Combination of LIVERfASt (LF) & Liver Stiffness Measurement (LSM) using Fibroscan outperforms FIB-4 & LSM, for the identification of MASLD advanced fibrosis (AF) in patients with type 2 diabetes (T2D)

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INTRODUCTION

- Better identification of MASH-related advanced fibrosis in T2D patients is mandatory as patient may require further assessment, specific surveillance (cirrhosis) or may benefit from targeted interventions.
- LIVERFASt, is an AI-based blood test that assess the severity of presumed MASLD lesions, steatosis, activity and fibrosis.
- LIVERFASt Fibrosis predicted the long-term liver outcomes and the overall mortality (1) and outperformed ELF for the identification of clinically significant fibrosis (2).

AIMS

To compare retrospectively two combinations for one-step assessment of advanced fibrosis: LIVERFASt Fibrosis & Liver Stiffness Measurement (LSM, Fibroscan) versus FIB-4 & LSM, for the identification of histological advanced fibrosis in patients with Type 2 diabetes (T2D) that undergone liver biopsy (LB).

METHODS

- In this retrospective study, we reviewed patients diagnosed with T2D and MASLD with various demographic and clinical factors attending the Liver center in a tertiary university hospital. (NCT01241227)
- Cut-offs for advanced fibrosis were those recommended by AASLD clinical practice guidelines (Hepatology 2023):
  - LSM to rule-in F3F4 /F2-F4 12kPa / 8KPa
  - FIB-4 to rule-in/-out F3F4 1.3 / 2.67
  - LIVERFASt Fibrosis used a single cut-off of 0.59 for F3F4

LIVERFASt (Fibronostics, Florida, US)

- LIVERFASt Fibrosis test combines usual biochemistry blood biomarkers and anthropometrics to generate scores correlated to biopsy fibrosis staging (fibronostics.com).
- LIVERFASt Fibrosis test has similar performance in patients with T2D as in patients without T2D (3)

FIB-4

- Algorithm: platelet count, age, AST and ALT
- Dual cut-off for advanced fibrosis (<1.3, >2.67)
- Over/underestimation factors: age, cytolysis, T2D
- Lower diagnostic performance for cirrhosis in T2D

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

Fibroscan (Echosens, Paris, France)

- Quality criteria: IQR/median<30%, Success rate≥60%, 10 valid LSM
- Variability in 531 NAFLD (MASLD) patients paired measurements: one stage difference in 32%, two stages difference in 10%
- Overestimation: Cytolysis with ALT > 3x ULN, non fasting, MetS: T2D, BMI>30, high-blood pressure

RESULTS

Study Flow Chart

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

Excluded
- Missing Data N=170

Tertiary Center MASLD Cohort with liver assessment with LSM, FIB-4 and LIVERFASt Fibrosis test N=583

Excluded
- Liver biopsy sample <2 cm
- Biopsy to blood draw time lapse > 6 months apart N=184

Included N=399 (T2D N=235) liver assessment with LSM, FIB-4 and LIVERFASt Fibrosis test With biopsy sample ≥2cm and <6 months between biopsy and biomarkers collection

