LIVERFASt (L-FAST) identifies advanced (F3F4, AF) and clinically significant fibrosis (F2-F4, CSF) especially well with Fibroscan in MASLD patients (pts) from a tertiary hepatology center.

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BACKGROUND

- The identification of patients (pts.) with *advanced fibrosis (AF, F3F4)* and *clinically significant fibrosis (CSF, F2-F4)* is mandatory in the specialty settings as they require further assessment or specific surveillance or may benefit from targeted interventions.
- **LIVERFASt** is an AI-based blood test that offers an overall assessment of the severity of presumed steatosis, activity, fibrosis (SAF) histological scores for MASLD. LIVERFASt Fibrosis test:
  - ✓ Demonstrated long-term prognostic value in MAFLD patients for liver-related morbidity and mortality

    Decraecker M. et al., Alim Pharmacol Ther 2022
  - ✓ Outperformed **ELF test** for CSF in a miscellaneous cohort

    Tangvoraphonkchai K. et al., J Hepatol Suppl. 2022
  - ✓ Outperformed **FIB-4** in patients with type 2 diabetes

    deLédinghen V., et al., Hepatology Suppl. 2020

Recently released clinical practice guidelines stated that the primary risk assessment could be done with FIB-4 and those with CSF risk should be reffered for secondary risk assessment with either a standard-of-care, liver stiffness measurement (LSM) with Fibroscan, or other noninvasive test.

Rinella M. et al. Hepatology 2023

AIMS

To compare retrospectively the performance of one-step strategy with two noninvasive combinations, the standard-of care, ***FIB-4 & LSM,*** versus ***LIVERFASt-Fibrosis & LSM,***

for the identification of histological AF and CSF in MAFLD pts.

- *As defined by Eslam M. et al. (J. Hepatol. 2020, MAFLD: metabolic-associated fatty liver disease*

METHODS

Patients:
MAFLD pts prospectively collected data between 2003 and 2020 in a tertiary hepatology center (NCT01241227).
Histopathology fibrosis scoring used NASH-CRN and SAF (*Bedossa P. Et al., Hepatology 2012*).

Cutoffs for AF (F3F4) and for CSF (F2-F4)
Cutoffs for FIB-4 and LSM were established according to AASLD CPG.
- FIB-4 cutoffs to rule out and to rule in AF were 1.3 and 2.68, respectively.
- LSM cutoffs for AF and CSF were 12kPa and 8 kPa, respectively.
- LIVERFASt for AF and CSF were 0.59 and 0.48, respectively

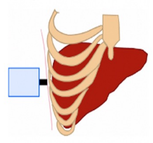
Statistics:
Strengh of concordance with biopsy for the combination blood biomarker and LSM.
Scatterplots of three evaluators of fibrosis

Quality data selection
- Quality LSM were selected : IQR/LSM <30%, Success rate ≥60%, 10 valid LSM
- Quality biopsy: ≥20mm , nonfragmented (with the exception of F4 pts.)
- Time lapse between biopsy and blood biomarkers and LSM ≤6 months

- We extracted data (N= 583 subjects) from a tertiary center , data collected between 2003 and 2020
- Selected subjects aged 18 years or more without missing data for FIB-4, LiverSTAT and with applicable LSM
- Among them, patients with data have been selected (≥20mm) and with lesser than 6 months time lapse between biopsy and noninvasive biomarkers and biopsy sizes ≥20mm.

LSM by Fibroscan (Echosens, Paris, France)

- Quality criteria: IQR/median<30%, Success rate≥60%, 10 valid LSM
- Variability in 531 NAFLD patients paired measurements: one stage difference in 32%, two stages difference in 10%
- Overestimation: Cytolysis with ALT > 3x ULN, non fasting, MetS (T2DM, BMI>30, high-blood pressure)



Castera L., et al., Hepatology 2010, Nascimbeni F. et al., , CGH 2014

LIVERSTAT (Fibronostics, Florida, US)

- AI computer aided proprietary algorithm for assessing fibrosis, steatosis,activity in MASLD pts.
- Combines blood biomarkers (GGT, bilirubin, haptoglobin, apolipoprotein A1, alpha2 macroglobulin, ALT, AST, cholesterol, triglycerids, glucose) adjusted on anthropometrics (age, gender, BMI) to generate three quantitatives scores (fibrosis, steatosis and activity) and a conversion into a category
- Can be used in fasting or non-fasting patient

