.03) and HBV genotype G infection (vs non-G, P <0.01).

The rate of FibroTest mean increase was faster in genotype G vs non-G-infected patients with baseline F0-F1-F2 fibrosis (P for interaction = 0.002).

Authors concluded that in HIV-HBV coinfected patients, HBV genotype G is an independent risk factor for liver fibrosis progression as determined by FibroTest. HBV genotype G-infected patients with low initial liver fibrosis levels may require more careful monitoring.

TAIBI 2018

FibroTest
Hepascore

HIV+HBV

MALAGNINO 2019

FibroTest

HBV+HIV

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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.

AKUTA 2018

FibroTest,
HCV,
HCC

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

100% sustained virological response and fibrosis improvement in real-life use of direct acting antivirals in genotype-1b recurrent hepatitis C following liver transplantation.

Iacob S, Cerban R, Pietrareanu C, et al. J Gastrointestin Liver Dis. 2018;27:139-144.

IACOB 2018
Liver Transplantation

Risk of hepatitis B virus reactivation in hepatitis B virus + hepatitis C virus-co-infected patients with compensated liver cirrhosis treated with ombitasvir, paritaprevir/r + dasabuvir + ribavirin.

Preda CM, Popescu CP, Baicus C et al. J Viral Hepat. 2018;25:834-841.

PREDA 2018

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. Liver Int. 2018;38:602-610.

PREDA 2018

Diagnostic value of combined serum biomarkers for the evaluation of liver fibrosis in chronic hepatitis C infection: A multicenter, noninterventional, observational study.

Köksal, Yılmaz G, Parlak M, et al., Study Group TCHC. Turk J Gastroenterol. 2018;29:464-72.

KÖKSAL 2018

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