COMPARATIVE PERFORMANCES OF LIVERFASt™, FIBROSCAN AND OTHER NON-INVASIVE TESTS FOR SEVERE FIBROSIS IN NAFLD PATIENTS.

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ABSTRACT

Objectives.

The study aimed to assess comparatively the diagnostic values of AI neural network constructed blood marker Liverfast (LF), transient elastography liver stiffness measurements (TE M/XL probes), Hepascore (HS), Fibrosure (FS), FIB4, APRI and Forns index for cirrhosis (F4 stage) and severe fibrosis (F3F4 stage), taking liver biopsy (LB) as reference in NAFLD patients.

Methods.

Data was prospectively collected among NAFLD patients between 2003 to 2020 in the University Hospital Center (CHU) of Bordeaux, France (NCT01241227) with NASH suspected (TE, liver function tests) and eligible for LB. LB was scored using SAF classification. Binary-AUROC (BinAUROC), 95%CI (p<0.05 vs 0.50) was used in per protocol (PP) and in-intention-to-diagnose (ITD) analysis, taking into account the TE non-applicability (NA) rate (TE-XL was used if TE-M NA).

Results.

A total of 583/753 patients were included (170 missing/NA NITs); 66/583 had NA-TE. Patients characteristics were: 56.4%males, median age 56.4yrs, 51.6%T2DM, BMI 31.5Kg/m2, median TE 9.6KPa, 71% F2-F4, 17% cirrhosis staging.

LF binAUROC(95%IC) for F4 and F3F4 staging were 0.810(.76-.85) and 0.720(.68-.76), respectively, without differences between non-T2DM and T2DM neither for F4 [0.827(.74-.89) vs. 0.788(.72-.84), p=0.45] nor for F3F4 [0.736(.67-.79) vs. 0.700(.64-.75), p=0.39]. In ITD analysis (n=564), LF binAUROC(95%IC) for F4 was 0.800(.75-0.84), not different from TE [0.746(.68-.80), p=0.08)], HS 0.774(.71-.82), FS 0.805(.75-.85), FIB4 0.756(.69- 0.81), Forns 0.783(.73-.83), all p=ns, and superior to APRI [0.650(.59- 0.71), p<0.001]; PP analysis had similar results, excepted for LF vs TE [0.797 vs 0.807, p=0.02, respectively].

In ITD in T2DM patients (n=287), LF binAUROC(95%IC) for cirrhosis was 0.774(.70-.83), not different from TE 0.720(.63-.79), HS 0.748(.67-0.81), FS 0.774(.70-0.83), Forns 0.744(.66-.81), all p=ns , and superior to FIB4 and APRI (p<0.001) (Figure 1) and without difference for F4 in non-T2DM (n=277) between LF-Fib and TE [0.824(.73-.89) vs 0.768(.65-0.85), p=0.29, respectively].

Conclusion.

Liverfast-Fibrosis is a NIT for the diagnosis of advanced chronic liver disease in NAFLD patients either in T2DM or non-T2DM patients. This score could be very useful

BACKGROUND

There is a call for action in the management of patients with type 2 diabetes mellitus (T2DM) and non-alcoholic steatohepatitis (NASH). (1)

However, the performance of NITs for the diagnostic of NAFLD, including steatohepatitis (NASH), was less evaluated than in viral hepatitis, particularly among T2DM patients. (2)

LIVERFASt™ (LF) is a new serum-based proprietary panel for assessing fibrosis, steatosis and activity in NAFLD patients with or without T2DM co-morbidity. (3) LIVERFASt system utilizes the AI machine learning technology and clinical scoring algorithms for all stages of liver diseases. (5,6,7)

The derived score is translated to a stage, based on the SAF liver scoring system (4) and predetermined cutoffs, to correspond to the level of histological stage or grade in that liver lesion.

AIMS

The study aimed to assess comparatively the diagnostic values of AI neural network constructed blood marker LIVERFASt, transient elastography liver stiffness measurements (TE, LSM-M/XL probes), Hepascore (HS), Fibrosure Fibrotest (FS), FIB4, APRI and Forns index for cirrhosis (F4 stage) and severe fibrosis (F3F4 stage), taking liver biopsy (LB) as reference in a prospectively collected cohort of NAFLD patients from the University Hospital Center (CHU) of Bordeaux, France (NCT01241227).

PATIENTS & METHODS

Patients

Retrospective study in a Prospectively collected cohort between 2003 to 2020

Patients undergone liver biopsy for NAFLD suspicion in the University Hospital Center (CHU) of Bordeaux, France

Eligibility for liver biopsy was determined by suspected NASH based on VCTE and liver function tests).

