

XXVIII IFSO World Congress

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PERFORMANCE OF FIB4, NFS AND APRI IN DETECTING ADVANCED FIBROSIS IN ADULTS WITH OBESITY AND METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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IFSO 2025 Santiago

Combined Therapies, The Dawn of a New Era

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Nothing to disclose



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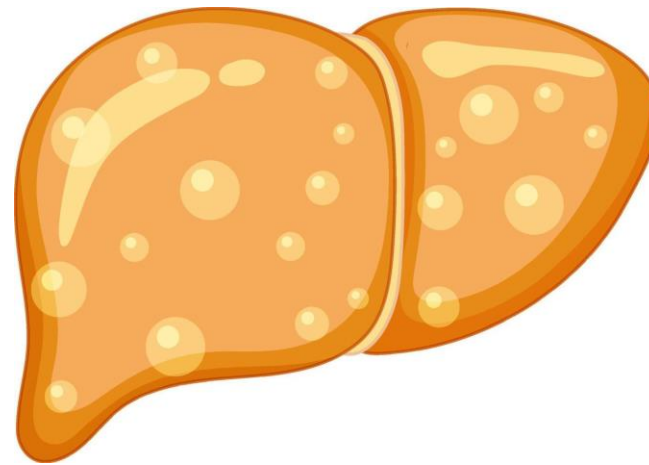
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Introduction

Metabolic dysfunction–Associated Steatotic Liver Disease (MASLD)



Affects 38%
adult population



Most common
chronic liver disease



One of the most
frequent
comorbidity 70-90%

- Giovanni T. Metabolic Dysfunction–Associated Steatotic Liver Disease. N Engl J Med. 2025.
- Younossi ZM. Global epidemiology of NAFLD — meta-analysis. Hepatology. 2016
- Chalasani N. AASLD Practice Guidance on the clinical assessment and management of NAFLD. Hepatology. 2018
- Powell EE. Obesity and non-alcoholic fatty liver disease: epidemiology to pathophysiology. Nat Rev Gastroenterol Hepatol. 2021

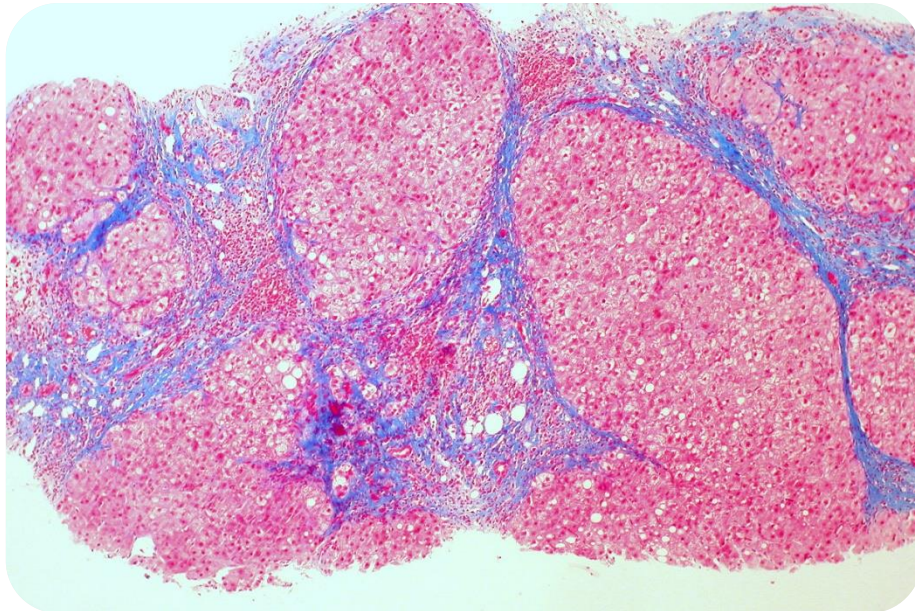
Introduction



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Evaluation of fibrosis stage



Biopsy

Transient
ARFI / Shear wave
MRI

Elastography

Serum markers
(FibroTest®, Enhanced Liver Fibrosis)

Serum scores (FIB-4, NFS, etc)



- Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 2021.
- AASLD Practice Guidance on NAFLD. Hepatology 2023.
- Noninvasive Evaluation of Liver Fibrosis Using Transient Elastography. J Hepatol 2012.

