MÁSTER EN HEPATOLOGÍA

UAM Universidad Autónoma de Madrid

Universidad de Alcalá

Asignatura: Enfermedades Metabólicas del hígado

“Diagnóstico de la Esteatosis Hepática Metabólica”

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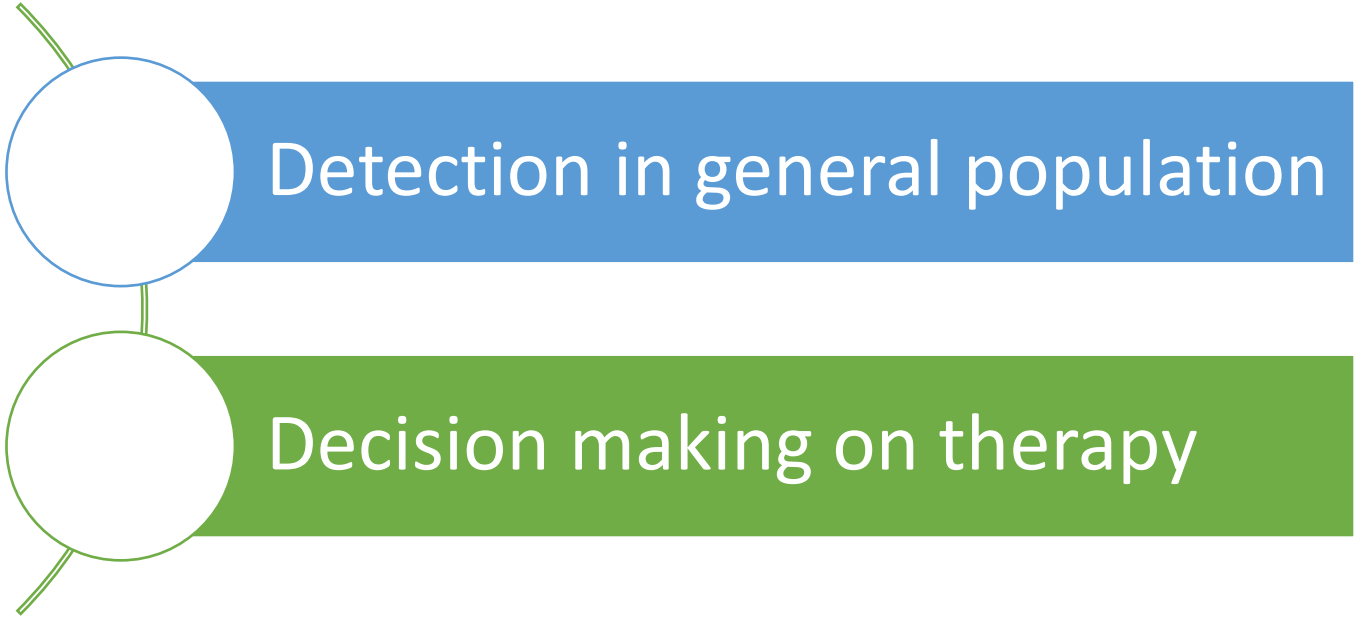
Hospital Universitario Virgen del Rocío, IBIS, Universidad de Sevilla, CiberEHD, Sevilla


Detection in general population
Decision making on therapy

Female 58 yo old with metabolic syndrome & steatosis

Patient attended out patient office at primary care due to hyperecogenicity of the liver in abdominal ultrasound.

Personal history

- No drug allergies.
- Never smoked.
- No alcohol consumption.
- Menopause at 47 years old.
- Arterial hypertension.

Family history

- Father died due to lung cancer.
- Mother alive at 76 years old suffering from type 2 diabetes.
- Two brothers with arterial hypertension.
- No cardiovascular events in the family.

Physical exploration

Systolic arterial pressure: 150 mmHg; **Diastolic arterial pression: 85 mmHg;** Weight: 83 kg; Height: 166 cms; **Body mass index: 30.6 kg/m2 (Obesity degree 1);** **a**canthosis nigricans. Waist perimeter: 100 cms; Abdomen and cardiorespiratory exploration without alterations.

Blood test

Biochemistry	**Glucose 116 mg/dL Urea 48 mg/dL Creatinine 0,76 mg/dL ; Uric acid 5,4 mg/dL; Lipids: Total Cholesterol: 226 mg/dL; HDL: 34 mg/dL; LDL: 146 mg/dL; Triglycerides: 194 mg/dL; LFT: Total bilirubin 1.31 mg/dL; AST: 35 U/L; ALT: 32 U/L; GGT: 77 U/L; AP: 110 U/L; LDH 207 U/L, total proteins: 7.2 g/dL; Albumin: 4.6 g/dL; Iron metabolism: Iron in blood: 118 µg/dL; TSI: 31 %; ferritin: 507 ng/mL**
Coagulation	**Haemoglobin: 15 g/dL, Platelets: 195 x 10^9/L; INR: 1.03**
Virus	**Hepatitis B, C, E negatives**
Metabolic	**Baseline Insulin: 48.3 µU/mL; HOMA: 13,8; HbA1c 6.5 %; Ceruloplasmine: 31 mg/dl; TSH 6.37 µUI/ml, T4-L 1.06 ng/dl; A1AT: 145 mg/dl**

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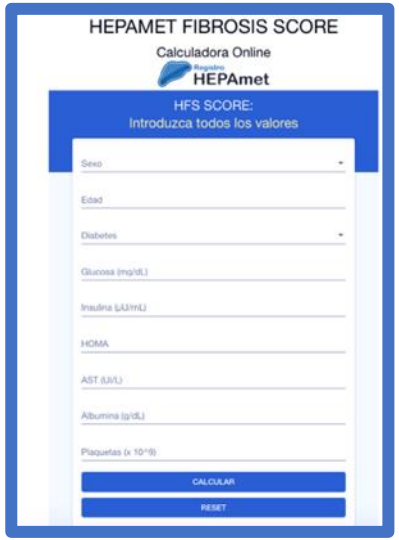
Detection of advanced fibrosis in general population

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

http://nafldscore.com/

https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

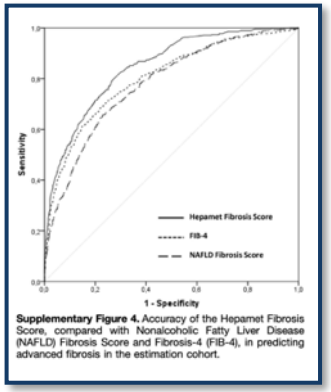


NAFLD Fibrosis Score

NAFLD fibrosis score = -1.675 + 0.037 × age (year) + 0.094 × BMI (kg/m^2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio - 0.013 × platelet count (×10^9/L) - 0.66 × albumin (g/dL)

FIB-4

$$\frac{\text{AST(U/L)} \times \text{Edad(años)}}{\text{Plaq(miles)} \times \sqrt{\text{ALT (U/L)}}}$$



Supplementary Figure 4. Accuracy of the Hepamet Fibrosis Score, compared with Nonalcoholic Fatty Liver Disease (NAFLD) Fibrosis Score and Fibrosis-4 (FIB-4), in predicting advanced fibrosis in the estimation cohort.

NIT	Parameters		
NAFLD-fibrosis score (NFS)	Age, AST, ALT, Platelets, BMI, albúmina & glucemia	**-0.723**	Grey zone
FIB-4	Age, AST, ALT & platelets	**1.24**	No fibrosis
Hepamet Fibrosis Score (HFS)	Age, Sex, T2DM, HOMA, AST, Albumin & platelets	**0.24**	Grey zone