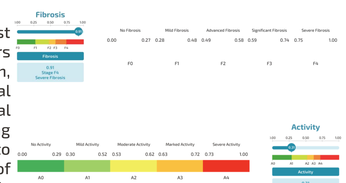
LB was scored using SAF classification (4): fibrosis scored F0-F4, Inflammatory activity A0 - A4 and steatosis S0 - S3.

Statistics

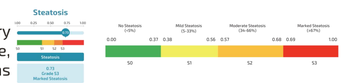
Binary-AUROC (BinAUROC), 95%CI (p<0.05 vs 0.50) was used in per protocol (PP) and in-intention-to-diagnose (ITD) analysis, taking into account the TE non-applicability rate.

LIVERFASt™ (Orlando, Florida USA)

LIVERFASt™ is a blood based diagnostic test that combines liver specific biomarkers (apolipoprotein A1, alpha2-macroglobulin, haptoglobin) with liver function tests (total bilirubin, GGT, AST, ALT), lipid panel (total cholesterol, triglycerides) and fasting glucose, as well as age, gender, and BMI to determine the severity of liver lesions of fibrosis stages and activity and steatosis grades.

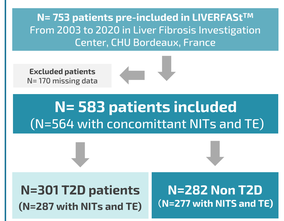


Other NITs evaluated were proprietary technologies (Hepascore, Fibrosure, Fibroscan) and free tests (APRI, FIB4, Forns index).



RESULTS

Cohort Flow Chart



Patient characteristics

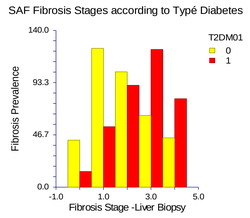
Characteristics	Prevalences, median (SE or range)
Male Gender	56.4%
Age, years	59.5 (18-85)
BMI, Kg/m2	31.5 (20.1-54.0)
ALT, IU/L	55 (0.5)
AST, IU/L	59 (0.12)
HbA1c,%	6.6 (0.14)
Total cholesterol, mmol/l	5.14 (0.54)
Triglycerids, mmol/l	1.58 (0.43)

Characteristics of included patients

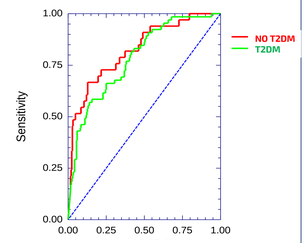
Characteristics	Prevalences, median (SE or range)
Noninvasive tests	Median (SE) scores
LIVERFASt Fibrosis score	**0.48** (0.01)
LIVERFASt Steatosis score	**0.74** (0.01)
LIVERFASt Activity score	**0.41** (0.01)
Fibroscan LSM CAP	 **9.6** (0.5) kPa **324** (2.6) dB/m
Fibrosure (Fibrotest)	0.44 (0.01)
Hepascore	0.28 (0.01)
FIB4	1.55 (0.08)
APRI	0.52 (0.05)
Forns Index	5.79 (0.08)
Liver Biopsy	
Biopsy length, mm Biopsy no.fragments	25 (11-95)mm 3 (1-25)
NAS score (Kleiner) 0-2 3-4 5-8	 8% (39) 33.3% (162) 58.7% (285)

Similar LIVERFASt™ performance for CIRRHOSIS in patients with DIABETES and without Diabetes

Prevalence of Fibrosis Stages at Liver Biopsy in T2DM and No-T2DM groups

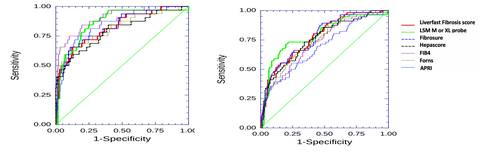


AUROC (95%CI) for cirrhosis



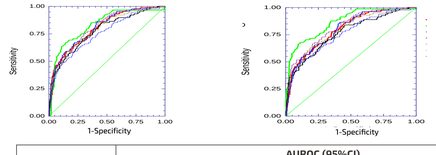
LIVERFASt™ performances were similar for F3F4 staging, without significant difference between non-diabetics and diabetic 0.736(.67-.79) vs. 0.700 (.64-.75), p=0.39

LIVERFASt™ performance for CIRRHOSIS is similar to that of VCTE in ITD in diabetics and not diabetics