Methods



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- Analytical cross-sectional observational study.
- Census sampling methodology.
- Patient information was obtained from the institutional database.
- Data was taken between 2016 and 2021.

Methods



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Inclusion criteria:

- ✓ Age 18-65 y
- ✓ Undergoing bariatric surgery
- ✓ Obesity (BMI ≥ 30 kg/m²)
- ✓ MASLD (steatosis $\geq 5\%$ on liver biopsy)

Exclusion criteria:

- ❖ Harmful alcohol use
- ❖ Previous bariatric surgery
- ❖ Liver biopsies <11 portal spaces
- ❖ Alternative causes of fibrosis (medications, viral hepatitis, autoimmune diseases, etc.)

Methods



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Reference test: Liver biopsy

Index test: Non-invasive liver fibrosis test

- **APRI** (AST to Platelet Ratio Index) ≥ 0.98 high risk of significant fibrosis - cirrhosis

$$[(AST / \text{reference } AST) \times 100] / PLT$$

- **FIB-4** (Fibrosis-4) ≥ 2.67 high risk of advanced fibrosis

$$(Age \times AST) / (PLT)^{1/2}$$

- **NFS** (Non-alcoholic Fatty Liver Disease Fibrosis Score) ≥ 0.672 high risk of advanced fibrosis

$$-1.675 + 0.037 \times age + 0.094 \times BMI + 1.13 \times \text{impaired fasting glucose/DM} + 0.99 \times AST/ALT \text{ ratio} - 0.013 \times PLT - 0.66 \times \text{serum albumin}$$

Methods



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Lab test

→ Cobas 6000 Module C50 analyzer

Fasting

→ ≥ 8 h.

Body Composition Analyzer

→ *SECA 514 M / TANITA TBF-310.*

Height

→ SECA stadiometer.

Waist circumference

→ Midpoint: lower border of the last rib - iliac crest.

Liver biopsies

→ Wedged, cold scissors, at the start of each surgery.

Biopsies

→ Two expert liver pathologists.

Methods: Statistical analysis



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Database **quality control** → detect missing or inconsistent values.

Verification → **original medical records** (physical/electronic).

Data were analyzed using statistical software **Stata v16.0** (StataCorp, TX, USA).



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Methods: Statistical analysis

- Dependent variable vs categorical covariates → Chi-square test / Fisher's exact test.
- Dependent variable vs numerical variables → Student's T test / Mann-Whitney U test.
- Performance → areas under the ROC curve (AUC).
- Optimal cutoff points → Liu product Method.
- Sensitivity analyses → bootstrapping technique (1,000 replicates), and confidence intervals were calculated.
- Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) were estimated.



Methods: Ethical considerations



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The protocol was approved:

- ✓ Ethics Committee of the Peruvian University of Applied Sciences (FCS-CEI/727-11-20)
- ✓ Multidisciplinary Research Unit of the Avendaño Clinic.

Results



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n=426

Characteristics		N (%)
Sex	Female	294 (69.0)
	Male	132 (31.0)
BMI (kg/m ²)		37.6 [33.8-41.1]
Obesity classification	I	140 (32.9)
	II	140 (32.9)
	III, IV, V	146 (34.3)
Waist circumference (cm)	Female	109.2 ± 12.4
	Male	125.4 ± 13.5
High blood pressure	No	349 (81.9)
	Yes	77 (18.1)
Diabetes Mellitus	No	346 (81.2)
	Yes	80 (18.8)
Insulin resistance	No	34 (8.3)
	Yes	378 (91.8)
Hypothyroidism	No	360 (84.51)
	Yes	66 (15.49)