Blood test	
Biochemistry	**Glucose 116 mg/dL Urea 48 mg/dL Creatinine 0,76 mg/dL ; Uric acid 5,4 mg/dL; Lipids: Total Cholesterol: 226 mg/dL; HDL: 34 mg/dL; LDL: 146 mg/dL; Triglycerides: 194 mg/dL; LFT: Total bilirubin 1.31 mg/dL; AST: 35 U/L; ALT: 32 U/L; GGT: 77 U/L; AP: 110 U/L; LDH 207 U/L, total proteins: 7.2 g/dL; Albumin: 4.6 g/dL; Iron metabolism: Iron in blood: 118 µg/dL; TSI: 31 %; ferritin: 507 ng/mL**
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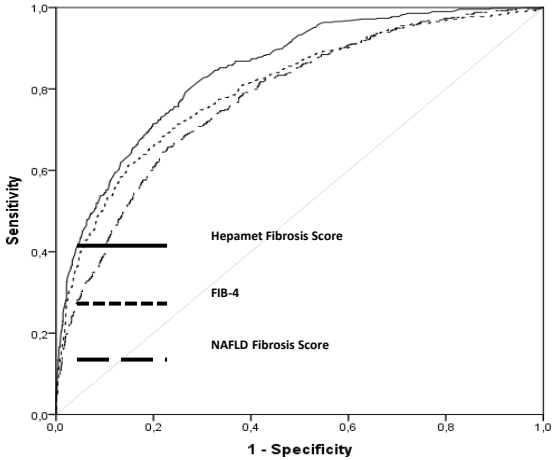
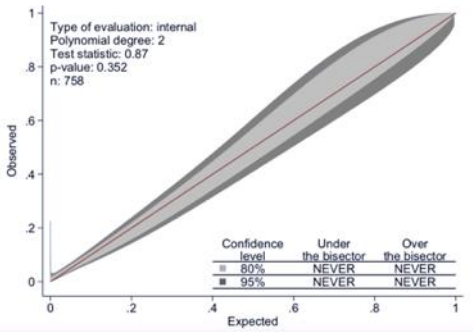
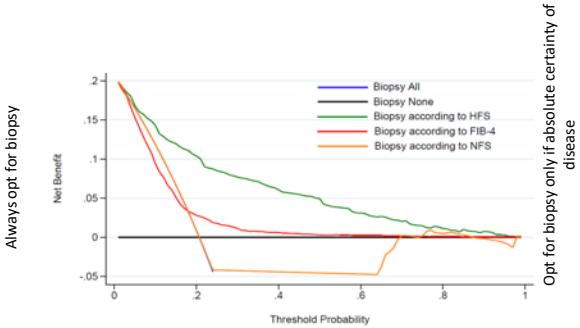
NAFLD: *non-alcoholic fatty liver disease*, **FIB-4:** *Fibrosis-4.*

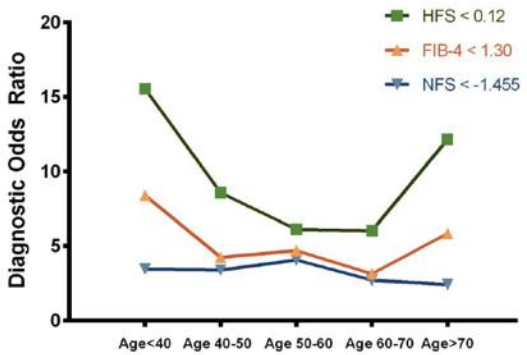
1. Ampuero J, *et al.* Development and Validation of Hepamet Fibrosis Scoring System–A Simple, Noninvasive Test to Identify Patients With Nonalcoholic Fatty Liver Disease With Advanced Fibrosis. Clin Gastroenterol Hepatol. 2020; 18(1):216-225.e5.

Detection and referral: fNITs





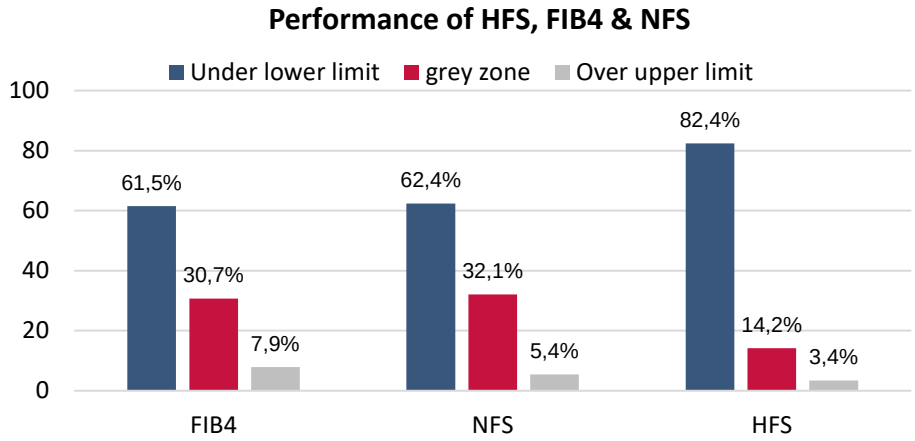




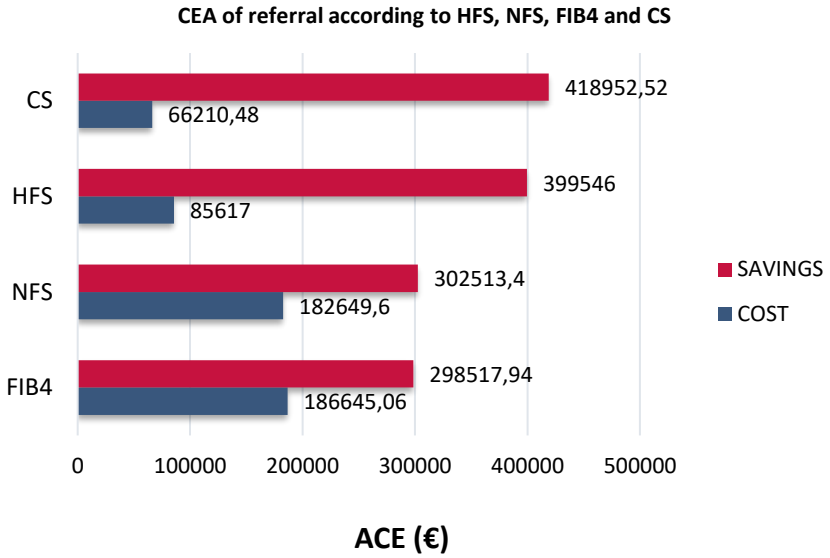
Ampuero et al. CGH 2020

Detection of Fibrosis in MAFLD: Combined score

Score	FIB-4	NFS	HFS
0	< 1.30	< -1.455	< 0.12
1	1.30 - 2.67	-1.455 - 0.675	0.12 - 0.47
2	> 2.67	> 0.675	> 0.48



IFH	0	1	2	3	4	5	6
N=1127	527 (47%)	211 (19%)	174 (15%)	111 (10%)	55 (5%)	23 (2%)	26 (2%)



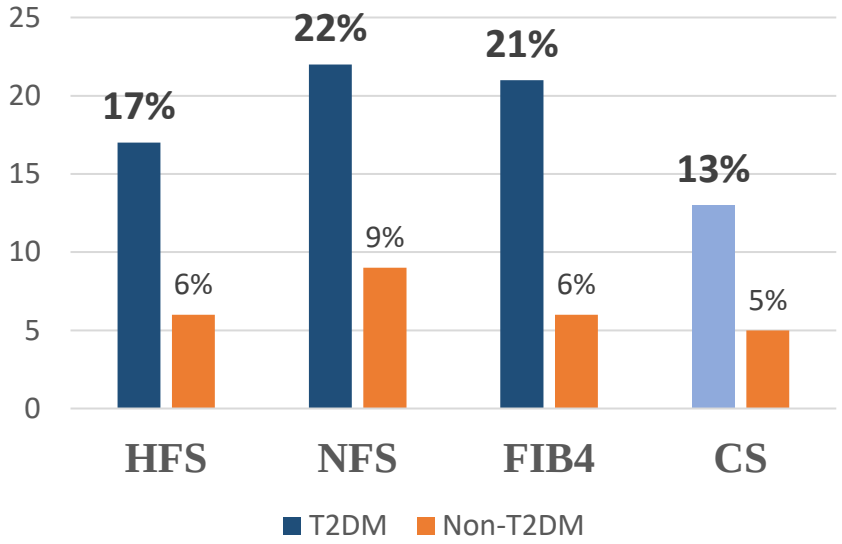
Three advantages of the Combined score:
1. Avoid missing patients with T2DM and advanced fibrosis under the lower cut-off o a single test
2. Select patients in the gray zone to underwent a second test: OWL-Liver® - ELF ® - FIBROSCAN ®
3. Improve efficacy rate in referral of patients at risk of advanced fibrosis

MAFLD: *metabolic associated fatty liver disease,* **FIB4:** *Fibrosis-4,* **NFS:** *NAFLD Fibrosis Score,* **HFS:** *Hepamet Fibrosis Score* **T2DB:** *type 2 diabetes mellitus.*
Ampuero J, et al. EASL 2018; Ampuero et al. EASL 2020

One single test like FIB4 or NFS failed in diabetic patients missing advanced fibrosis and referring the double of patients