Decraecker M. et al., APT 2022
De Lédinghen V. et al., Hepatology Suppl 2020

FIB-4 Index

- Algorithm: **platelet count, age, AST and ALT**
- **Dual cut-off** for advanced fibrosis (<1.3, ≥2.68)
- **Over or underestimation**: age range, cytosis, normal ALT and AST (T2DM)
- Lower diagnostic performance for cirrhosis in T2D

$$\text{FIB-4} = \frac{\text{age(years)} \times \text{AS(IU/L)}}{\text{Platelet count } (10^9/\text{L}) \times \text{ALT(IU/L)}^{\frac{1}{2}}}$$

Sterling RK. et al., Hepatology 2006
Hagström H. et al., J Hepatol 2020

Cohort Flow chart

N= 753 patients pre-included with LIVERFASt™ and liver biopsy
From 2003 to 2020 in Liver Fibrosis Investigation Center, CHU Bordeaux,

Excluded patients
N= 170 missing data

N= 583 patients included (301 T2DM pts.)
N=564 with concomittant FIB-4, LIVERFASts and TE (277 T2DM pts.)

Excluded patients
N= 170
- more than 6 months between NITs and biopsy or
- Biopsy sample <20mm

N= 399 patients included
- **less than 6 months between NITs and biopsy or**
- **Biopsy sample ≥20mm**

Patients characteristics

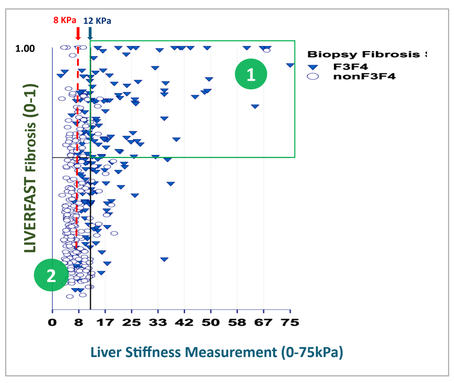
Characteristics	Prevalences , median (SE or range)	
	N=583 Overall included cohort	N=399 with high quality subgroup
Male Gender	56.4%	57.4%
Age, years	59.5 (18-85)	56.9% (18-85)
BMI, Kg/m2	31.5 (20.1-54.0)	31.1 (20.3-49.5)
ALT, IU/L	55 (0.5)	56 (3)
AST, IU/L	59 (0.12)	43 (2)
Type 2 Diabetes	301 (51.6%)	208 (52.1%)
HbA1c,%	6.6 (0.14)	6.6 (0.13)
Total cholesterol, mmol/l	5.14 (0.05)	5.18 (0.06)
Triglycerids, mmol/l	1.58 (0.43)	1.88 (0.05)
NITs		
LIVERFASt Fibrosis score	**0.48** (0.01)	**0.48** (0.91)
LIVERFASt Steatosis score	**0.74** (0.01)	**0.75** (0.01)
LIVERFASt Activity score	**0.41** (0.01)	**0.42** (0.01)
Fibroscan LSM , kPa CAP , dB/m	 **9.6** (0.5) **324** (2.6)	 **9.4** (0.53) **325** (134-400)
FIB-4	**1.55** (0.08)	1.55 (0.08)
Liver Biopsy	**Liver Biopsy**	
Biopsy length, mm Biopsy no.fragments	25 (11-95) 3 (1-25)	29.5 (11-95) 3 (1-25)
NAS score (Kleiner) 0-2 3-4 5-8	 8% (39) 33.3% (162) 58.7% (285)	 6% (20) 32.9% (109) 61.1% (271)

Summary of the results

F3F4 staging	LIVERFASt & Fibroscan	FIB-4 & Fibroscan
F3F4 correctly identified	**70**/74 (95%)	**47**/51 (92%)
Missed F3F4	**47**/194 (24%)	**63**/254 (25%)
NonF3F4 correctly identified	**147**/194 (76%)	**118**/254 (46.5%)
Overestimated F3F4	**4**/74 (5%)	**4**/51 (8%)
Unclassified	0	**73**/245 (29%)*