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Results



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Characteristics (Liver Biopsy)		N (%)
Steatosis	Mild	226 (53.05)
	Moderate	113 (26.53)
	Severe	87 (20.42)
Steatohepatitis	No	21 (4.98)
	Yes	401 (95.02)
Fibrosis	F0	65 (15.3)
	F1	249 (58.45)
	F2	71 (16.67)
	F3	41 (9.62)
Significant fibrosis (F2-F4)	No	314 (73.7)
	Yes	112 (26.3)
Advanced fibrosis (F3-F4)	No	385 (90.4)
	Yes	41 (9.6)

Characteristics		N (%)
FIB-4		0.5 [0.36 - 0.72]
F3-F4 risk	Low	402 (94.4)
	Indeterminate	23 (5.4)
	High	1 (0.2)
NFS		-2.9 ± 1.3
F3-F4 risk	Low	361 (84.7)
	Indeterminate	59 (13.9)
	High	6 (1.4)
APRI		0.24 [0.16 - 0.38]
F2-F4 risk	Low	406 (95.3)
	High	20 (4.7)

Results

Characteristics associated with advanced liver fibrosis according to biopsy in bivariate analysis

Characteristics		Advanced liver fibrosis (F3-F4)		<i>p-value</i>
		No (n=385) n (%)	Yes (n=41) n (%)	
Sex	Female	270 (91.8)	24 (8.2)	0.127 ‡
	Male	115 (87.1)	17 (12.9)	
Age (years)*		36.9 ± 9.9	43.0 ± 10.3	<0.001 †
Total cholesterol (mg/dL) *		197.1 ± 39.3	187.4 ± 40.1	0.134 †
HDL cholesterol (mg/dL) **		43 [36-50]	39 [34 -47]	0.085 ††
LDL cholesterol (mg/dL) *		119 ± 34.8	111.8 ± 34.6	0.210 †
Triglycerides (mg/dL) **		150.5 [110 - 207.5]	150 [119 - 202]	0.868 ††
Glucose (mg/dL) **		92 [85 -98]	96 [88.5-112]	0.008 ††
HOMA - IR**		5.2 [3.6 - 7.3]	7.5 [5.3 - 13.0]	<0.001 ††
AST (U/L) **		23 [17 - 34.6]	33 [19-54]	0.008 ††
ALT (U/L) **		33 [22-56]	48 [21-67]	0.255 ††
Platelets *		320.4 ± 67.9	304.2 ± 72.7	0.151 †
Albumin*		4.6 ± 0.3	4.5 ± 0.4	0.113 †

*: Mean ± standard deviation; **: Median [Interquartile Range]; †: Student's T-test; ††: Mann-Whitney U-test; ‡: Chi-square test; ††: Fisher's exact test



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Results

Characteristics associated with advanced liver fibrosis according to biopsy in bivariate analysis



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Characteristics		Advanced liver fibrosis (F3-F4)		<i>p-value</i>
		No (n=385) n (%)	Yes (n=41) n (%)	
BMI ≥ 40 kg/m ²	No	264 (94.3)	16 (5.71)	<0.001 ‡
	Yes	121 (82.9)	25 (17.1)	
Waist circumference (cm)**	Female (n=260)	107 [101 - 116]	115.5 [100 - 129]	0.047 ††
	Male (n=110)	123 [115 - 132.5]	135.5 [127 -151]	0.014 ††
High blood pressure	No	325 (93.1)	24 (6.9)	<0.001 ‡
	Yes	60 (77.9)	17 (22.1)	
Diabetes Mellitus	No	318 (91.9)	28 (8.1)	0.026 ‡
	Yes	67 (83.8)	13 (16.25)	
Insulin resistance	No	32 (94.1)	2 (5.9)	0.758 ‡ ‡
	Yes	341 (90.2)	37 (9.8)	
Hypothyroidism	No	327 (90.8)	33 (9.2)	0.454 ‡
	Yes	58 (87.9)	8 (12.1)	