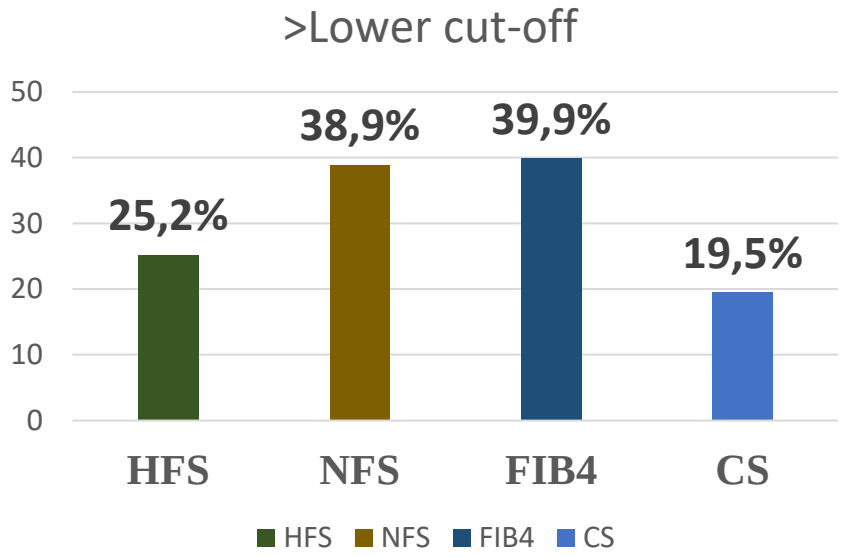
Prevalence of advanced fibrosis in patients under lower cut-off

N=2392; T2DM: 836; Advanced Fibrosis: 494



Referral rate from Primary Care using one single test

N=1127; age: 55±14; Females: 43,1% (486/1127);
T2DM: 307/1127 (27%)



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FIB4: *Fibrosis-4*, **NFS:** *NAFLD Fibrosis Score*, **T2DB:** *type 2 diabetes mellitus*, **HFS:** *Hepamet Fibrosis Score.*

1. Ampuero J, *et al.* Development and Validation of Hepamet Fibrosis Scoring System–A Simple, Noninvasive Test to Identify Patients With Nonalcoholic Fatty Liver Disease With Advanced Fibrosis. Clin Gastroenterol Hepatol. 2020; 18(1):216-225.e5.

HFS in Primary Care

N=425

Age: 55±13
Males: 61% (258/425)
Females: 39% (158/425)

HFS > 0.12 [58/425 (14%)]
FIB4 > 1.30 [166/425 (39%)]
NFS > -1.455 [157/424 (37%)]

IFH					N=427
0	214 (50%)				**214 (50%)**
1 - 2	88 (21%)	66 (17%)			**154 (36%)**
≥ 3	22 (5%)	20 (4%)	10 (2%)	7 (2%)	**58 (14%)**

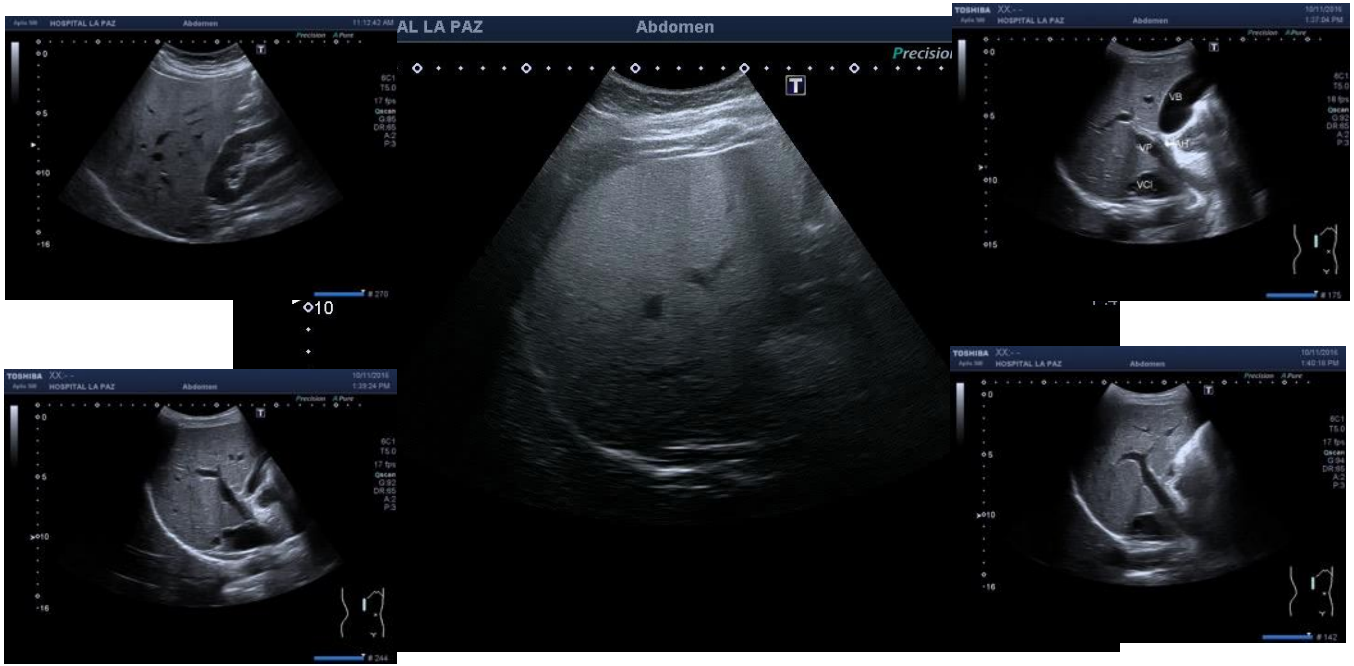
HFS < 0.12 ---- RISK OF CIRRHOSIS 0.9%

HFS advantages:

- ✓ Metabolic status + fibrosis stage
- ✓ Potential for monitoring
- ✓ NPV > 96% when HFS ≤ 0.12
- ✓ Cost-effectiveness reducing significantly referral rate.

Ampuero et al. CGH 2019
Gimena J et al. TFG. Medicina. US.

Liver Ultrasonography



Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease☆

European Association for the Study of the Liver (EASL)*, European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO)

Liver ultrasonography

Recommendations

- US is the preferred first-line diagnostic procedure for imaging of NAFLD, as it provides additional diagnostic information (**A1**)

J Hepatol 2016

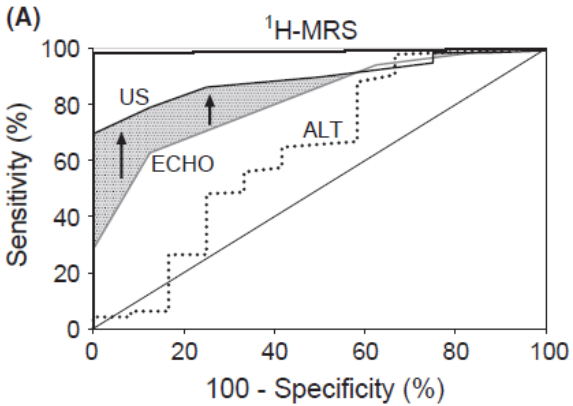
AUROC
0,96
0,89
0,82

Clinical value of liver ultrasound for the diagnosis of non-alcoholic fatty liver disease in overweight and obese patients. Brill F et al. Liver Int 2015;35:2139-2146

N=146

Parenchymal echogenicity	Far gain attenuation	GB wall blurring	Portal vein blurring	Hepatic vein blurring

Threshold for steatosis detection: 12.5%



Ultrasonography limitations:

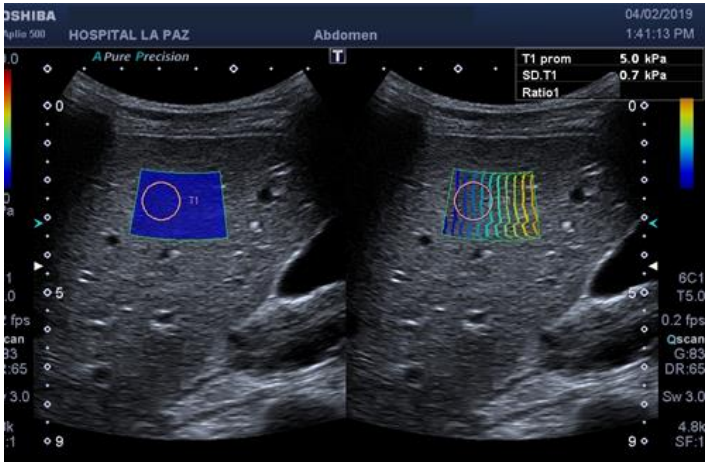
- Not able to segregate steatohepatitis from steatosis.
- Liver hyper-ecogenicity do not correlate with hepatic injury
- Brilliant liver requires differential diagnosis
- Steatosis detected by ultrasonography when higher than **12.5%**

Taking care of NAFLD at hepatology clinics: Ultrasonography, shear-wave and transient elastography

LIVER ULTRASONOGRAPHY:

- *Hyper-echogenicity*
- *Far gain attenuation*
- *Blurred border with gallbladder*
- *Blurred border to vessels*

Shear-wave elastometry: 6,6 kPa



Fibroscan (sonda XL):	
Median	**10.0 kPa**
IQR	1.4
% success	100 %
CAP	**304 dB/m**