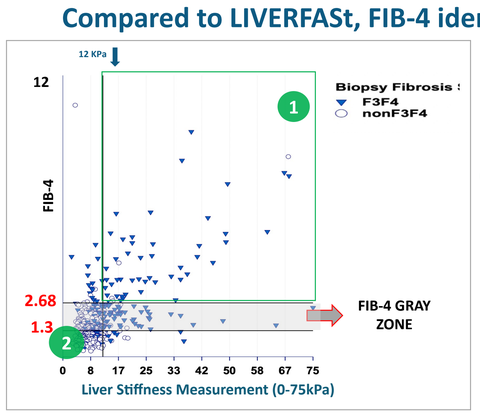
RESULTS

According to liver biopsy, LIVERFASt identifies F3F4 and F2-F4 especially well with LSM by Fibroscan when both agree



N=399 MASLD, with LB sample size ≥20mm and time lapse to biopsy < 6 months						
		LSM cutoff 12kPa		LSM cutoff 8kPa		
	LIVERFASt & LSM agree	Number	Biopsy confirms both NITs	Biopsy disagrees with both NITs	LIVERFASt & Fibroscan agree	Biopsy confirms both NITs	Biopsy disagrees with both NITs
1	LIVERFASt & LSM agree for F3F4	**74**	**70 (94.6%)**	4 (5.4%)	**117**	**94 (80.3%)**	23 (19.7%)
2	LIVERFASt & LSM agree for F0-F2	**194**	**147 (75.8%)**	47 (24.2%)	**116**	**103 (88.8%)**	13 (11.2%

Compared to LIVERFASt, FIB-4 identifies F3F4 patients to a lesser extent when together with LSM



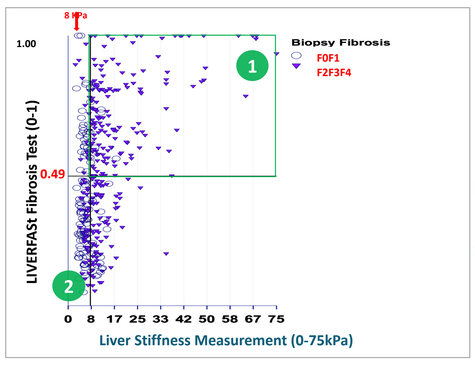
330 MASLD, with LB sample size ≥20mm and time lapse to biopsy < 6 months			
		LSM cutoff 12kPa	
	FIB-4 & Fibroscan agree	Number	Biopsy confirms both NITs, n(%)	Biopsy disagrees with both NITs, n(%)
1	FIB-4 & LSM agree on F3F4	**51**	**47/51 (92%)**	4/51 (8%)
2	FIB-4 & LSM agree on the absence of F3F4 (grey zone+ low risk zone)	**139**	**118/139 (85%)**	21 (15%)

LIVERFASt can palliate to FIB-4 false negatives

93/172 (54%) of patients with FIB-4 in the Gray zone (1.3-2.67) staged F3F4 at biopsy
➢ **46/93 (49.5%) of F3F4 are identified as F3F4 with LIVERFASt**

30/158 (20%) of patients with FIB-4 in the Low risk zone (<1.3) staged F3F4 at biopsies
➢ **6/30 (20%) F3F4 can be identified with LIVERFASt**

LIVERFASt, identifies F2F3F4 patients especially well together with LSM



N=399 MASLD, with LB sample size ≥20mm and time lapse to biopsy < 6 months			
		LSM cutoff 8kPa	
	LIVERFASt & LSM agree	Number	Biopsy confirms both NITs	Biopsy disagrees with both NITs
1	LIVERFASt & LSM agree on F2F3F4	**146**	**138/146 (94.5%)**	8 (5.5%)
2	LIVERFASt & LSM agree on F0F1	**102**	**57/102 (55.9%)**	45 (44.1%)

CONCLUSIONS

- The combination LIVERFASt-Fibrosis & LSM (Fibroscan) identified advanced fibrosis and clinically significant fibrosis with the highest confirmatory rate with liver biopsy (94%)
- Using a lower than 12kPa LSM cutoff, a higher number of patients with advanced fibrosis were identified
- Acording to the LSM cutoff that is used, between 50% and 150% more patients were identified with advanced fibrosis (F3F4) than with the combination between FIB-4 & LSM.
- LIVERFASt can reveal 50% of FIB-4 grey zone missed cases and palliate the false negative rate of FIB-4

DISCLOSURES

RQ, MM Fibronostics employment

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