

LIVERFAST OUTPERFORMS FIB-4, IN SEQUENTIAL COMBINATION WITH VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY (VCTE) FOR IDENTIFYING ≥F3 STAGES IN PATIENTS WITH MASLD INCLUDING PATIENTS WITH TYPE 2 DIABETES (T2DM).

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INTRODUCTION

- FIB-4** followed by vibration-controlled transient elastography (**VCTE**, Echosens, Paris, France) is recommended to detect advanced fibrosis (≥F3). (Rinella M. et al. AASLD CPG Hepatology 2023)
- LIVERFAST** (Fibronostics U.S., Inc.) is a novel blood-based test reimbursed in US to identify liver fibrosis with high performance against histology, including inpatients with type 2 diabetes mellitus (T2DM) (2)
- Along with assessing liver fibrosis, LIVERFAST assesses steatosis and MASH-related activity.

AIMS

The study aimed to compare the performance of LIVERFAST Fibrosis test and FIB-4, sequentially with VCTE (Fibroscan), for the identification of advanced fibrosis (≥F3) including analyses in patients with type 2 diabetes (T2DM).

Cross-sectional retrospective study, conducted on patients ≥ 18 years old with established MASLD from a tertiary hepatology center, University Hospital Center of Bordeaux, France.

Inclusion criteria:

- Available blood tests, LIVERFAST and FIB-4, VCTE, and high quality (≥20 mm) liver biopsy

Fibrosis assessed using the following cut-offs:

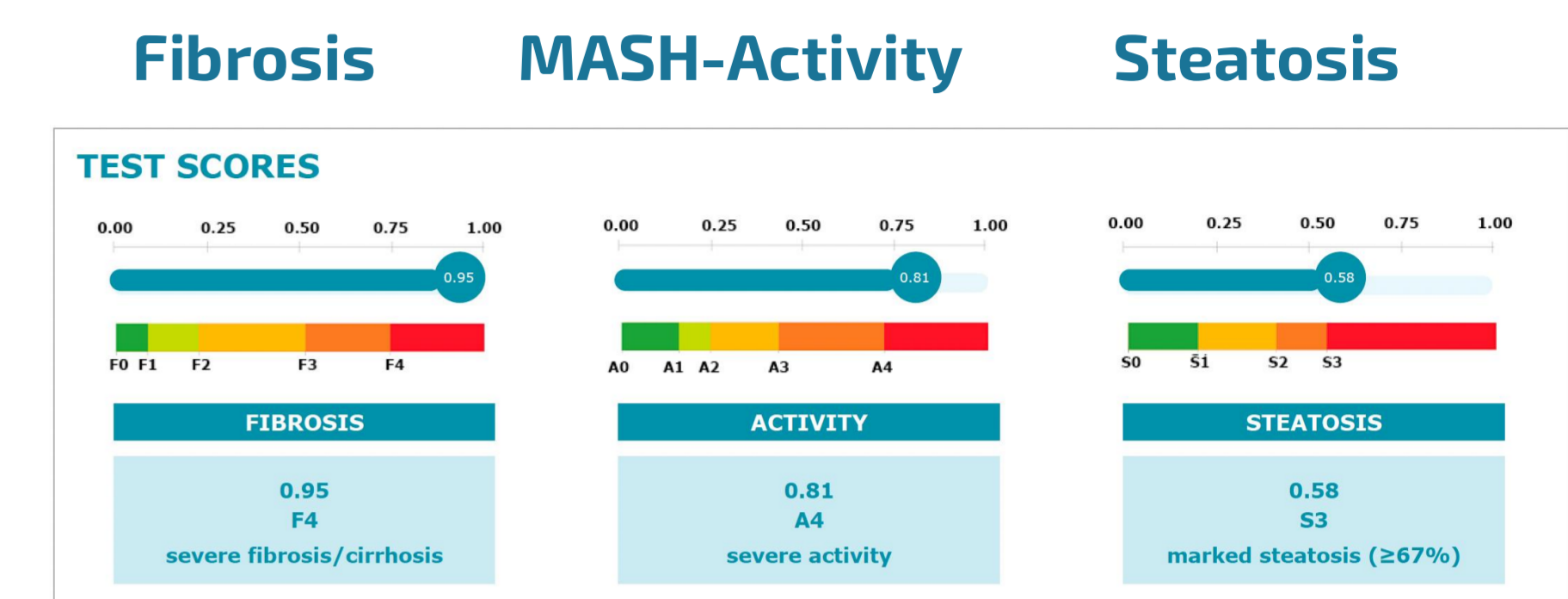
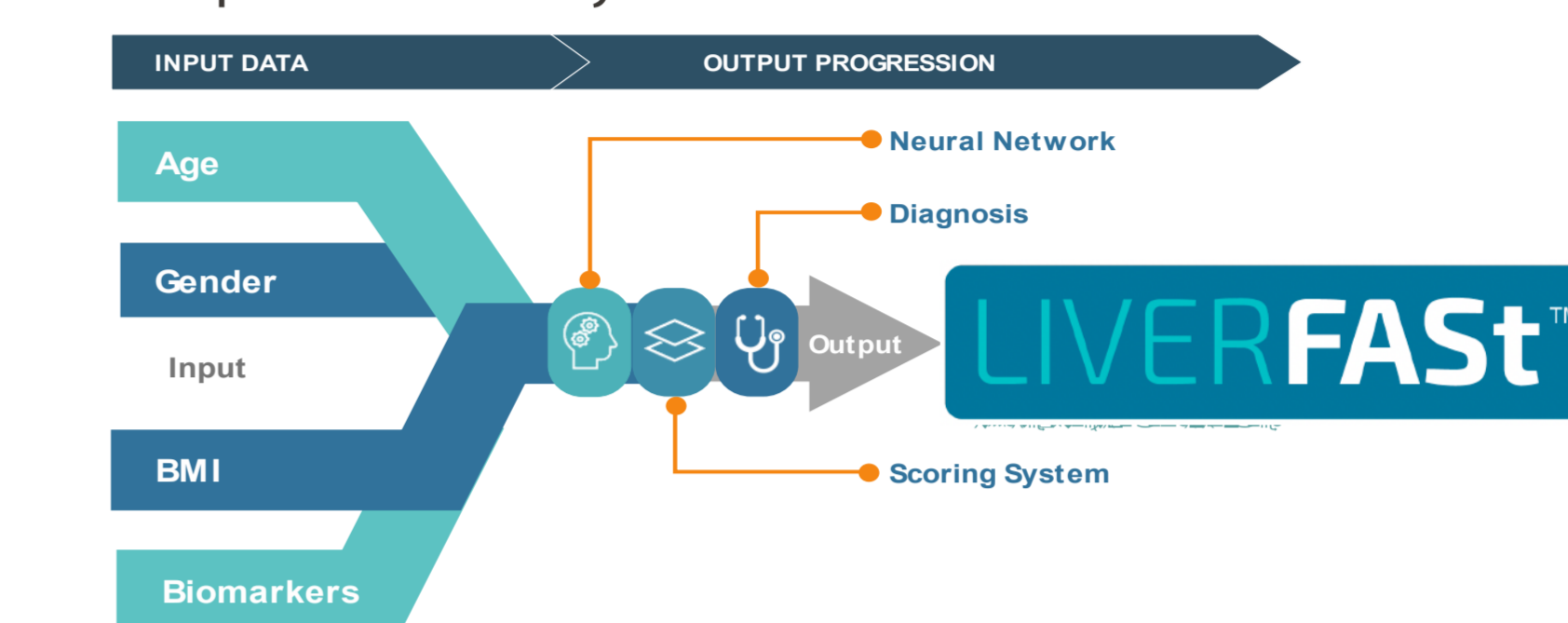
- FIB-4: ≥1.30 (or 2.00 for age ≥65 years) = intermediate/high risk for ≥F3 and >2.67 = high risk for ≥F3
- LIVERFAST fibrosis test: cut-off 0.52 for ≥F3
- VCTE ≥12kPa for ruling in ≥F3

Statistics

Performances were assessed using sensitivity, specificity, PPV, NPV, and number needed to diagnose one case (NND).