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shear-wave elastography

Individual patient data meta-analysis CAP detecting steatosis

N=2735

NAFLD (n=537); HepC (n=997); HepB (n=1003); Others (n=198)

F0: 304 (11%); F1: 970 (36%); F2: 725 (27%); F3:334 (12%; F4: 350 (13%)

Clinical case

Etiology – Diabetes – BMI

CAP values dB/m

- **NAFLD/NASH** Deduct 10 dB/m
- **Diabetes** Deduct 10 dB/m
- **BMI** (20-30 Kg/m²) Deduct 4.4 dB/m for each Unit>25 Add 4.4 for each Unit below 25

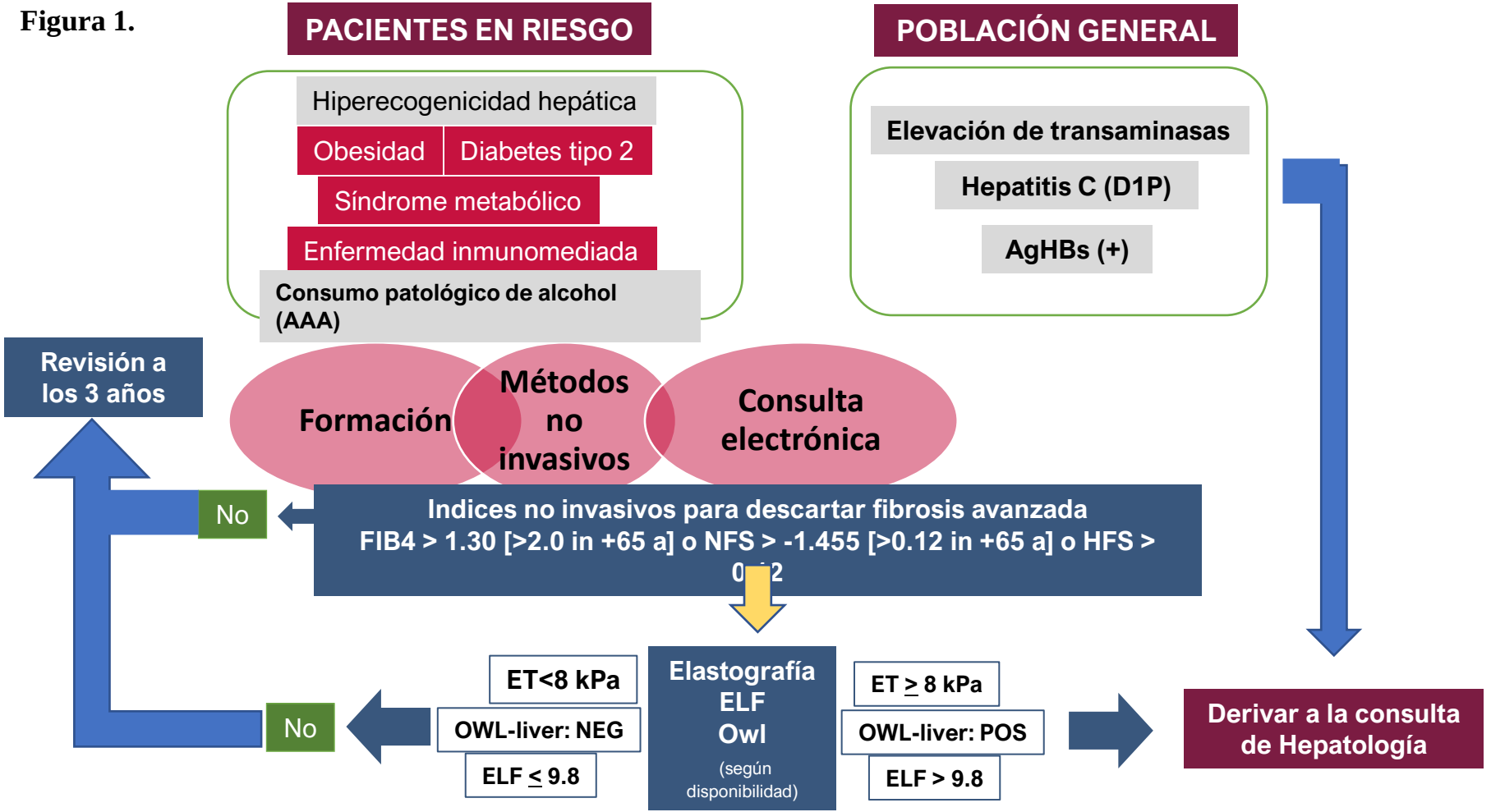
Recalculated CAP value

>S0	>S1	>S2
248 (237 to 261)	**268** (257 to 284)	**280** (268 to 294)

	AUROC
S0 vs. S1-S3	0.82 (0.81-0.84)
S0-S1 vs. S2-S3	0.87 (0.85-0.88)
S0-S1-S2 vs. S3	0.88 (0.86-0.91)

Karlas et al. J Hepatol 2017;66:1022-1030
Romero-Gómez M, Cortez-Pinto H. J Hepatol 2017

Figura 1.



VHC: virus de la hepatitis C, **HFS:** *Hepamet Fibrosis Score*, **NFS:** *NAFLD Fibrosis Score*, **FIB4:** *Fibrosis-4*.
Romero Gómez M *et al*. Consenso AEEH 2021

Second line test: OWL-Liver

OWLiver® in patients with T2DM

Estimation cohort: n=616 biopsy proven-MAFLD

- **N=616 patients**
- 53% males
- AST = 65,8 ±11,7U/L y ALT = 53,33 ±38,27U/L
- IMC 34,5 ±6,44 kg/m^2
- **% Patients with bad control of T2DM (24% pacientes con HbAc1> 7%)**
- **Steatosis: 263 (42%)**
- **Steatohepatitis 353 (57,3%)**

16 metabolites together with variables like BMI, ALT & AST

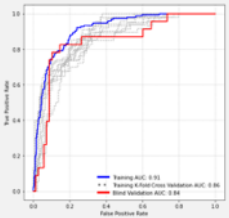
	Estimation	Validation
AUC	0.805 ± 0.047	0.809 ± 0,064
S	0.671 ± 0,049	0.722 ± 0,147
E	0,799 ± 0,029	0,723 ± 0,113

Algorithm OWLiver ®F2+

Estimation cohort n= 790 patients with biopsy proven NAFLD (F2-F3 and NAS ≥ 4)

12 metabolites together with variables like BMI, ALT & AST

	Estimation	Validation
AUC	0.81	0.82
S	0.96	0.95
E	**0.36**	**0.20**
VPP	0.86	0.62
VPN	0.62	**0.75**



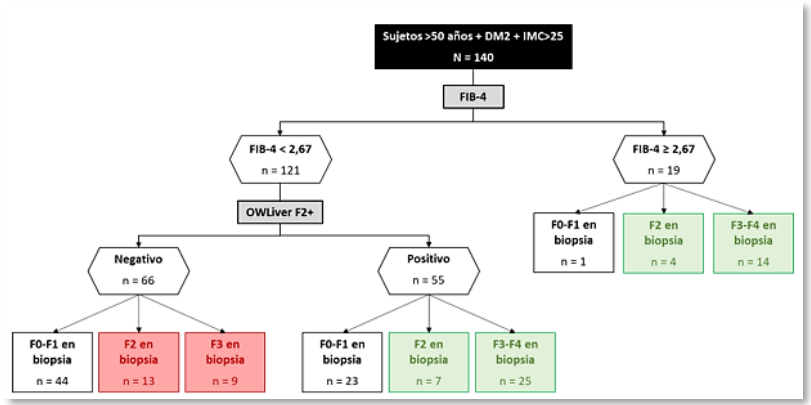
OWLiver® confirma su uso como **herramienta no invasiva para identificar pacientes NASH y fibrosis ≥ F2-F3** en la población general y en **pacientes diabéticos.**

1. Martínez-Arranz I, *et al*. Non-invasive serum lipidomic approach to discriminate non-alcoholic steatohepatitis in multiethnic patients with type 2 diabetes mellitus. Hepatol. 2019; 70(1):1030A. **2.** Mincholé I, *et al*. Serum metabolomics-based steatohepatitis score for the noninvasive identification of patients with non-alcoholic steatohepatitis (NASH) in multiethnic, including type 2 diabetes mellitus population. International Liver Congress 2021 (EASL). PO-1518. **3.** Noureddin AM, *et al*. Serum-based Metabolomics-Advanced StEatohepatitis Fibrosis Score (MASEF) fot the non-invasive identification of patients with non-alcoholic steatohepatitis with significant fibrosis. Digital International Liver Congress 2020 (EASL). LBP21.

