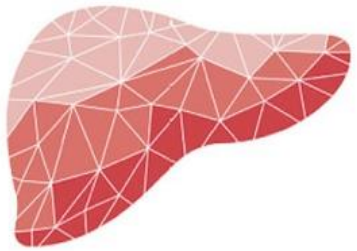
ciberehd
Centro de Investigación Biomédica en Red
Enfermedades Hepáticas y Digestivas

IBiS
INSTITUTODEBIOMEDICINADESEVILLA

Hospital U Virgen del Rocío
UGC Aparato Digestivo

Universidad de Sevilla

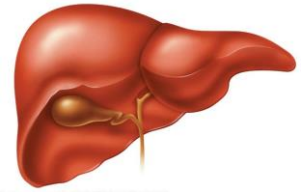


MÁSTER EN HEPATOLOGÍA

UAM
Universidad Autónoma de Madrid

Universidad de Alcalá

Diagnóstico no invasivo de la enfermedad hepática metabólica

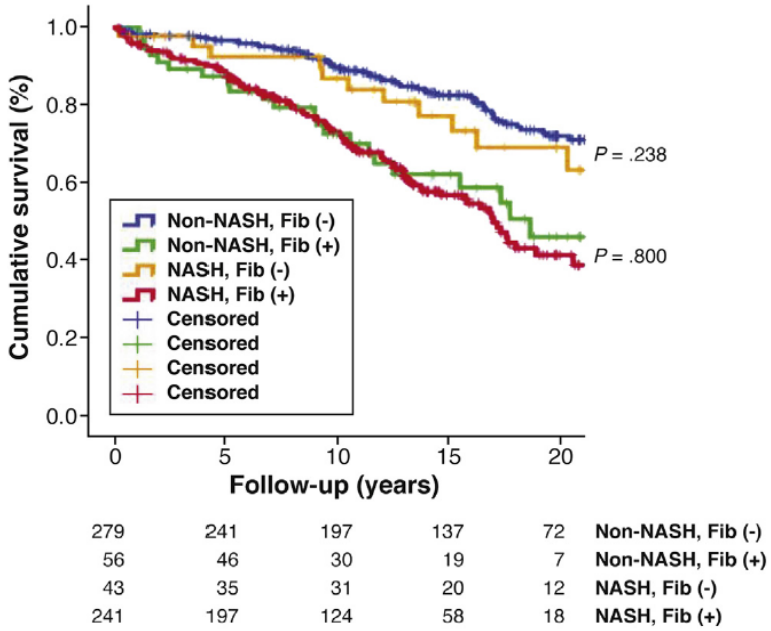


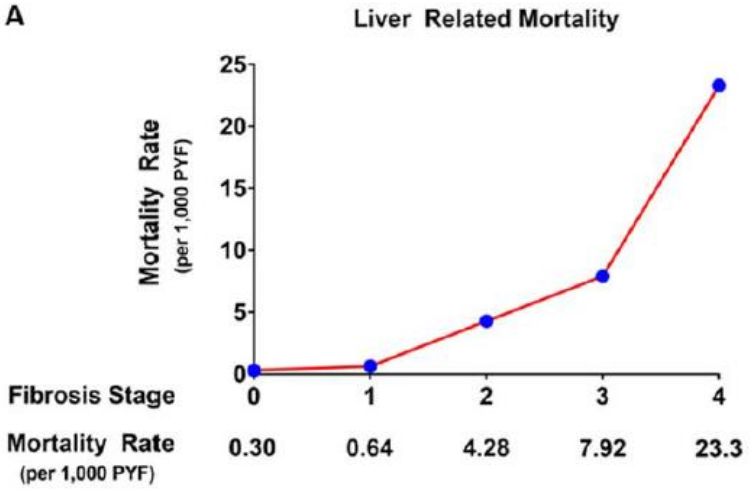
Dr. Javier Ampuero
UGC Enfermedades Digestivas
Hospital Universitario Virgen del Rocío
Sevilla, España

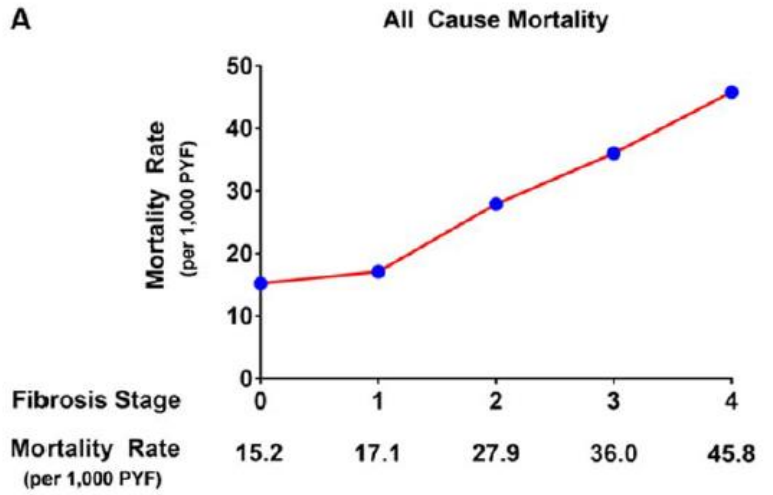
¿Qué es más importante detectar?

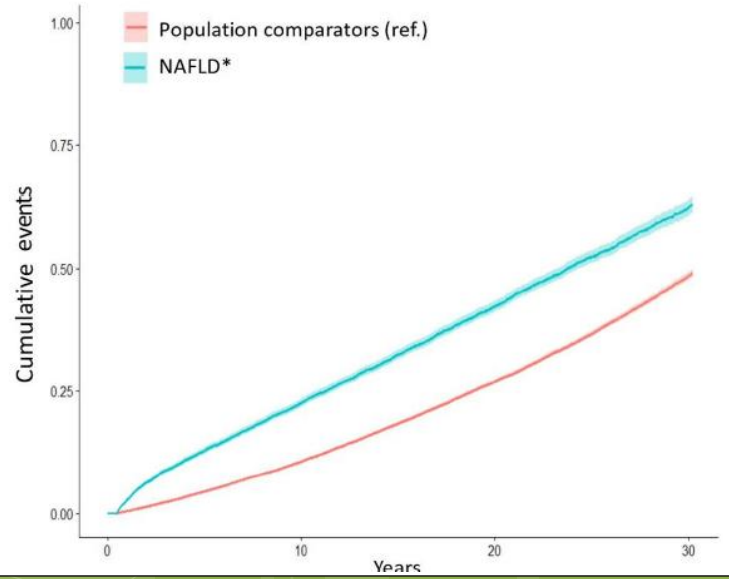
Una mirada al escenario

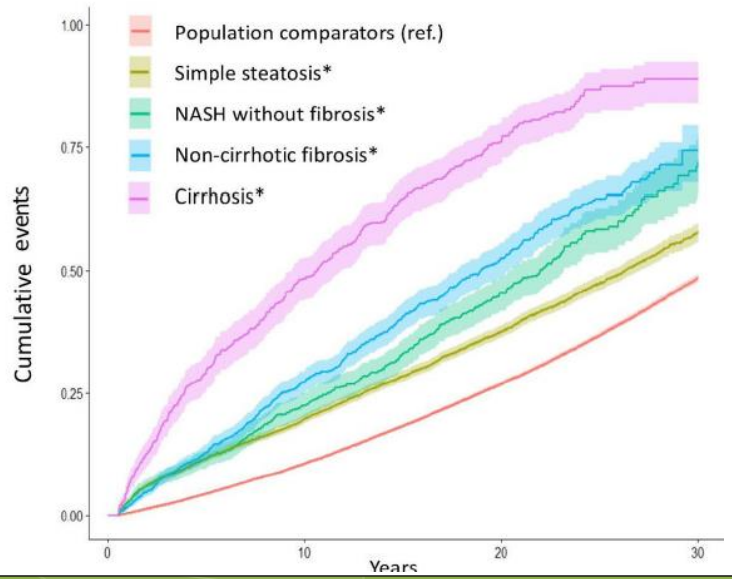
MORTALIDAD SEGÚN DAÑO HISTOLÓGICO











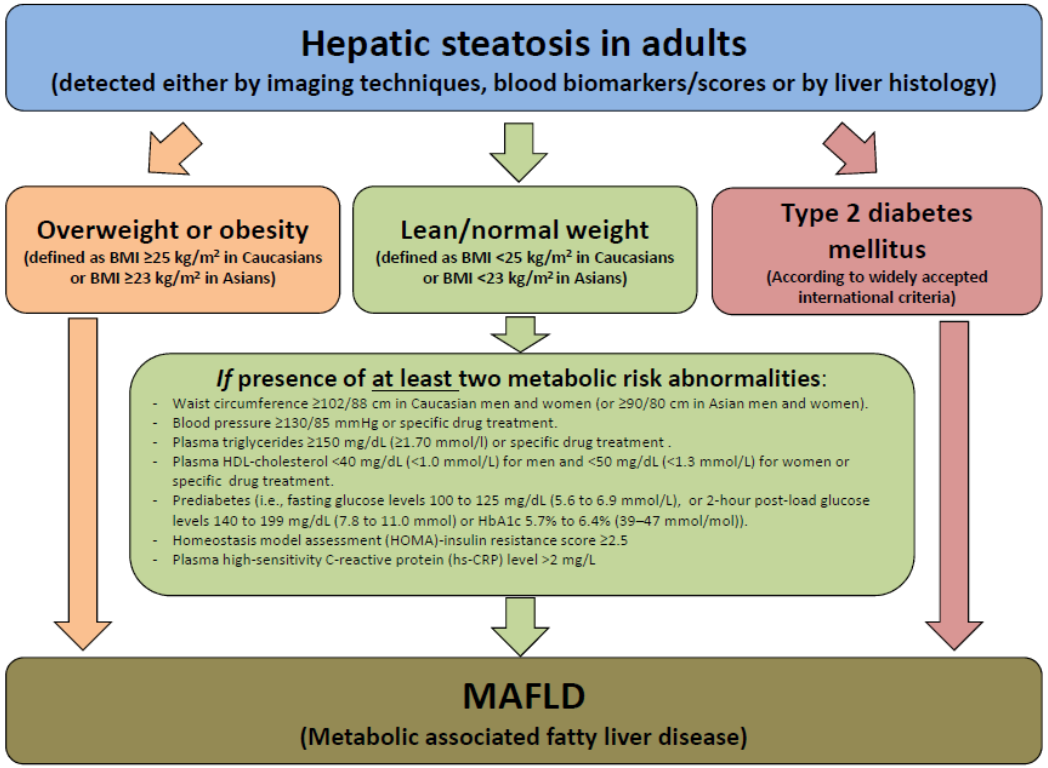
Angulo et al. Gastroenterology 2017

Simon et al, Gut 2021

Dulai et al, Hepatology 2017

¿Cómo abordar la esteatosis hepática?

Métodos bioquímicos y de imagen



Eslam et al. J Hepatol 2020

Hepatic Steatosis Index (HSI)

Fórmula: 8 * (**ALT/AST) ratio** + **BMI** + 2 (if **DM**) + 2 (if **female**)

Interpretación: HSI<30: No NAFLD; HSI>36 NAFLD

HEPATIC STEATOSIS INDEX		
AST		U/L
ALT		U/L
SEXO FEMENINO		SI/NO
DIABETES TIPO 2		SI/NO
PESO		kg
TALLA		m
IMC (kg/m²)		Kg/m²
HSI		

FATTY LIVER INDEX		
Triglicéridos		mg/dl
GGT		U/L
Perímetro abdominal		cm
PESO		kg
TALLA		m
IMC (kg/m²)		Kg/m²
FLI		

Fatty Liver Index (FLI)

Fórmula:
100/(1+EXP((1)*(0.953*Ln(**Tg**))+(0.139*****BMI**)+(0.718*Ln(**GGT**))+(0.053*(**WC**))-15.475))

Interpretación: FLI<30: No NAFLD; FLI>60 NAFLD

Esteatosis Hepática

Ultrasonography

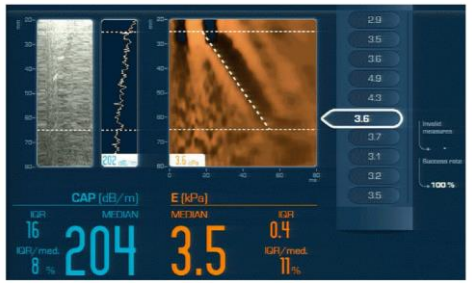
Sensitivity 60-70%, Specificity 90-95%

Low sensitivity when fat infiltration < 30%!!!!

Table 1. Comparison between commonly used modalities for liver fat quantification.