*: Mean ± standard deviation; **: Median [Interquartile Range]; †: Student's T-test; ††: Mann-Whitney U-test; ‡: Chi-square test; ‡‡: Fisher's exact test



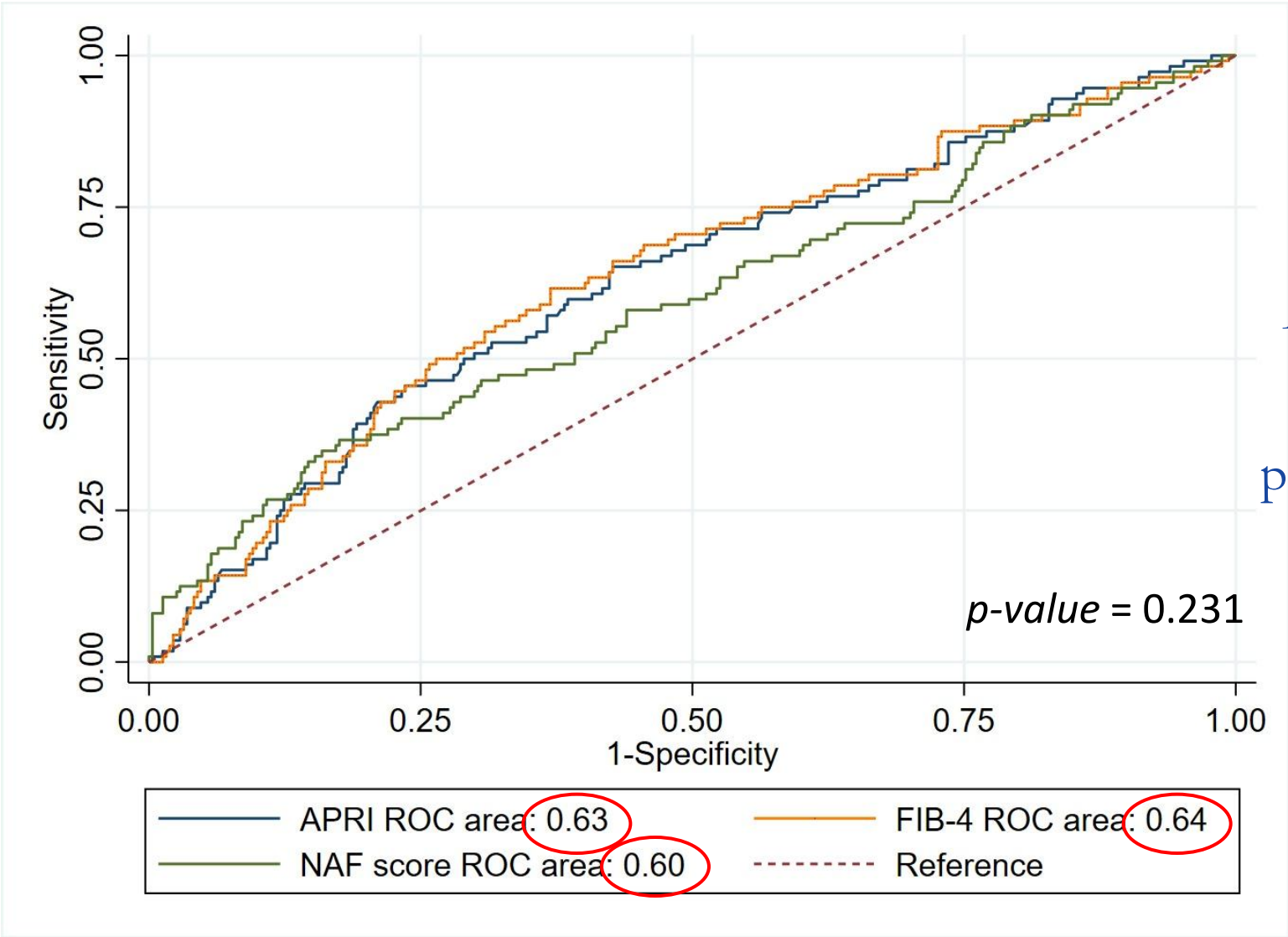
Results

AUROC of APRI, FIB-4 and NFS for significant fibrosis in patients with MASLD



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AUROC 0.6-0.7
=
poor performance