Second line test: OWL-Liver

Capacidad diagnóstica del panel metabolómico en la detección de esteatohepatitis y fibrosis significativa

140 pacientes con biopsia
DM2, >50 años e IMC>25



La combinación de FIB-4 y OWLiver® F2+ respecto la biopsia hepática

OWLiver® es una herramienta útil como cribado para la detección de NASH y fibrosis entre los sujetos con un riesgo elevado de desarrollar MALFD, complementaria a los scores de fibrosis

Estudio observacional de estimación y validación de modelos predictivos diagnósticos en las Unidades de Hígado de 6 hospitales nacionales

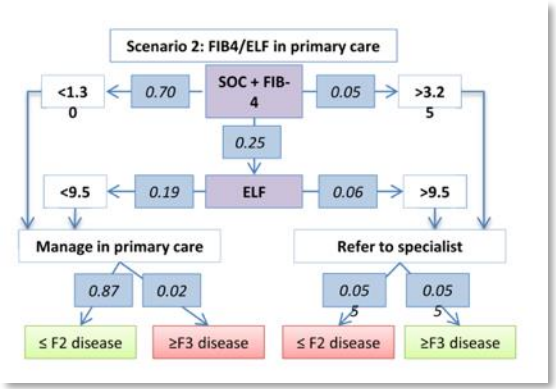
- Fibrosis significativa F≥2 fue detectada con FIB-4 < 2,67 (n=121) y el OWLiver® F2+ presentando una sensibilidad del 59,3%
- En pacientes con FIB-4<2,67 (n=121) OWLiver®F2+ **recuperó 25 de los 34 con fibrosis**

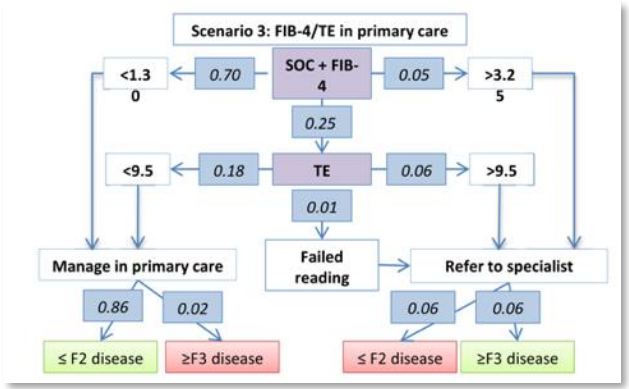
La combinación de FIB-4 y OWLiver® respecto la biopsia hepática:

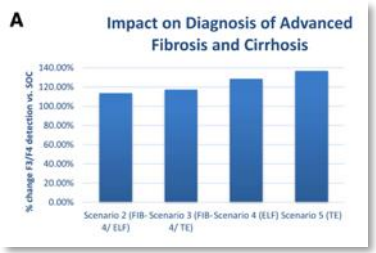
- Identificar al **63,9%** de los pacientes con **F≥2** (n=72)
- Identifican **95,8%** de los pacientes con **F3-F4** (n=48)

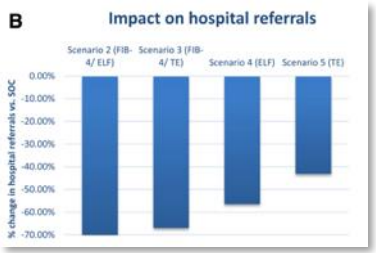
DM2: diabetes mellitus tipo 2, **IMC:** índice de masa corporal; **NASH**: esteatohepatitis no alcohólica, **MALFD:** enfermedad del hígado graso asociada a la disfunción metabólica. **1.** Iruzubieta P, *et al.* Capacidad diagnóstica de diferentes paneles metabolómicos para detector esteatohepatitis y fibrosis significativa en pacientes con alto riesgo de esteatosis hepática metabólica (EHMET). LXXX Congreso de la Sociedad Española de Patología Digestiva (SEPD). OB-034.

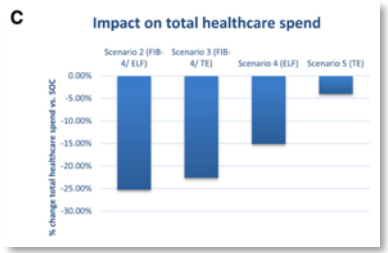
Second line test: ELF







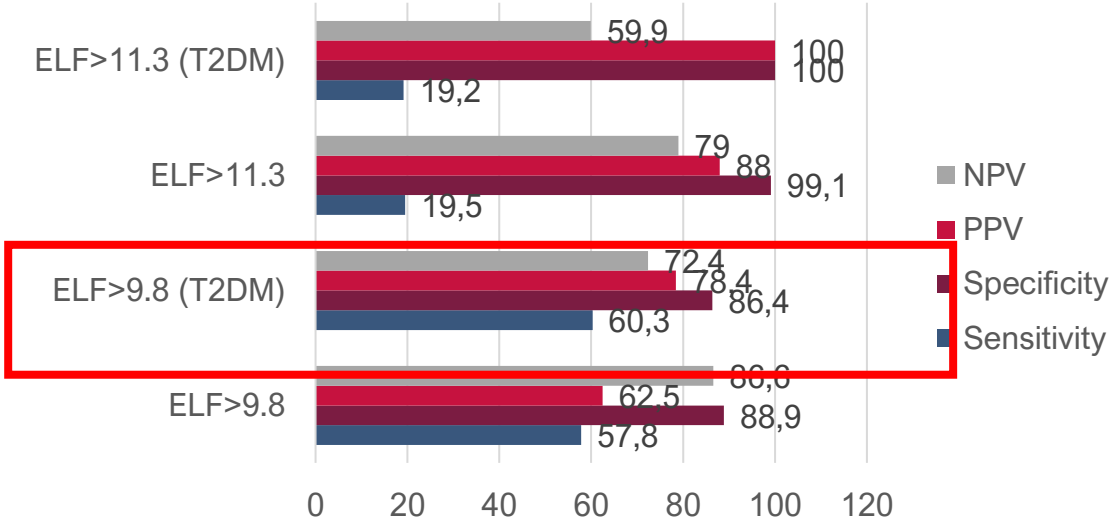




ELF: *enhanced liver fibrosis,* **FIB4:** *fibrosis-4,* **SOC:** *standard of care.* **1.** Srivastava A, *et al.* Cost-comparison analysis of FIB-4, ELF and fibroscan in community pathways for non-alcoholic fatty liver disease. BMC Gastroenterol. 2019;19(1):122.

Diagnostic accuracy of estimating advanced fibrosis with ELF score

N=463 biopsy proven NAFLD



ELF: *enhanced liver fibrosis,* **NAFLD:** *non-alcoholic fatty liver disease,* **T2DB:** *type 2 diabetes mellitus,* **NPV:** *negative predictive value,* **PPV:** *positive predictive value.*

1. Younossi Z, et al. Performance of the Enhanced Liver Fibrosis Test to Estimate Advanced Fibrosis Among Patients With Nonalcoholic Fatty Liver Disease. JAMA Netw Open 2021;4(9):e2321923.

Second line test: Transient Elastography

Patients referred for high risk of fibrosis: Individual patient data meta-analysis of CAP detecting steatosis

N=2735; NAFLD (n=537); HepC (n=997); HepB (n=1003); Others (n=198)

F0: 304 (11%); F1: 970 (36%); F2: 725 (27%); F3:334 (12%; F4: 350 (13%)

Transient Elastography
CAP (dB/m)

Etiology – Diabetes – BMI

	AUROC
S0 vs. S1-S3	0.82 (0.81-0.84)
S0-S1 vs. S2-S3	0.87 (0.85-0.88)
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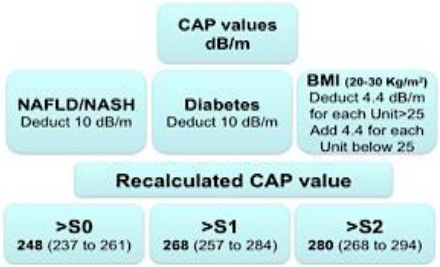
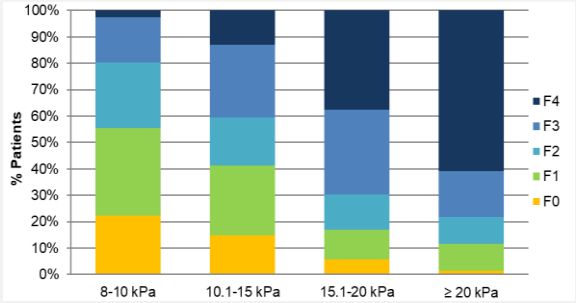


QoTE:
Median IQR/kPa < 30%

Diagnostic accuracy of transient elastography in fibrosis detection: a Spanish multicenter study in patients with biopsy proven NAFLD

N= 501 Spanish biopsy-proven NAFLD patients with Elastography



TE (kPa)