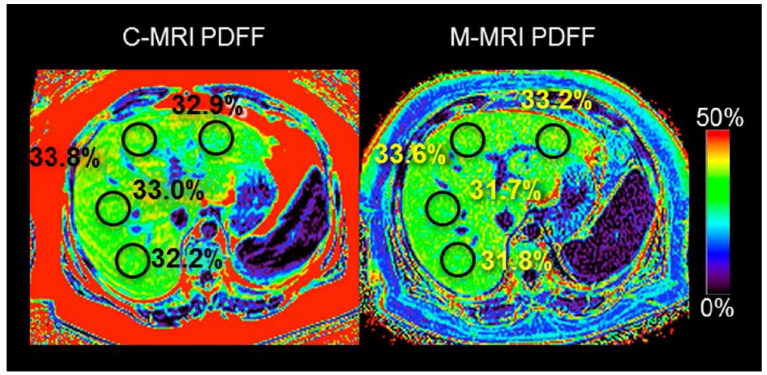
Modality	Cost	Accuracy	Point of care	Quantitative
CUS	+	++	Yes	No
CAP	+	++	Yes	Yes, but not linear in higher liver fat content
CT	++	++	No	Semi-quantitative
MRI-PDFF	++	+++	No	Yes

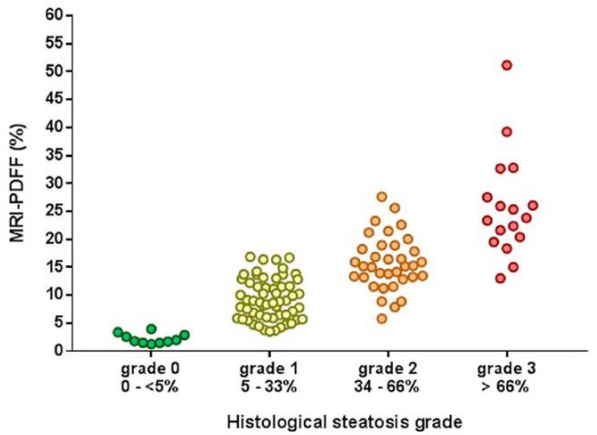
Controlled Attenuation Parameter (CAP)

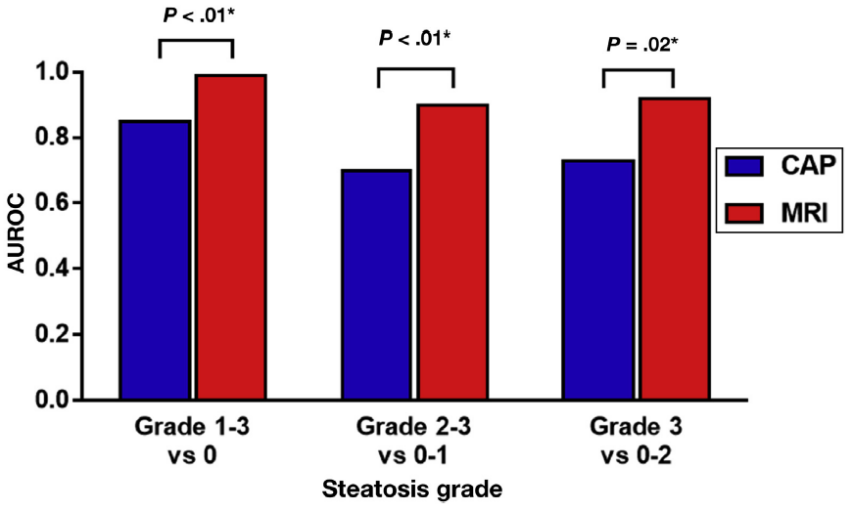


	S0 *vs.* S1–S3	S0–S1 *vs.* S2–S3	S0–S2 *vs.* S3*
AUC	0.823 (0.809–0.837)	0.865 (0.850–0.880)	0.882 (0.858–0.906)
Sensitivity	0.688 (0.600–0.750)	0.773 (0.690–0.838)	0.882 (0.765–0.956)
False negative rate (1-sensitivity)	0.312 (0.250–0.400)	0.227 (0.162–0.310)	0.118 (0.044–0.235)
Specificity	0.822 (0.761–0.897)	0.812 (0.749–0.879)	0.776 (0.720–0.821)
False positive rate (1-specificity)	0.178 (0.103–0.239)	0.188 (0.121–0.251)	0.224 (0.179–0.280)
Optimal cut-off, dB/m	248 (237–261)	268 (257–284)	280 (268–294)

Proton Density Fat Fraction (MRI-PDFF)



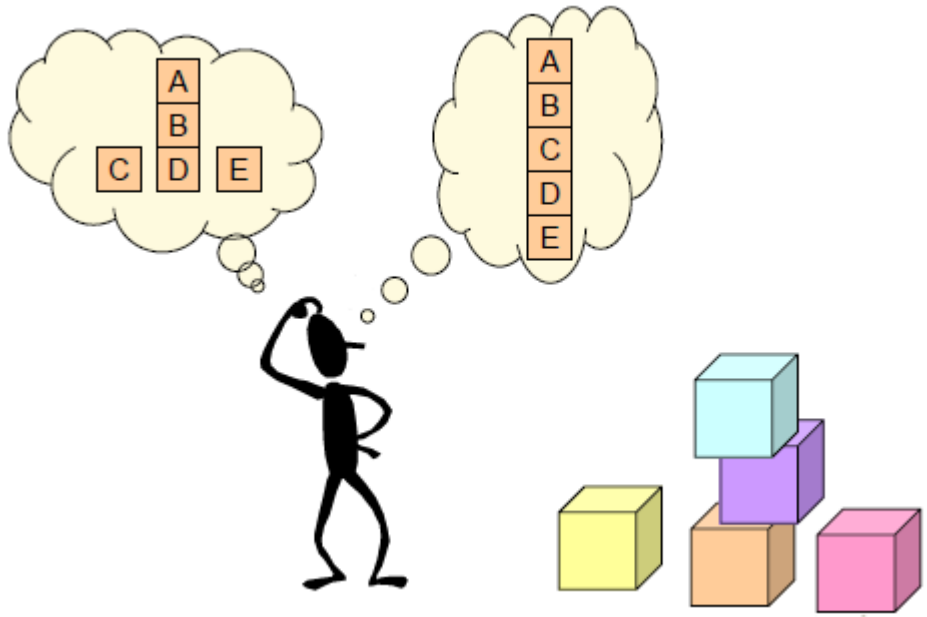




Loomba et al. J Hepatol 2018 Karlas et al. J Hepatol 2017 Park et al. Gastroenterology 2017 Caussy et al. Hepatology 2018

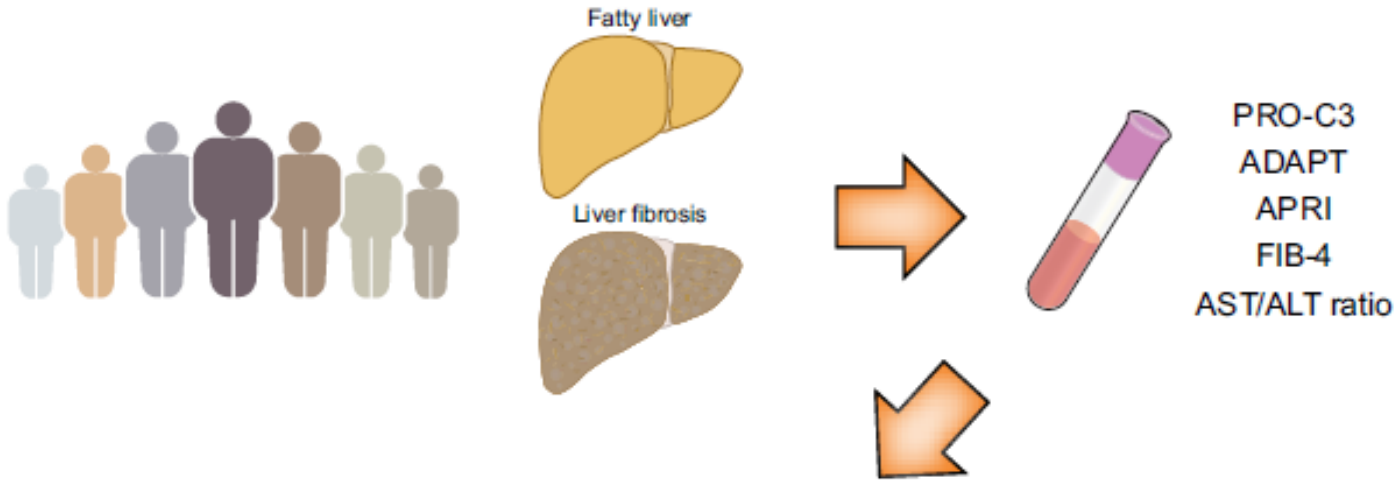
¿Cómo abordar la esteatohepatitis?

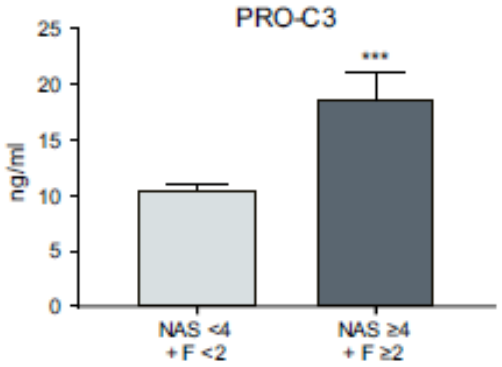
Métodos bioquímicos y de imagen



Esteatohepatitis

CENTAUR screening population (n = 517)





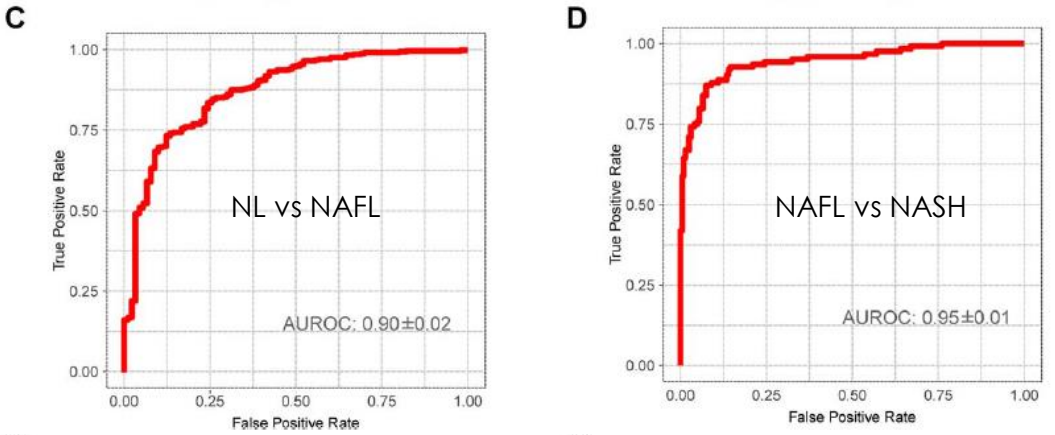
	PRO-C3 AUC	ADAPT AUC	APRI AUC	FIB-4 AUC	AST/ALT AUC
Significant fibrosis (F2-F4)	0.70	0.76	0.66	0.71	0.58
Advanced fibrosis (F3-F4)	0.73	0.80	0.68	0.79	0.68
NASH	0.74	0.78	0.68	0.68	0.53

Nielsen et al. J Hepatol 2022

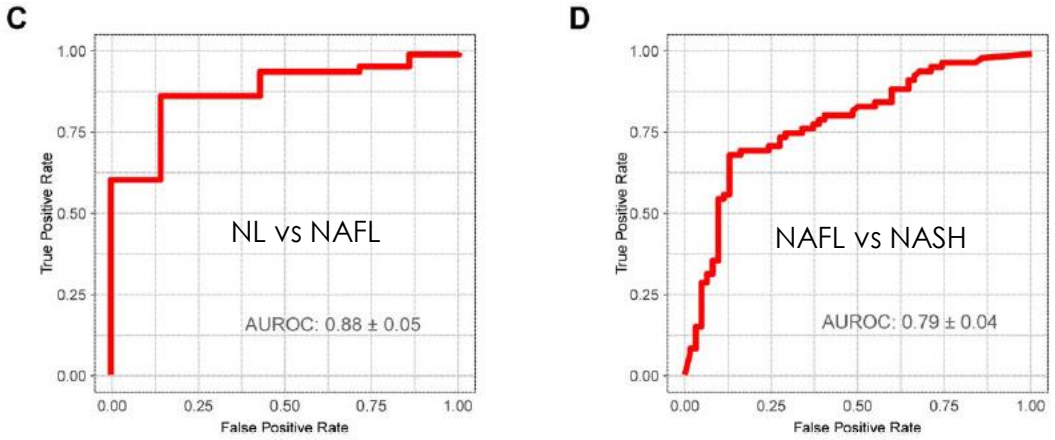
Esteatohepatitis

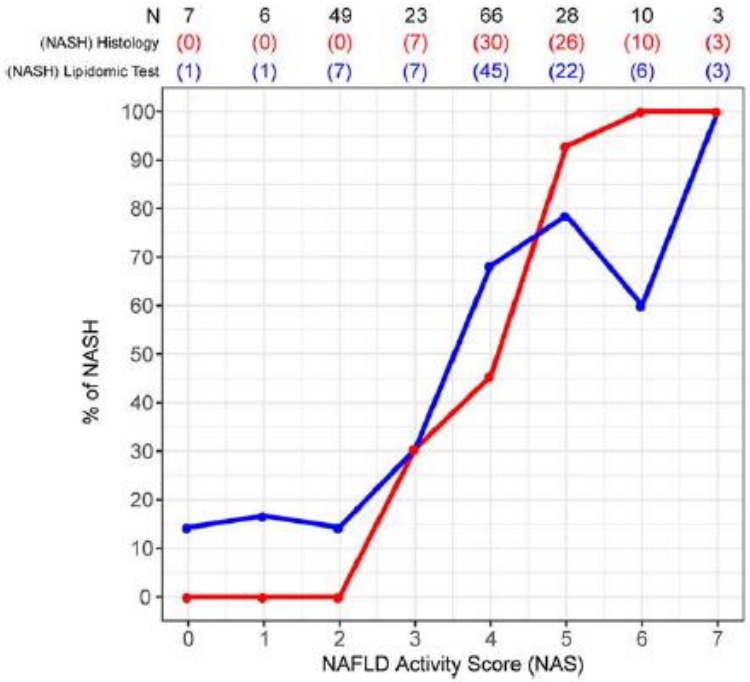
Histology	Discovery Cohort			Validation Cohort		
	NL	NAFL	NASH	NL	NAFL	NASH
n	90	246	131	7	109	76
Age (years)	44.8 ± 13.1	42.7 ± 12.2	45.1 ± 10.8	43.1 ± 11.0	45.0 ± 11.3	48.1 ± 12.4
Sex (Female %)	88.1*,†	70.4‡	74.6‡	71.4	51.4	56.6
BMI (kg/m^2)	39.4 ± 13.3†	42.9 ± 11.4‡	45.9 ± 11.2	39.8 ± 13.2	40.2 ± 9.6	43.2 ± 8.6
AST (U/L)	21.2 ± 12.6*,†	35.2 ± 29.0	31.2 ± 33.0	25.6 ± 14.2	31.4 ± 18.6	38.1 ± 35.3
ALT (U/L)	19.0 ± 7.4 *,†,‡	46.7 ± 35.2	40.6 ± 30.8‡	38.4 ± 37.7	49.4 ± 40.0	52.1 ± 47.5
Total fasting cholesterol (mg/dL)	186.2 ± 32.5	203.4 ± 42.6	204.9 ± 43.1	170.4 ± 27.1	198.0 ± 41.6	206.2 ± 41.7
Fasting triglycerides (mg/dL)	120.3 ± 54.3	155.9 ± 98.4	141.2 ± 88.2	93.0 ± 49.6	167.6 ± 89.9	165.6 ± 83.8
Fasting glucose (mg/dL)	102.1 ± 34.7	109.5 ± 29.7	111.0 ± 38.1	91.4 ± 15.5	111.8 ± 32.5	119.7 ± 42.5