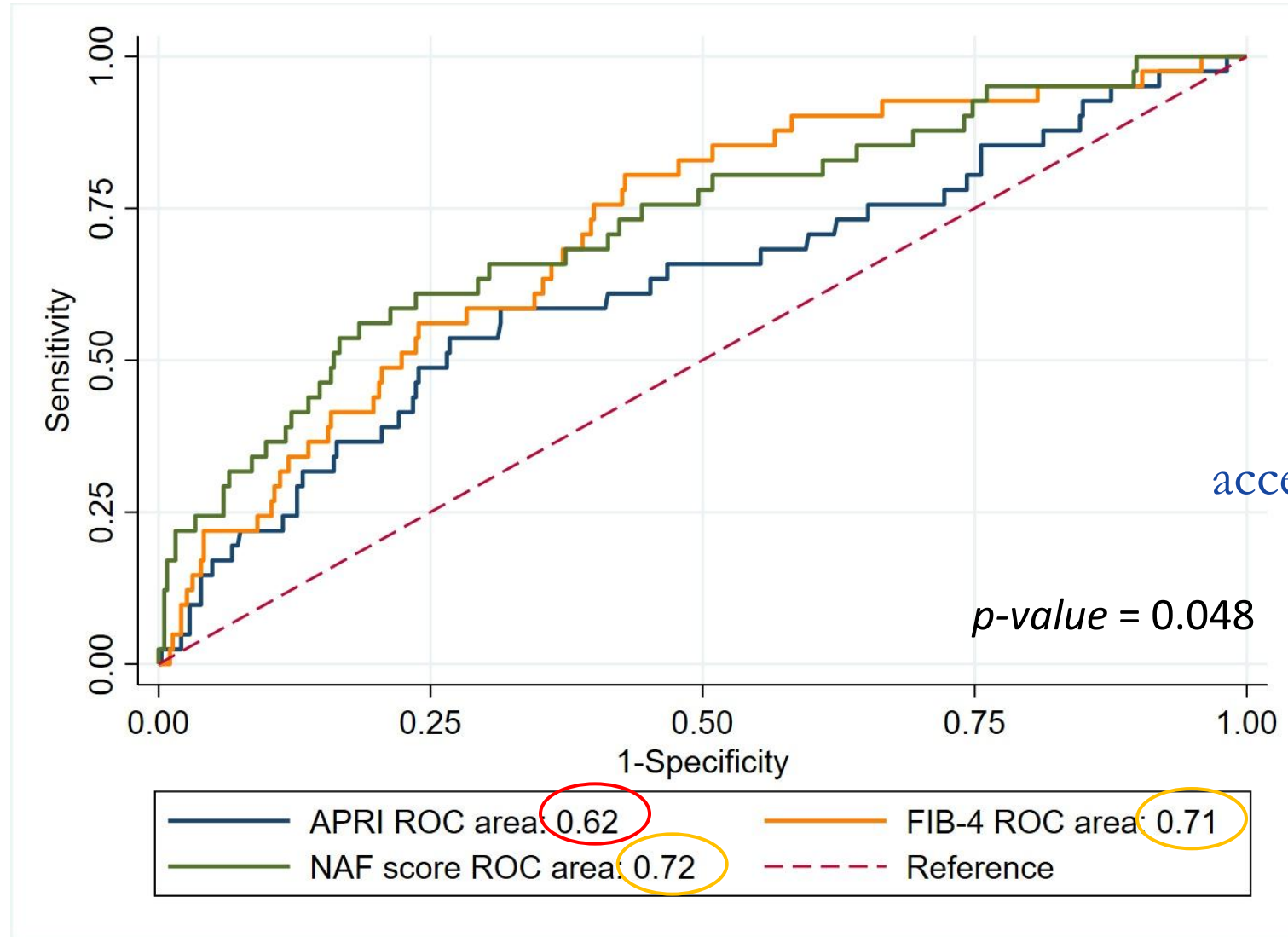
Results

AUROC of APRI, FIB-4 and NFS for advanced fibrosis in patients with MASLD



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AUROC 0.7-0.8
=
acceptable performance



Results

Discriminative capacity of APRI, FIB-4 and NFS to detect advanced fibrosis in patients with MASLD, overall and by subgroup



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		APRI		FIB4		NFS		<i>p-value</i> †
		AUROC	95% CI	AUROC	95% CI	AUROC	95% CI	
Global		0.62	0.52-0.72	0.71	0.63 – 0.79	0.72	0.63 - 0.81	0.048
Age	<35 years	0.65	0.44 – 0.85	0.71	0.49 – 0.92	0.69	0.48 - 0.83	0.404
	≥35 years	0.61	0.49 – 0.72	0.66	0.55 – 0.76	0.71	0.61 - 0.82	0.170
Sex	Female	0.63	0.50 – 0.77	0.78	0.70 – 0.86	0.77	0.68 – 0.87	0.014
	Male	0.54	0.39 - 0.68	0.62	0.47 - 0.76	0.67	0.50 - 0.84	0.174
BMI ≥ 40 kg/m²	Yes	0.71	0.59 – 0.82	0.78	0.69 – 0.87	0.75	0.64 – 0.86	0.040
	No	0.47	0.31 - 0.64	0.63	0.49 – 0.78	0.62	0.48 – 0.77	0.021
Diabetes Mellitus	Yes	0.64	0.46 - 0.83	0.74	0.59 – 0.89	0.72	0.57 – 0.88	0.206
	No	0.60	0.48 - 0.72	0.69	0.60- 0.79	0.69	0.58 - 0.80	0.190
High blood pressure	Yes	0.66	0.52 - 0.80	0.70	0.55 – 0.85	0.72	0.57 - 0.86	0.732
	No	0.56	0.42-0.70	0.68	0.58 – 0.79	0.69	0.57 – 0.80	0.101

slightly
improve



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AUROC: Area Under ROC ; 95% CI: 95% Confidence Interval †: Test equality of ROC areas

Results



