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RETROSPECTIVE CROSS SECTIONAL EVALUATION OF THE LIVERFAST TEST FOR STAGING LIVER FIBROSIS IN MASLD PATIENTS IN NIDDK STUDIES' POPULATIONS USING LIVER BIOPSY

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INTRODUCTION

MASLD affects more than 25% of subjects of the general population and can progress to advanced fibrosis (AF) and cirrhosis, especially in patients with type 2 diabetes (T2D). (Younossi ZM et al. Hepatology 2023)

Given the limitations of the liver biopsy there is a growing need for non-invasive cost-effective blood-based tests (NITs) for liver fibrosis assessment.

Clinical care pathways are already integrating NITs in a two-steps sequential approach (Rinella M. et al. Hepatology 2023)

LIVERFASt (LF) device developed by Fibronostics US, Inc. (Florida, USA), is a software-based system that uses a proprietary algorithm to generate s a blood-based non-invasive device for staging liver fibrosis along with grading steatosis and activity features in patients with MASLD.

AIM

We aimed to retrospectively assess the diagnostic performance of LIVERFASt fibrosis test against historically collected liver biopsy from a MASLD adult dataset from the National Institute of Diabetes and Digestive and Kidney Diseases central biorepository (NIDDK-CR).

METHODS

The National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) has supported collection of data. Patients with biosample availability and histological results have been selected from several MASLD. LIVERFASt is an AI-based algorithm that uses 14 biomarkers (biochemistry and anthropometrics) that is providing three different assessments - fibrosis, steatosis and inflammatory activity.

Statistics uses AUC (95%CI), sensitivity (Se), Specificity (Sp), Positive and negative predictive values (PPV, NPV), positive likelihood ratio (LR+) and diagnostics odds ratio (DOR) for clinically significant fibrosis (CSF, ≥F2), advanced fibrosis (AF, ≥F3) and cirrhosis (F4).

LIVERFASt Fibrosis test combines usual biochemistry blood biomarkers and anthropometrics to generate scores correlated to biopsy fibrosis staging (fibronostics.com).

RESULTS

Characteristics of the included patients	
Demographics	
N	105
Age (years)	49 (18-75)
Female	62 (59%)
Male	43 (41%)
BMI (Kg/m²)	33.7 (24.0-54.8)
SLD Phenotype	
MASLD	105 (100%)
MetALD	0
Unknown alcohol consumption	0
Cardiometabolic criteria	
Type 2 Diabetes	44 (41.9%)
HbA1c ≥ 5.7% (39mmol/L)	62 (61.4%), n=101
Fasting glucose ≥ 5.6mmol/L (100 mg/dL)	56 (53.9%)
BMI ≥25 Kg/m²	100 (96.2%)
Waist circumference ≥ 94 cm (M) and ≥ 80 (F)	98 (94.2%)
Triglycerides ≥ 1.70 mmol/L (150 mg/dL)	60 (57.7%)
HDL-Cholesterol ≤ 1.0 mmol/L (40 mg/dL) (M) and ≤ 1.3 mmol/L (50 mg/dL) (F)	72 (69.2%), n=104
Hypertension	59 (56.7%)
Blood (Biochemistry and blood count)	
AST (IU/L)	38 (16-460)
ALT (IU/L)	47 (10-310)
GGT (IU/L)	54 (10-820)
Total Bilirubin (micromol/L)	7.0 (2.9-30.0)
Fasting glucose (mmol/L)	5.77 (3.88-19.09)
Triglyceride (mmol/L)	1.93 (0.47-9.03)
Total cholesterol (mmol/L)	4.94 (2.30-7.63)
HDL Cholesterol (mmol/L)	1.11 (0.44-1.78)
Alpha-2 macroglobulin (g/l)	1.81 (0.87-4.39)
Apolipoprotein A1 (g/L)	1.36 (0.88-1.96)
Haptoglobin (g/L)	1.26 (0.09-3.28)
Albumin (g/L)	4.20 (1.40-5.20)
HbA1c (%)	5.9 (4.1-12), n=101
Platelets count (x10⁹/L)	239 (74-457)
LIVERFASt	
LIVERFAST Fibrosis score (0-1)	0.28 (0.01-0.99)
LIVERFAST Steatosis score (0-1)	0.62 (0.04-0.94)
LIVERFAST Activity score (0-1)	0.53 (0.10-0.98)
Liver Histology	
Length of liver biopsy specimen (mm) *Sum of fragments sizes in DB2	27 (21-62)
Length of liver biopsy specimen (mm) ≥ 20 mm. *Sum of fragments sizes in DB2	105 (100%)
Fibrosis stage (NASH-CRN)	
0 – none	21 (20.0%)
1 - perisinusoidal or portal	27 (25.7%)
2 - perisinusoidal and periportal	19 (18.1%)
3 - bridging	25 (28.8%)
4 - cirrhosis	13 (12.4%)
Steatosis grade (NASH-CRN, SAF), CP1	
0 - <5%	3 (2.9%)
1 - 5–33%	40 (38.1%)
2 - 34–66%	34 (32.4%)
3 - >66%	28 (26.7%)
Time lapse between blood analyses and liver biopsy	
≤ 6 months	66 (62.9%)
>6 months	39 (37.1%)