- < 8 kPa (n=112) → ≥F2 (n=4; 3,9%) → Cirrhosis (0%)
- ≥ 8 kPa (n=389) → ≥F2 (n=245;63%) → Cirrhosis (n=86; 22%)

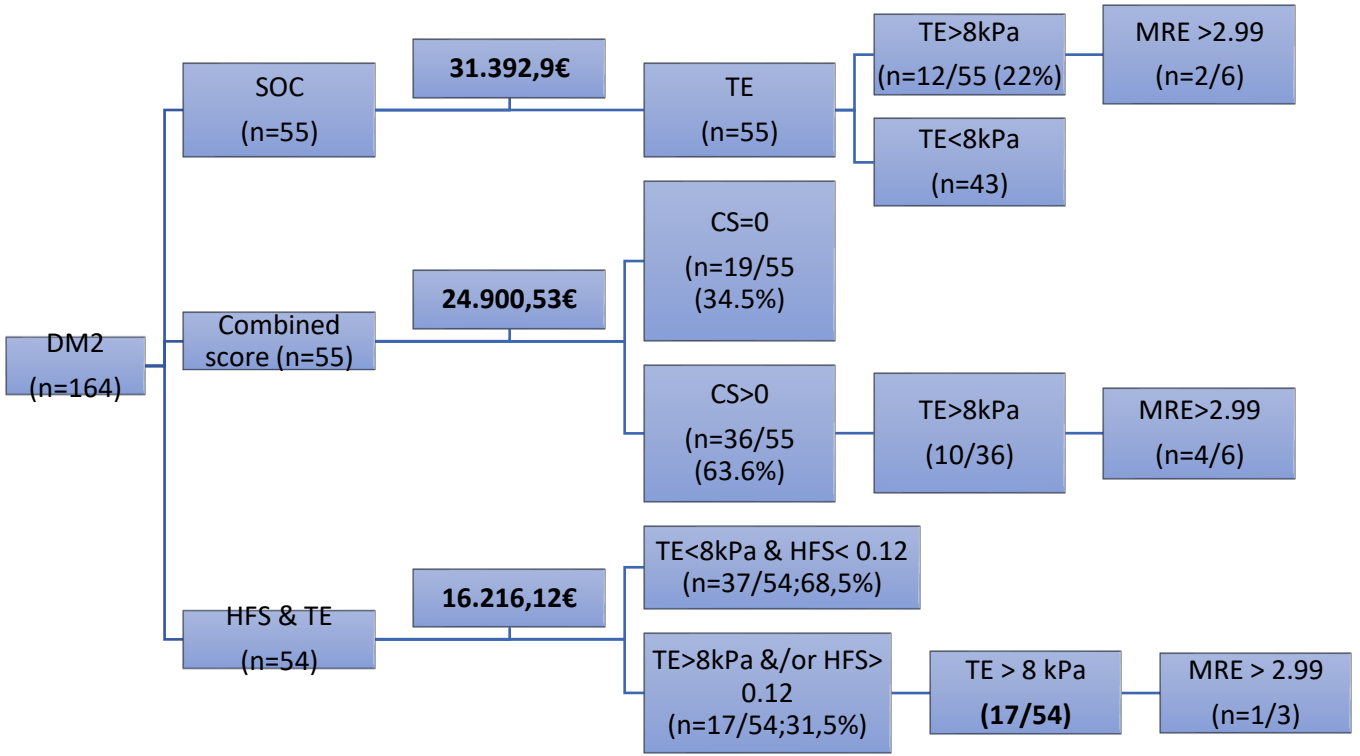
CAP: *controlled attenuation parameter*, **NAFLD**: *non-alcoholic fatty liver disease*, **BMI:** *body mass index*, **TE**:*transient elastography*, **IQR:** *interquartile range.*

1. Karlas T, *et al.* Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. J Hepatol. 2017;66(5):1022-1030. **2.** Romero-Gómez M, *et al.* Detecting liver fat from viscoelasticity: How good is CAP in clinical practice? The need for universal cut-offs. J Hepatol. 2017; 66(5):886-887. **3.** Rivera J, *et al.* Prevalence estimation of significant fibrosis due to non-alcoholic steatohepatitis combining transient elastography and histology.Liver Intern 2022; (In Press)

NASH-PI

Age average was 55±10y, 54.3% males, and 66.5% obese (BMI> 30Kg/m^2).

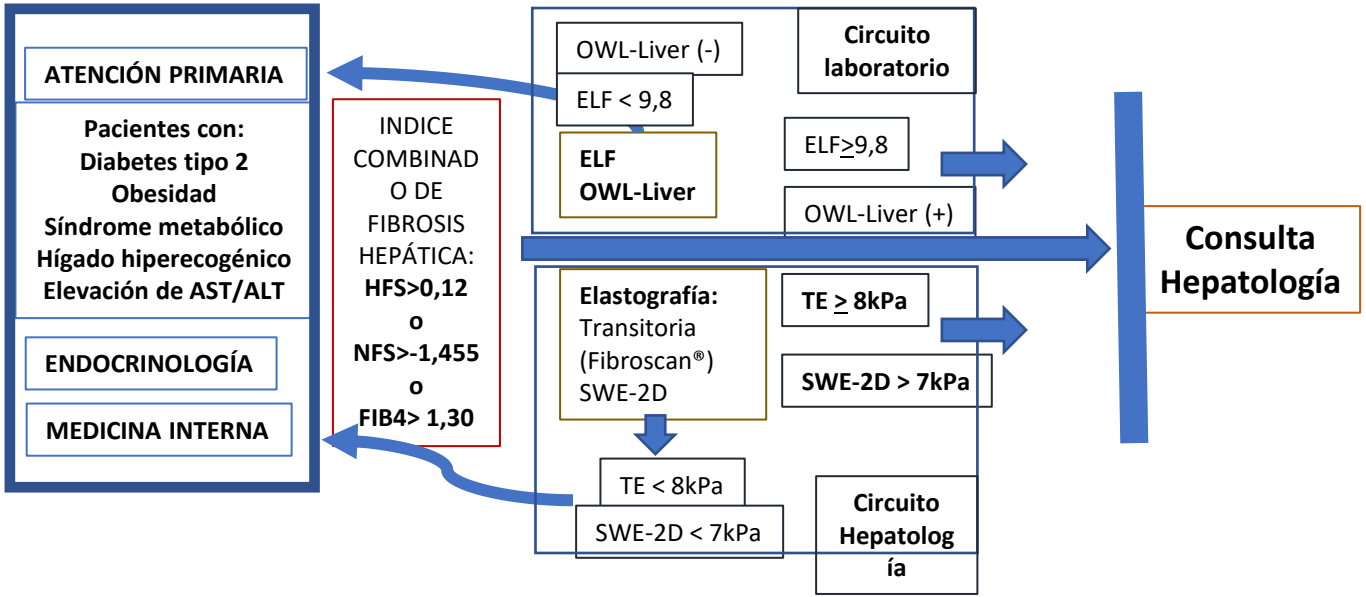
Transient elastography >8kP was found in 35/164 (21.3%); >10kPa 22/164 (13.4%) and >15kPa 12/164 (7.3%).



Advanced Fibrosis confirmed by MRE in 7 out of 15

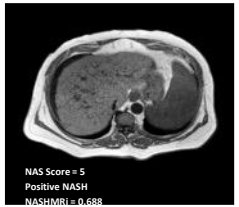
Romero-Gómez et al. EASL 2022

Circuito asistencial: Detección de Fibrosis Hepática

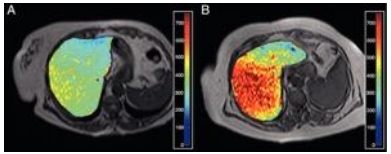


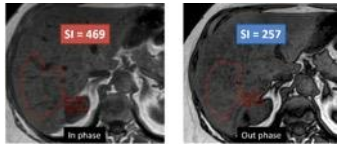
Romero Gomez M. Med Clin (Barc) 2022

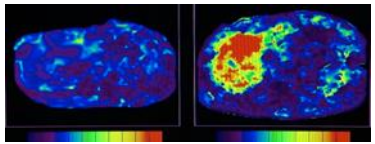
MR Imaging Biomarkers



- Imaging Biomarkers
  - MRI
    - PDFF
    - DeMILI
      - NASH-MRI
      - Fibro-MRI
    - LMS
    - MRE