Estimation cohort



Validation cohort





Mayo et al. Hepatol Commun 2018

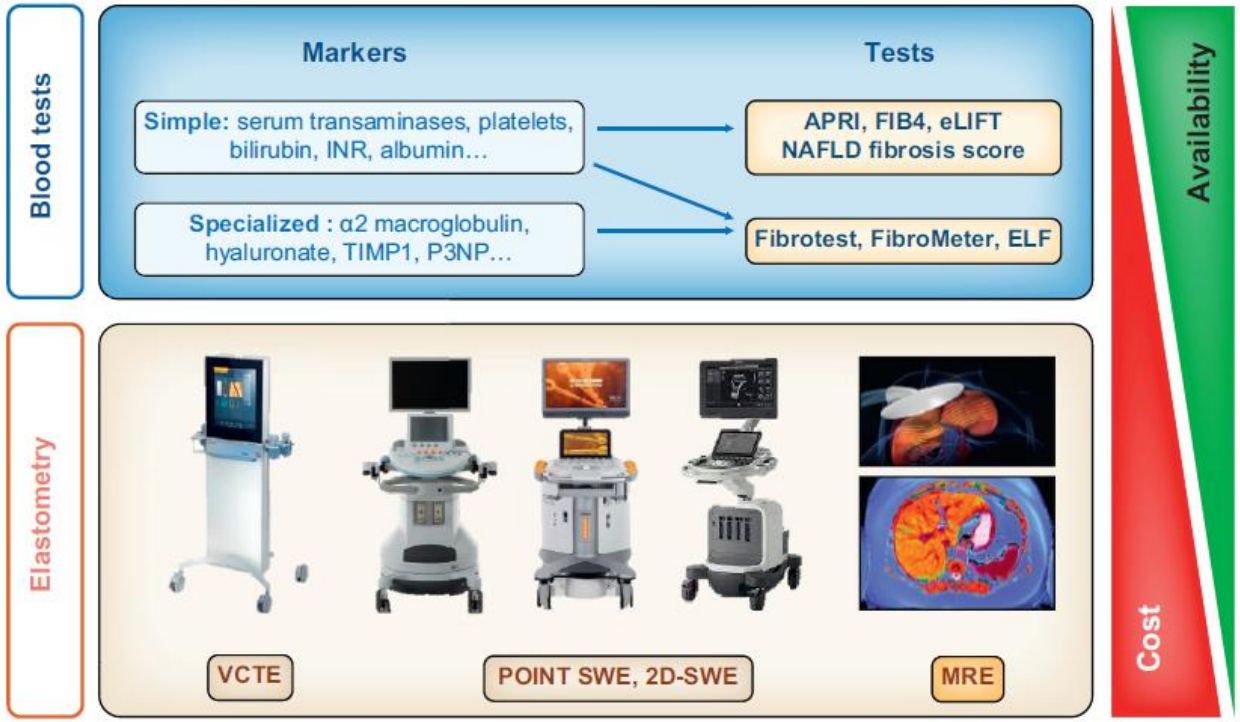
Esteatohepatitis

Author date	Study design N	Mode of elastography	NASH histology %	Distribution of fibrosis stage % 0–2/3–4	Optimal cutoff	Accuracy c-statistic
Chen et al 2011[45]	Retrospective cross-sectional N = 58	MRE 2D	62%[a]	81%/19%	2.74 kPa, sensitivity 94%, specificity 73% 2.90 kPa, sensitivity 83% specificity 82%	0.93
Loomba et al 2014[47]	Prospective cross-sectional N = 117	MRE 2D	91%[b]	81%/19%	3.26 kPa, sensitivity 42%, specificity 92%	0.73
Loomba et al 2016[50]	Prospective cross-sectional N = 100	MRE 2D and 3D	87%[b]	85%/15%	2D: 2.92 kPa 3D (60Hz): 2.42 kPa 3D (40Hz): 1.93 kPa	0.75 0.76 0.74
Imajo et al 2016[20]	Cross-sectional N = 142	MRE 2D	76%	68%/32%	Not reported	0.81
Imajo et al 2016[20]	Cross-sectional N = 142	VCTE	76%	68%/32%	Not reported	0.80
Lee et al 2016[65]	Cross-sectional N = 183	VCTE	51%	85%/15%	7.0 kPa, sensitivity 86%, specificity 58%	0.75
Park et al 2017[19]	Prospective cross-sectional N = 104	MRE 2D	73%[b]	80%/20%	2.53 kPa, sensitivity 64%, specificity 68%	0.70
Park et al 2017[19]	Prospective cross-sectional N = 104	VCTE	73%[b]	80%/20%	5.60 kPa, sensitivity 61%, specificity 59%	0.35

Ajmera et al. Semin Liver Dis 2018

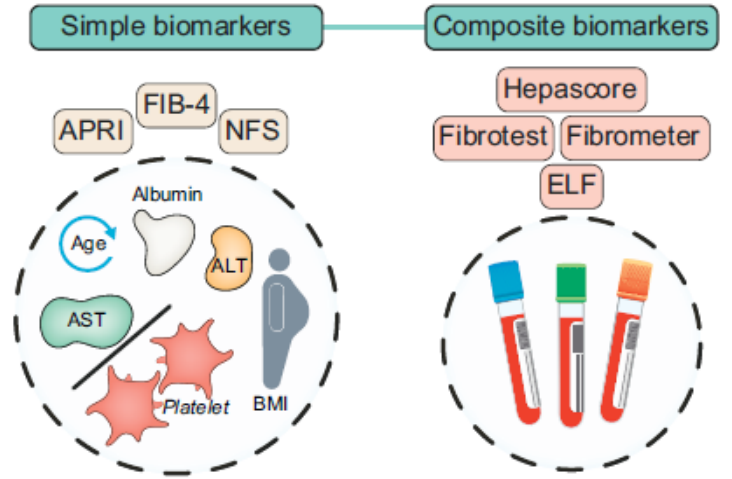
¿Cómo abordar la fibrosis avanzada?

Métodos bioquímicos



EVALUACIÓN DE FIBROSIS HEPÁTICA

Markers	n	NAFLD phenotype	AUC*	
Serum based variables			**Training set**	**Validation set**
AST/ALT[81–83]	174	All patients	0.83	0.83–0.90
Terminal peptide of procollagen III[49]	136	All patients	0.82	0.84
Pro-C3 levels[51]	150	All patients	0.91	NR
FibroTest: haptoglobin, α2-macroglobulin, apolipoprotein-A, bilirubin, and GGT[84–86]	1,202	All patients	0.86	0.85
APRI score: AST, Platelets[82,87]	175	All patients	080	0.56–0.67
ELF test: hyaluronic acid, PIIINP, and TIMP-1[46,48,88]	1,329	All patients	0.87	0.90
Combinations with serum based and clinical variables				
NAFLD fibrosis score: age, BMI, albumin, AST/ALT ratio, hyperglycaemia, and platelets[82,89,90,42]	733	All patients	0.88	0.77–0.84
Fibrometer: age, weight, glucose, AST, ALT, ferritin, and platelets[48]	1,021	All patients	0.94	0.94
FIB-4 index: age, AST, ALT, and platelets[38,82,90,42]	686	All patients	0.80	0.86
BARD score: BMI, diabetes, and AST/ALT ratio[40,82,90]	1,513	All patients	0.81	0.77–0.78
BARDI score: BMI, diabetes, AST/ALT ratio, and INR91	107	All patients	0.88	NR
Hepascore: age, sex, bilirubin, GGT, α2-macroglobulin, and hyaluronic acid[45]	242	All patients	–	0.81
Novel combinations				
HA, CK-18 and TIMP-1[53]	180	All patients	0.90	NR
FIB-C3: Pro-C3, age, BMI, diabetes, and platelets[52]	433	All patients	0.86	0.85
FIBROSpect test: α2-macroglubulin, hyaluronic acid, and TIMP-1[55]	792	All patients	0.87	0.85



Cost of patented tests — Local resources /cost

NFS is etiology specific; other biomarkers validated in several etiologies — Validation in specific etiology

Composite (patented) biomarkers performed in validated laboratories — Quality check

Acute hepatitis, Gilbert's, cholestasis, hemolysis, HIV infection — Risk factors for error

Vilar et al. J Hepatol 2018

Patel et al. J Hepatol 2019

NAFLD FIBROSIS SCORE

Fibrosis avanzada

ORIGINAL ARTICLES

The NAFLD Fibrosis Score: A Noninvasive System That Identifies Liver Fibrosis in Patients with NAFLD

Paul Angulo,[1] Jason M. Hui,[2] Giulio Marchesini,[3] Ellisabetta Bugianesi,[4] Jacob George,[2] Geoffrey C. Farrell,[2] Felicity Enders,[5] Sushma Saksena,[6] Alastair D. Burt,[6] John P. Bida,[5] Keith Lindor,[1] Schuyler O. Sanderson,[7] Marco Lenzi,[8] Leon A. Adams,[1] James Kench,[9] Terry M. Therneau,[5] and Christopher P. Day[6]

NFS = −1.675 + 0.037 × age (years) + 0.094 BMI (kg/m^2) + 1.13 × impaired glucose tolerance/diabetes (yes = 1, no = 0) + 0.99´AST/ALT ratio−0.013 × platelets (×10^9/l)−0.66 × albumin (g/dl) [19]

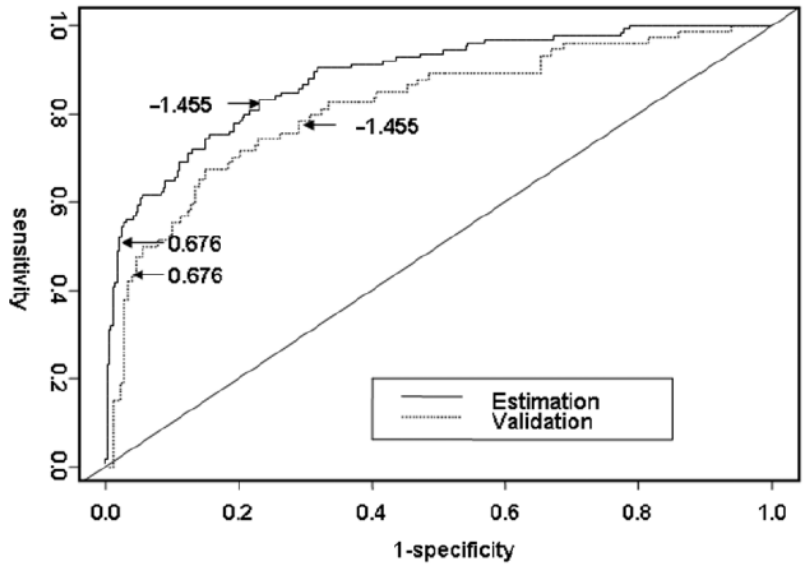


Table 3. Predictive Value of the Scoring System Obtained from the Estimation Group (n = 480)

	Low cutoff point (< −1.455)	Indeterminate (−1.455-0.676)	High cutoff point (> 0.676)	Total
Total	295	144	71	480
No significant fibrosis (stage 0-2)	273	**23.8%**	7	355
Significant fibrosis (stage 3-4)	22	39	64	125
Sensitivity	82%		51%	
Specificity	77%		98%	
Positive predictive value	56%		90%	
Negative predictive value	93%		85%	
Likelihood ratio (+)	3.567	**F3-F4: 17.9%**	25.966	
Likelihood ratio (−)	0.229		0.498	
Interpretation	Absence of significant fibrosis (93% certainty)		Presence of significant fibrosis (90% certainty)	

Table 4. Predictive Value of the Scoring System Obtained from the Validation Group (n = 253)

	Low Cutoff Point (< −1.455)	Indeterminate (−1.455-0.676)	High Cutoff Point (>0.676)	Total
Total	144	70	39	253
No significant fibrosis (stage 0-2)	127	**27.7%**	7	179
Significant fibrosis (stage 3-4)	17	25	32	74
Sensitivity	77%		43%	
Specificity	71%		96%	
Positive predictive value	52%		82%	
Negative predictive value	88%		80%	
Likelihood ratio (+)	2.652	**F3-F4: 19.3%**	11.058	
Likelihood ratio (−)	0.324		0.591	
Interpretation	Absence of significant fibrosis (88% certainty)		Presence of significant fibrosis (82% certainty)	

Angulo et al. Hepatology 2007

Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease

Stuart McPherson,[1] Stephen F Stewart,[1] Elsbeth Henderson,[1] Alastair D Burt,[2] Christopher P Day[2]

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

Table 3 A comparison of the performance of each test for the diagnosis of advanced fibrosis in 145 patients with non-alcoholic fatty liver disease (NAFLD)

Test	AUROC (95% CI)	Cut-off	Sens (%)	Spec (%)	PPV (%)	NPV (%)
AST/ALT ratio	0.83 (0.74 to 0.91)	0.8	74	78	44	93
		1	52	90	55	89
APRI	0.67 (0.54 to 0.8)	1	27	89	37	84
BARD score	0.77 (0.68 to 0.87)	2	89	44	27	95
FIB-4 score	0.86 (0.78 to 0.94)	1.30	85	65	36	95
		3.25	26	98	75	85
NAFLD fibrosis score	0.81 (0.71 to 0.91)	−1.455	78	58	30	92
		0.676	33	98	79	86

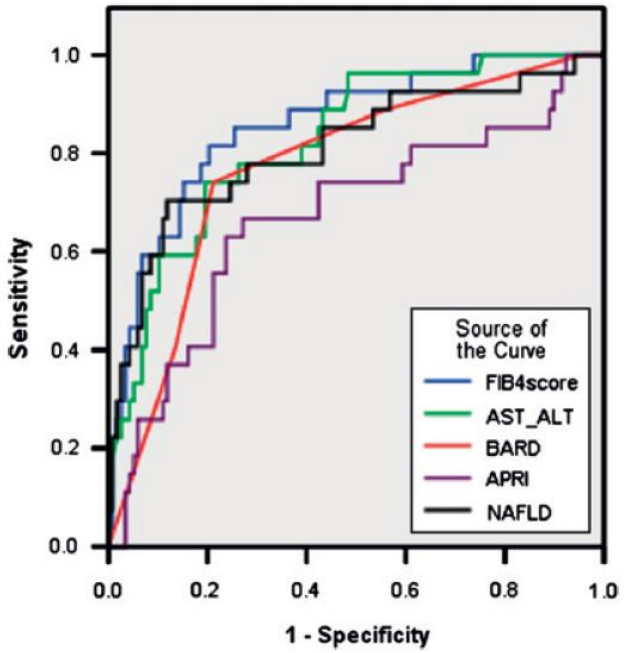


Table 4 Proportion of patients who may potentially avoid liver biopsy using the simple non-invasive tests to exclude advanced fibrosis