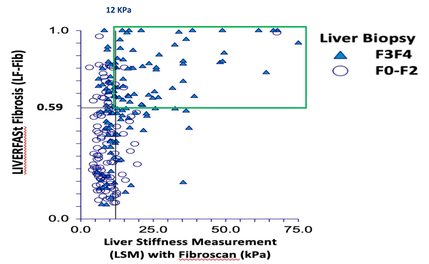
Characteristics of the MASLD cohort

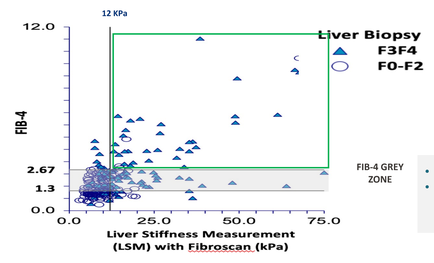
	N=583	N=399 overall with LB sample ≥2cm and <6 months apart from biomarkers	N=235 T2D patients with LB sample ≥2cm and <6 months apart from biomarkers
Age (years), median	56 yrs	60 yrs	61 yrs
Male Gender	56.4%	56.8%	49.5%
BMI (kg/m²)	31.5	31.3	32.8
Liver Stiffness Measurement, KPa	9.6 KPa	9.6 KPa	10.4 KPa
Liver Biopsy			
Advanced Fibrosis (F3F4)	45.2%	46.2%	58.3%
Cirrhosis	17.8%	21.0%	26.2%
NAS score ≥4	78.6%	79.6%	82.2%
Type 2 Diabetes	51.6%	52.4%	100%
HbA1c, %	6.6%	6.6%	6.9%
ALT, IU/L	55	55	55
AST, IU/L	59	42	43
FIB-4, median	1.55	1.55	1.67
LIVERFASt Fibrosis Test, median	0.48	0.48	0.56

Summary of the results	LIVERFASt & Fibroscan	FIB-4 & Fibroscan
F3F4 correctly identified	**70**/74 (95%)	**47**/51 (92%)
Missed F3F4	**47**/194 (24%)	**63**/254 (25%)
No-F3F4 correctly identified	**147**/194 (76%)	**118**/254 (46.5%)
Overestimated F3F4	**4**/74 (5%)	**4**/51 (8%)
Unclassified	0	**73**/245 (29%)*

Scatterplots of LIVERFASt & LSM and of FIB-4 & LSM plotted against liver biopsy staging in the overall cohort (N=399)

Right upper quadrants display patients in whom NITs agree for F3F4. Triangles show cases with biopsy staging F3F4





- 74% of F3F4 pts LB had FIB-4 <2.67;
- LIVERFASt &LSM correctly identified 41% oF3F4 pts having FIB-4 in the indeterminate (grey) zone.

MASLD cohort with LB sample size ≥20mm and time lapse to biopsy < 6 months	Overall cohort N=399 with LB sample ≥2cm and <6 months apart from biomarkers			Patients with T2D N=235 with LB sample ≥2cm and <6 months apart from biomarkers		
	No	Biopsy confirms both NITs	Biopsy disagrees with both NITs	No	Biopsy confirms both NITs	Biopsy disagrees with both NITs
LIVERFASt & LSM agree for F3F4 using 12KPa cutoff for LSM	74	70/74 (94.6%)	4/74 (5.4%)	56	53/56 (94.6%)	3/56 (5.4%)
LIVERFASt & LSM agree for F3F4 using 8KPa cutoff for LSM	117	94/117 (80.3%)	23/117 (19.7%)	88	72/88 (81.8%)	16/88 (18.2%)

MASLD cohort with LB sample size ≥20mm and time lapse to biopsy < 6 months	Overall cohort N=399 with LB sample ≥2cm and <6 months apart from biomarkers			Patients with T2D N=235 with LB sample ≥2cm and <6 months apart from biomarkers		
	No	Biopsy confirms both NITs	Biopsy disagrees with both NITs	No	Biopsy confirms both NITs	Biopsy disagrees with both NITs
FIB-4 & LSM agree for F3F4 using 12KPa cutoff for LSM	51	47/51 (92%)	4 (7.8%)	36	32/36 (88.9%)	4/36 (11.1%)
FIB-4 & LSM agree for F3F4 using 8KPa cutoff for LSM	76	69/76 (90.8%)	7/76 (9.2%)	41	37/41 (90.2%)	*4/41 (9.8%)*

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DISCLOSURES

RQ, MM _Fibronostics

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CONCLUSIONS

- **In patients with type 2 diabetes, the combination LIVERFASt Fibrosis Test & LSM outperformed FIB-4 & LSM for the identification of MASLD-related advanced fibrosis.**
- **According to liver biopsy, a lower cutoff for LSM, as 8KPa, could improve the identification of advanced fibrosis using LIVERFASt Fibrosis Test & LSM**