METHODS

The present study focused on LIVERFAST Fibrosis Test

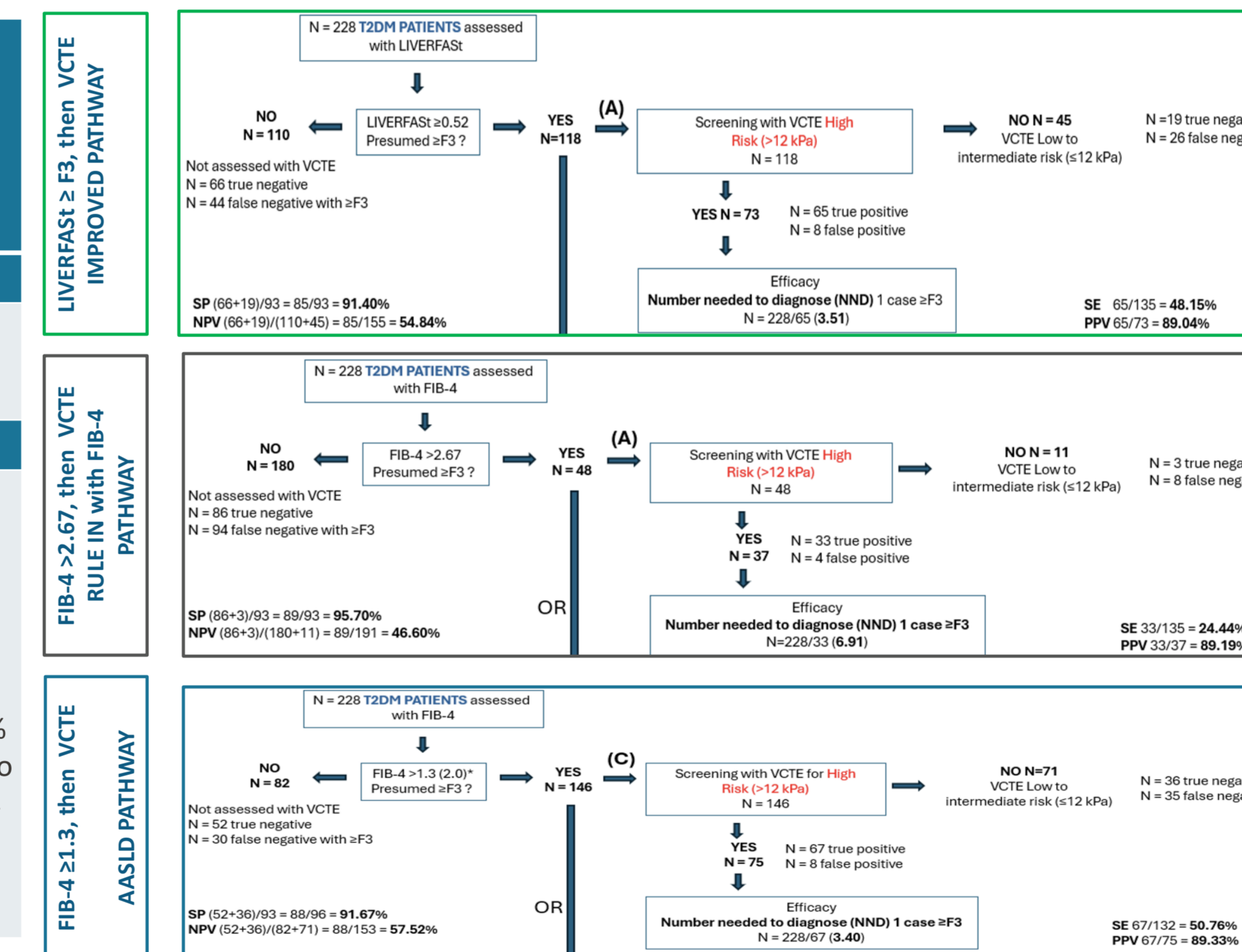


Serum biomarkers performed, including alpha-2 macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, GGT, ALT, AST, glucose, total cholesterol, triglycerides, age, sex, height, and weight were computed into LIVERFAST algorithms to analyze three scores (0.00–1.00) for fibrosis, MASH-related activity and steatosis.