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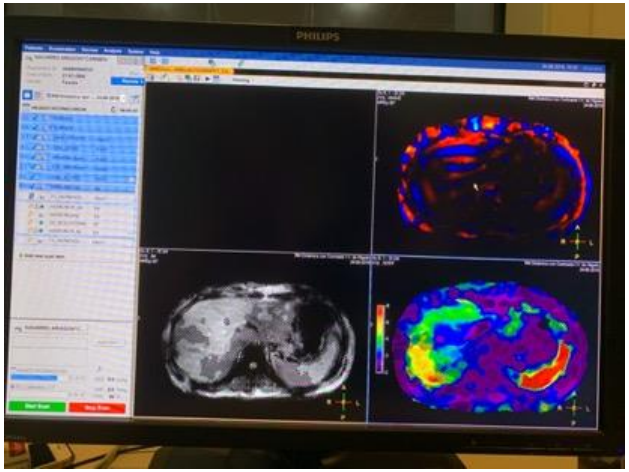
PHILIPS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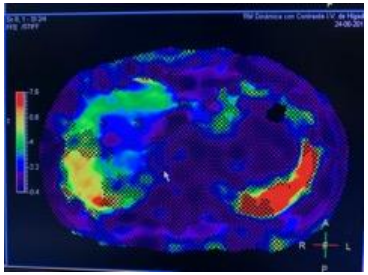
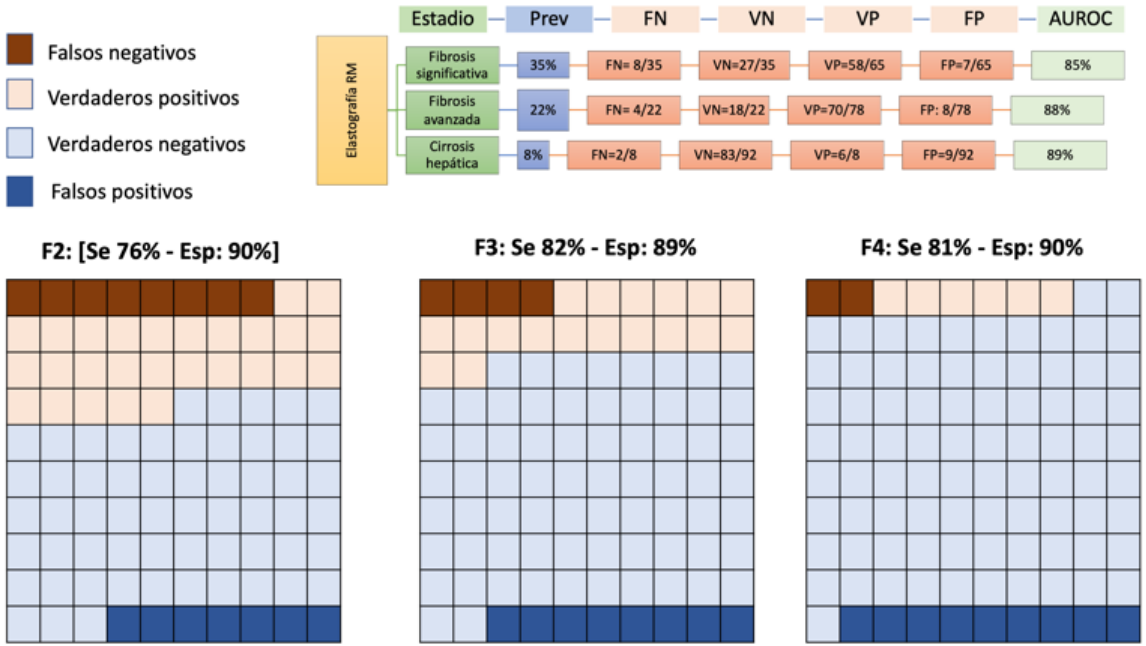


Diagnostic accuracy of elastography, and magnetic resonance imaging in patients with NAFLD: a systematic review and meta-analysis



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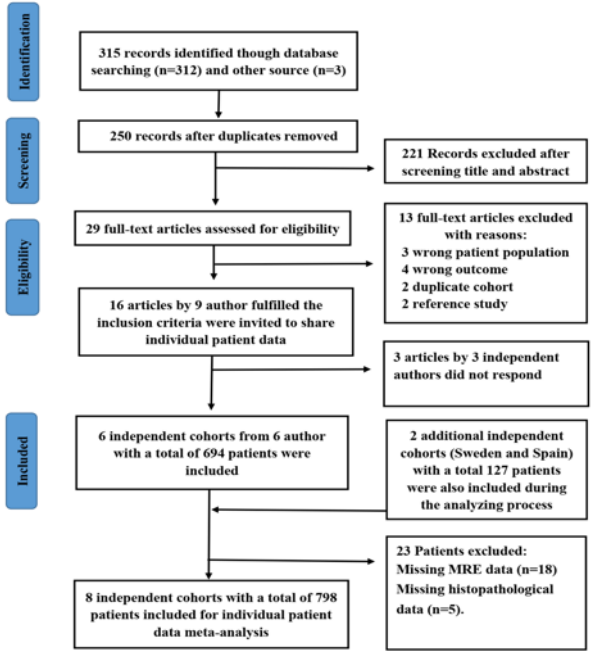
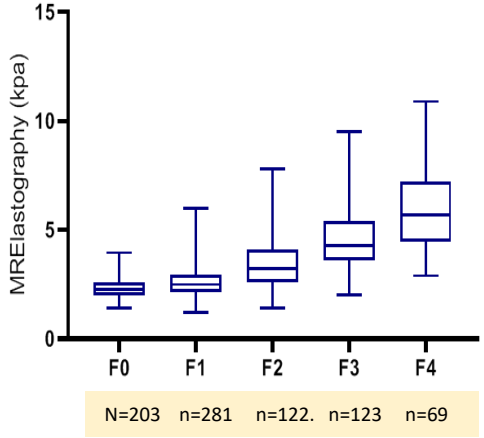
Selvaraj et al. JHep 2021

Study identification and selection flowchart.



Establishing the Cut-offs and Confounding factors of Magnetic Resonance Elastography for staging NAFLD-fibrosis: an IPD meta-analysis



Liang, Ampuero … Romero-Gómez. EASL 2022

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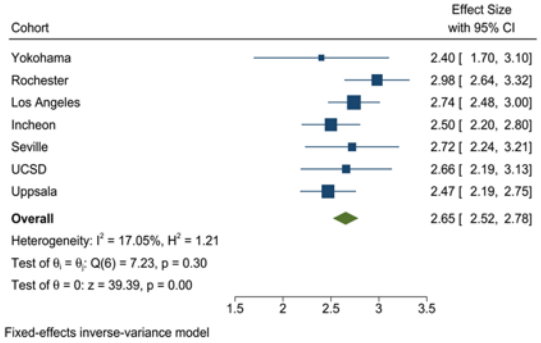
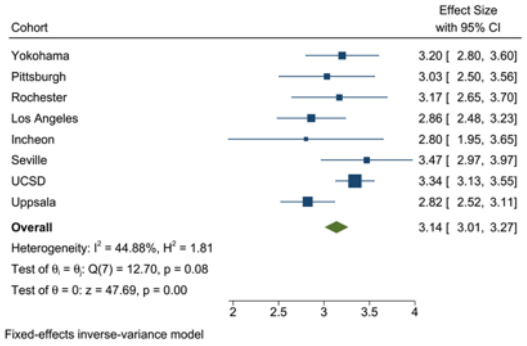
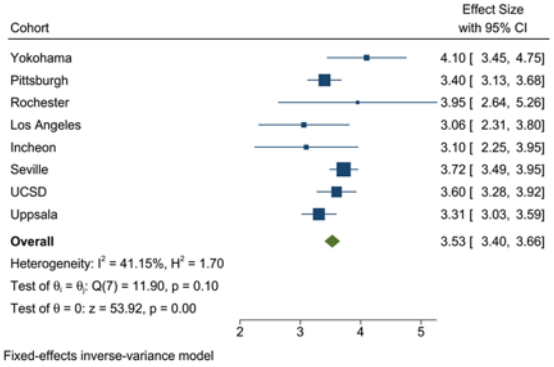