Design of the Study

129 adult subjects with MASLD randomly assigned from the NASH-CRM registry with histopathology and ≥ 20mm biopsy size and bio repository available for LIVERFASt inputs (retrospective)

24 subjects excluded (specimen related – insufficient quantity (1) sampling analytical failure (2), repeated measurements in same subjects (21)

105 adult subjects with MASLD from the NASH-CRN studies with histopathology assessment ≥ 20mm biopsy size and LIVERFASt assessed on biorepository specimens (retrospective)

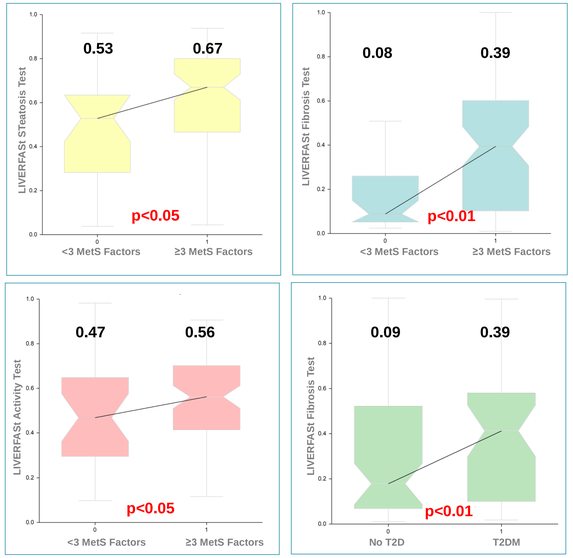
105 MASLD adult subjects
(including 25 subjects with T2DM)

Standard-area under the receiver operating curves according to the liver fibrosis endpoint

Case Group	AUC (95% CI), P value	SE (%)	SP(%)	PPV	NPV	Likelihood Ratio +	DOR
Cirrhosis (Fibrosis stage 4)							
Overall MASLD	**0.823** < 0.001	0.55	0.92	0.52	0.93	5.9	11.9
With T2DM	**0.876** < 0.001	0.43	0.91	0.43	0.91	4.7	7.5
Advanced fibrosis (fibrosis stages ≥ 3)							
Overall MASLD	**0.872** < 0.001	0.61	0.88	0.44	0.93	5.1	9.9
With T2DM	**0.859** < 0.001	0.50	0.85	0.35	0.91	3.3	5.5
Clinically significant fibrosis (Fibrosis stages ≥ 2)							
Overall MASLD	**0.783** < 0.001	0.75	0.68	0.28	0.95	2.3	6.2
With T2DM	**0.773** < 0.001	0.78	0.53	0.21	0.93	1.7	4.1

LIVERFASt fibrosis test performance was significant for patients with MASLD with T2DM and not different from that in patients without T2DM

Boxplots of LIVERFASt scores according to the MetS number of factors and to the presence or diabetes



Patients with ≥3 metabolic syndrome (MetS) factors had more presumed steatosis with LIVERFASt compared to those with less than 3.

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CONCLUSIONS

LIVERFASt Fibrosis test has high performances in MASLD patients can be used to identify patients with cirrhosis or those with MASH-related fibrosis.

LIVERFASt Fibrosis test performs equally in patients with MASLD and T2DM.

According to LIVERFASt, patients having three or more MetS factors or T2DM had more severe liver fibrosis than those with less than three MetS factors or without diabetes.

CONTACT INFORMATION

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