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Diagnostic performance of APRI, FIB-4 and NAF according to theoretical and empirical cut-off points*

	Sensitivity	Specificity	Correct classification	LR+	LR-
APRI					
Theoretical point: ≥ 0.98	14.6%	96.1%	88.3%	3.8	0.9
Empirical point: ≥ 0.300	58.5%	68.6%	67.61	1.9	0.6
FIB4					
Theoretical point: > 2.67	0.0%	99.5%	89.9%	0.0	1.0
Empirical point: ≥ 0.507	80.5%	56.9%	59.2%	1.9	0.3
NFS					
Theoretical point: > 0.672	12.2%	99.5%	91.1%	23.5	0.9
Empirical point: ≥ -2.104	61.0%	76.1%	74.7%	2.6	0.51

Calculated
optimal
cut-off

* Empirical optimum point calculated using the Liu method



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Conclusions



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1. Non-invasive scores in patients undergoing BMS tend to underestimate the grade of fibrosis in preoperative assessment.
2. The scores perform from poor to acceptable, with NFS and FIB-4 showing better discriminative ability, especially in women and in adults with severe obesity.
3. The commonly used and recommended cut-off points are oriented toward gaining specificity, but with very low sensitivity, which makes them less valuable as a screening test.
4. NFS achieves a higher percentage of correct classification when using **new empirical cut-off points** that optimize the balance between sensitivity and specificity.



thank you



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