	Cut-off	Patients avoiding liver biopsy*	False negative result
AST/ALT	<0.8	100/145 (69%)	7 (7%)
BARD score	<2	55/145 (38%)	3 (5%)
FIB-4 score	<1.30	90/145 (62%)	4 (5%)
NAFLD fibrosis score	<−1.455	75/145 (52%)	6 (8%)

F3-F4: 19.3%

McPherson et al. Gut 2010

NAFLD FIBROSIS SCORE Y FIB-4: META-ANÁLISIS

	FIB-4 (n=5393)			NFS (n=3248)			APRI (n=5477)			AST/ALT (n=5434)		
Advanced fibrosis, %	30			29			30			30		
AUROC	0.76 (0.74–0.77)			0.73 (0.71–0.75)			0.70 (0.69–0.72)			0.64 (0.62–0.65)		
	YI	90% Se	90% Sp	YI	90% Se	90% Sp	YI	90% Se	90% Sp	YI	90% Se	90% Sp
Threshold	1.44	0.88	2.31	−1.39	−2.55	0.28	0.49	0.29	0.91	0.64	0.51	1.34
Sensitivity, %	69 (67–72)	90 (88–91)	38 (36–41)	75 (72–78)	90 (88–92)	29 (26–32)	67 (64–69)	90 (89–92)	32 (30–34)	75 (73–77)	90 (87–91)	16 (14–18)
Specificity, %	70 (69–72)	39 (37–40)	90 (89–91)	63 (61–65)	36 (33–37)	90 (89–91)	63 (62–65)	29 (28–30)	90 (89–91)	47 (45–48)	25 (23–26)	90 (89–91)
Misclassified, %	30 (30–31)	46 (46–47)	26 (25–26)	34 (34–36)	48 (49–50)	28 (28–29)	36 (36–37)	53 (53–54)	27 (27–28)	45 (45–46)	56 (56–57)	32 (32–33)

	FIB-4 (n=5393)			NFS (n=3248)	
Advanced fibrosis, %	30			29	
AUROC	0.76 (0.74–0.77)			0.73 (0.71–0.75)	
Source	Shah *et al* [83]	McPherson *et al*[84]	This study	Angulo *et al* [16]	This study
Thresholds	<1.3, ≥2.67	<1.3, ≥3.25	<0.88, ≥2.31*	<−1.455, ≥0.676	<−2.55, ≥0.28*
Sensitivity, %	54 (52–56)	44 (42–46)	80 (76–83)	47 (44–50)	74 (70–79)
Specificity, %	91 (89–92)	95 (93–96)	79 (77–81)	91 (89–93)	78 (76–81)
Misclassified, %	12 (11–13)	10 (9–11)	10 (9–11)	11 (10–13)	10 (8–11)
Indeterminate, %	34 (33–35)	39 (37–40)	52 (50–53)	39 (37–41)	56 (54–59)

N=37 ESTUDIOS

Mozes et al. Gut 2021

HEPAMET FIBROSIS SCORE

Fibrosis avanzada

HFS SCORE:
Introduzca todos los valores

Sexo

Edad

Diabetes

Glucosa (mg/dL)

Insulina (µU/mL)

HOMA

AST (UI/L)

Albumina (g/dL)

Plaquetas (x 10^9)

CALCULAR

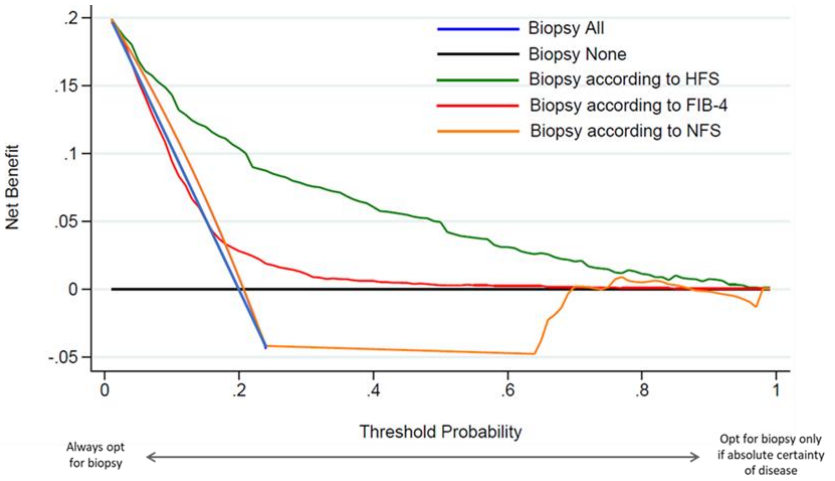
RESET

Table 3. Discrimination Ability of the Hepamet Fibrosis Score Compared With NAFLD Fibrosis Score and FIB-4 in the Estimation and Validation Cohorts

	Hepamet Fibrosis Score	NAFLD Fibrosis Score	FIB-4
Estimation cohort (n = 758)			
Advanced fibrosis (F0–F2 vs F3–F4)	0.850 (0.807–0.893)	0.775 (0.723–0.828); .0025	0.772 (0.713–0.832); .0002
Validation cohort (n = 1694)			
Advanced fibrosis (F0–F2 vs F3–F4)	0.844 (0.819–0.869)	0.789 (0.764–0.814); <.0001	0.801 (0.776–0.826); <.0001
Overall cohort (n = 2452)			
Advanced fibrosis (F0–F2 vs F3–F4)	0.848 (0.826–0.869)	0.778 (0.756–0.801); <.0001	0.802 (0.780–0.825); <.0001

HFS 21% vs FIB-4 26% vs NFS 31%

	Estimation cohort		Validation cohort	
Advanced fibrosis, %	12.1		24.6	
Cutoff	<0.12	≥0.47	<0.12	≥0.47
Sensitivity, %	70.7	38	74.6	34.6
Specificity, %	80.9	98	75.5	96.7
PPV, %	33.9	72.9	49.8	77.2
NPV, %	95.2	92	90.1	81.9
LR+	3.71	15.24	3.05	10.40
LR–	0.36	0.63	0.34	0.68



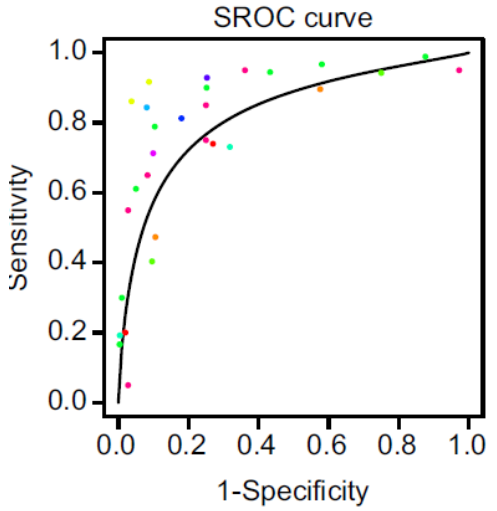
Hepamet Fibrosis Score	Fibrosis significativa (F2-F4)	Fibrosis avanzada (F3-F4)	Cirrosis (F4)
Riesgo bajo (<0.12)	23,6%	8,1%	0,9%
Riesgo intermedio (0.12-0.47)	57,1%	33,7%	7,4%
Riesgo alto (≥0.47)	86,4%	76,3%	35,5%

Ampuero et al. Clin Gastroenterol Hepatol 2020

https://www.hepamet-fibrosis-score.eu/

Table 3. Performance of ELF Panel and Simple Markers Panel in Distinguishing Different Stages of Fibrosis as Measured by AUC Values With Confidence Intervals (n = 91)

	0 Versus 1/2/3/4 Any Fibrosis	0/1 Versus 2/3/4 Moderate Fibrosis	0/1/2 Versus 3 /4 Severe Fibrosis
Simple	0.79 (0.69–0.88)	0.86 (0.78–0.94)	0.89 (0.81–0.97)
ELF	0.82 (0.73–0.90)	0.90 (0.84–0.96)	0.93 (0.88–0.98)
Simple + ELF	0.84 (0.76–0.92)	0.93 (0.88–0.99)	0.98 (0.96–1)



11 studies were included in the meta-analysis of advanced fibrosis
AUC: 0.83 (0.71, 0.90)
Sensitivity: 0.73 (0.60, 0.83)
Specificity: 0.80 (0.68, 0.88)

Model	*P*-value	Odds ratio (95% CI)
Model for overall discordance		
Age (≥45)	0.001	3.706 (1.740–7.892)
Steatosis (present)	0.006	0.367 (0.179–0.754)
METAVIR inflammatory grade	0.007	2.624 (1.295–5.318)

TABLE 4. Performance of Individual NITs at Low and High Thresholds Derived From the Literature to Discriminate Advanced Fibrosis (F3-F4 vs. F0-F2)

Variable	NFS (n = 2,417)	FIB-4 (n = 3,123)	ELF (n = 3,173)	LS by VCTE (n = 1,765)
Prevalence of F3-F4	80%	71%	71%	84%
AUROC (95% CI)	0.74 (0.74, 0.74)	0.78 (0.78, 0.78)	0.80 (0.80, 0.80)	0.80 (0.79, 0.8)
Thresholds	<–1.455, ≥0.676	<1.3, ≥2.67	<9.8, ≥11.3	<9.9, ≥11.4 kPa
Sensitivity*	89 (88, 91)	82 (81, 84)	74 (72, 75)	83 (81, 85)
Specificity*	89 (86, 92)	93 (91, 94)	98 (96, 99)	71 (66, 76)
PPV*	97 (96, 98)	97 (96, 97)	99 (98, 99)	94 (92, 95)
NPV*	67 (63, 71)	68 (65, 70)	60 (58, 63)	45 (40, 50)
Indeterminate*	51 (49, 53)	43 (41, 45)	45 (43, 47)	8 (7, 9)
Misclassified*	11 (10, 12)	15 (13, 16)	19 (18, 21)	19 (17, 21)

F3-F4: 70.6%

Guha et al. Hepatology 2008 Fagan et al. Liver Int 2015 Anstee et al. Hepatology 2019 Vali et al. J Hepatol 2020

¿Existen límites en la interpretación de los scores?

Rehenes de sus variables

EDAD: MAYORES 65 AÑOS

Limitaciones NITs en EHmet

Hospital U. Virgen del Rocío

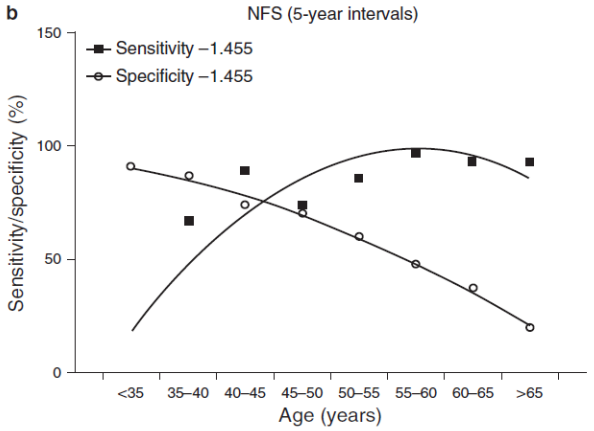
LIVER

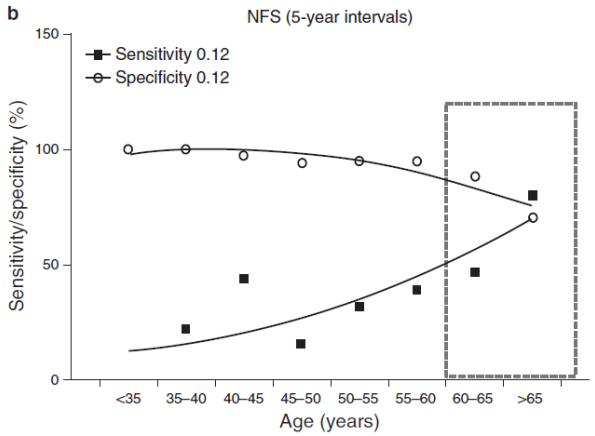
Open

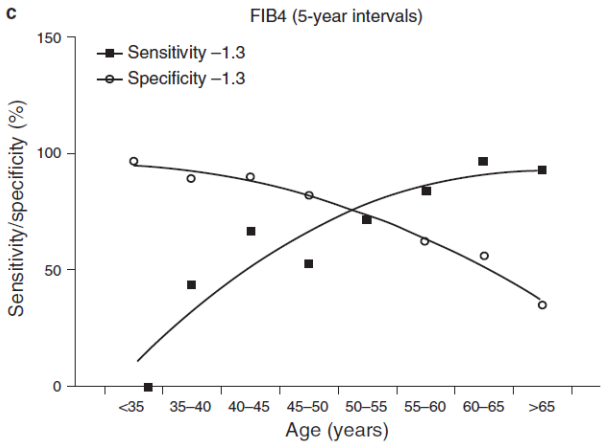
see related editorial on page 752

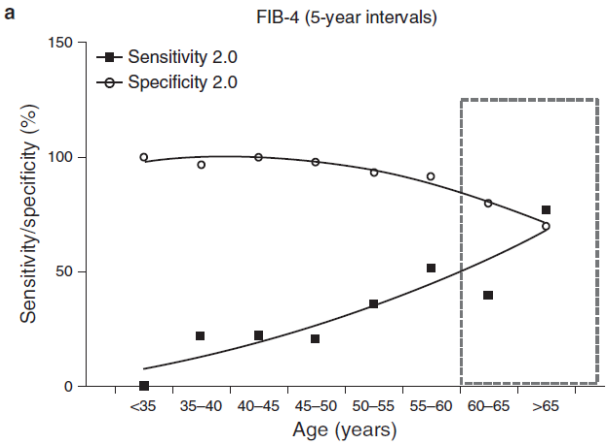
Age as a Confounding Factor for the Accurate Non-Invasive Diagnosis of Advanced NAFLD Fibrosis