RESULTS

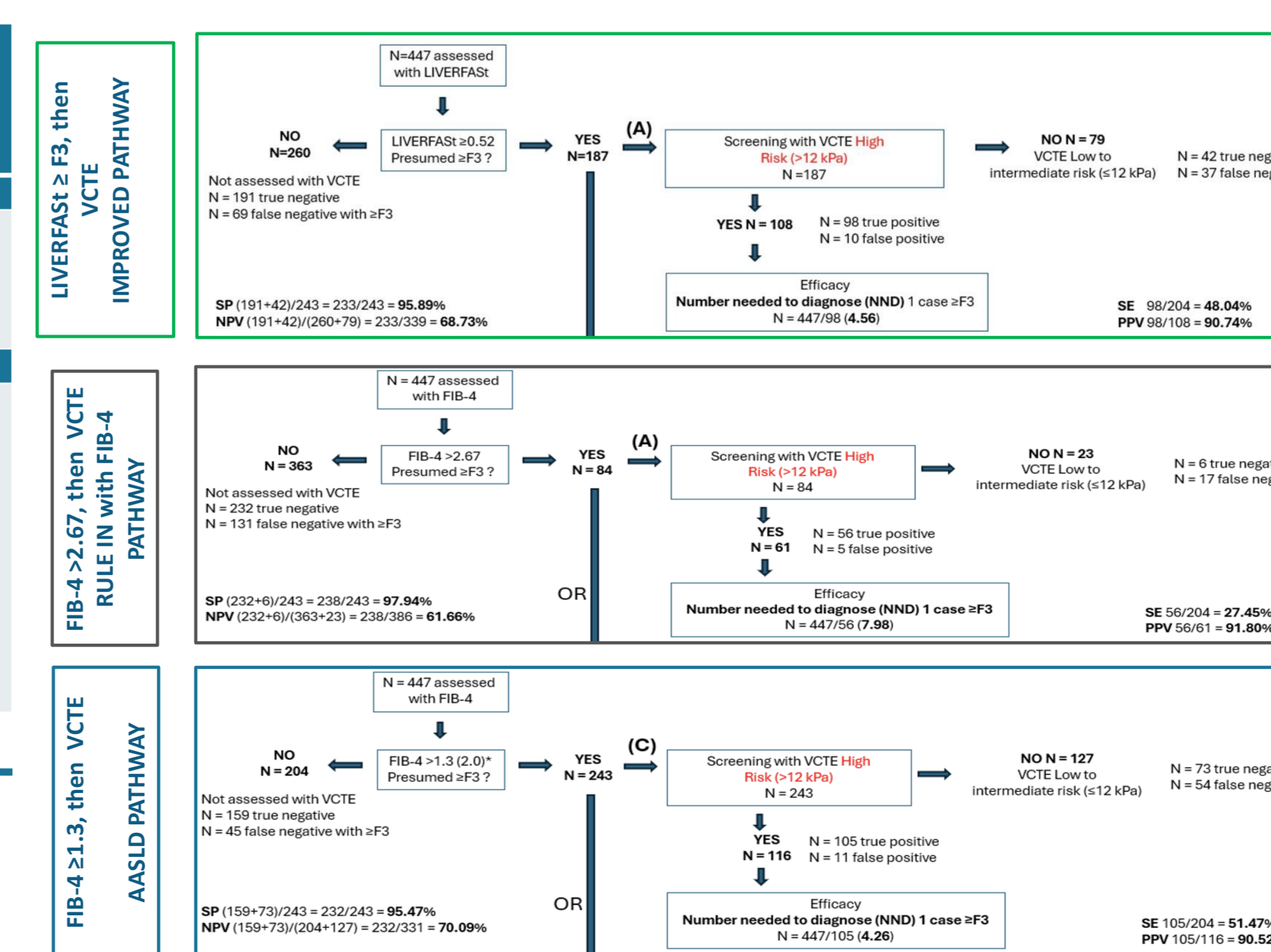
Performance and efficacy of the NITs sequential combinations in the two-step approach for ≥F3 fibrosis in the MASLD population with T2DM

Non-Invasive Liver Disease Assessment for ≥ F3 stage	SE	SP	PPV	NPV	Efficacy NND(no.)	Efficacy measured on VCTE referrals No(NND)
MASLD population with T2DM						
LIVERFAST followed by VCTE						
LIVERFAST ≥0.52 followed by VCTE >12 kPa (high risk for ≥F3 stages)	48%	91%	89%	55%	3.51	118 (1.82)
FIB-4 followed by VCTE						
FIB-4 >2.67, followed by VCTE >12 kPa (high risk for ≥F3 stage)	24%	96%	89%	47%	6.91	48 (1.45)
FIB-4 >1.3 (2.0)*, followed by VCTE >12 kPa, intermediate/ high risk for ≥F3 stage	51%	92%	89%	58%	3.40	146** (2.18)
AASLD PATHWAY						



Performance and efficacy of the NITs sequential combinations in the two-step approach for ≥F3 fibrosis in the overall MASLD population