	AUROC (95%CI)	
NITs	No DIABETES patients N=277	DIABETES N=287
LIVERFASt	**0.824 (.732-.887)***	**0.774 (.702-.831)***
LSM (VCTE)	0.768 (.647-.852)	0.720 (.629-.791)
Fibrosure	0.833 (.741-.895)	0.774 (.701-.831)
Hepascore	0.794 (.684-.869)	0.748 (.668-.811)
FIB4	0.855 (.732-.924)	0.676 (.584-.751)
Forns Index	0.811 (.708-.880)	0.744 (.663-.808)
APRI	0.693 (.590-.774)	0.635 (.549-.707)
	*P= NS LIVERFASt vs LSM and p<0.01 vs APRI	P= NS LIVERFASt vs LSM and p<0.001 vs APRI and FIB4

LIVERFASt™ has similar performance with VCTE for CIRRHOSIS in ITD analysis

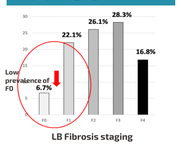


	AUROC (95%CI)	
NITs	In-intention-to-diagnose (ITD), N=564	Per protocol (PP) , N=499
LIVERFASt	**0.800 (.747-.843)***	**0.797 (.741-.842)***
LSM (VCTE)	0.746 (.678-.802)	0.807 (.731-.863)
Fibrosure	0.805 (.751-.848)	0.799 (.744-.845)
Hepascore	0.774 (.713-.823)	0.759 (.693-.812)
FIB4	0.756 (.685-.814)	0.759 (.686-.818)
Forns Index	0.783 (.725-.830)	0.784 (.723-.832)
APRI	0.650 (.588-.705)	0.643 (.579-.699)
	*P= NS LIVERFASt vs LSM and p<0.01 vs APRI	*P= 0.02 LIVERFASt vs LSM and <0.001 vs APRI

Prevalences of liver lesions according to biopsy

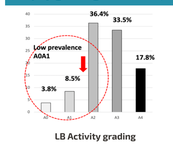
Highly selected population having high prevalence of severe lesions, lack of controls. Impact on performances evaluation of NITs for discriminating between early and intermediate stages

Biopsy staging of FIBROSIS



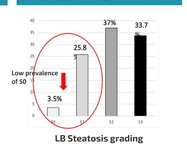
LB Fibrosis staging

Biopsy grading ACTIVITY (SAF)



LB Activity grading

Biopsy grading STEATOSIS

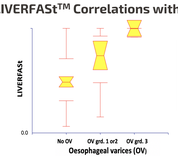


LB Steatosis grading

SAF Fibrosis	
F0	**6.7%. (39)**
F1	22.1% (129)
F2	26.1% (152)
F3	28.3% (165)
F4	16.8% (98)
SAF Steatosis	
S0 (<5%)	**3.5% (20)**
S1 (5-33%)	25.8% (148)
S2 (33-66%)	37.0% (212)
S3 (>66%)	33.7% (193)
SAF Activity	
A0	**3.8% (19)**
A1	**8.5% (43)**
A2	36.4% (184)
A3	33.5% (169)
A4	17.8% (90)

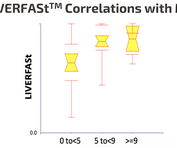
LIVERFASt™ Correlations with cirrhosis signs and complications

LIVERFASt™ Correlations with oesophageal varices (OV)



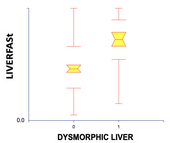
OV Grade	LIVERFASt™ Median score
Grade 0 (n=160)	0.49
Grade ½ (n=26)	0.74
Grade 3 (n=3)	1.00

LIVERFASt™ Correlations with MELD in cirrhotic patients



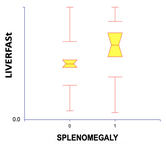
MELD	LIVERFASt™ Median score
0 to <5 (n=41)	0.64
5 to <9 (n=49)	0.84
>=9 (n=7)	0.86

LIVERFASt™ correlation with dysmorphic liver



US dysmorphic liver	LIVERFASt™ Median score
No (n=301)	0.46
Yes (n=78)	0.72

LIVERFASt™ correlation with splenomegaly



Splenomegaly	LIVERFASt™ Median score
No (n=334)	0.48
Yes (153)	0.72

CONCLUSION

LIVERFASt-Fibrosis is a NIT for the diagnosis of advanced chronic liver disease in NAFLD patients either in T2DM or non-T2DM patients.

LIVERFASt™ could be very useful to select patients for clinical trials and as screening test in general population.

References

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Disclosures

Fibronostics: RQ, MM, IA

FIBRONOSTICS