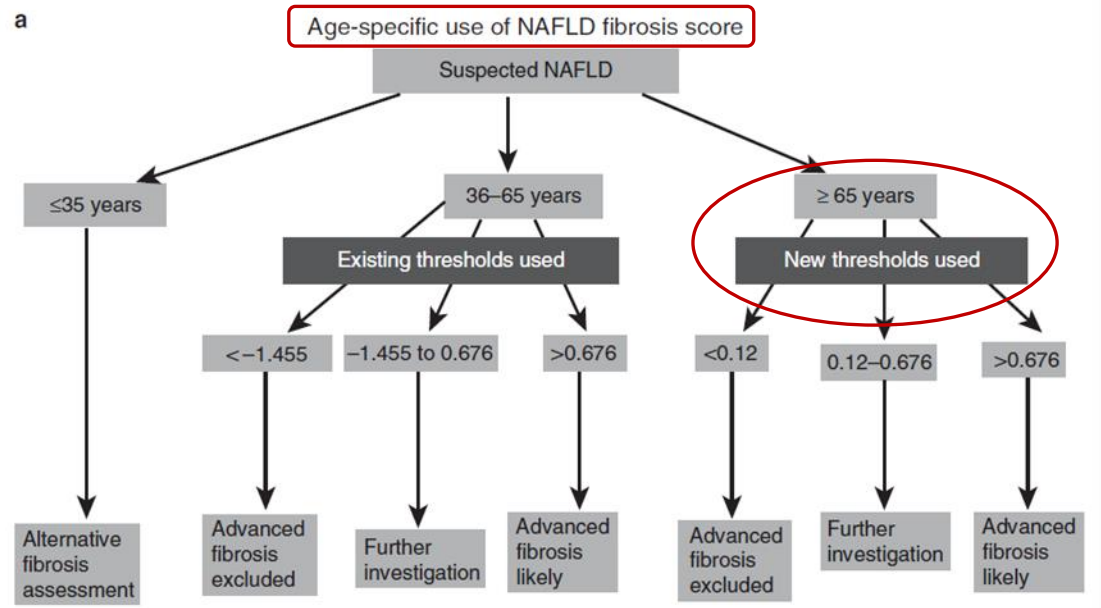
Stuart McPherson, BSc, MBChB, MD, FRCP[1,2], Tim Hardy, BSc, MBBS[1,2], Jean-Francois Dufour, MD, PhD[3], Salvatore Petta, MD, PhD[4], Manuel Romero-Gomez, MD, PhD[5], Mike Allison, BSc(Hons), MD, PhD[6], Claudia P. Oliveira, MD, PhD[7], Sven Francque, MD, PhD[8], Luc Van Gaal, MD, PhD[9], Jörn M. Schattenberg, MD, PhD[10], Dina Tiniakos, MD, PhD[1,2], Alastair Burt, BSc (Hons), MBChB, MD (Hons), FRCPath, FRCP, FRCPA, FRSB, F AcadMEd, FAHMS[11], Elisabetta Bugianesi, MD, PhD[12], Vlad Ratziu, MD, PhD[13], Christopher P. Day, MA, MB BChir, MD, PhD, FRCP, FRCPE, FMedSci[1,2] and Quentin M. Anstee, BSc, MB BS, PhD, FRCP[1,2]

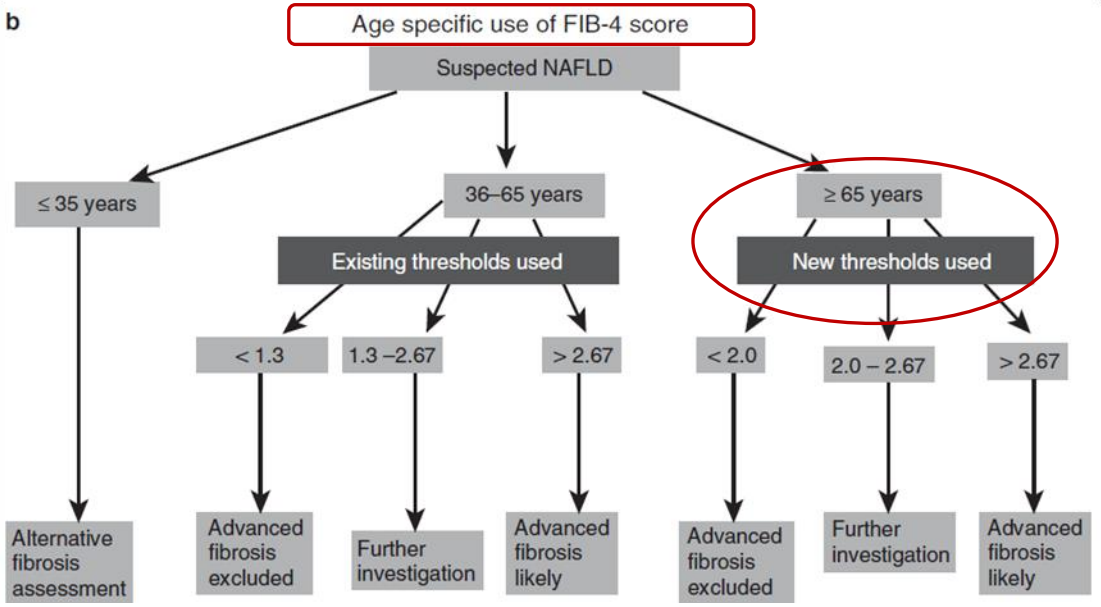












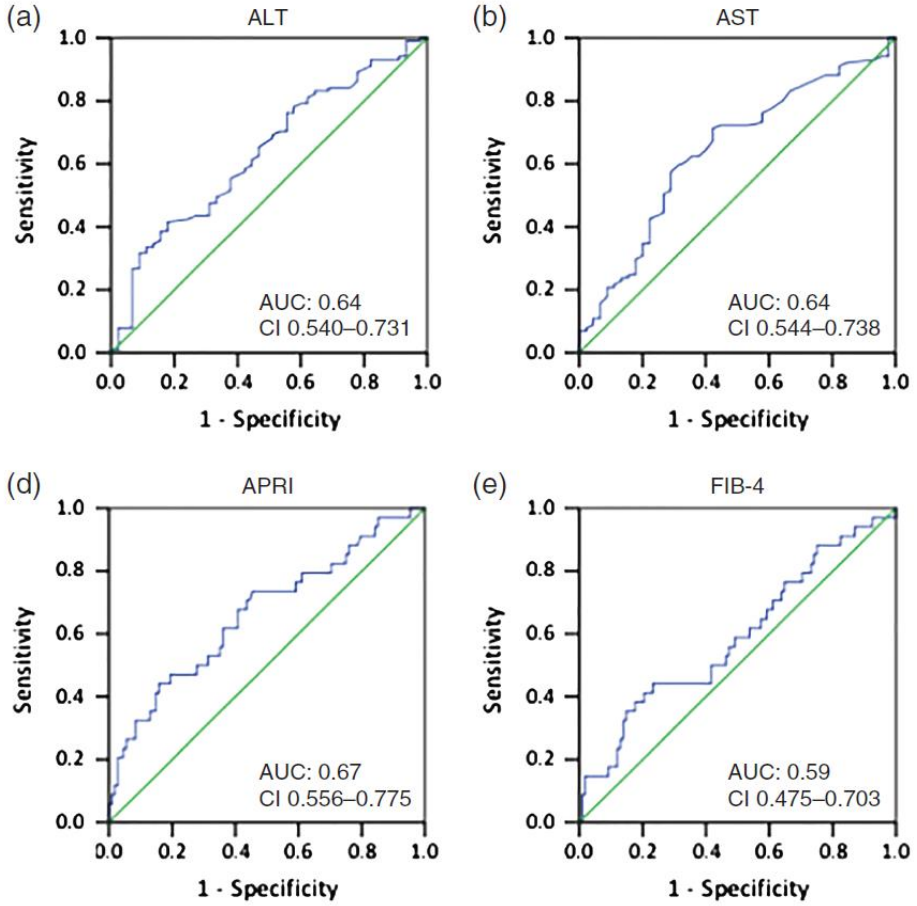
McPherson al. Am J Gastroenterol 2016

ORIGINAL ARTICLE

Performance of fibrosis prediction scores in paediatric non-alcoholic fatty liver disease

Jasmine A Jackson,[1] Juna V Konomi,[2] Michael V Mendoza,[2] Alyssa Krasinskas,[3] Ran Jin,[2] Shelley Caltharp,[3] Marialena Mouzaki[4] and Miriam B Vos[2]

[1]Emory University School of Medicine, [2]Department of Paediatric Gastroenterology, Hepatology and Nutrition, Emory University School of Medicine, [3]Department of Pathology, Emory University, Atlanta, Georgia, United States and [4]Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada



Jackson al. J Paedriatr Child Health 2018

ORIGINAL ARTICLE

The Evaluation of Hepatic Fibrosis Scores in Children with Nonalcoholic Fatty Liver Disease

Sana Mansoor · Lisa Yerian · Rohit Kohli · Stavra Xanthakos · Paul Angulo · Simon Ling · Rocio Lopez · Carter-Kent Christine · Ariel E. Feldstein · Naim Alkhouri

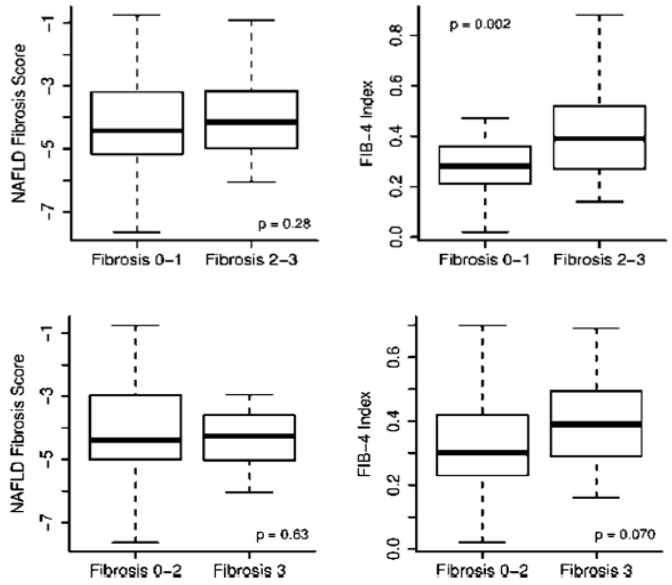


Table 3 Noninvasive hepatic fibrosis scores: receiver operating characteristics (ROC) analysis

Noninvasive hepatic fibrosis scores	Fibrosis 1–4	Fibrosis 2–4	Fibrosis 3–4
AST/ALT	0.572 (0.350, 0.793)	0.585 (0.466, 0.703)	0.441 (0.316, 0.565)
APRI	0.800 (0.695, 0.904)	0.666 (0.553, 0.778)	0.628 (0.478, 0.778)
NAFLD fibrosis score	0.470 (0.259, 0.681)	0.554 (0.435, 0.673)	0.521 (0.385, 0.657)
FIB-4 index	0.547 (0.375, 0.719)	0.686 (0.576, 0.797)	0.367 (0.231, 0.503)

Mansoor et al. Dig Dis Sci 2015

Limitaciones NITs en EHmet

CIRRHOSIS AND LIVER FAILURE

WILEY Liver INTERNATIONAL

Diabetes impacts prediction of cirrhosis and prognosis by non-invasive fibrosis models in non-alcoholic fatty liver disease

Luis C. Bertot[1] | Gary P. Jeffrey[1,2] | Bastiaan de Boer[3] | Gerry MacQuillan[1,2] | George Garas[1,2] | Justin Chin[2] | Yi Huang[1] | Leon A. Adams[1,2]

Models	Fibrosis ≥3 Overall AUC (95% CI)	Non-diabetics AUC (95% CI)	Diabetics AUC (95% CI)	Non-DM vs DM P value
Hepascore	0.87 (0.82 -0.92)	0.93 (0.89-0.98)	0.84 (0.77-0.91)	.03
FIB-4	0.82 (0.76-0.88)	0.87 (0.76-0.97)	0.79 (0.71-0.87)	.25
APRI	0.77 (0.70-0.83)	0.85 (0.75-0.95)	0.75 (0.66-0.83)	.13
NAFLD-FS	0.72 (0.65-0.80)	0.70 (0.57-0.87)	0.67 (0.54-0.77)	.94
F4 Fibrosis (cirrhosis)				
Hepascore	0.85 (0.78-0.93)	0.95 (0.91-0.99)	0.80 (0.69-0.90)	.005
FIB-4	0.86 (0.79-0.93)	0.96 (0.92-0.99)	0.80 (0.71-0.90)	.003
APRI	0.78 (0.70-0.86)	0.92 (0.85-0.98)	0.73 (0.63-0.83)	.002
NAFLD-FS	0.81 (0.72-0.89)	0.82 (0.70-0.94)	0.77 (0.66-0.89)	.57

OBES SURG
DOI 10.1007/s11695-016-2246-5

ORIGINAL CONTRIBUTIONS

Modified thresholds for fibrosis risk scores in nonalcoholic fatty liver disease are necessary in the obese

Geraldine J. Ooi[1] · Paul R. Burton[1,2] · Lisa Doyle[1] · John M. Wentworth[1,3] · Prithi S. Bhathal[4] · Ken Sikaris[5] · Michael A. Cowley[6] · Stuart K. Roberts[7] · William Kemp[7] · Paul E. O'Brien[1] · Wendy A. Brown[1,2]

TABLE 5 Comparisons of the diagnostic performances of noninvasive fibrosis tests for advanced fibrosis among the NAFLD subgroups