Non-Invasive Liver Disease Assessment for ≥ F3 stage	SE	SP	PPV	NPV	Efficacy NND(no.)	Efficacy measured on VCTE referrals No(NND)
OVERALL MASLD population						
LIVERFAST followed by VCTE						
LIVERFAST ≥F3 followed by VCTE >12 kPa (high risk for ≥F3 stages)	48%	96%	91%	69%	4.56	187 (1.91)
FIB-4 followed by VCTE						
FIB-4 >2.67, followed by VCTE >12 kPa (high risk for ≥F3 stage)	28%	98%	92%	62%	7.98	84 (1.50)
FIB-4 >1.3 (2.0)*, followed by VCTE >12 kPa (intermediate/ high risk for ≥F3 stages)	52%	96%	91%	70%	4.26	243* (2.31)
AASLD PATHWAY						



Compared to the recommended pathway (AASLD), the improved pathway using LIVERFAST instead of FIB-4 before VCTE had several advantages:

- Improves the false positive rate referrals to VCTE
- Improves the true negative rate
- Generates 20% more correctly classified patients
- High efficacy in T2DM patients

Summary:

The combination LIVERFAST and VCTE achieved:

- Higher PPV (90.4%) than FIB-4 and VCTE (76% both) for similar NPV.
- Almost twice more of ≥F3 cases than the combination FIB-4 at the cut-off >2.67
- Stronger NND** was 4.56 vs 7.98, respectively.
- LIVERFAST identified a similar number of ≥F3 cases as FIB-4 at the recommended ≥1.3 [2.0] cut-off with a significantly lower number of required false positive referrals to VCTE [187/447 vs 243/447, respectively, p<0.001].
- Similar results have been observed in the T2DM subanalysis with a lower number of required VCTEs referrals of 118/228 vs 146/228 (p<0.01), respectively.

- A higher proportion of patients correctly classified without suspected fibrosis (true negatives) during the first step by LIVERFAST alone versus FIB-4 alone at the recommended cut-off: 42.7% vs 35.6%, p<0.05, respectively.

CONCLUSIONS

- LIVERFAST outperformed FIB-4 and its integration into MASLD pathways may enhance screening efficiency, including in high-risk T2DM patients.
- The study showed that LIVERFAST plays also crucial role in ruling out fibrosis in a higher proportion of patients than FIB-4, identifying those that do not require a second test as far as the first correctly classified fibrosis.

MASLD WITH T2DM

LIVERFAST as a stand-alone NIT outperformed FIB-4 for identifying ≥F3 fibrosis:

- Almost twice the sensitivity and higher NPV of FIB-4 (cut-off >2.67)
- Higher specificity and PPV at the recommended cut-off (≥1.3 [2.0])*

Performance of the NITs as a stand-alone assessment for ≥F3 fibrosis in the MASLD population with T2DM

Assessment for ≥F3 stage in the overall MASLD population with T2DM	SE	SP	PPV	NPV
LIVERFAST	67%	71%	77%	60%
≥0.52 for ≥F3 stage	(91/135)	(66/93)	(91/118)	(66/110)
FIB-4				
≥2.67, high risk for ≥F3 stage	30%	93%	85%	48%
	(41/135)	(86/93)	(41/48)	(86/180)
≥1.3 (2.0) intermediate to high risk for ≥F3 stage	76%	53%	70%	60%
	(102/135)	(49/93)	(102/146)	(49/82)
VCTE				
>12 kPa, high risk for ≥F3 stage	57%	86%	86%	58%
	(77/135)	(80/93)	(77/90)	(80/138)

*FIB-4 lower cut-off 2.0 in patients aged ≥65 years; T2DM type 2 diabetes mellitus

Performance of the NITs as a stand-alone assessment for ≥F3 fibrosis in the overall MASLD population

Assessment for ≥F3 stage in the overall MASLD population	SE	SP	PPV	NPV
LIVERFAST	66%	79%	72%	74%
≥0.52 for ≥F3 stage	(135/204)	(191/243)	(135/187)	(191/260)
FIB-4				
≥2.67, high risk for ≥F3 stage	36%	96%	87%	64%
	(73/204)	(232/243)	(73/84)	(232/363)
≥1.3 (2.0)* intermediate to high risk for ≥F3 stage	78%	65%	65%	78%
	(159/204)	(159/243)	(159/243)	(159/204)
VCTE				
>12 kPa, high risk for ≥F3 stage	58%	91%	84%	73%
	(119/204)	(221/243)	(119/141)	(221/306)

*FIB-4 lower cut-off 2.0 in patients aged ≥65 years; T2DM type 2 diabetes mellitus

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