Parameters			AUROC (95% CI)	Cutoff	Se (%)	Sp (%)	DA (%)	PPV (%)	NPV (%)	P value[a]
Obesity (Nonobese: n = 71 vs Obese: n = 244)	No	AAR	0.789 (0.670–0.909)	1.131	73.3	75.0	74.6	44.0	91.3	.326
	Yes		0.715 (0.627–0.803)	0.953	67.5	72.5	71.7	32.5	91.9	
	No	APRI	0.896 (0.770–1.000)	0.702	86.7	94.6	93.0	81.3	96.4	.196
	Yes		0.801 (0.732–0.870)	0.558	80.0	69.6	71.3	34.0	94.7	
	No	FIB-4[b]	0.965 (0.924–1.000)	<1.3, >2.670	86.7-100	48.2-92.9	59.2-91.5	34.1-76.5	96.3-100	.002
	Yes		0.835 (0.766–0.905)	<1.3, >2.670	60.0-85.0	58.8-90.7	63.1-85.7	28.8-55.8	92.0-95.2	
	No	NFS[b]	0.965 (0.924–1.000)	<-1.455, >0.676	60.0-100	60.7-98.2	69.0-90.1	40.5-90.0	90.2-100	<.001
	Yes		0.801 (0.726–0.876)	<-1.455, >0.676	42.5-82.5	59.8-92.2	63.5-84.0	28.7-51.5	89.1-94.6	
	No	BARD	0.777 (0.679–0.874)	2.000[20]	80.0	69.6	71.8	41.4	92.9	.093
	Yes		0.661 (0.568–0.754)	2.000[20]	65.0	57.8	59.0	23.2	89.4	
	No	ARFI	0.924 (0.836–1.000)	1.435	80.0	94.6	91.5	80.0	94.6	.164
	Yes		0.842 (0.767–0.917)	1.395	67.5	91.7	87.7	61.4	93.5	

Bertot al. Liver Int 2018

Joo et al. Liver Int 2018

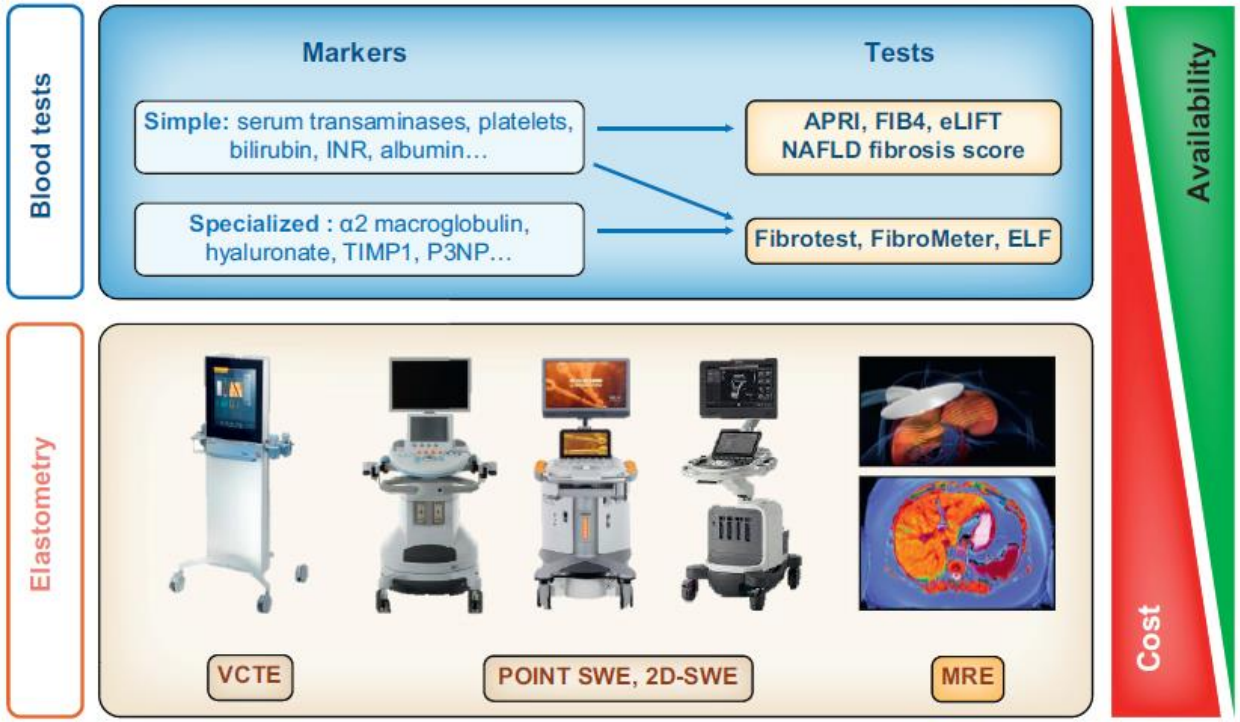
TABLE 6 Comparisons of the diagnostic performances of noninvasive fibrosis tests for advanced fibrosis among the radiological or histological steatosis subgroups

Parameters	Steatosis severity		AUROC (95% CI)	Cutoff	Se (%)	Sp (%)	DA (%)	PPV (%)	NPV (%)
AAR	Radiological	Mild	0.740 (0.638–0.842)	1.119	68.8	76.7	74.3	56.4	84.8
		Moderate	0.601 (0.438–0.764)	0.956	56.3	66.4	65.2	18.0	92.0
		Severe	0.831 (0.607–0.991)	0.856	85.7	75.4	76.4	27.3	98.0
	Histological	Mild	0.779 (0.683–0.875)	1.121	71.0	78.6	76.2	59.5	85.9
		Moderate	0.666 (0.519–0.813)	0.823	92.3	49.5	54.6	20.0	97.9
		Severe	0.651 (0.473–0.829)	0.953	54.5	78.9	76.4	23.1	93.8
APRI	Radiological	Mild	0.912 (0.845-0.980)	0.480	93.8	78.1	82.9	65.2	96.6
		Moderate	0.812 (0.707-0.917)	0.680	75.0	81.1	80.4	34.3	96.1
		Severe	0.578 (0.344-0.812)	0.561	57.1	61.5	61.1	13.8	93.0
	Histological	Mild	0.938 (0.872-1.000)	0.487	93.5	92.9	93.1	85.3	97.3
		Moderate	0.815 (0.689-0.941)	0.813	61.5	93.7	89.8	57.1	94.7
		Severe	0.617 (0.460-0.774)	0.681	63.6	64.2	64.2	17.1	93.8
FIB-4[a]	Radiological	Mild	0.927 (0.868–0.985)	<1.3, >2.670	87.5-96.9	49.3-89.0	63.8-88.6	45.6-77.8	94.2-97.3
		Moderate	0.733 (0.591–0.875)	<1.3, >2.670	43.8-75.0	53.3-91.8	55.8-86.2	17.4-41.2	92.6-94.2
		Severe	0.829 (0.714–0.943)	<1.3, >2.670	28.6-85.7	70.8-92.3	72.2-86.1	24.0-28.6	92.3-97.9
	Histological	Mild	0.951 (0.906-0.995)	<1.3, >2.670	87.1-96.8	58.6-94.3	70.3-92.1	50.8-87.1	94.3-97.6
		Moderate	0.840 (0.717-0.963)	<1.3, >2.670	53.8-92.3	52.6-90.5	57.4-86.1	21.1-43.8	93.5-98.0
		Severe	0.685 (0.542-0.828)	<1.3, >2.670	27.3-63.6	58.9-89.5	59.4-83.0	15.2-23.1	91.4-93.3
NFS[a]	Radiological	Mild	0.866 (0.786–0.946)	<-1.455, >0.676	59.4–96.9	49.3–87.7	63.8–79.0	45.6–67.9	83.1–97.3
		Moderate	0.700 (0.564–0.835)	<-1.455, >0.676	25.0–62.5	56.6–96.7	57.2–88.4	15.9–50.0	90.8–92.0
		Severe	0.904 (0.829–0.980)	<-1.455, >0.676	42.9–100	78.5–93.8	80.6–88.9	33.3–42.9	93.8–100
	Histological	Mild	0.886 (0.818–0.954)	<-1.455, >0.676	61.3–93.5	50.0–90.0	63.3–81.2	45.3–73.1	84.0–94.6
		Moderate	0.828 (0.710–0.945)	<-1.455, >0.676	23.1–92.3	55.8–92.6	60.2–84.3	22.2–30.0	89.8–98.1
		Severe	0.735 (0.574–0.896)	<-1.455, >0.676	36.4–63.6	71.6–96.8	70.8–90.6	20.6–57.1	92.9–94.4
BARD	Radiological	Mild	0.650 (0.549-0.750)	2.000[20]	71.9	53.4	59.0	40.4	81.3
		Moderate	0.599 (0.452-0.746)	2.000[20]	50.0	57.4	56.5	13.3	89.7
		Severe	0.932 (0.871-0.993)	2.000[20]	100	73.8	76.4	29.2	100
	Histological	Mild	0.630 (0.529–0.731)	2.000[20]	71.0	51.4	57.4	39.3	80.0
		Moderate	0.702 (0.555–0.849)	2.000[20]	69.2	52.6	54.6	16.7	92.6
		Severe	0.700 (0.489–0.910)	2.000[20]	63.6	74.7	73.6	22.6	94.7

Joo et al. Liver Int 2018

¿Cómo abordar la fibrosis avanzada?

Métodos de elastografía



EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2021 update

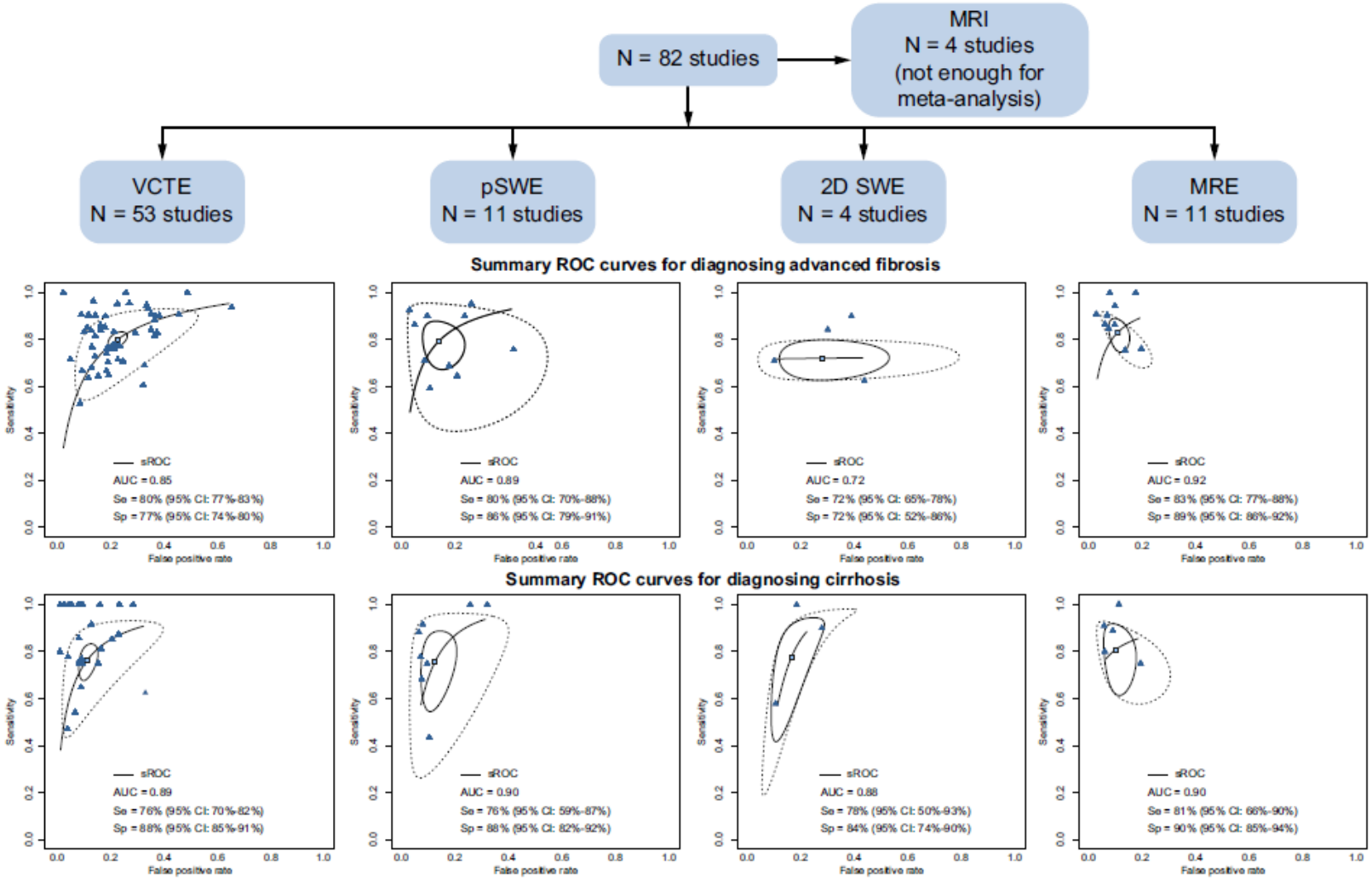
Table 2. Advantages and disadvantages of the main non-invasive tests used to diagnose and stage liver fibrosis.

	Serum markers		Transient elastography	pSWE	2D-SWE	MRE
Advantages	Non-patented • Good reproducibility • High applicability (95%) • No cost and wide availability • Well validated • Can be performed in the outpatient clinic • Prognostic value of some has been validated for some aetiologies of chronic liver disease on population level	Patented Good reproducibility • High applicability (95%) • Well validated • Can be performed in the outpatient clinic • Prognostic value of some has been validated for some aetiologies of chronic liver disease	• Most widely used and validated technique • Point-of-care (bedside; rapid, easy to learn) • Quality criteria well defined • Good reproducibility • High performance for cirrhosis (AUROC >0.9) • Prognostic value in compensated cirrhosis well validated	• Can be performed in combination with regular ultrasound if the device is provided with adequate software • ROI smaller than TE and location chosen by the operator • Higher applicability than TE (ascites and obesity) • Performance equivalent to that of TE for advanced fibrosis and cirrhosis • Prognostic value in cirrhosis • High applicability for spleen stiffness measurement	• Can be performed in combination with regular ultrasound if the device is provided with adequate software • Large ROI that can be adjusted in size and location chosen by the operator • Measures liver stiffness in real time • Good applicability • High performance for the diagnosis of significant fibrosis and cirrhosis • Prognostic value in compensated cirrhosis	• Can be implemented on a regular MRI machine • Examination of the whole liver • Higher applicability than TE (ascites and obesity) • High performance for the earlier fibrosis stage and for diagnosis of cirrhosis
Disadvantages	• Non-liver-specific • Performance not as good as TE and patented serum markers • False positive results with FIB-4 and NFS in case of age>65 yrs	• Cost • Non-liver-specific • Performance not as good as TE for cirrhosis • False positive results in case of extrahepatic inflammatory conditions, profibrotic, extrahepatic disease and other (*e.g.* haemolysis, Gilbert syndrome)	• Requires a dedicated device • ROI cannot be chosen • Applicability (>95%) lower than serum biomarker: (obesity, ascites, operator experience) • False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake	• False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake	• False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake	• Not applicable in case of iron overload • Requires a MRI facility • Time consuming • Costly • No clear data on prognostic value

2D-SWE, bidimensional shear wave elastography; FIB-4, fibrosis-4; MRE, magnetic resonance elastography; MRI, magnetic resonance imaging; NFS, NAFLD fibrosis score; pSWE, point-shear wave elastography; ROI, region of interest; TE, transient elastography.

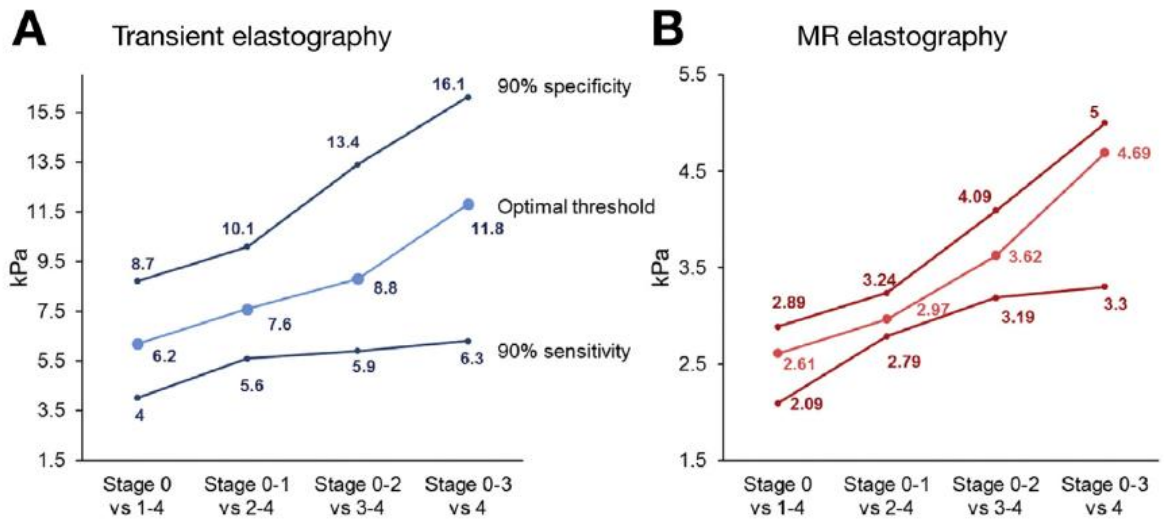
EASL Clinical Practice Guidelines. J Hepatol 2021

Fibrosis avanzada



Selvaraj et al. J Hepatol 2021

Studies, n (patients; n)	Prevalence, % (95% CI)	Cut-off range	sAUC (95%CI)	sSe, % (95% CI)	sSp, % (95% CI)
VCTE (kPa)					
F≥1	14 (1,064)	67 (23–94)	5.3–8.2	0.82 (0.78–0.85)	78 (73–82)	72 (65–79)
F≥2	37 (2,763)	45 (5–77)	3.8–10.2	0.83 (0.80–0.87)	80 (76–83)	73 (68–77)
F≥3	44 (4,219)	25 (5–54)	6.8–12.9	0.85 (0.83–0.87)	80 (77–83)	77 (74–80)
F=4	22 (337)	9 (3–31)	6.9–19.4	0.89 (0.84–0.93)	76 (70–82)	88 (85–91)
MRE (kPa)					
F≥1	6 (391)	60 (54–90)	2.50–3.14	0.87 (0.80–0.94)	71 (60–81)	85 (78–91)
F≥2	6 (209)	31 (25–54)	2.86–4.14	0.91 (0.80–0.97)	78 (67–85)	89 (83–94)
F≥3	10 (214)	19 (12–32)	2.99–4.80	0.92 (0.88–0.95)	**83 (77–88)**	**89 (86–92)**
F=4	5 (41)	8 (6–9)	3.35–6.70	0.90 (0.81–0.95)	**81 (66–90)**	**90 (85–94)**
NASH	4 (224)	69 (51–78)	2.53–3.26	0.83 (0.69–0.91)	65 (46–80)	83 (69–91)
pSWE (m/s)					
F≥1	4 (276)	73 (58–95)	1.11–1.81	0.77 (0.55–0.92)	64 (48–77)	76 (65–84)
F≥2	9 (805)	46 (17–73)	1.18–1.81	0.86 (0.78–0.90)	69 (59–77)	85 (80–88)
F≥3	11 (1,209)	30 (17–52)	1.34–4.24	0.89 (0.83–0.95)	**80 (70–88)**	**86 (82–92)**
F=4	8 (759)	17 (6–32)	1.36–2.54	0.90 (0.82–0.95)	76 (59–87)	88 (82–92)
2DSWE (kPa)					
F≥2	4 (488)	55 (26–71)	8.3–11.6	0.75 (0.58–0.87)	71 (56–83)	67 (43–84)
F≥3	4 (488)	36 (16–45)	9.3–13.1	0.72 (0.60–0.84)	72 (65–78)	72 (52–86)
F=4	3 (372)	15 (7–16)	14.4–15.7	0.88 (0.81–0.91)	78 (50–93)	84 (74–90)



Selvaraj et al. J Hepatol 2021

Hsu et al, Clin Gastroenterol Hepatol 2018

Limitaciones

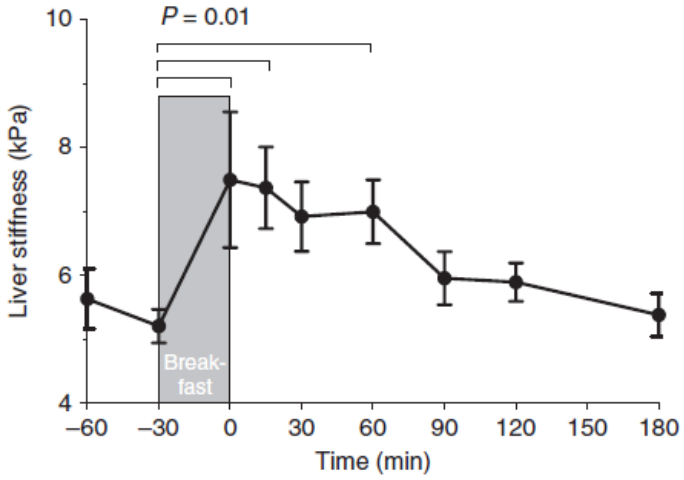
Patología cardiaca

Table 4 Liver stiffness measurement values expressed as median

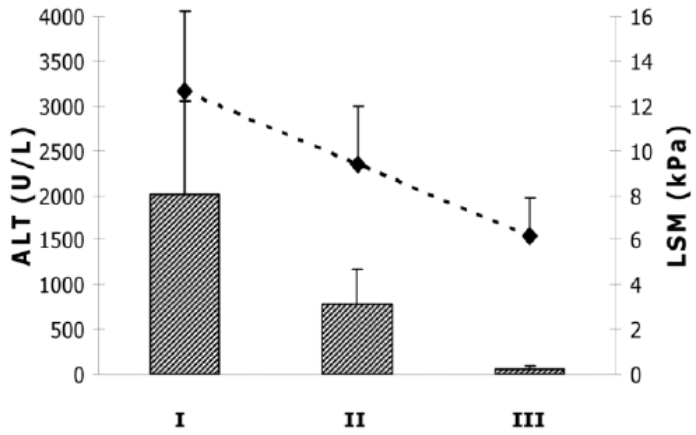
Group	LSM	IQR	IQR:LSM
Stable LHF	4.7 (4.0, 8.7)	1.0	0.20
Stable RHF	9.7 (5.0, 10.8)	1.6	0.16
ADHF	11.2 (6.7, 14.3)	1.4	0.19
HD	6.0 (4.4, 7.2)	0.8	0.13
Control	4.4 (3.6, 5.1)	0.8	0.17

ADHF, acute decompensated left-sided heart failure; HD, haemodialysis group; IQR, interquartile
right-sided heart failure.

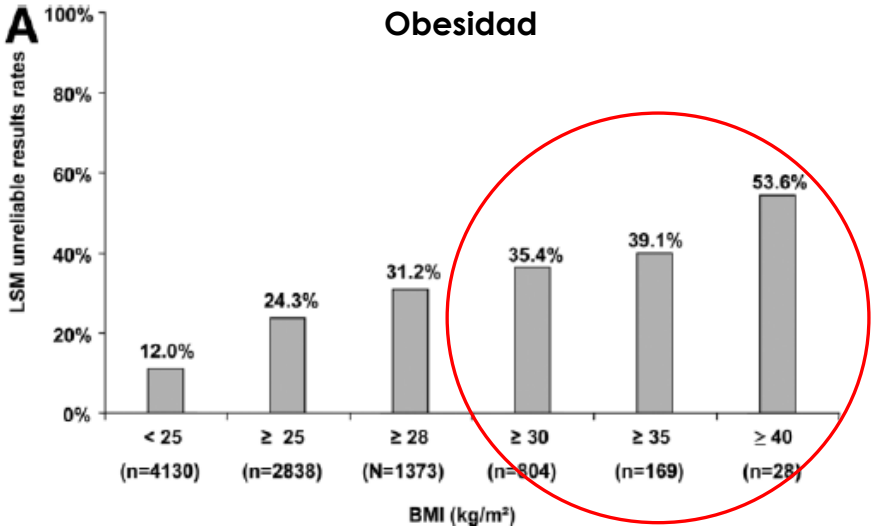
Necesidad de ayuno



Inflamación hepática



Obesidad



Importancia del explorador

Table 1. Factors Associated with LSM Failure in Univariate and Multivariate Analyses

Parameter	Univariate OR	Univariate 95% CI	Univariate P	Multivariate OR	Multivariate 95% CI	Multivariate P
BMI (>30 kg/m²)	10.5	8.6-12.8	0.0001	8.4	6.6-10.8	0.0001
Operator experience (<500 versus >500 examinations)	2.8	2.1-3.6	0.0001	2.6	1.8-3.9	0.0001
Age (>52 years)	3.5	2.7-4.4	0.0001	2.2	1.6-2.9	0.0001
Type 2 diabetes (yes versus no)	4.0	3.3-5.0	0.0001	2.0	1.5-2.6	0.0001
Hypertension (yes versus no)	3.1	2.5-3.9	0.0001			
Time of examination (first versus others)	2.0	1.6-2.4	0.0001	1.5	1.2-2.0	0.0001
GGT (>3× ULN)	1.5	1.2-1.8	0.001			

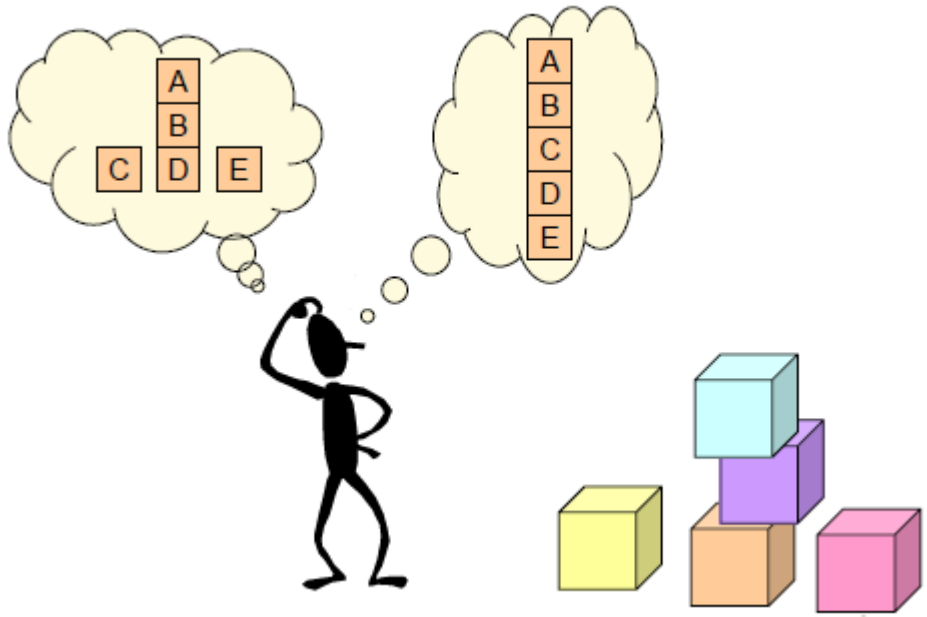
Castera et al, Hepatology 2010

Hopper et al, Eur J Heart Fail 2012

Mederacke et al, Liver Int 2009

¿Existen otros matices a considerar?

Combinación de endpoints



FAST

Fibrosis ≥2 + NAS ≥4

	Derivation cohort (UK NAFLD)	French bariatric surgery cohort	USA screening cohort	China Hong-Kong NAFLD cohort	China Wenzhou NAFLD cohort	French NAFLD cohort	Malaysian NAFLD cohort	Turkish NAFLD cohort	Pooled external cohort
N Patients	**350**	**110**	**242**	**83**	**104**	**182**	**176**	**129**	**1026**
AUROC [95% CI]	0.80	0.95	0.86	0.85	0.84	0.80	0.85	0.74	0.85
Rule out cut-off					**≤0.35**				
% patients	**32%**	**63%**	**80%**	**34%**	**53%**	**37%**	**44%**	**20%**	**51%**
Se / Sp	0.90/0.53	1/0.73	0.64/0.86	0.94/0.55	0.89/0.56	0.88/0.56	0.94/0.54	0.91/0.35	0.89/0.64
NPV	0.85	1	0.95	0.93	0.98	0.87	0.97	0.73	0.94
Indeterminate					**0.35 - 0.67**				
% patients	**39%**	**20%**	**16%**	**35%**	**36%**	**38%**	**34%**	**44%**	**30%**
Rule in cut-off					**≥0.67**				
% patients	**29%**	**17%**	**4%**	**31%**	**11%**	**24%**	**22%**	**36%**	**19%**
Se/Sp	0.90/0.48	0.93/0.75	0.99/0.25	0.89/0.58	0.92/0.44	0.89/0.45	0.87/0.58	0.82/0.49	0.92/0.49
PPV	0.83	0.63	0.78	0.81	0.33	0.76	0.54	0.78	0.69

Newsome et al. Lancet Gastroenterol Hepatol 2020

NIS4® based on blood/serum levels of 4 biomarkers: miR-34a-5p, YKL-40, alpha2-macroglobulin, and HbA1c

$$NIS4_{score} = \frac{e^{\gamma}}{(1+e^{\gamma})}$$

$$\text{Where } \gamma = \beta_0 + \beta_1 \times (\text{miR-34a-5p log [copies/µL]}) + \beta_2 \times (\text{A2M [g/L]}) + \beta_3 \times (\text{YKL40 [ng/mL]}) + \beta_4 \times (HbA_{1c}\ [\%])$$

	Discovery cohort (n=239)	RESOLVE-IT diag validation cohort (n=475)	Angers validation cohort (n=227)	Pooled validation cohort (n=702)
Prevalence of at-risk NASH*	104 (44%)	260 (55%)	85 (37%)	345 (49%)
AUROC (95% CI)	0·80 (0·73–0·85)	0·83 (0·79–0·86)	0·76 (0·69–0·82)	0·80 (0·77–0·84)
Rule out				
Low cutoff	<0·36	<0·36	<0·36	<0·36
n	108 (45%)	175 (37%)	114 (50%)	289 (41%)
Sensitivity	80·8% (71·6–87·6)	83·5% (78·3–87·7)	75·3% (64·5–83·7)	81·5% (76·9–85·3)
Specificity	65·2% (56·5–73·0)	61·4% (54·5–67·9)	65·5% (57·0–73·1)	63·0% (57·8–68·0)
Negative predictive value	81·5% (72·6–88·1)	75·4% (68·3–81·5)	81·6% (73·0–88·0)	77·9% (72·5–82·4)
Indeterminate				
n	71 (30%)	143 (30%)	49 (22%)	192 (27%)
Rule in				
High cutoff	≥0·63	≥0·63	≥0·63	≥0·63
n	60 (25%)	157 (33%)	64 (28%)	221 (31%)
Sensitivity	45·2% (35·5–55·2)	51·5% (45·3–57·7)	48·2% (37·4–59·3)	50·7% (45·3–56·1)
Specificity	90·4% (83·8–94·6)	89·3% (84·2–93·0)	83·8% (76·5–89·3)	87·1% (83·1–90·3)
Positive predictive value	78·3% (65·5–87·5)	85·4% (78·6–90·3)	64·1% (51·0–75·4)	79·2% (73·1–84·2)

Data are n (%) or percentage (95% CI), unless otherwise specified. AUROC=area under the receiver operating characteristics curve. NASH=non-alcoholic steatohepatitis. *At-risk NASH was defined as non-alcoholic fatty liver disease activity score 4 or more and liver fibrosis stage 2 or more.

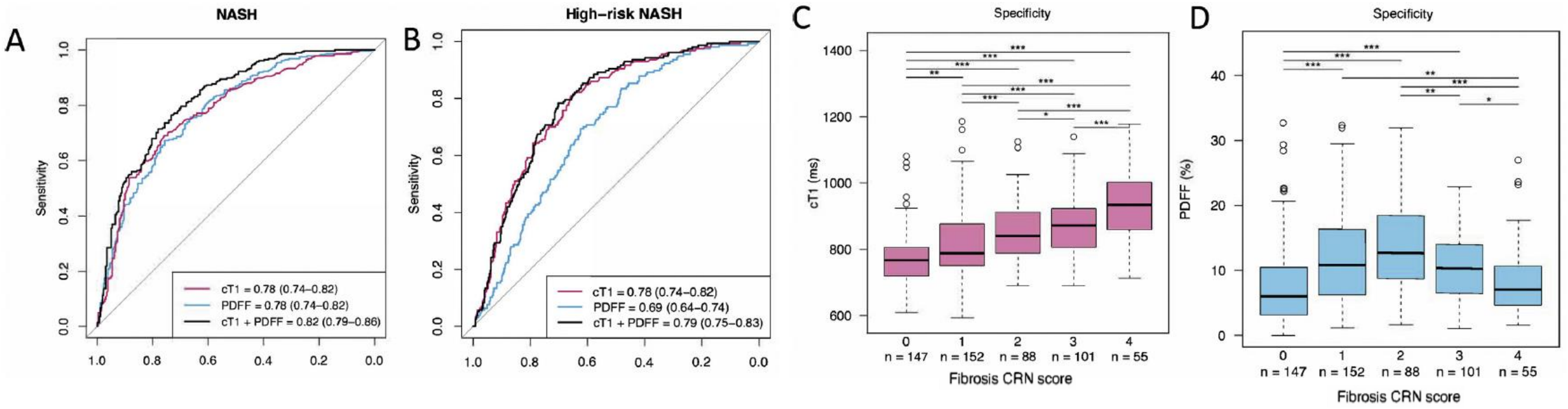
Table 2: NIS4 performance metrics to discriminate patients with or without at-risk NASH

	Number of patients with both comparator test and NIS4 data	Number of patients with condition	Comparator test AUROC (95% CI)	NIS4 reference AUROC (95% CI)	p value
At-risk NASH (NAS ≥4 and fibrosis stage ≥2)					
NIS4	702	345	..	0·80 (0·77–0·84)	..
FIB-4	694	341	0·70 (0·67–0·75)	0·81 (0·77–0·84)	<0·0001
NFS	694	341	0·66 (0·62–0·70)	0·81 (0·77–0·84)	<0·0001
ELF*	474	259	0·77 (0·72–0·81)	0·83 (0·79–0·86)	0·0067
BARD	702	345	0·58 (0·54–0·62)	0·80 (0·77–0·84)	<0·0001
APRI	694	341	0·74 (0·70–0·78)	0·81 (0·77–0·84)	0·0010
VCTE†	196	71	0·75 (0·68–0·82)	0·76 (0·69–0·82)	0·92
Advanced fibrosis (NAS ≥4 and fibrosis stage ≥3)					
NIS4	702	182	..	0·81 (0·77–0·84)	..
FIB-4	694	179	0·74 (0·70–0·78)	0·80 (0·77–0·84)	0·0044
NFS	694	179	0·68 (0·64–0·73)	0·80 (0·77–0·84)	<0·0001
ELF*	474	135	0·77 (0·72–0·81)	0·80 (0·76–0·84)	0·16
BARD	702	182	0·62 (0·57–0·67)	0·81 (0·77–0·84)	<0·0001
APRI	694	179	0·75 (0·71–0·79)	0·80 (0·77–0·84)	0·017
VCTE†	196	39	0·81 (0·73–0·88)	0·80 (0·72–0·87)	0·84

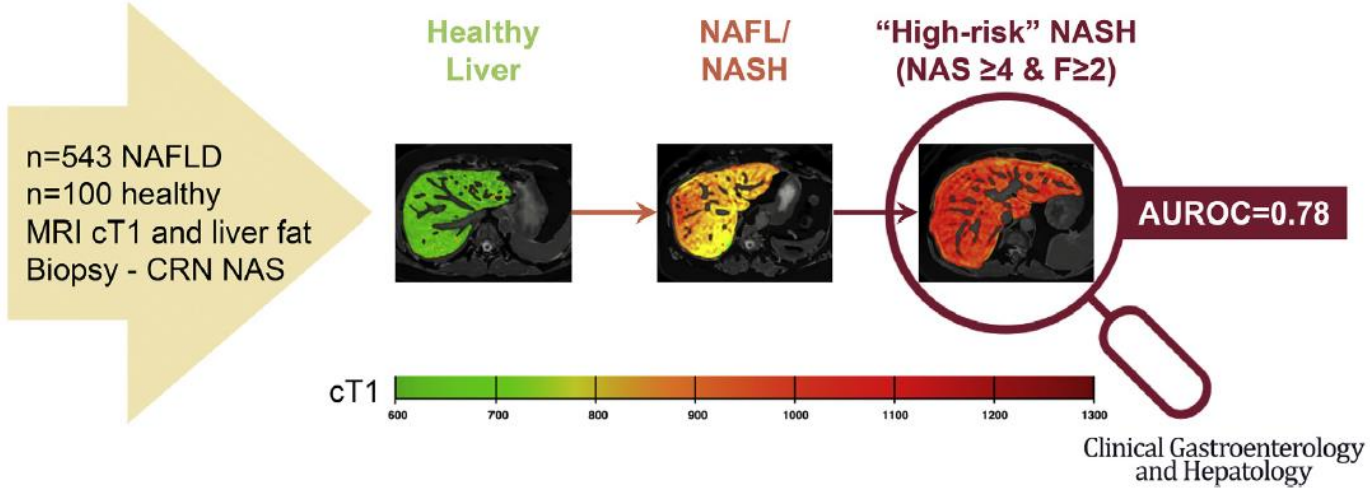
Harrison et al. Lancet Gastroenterol Hepatol 2020

RESONANCIA MAGNÉTICA

Fibrosis ≥2 + NAS ≥4



MRI cT1 accurately identifies NASH patients at high risk of disease progression



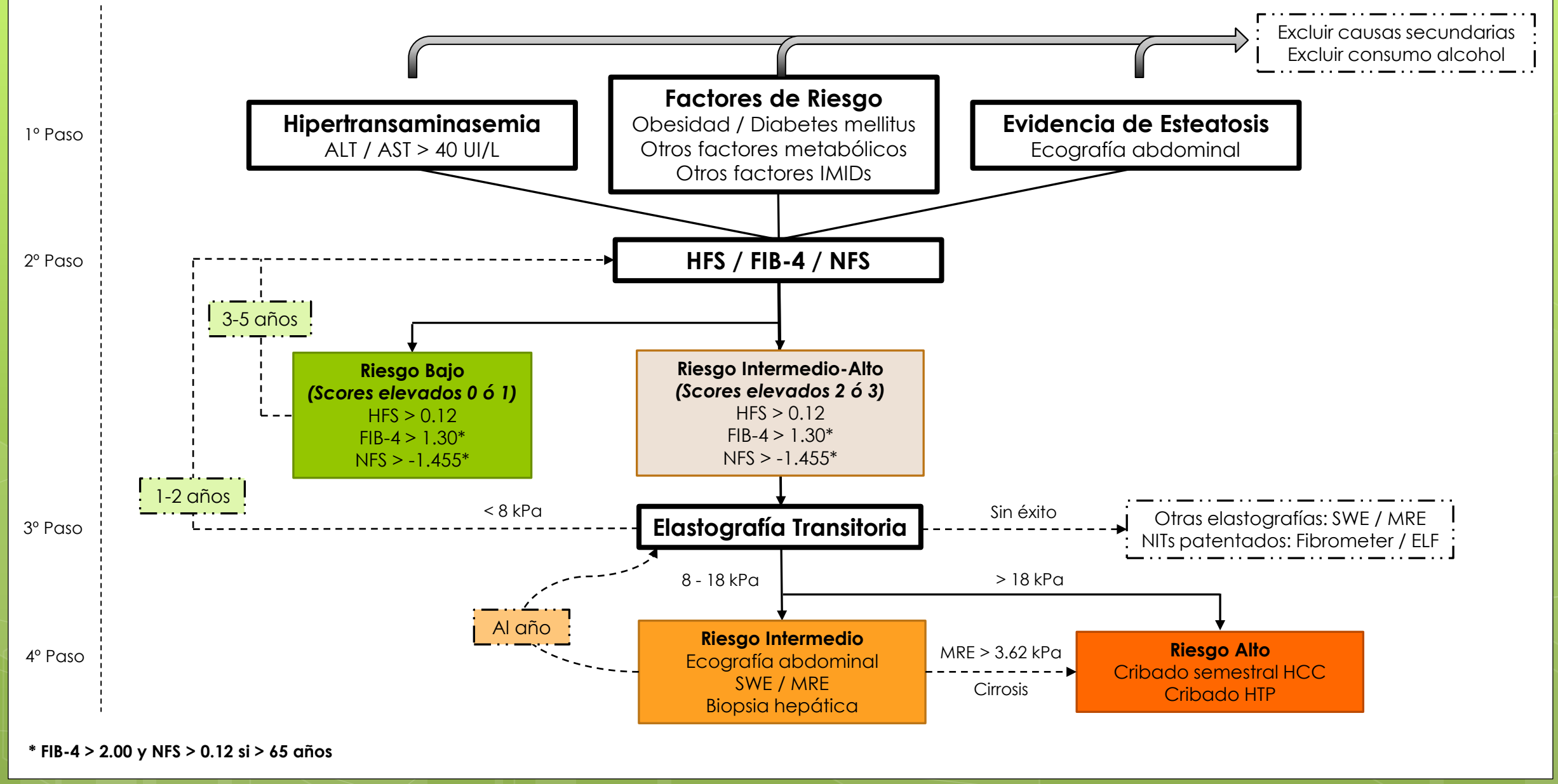
Andersson et al. Clin Gastroenterol Hepatol 2022

¿Cuál sería la estrategia más ideal?

Paso a paso

MANEJO DIAGNÓSTICO

Algoritmo en MAFLD



*** FIB-4 > 2.00 y NFS > 0.12 si > 65 años**

Ampuero J. Opinión personal

Conclusiones

¿Qué nos llevamos a casa?

CONCLUSIONES

- La enfermedad hepática metabólica tiene diferentes endpoints a detectar, debiendo ajustarse los recursos diagnósticos a la relevancia clínica.
  - La fibrosis hepática es el endpoint de mayor impacto y, en consecuencia, es el área con mayor número de estudios y opciones diagnósticas.
    - Los scores bioquímicos no patentados son razonablemente precisos y deben ser usados de rutina.
  - La esteatohepatitis es un endpoint relevante que requiere un abordaje metabolómico.

- Existen limitaciones tanto de los métodos bioquímicos como elastográficos que se deben conocer en aras de evitar tomar decisiones precipitadas (especialmente, falsos positivos en determinados escenarios).

- La estrategia más adecuada es la combinación secuencial de métodos.
  - En un primer paso utilizar algún método bioquímico no patentado y en un segundo paso una técnica elastográfica.

GRACIAS

Dr. Javier Ampuero

Hospital Universitario Virgen del Rocío

jampuero-ibis@us.es

@Dr_Ampuero