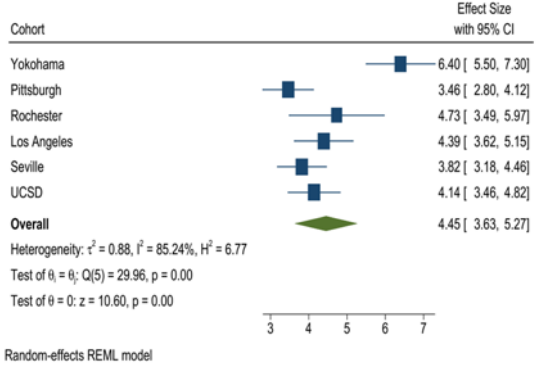
≥F1 cut-off：2.65 kpa



≥F2 cut-off：3.14 kpa



≥F3 cut-off：3.53 kpa



F4 cut-off：4.45 kpa

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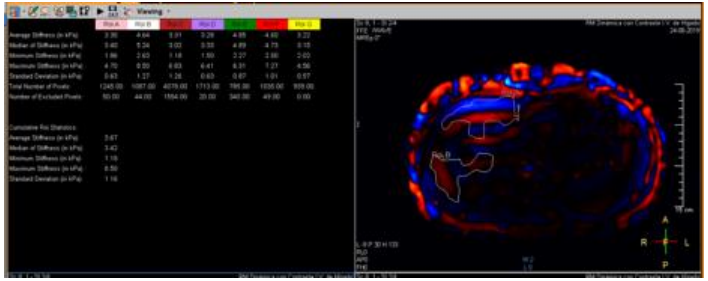
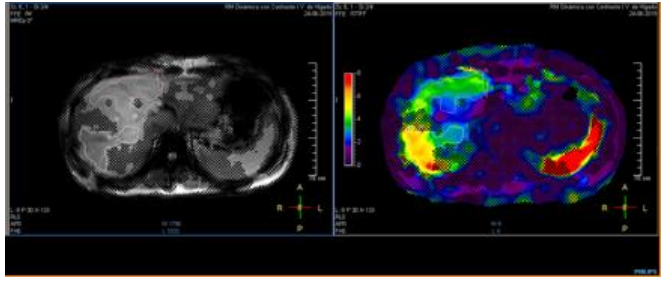
Magnetic Resonance Elastography to detect liver fibrosis in MAFLD





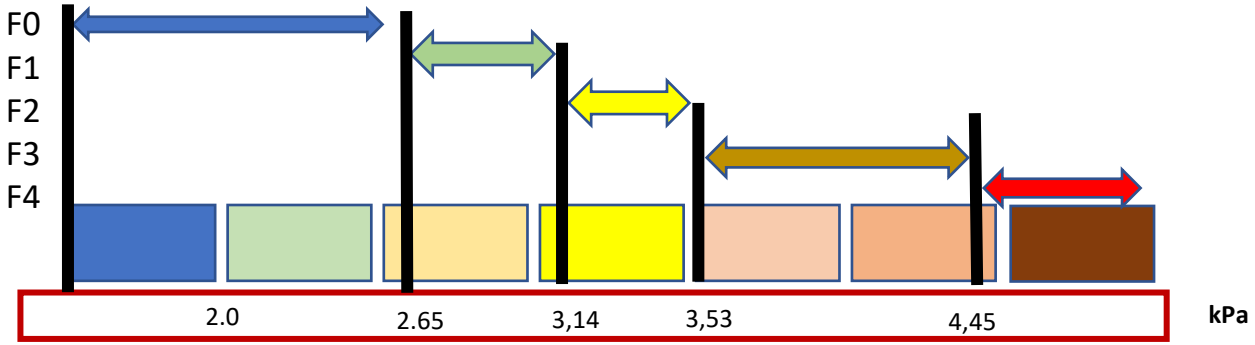


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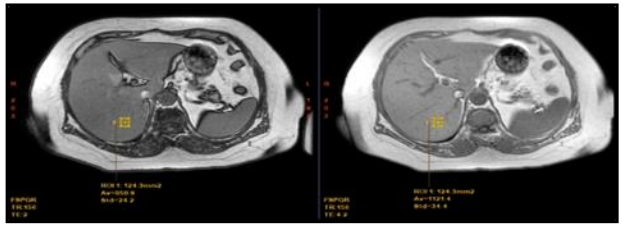
Table 6 GLMM (generalized linear mixed model) explore variables associated with prediction failure (overestimation and underestimation)

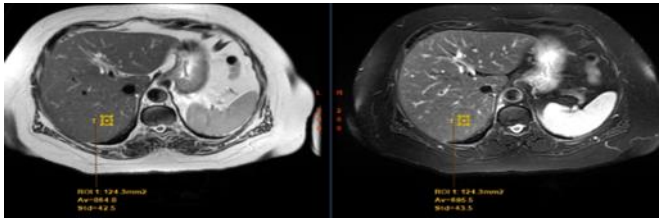
	Concordance vs Overestimation				Concordance vs Underestimation			
Variables	**Odds Ratio**	**95%CI**	**Z-value**	**P-value**	**Odds Ratio**	**95%CI**	**Z-value**	**P-value**
BMI	1.055	0.992-1.122	1.71	0.087	0.999	0.945-1.057	-0.03	0.979
Age	1.016	0.989-1.044	1.15	0.251	0.901	0.967-1.016	-0.71	0.479
T2DM (yes/no)	1.511	0.803-2.840	1.28	0.200	0.857	0.444-1.655	-0.46	0.646
ALT	0.994	0.984-1.004	-1.14	0.253	1.001	0.992-1.009	0.14	0.891
AST	1.008	0.997-1.019	1.37	0.172	0.998	0.985-1.011	-0.32	0.752
GGT	1.004	1.001-1.007	2.51	0.012	1.001	0.997-1.005	0.25	0.800
platelet	0.999	0.995-1.004	-0.33	0.745	0.999	0.994-1.003	-0.59	0.556
Steatosis stage								
S1 vs S0	0.926	0.094-9.114	-0.07	0.948				
S2 vs S0	0.480	0.043-5.383	-0.60	0.551	S2vs S1:0.644	0.261-1.586	-0.96	0.338
S3 vs S0	0.497	0.039-6.398	-0.54	0.592	S3vs S1:0.596	0.176-2.022	-0.83	0.407
NASH(no/MMA /SA)								
MMA-NASH vs no	1.618	0.573-4.565	0.91	0.363	2.530	0.977-6.555	1.91	0.056
SA-NASH vs no	3.229	1.433-7.278	2.83	0.005	2.329	0.958-5.659	1.87	0.062
MRI-PDFF	1.029	0.985-1.076	1.28	0.200	0.996	0.948-1.047	-0.14	0.888

Proton Density Fat Fraction (PDFF)

PDFF = Pdfat / (PDfat+PDwater)



Chemical shift



T2 vs T2 FAT SAT

Multi-echo Chemical-Shift-Encoded MR (MECSE-MR) sequences

In our patient: PDFF 40%

- High sensitivity and specificity (**Gold standard method for hepatocyte steatosis**)
- Reproducible
- Whole liver analysis
- Not time-consuming
- Expensive

Redor SB et al. J Magn Reson Imaging 2011
Idilman IS et al. Acta Radiol 2016

Highlight:

- 1. MRE has excellent diagnostic performance for the diagnosis of significant, advanced fibrosis and cirrhosis in patients with NAFLD.

- 2. We established cut-offs of 2.65kPa, 3.14kPa, 3.53kPa and 4.45kPa for any(≥F1), significant(≥F2), advanced(≥F3) fibrosis and cirrhosis, respectively.

- 3. Severe activity NASH and raised GGT level may affect diagnostic accuracy of MRE in staging early liver fibrosis.

Limitations of liver biopsy as gold standard:

a) Diagnostic criteria for steatohepatitis

NASH diagnosis	Yes	No

NAScore	Steatosis	Ballooning	Inflammation
0	< 5%	No	No
1	5%-33%	Few	<2 foci
2	33%-66%	prominent	2-4 foci
3	>66%		> 4 foci

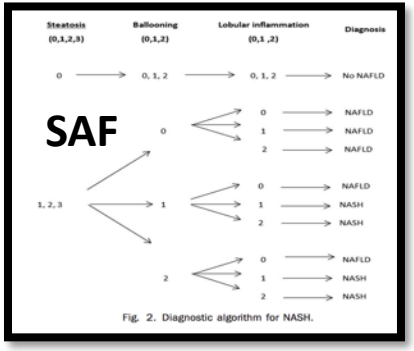


Fig. 2. Diagnostic algorithm for NASH.

b) Overlap between inflammatory activity and fibrosis stage

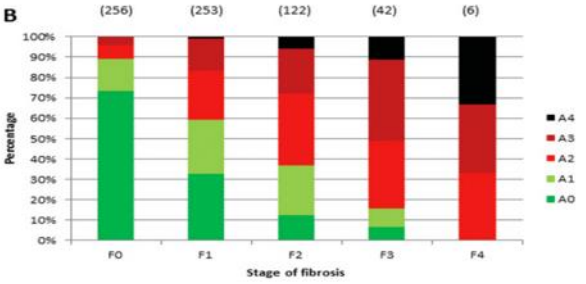
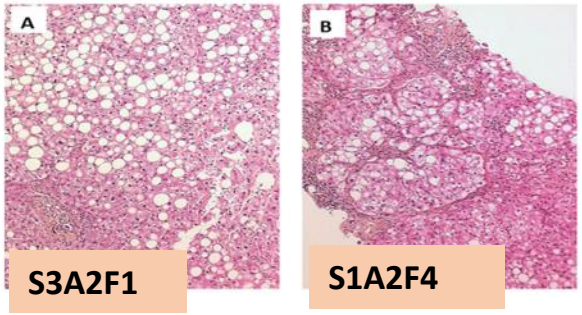


Fig. 6. (A) Correlation between activity grade and fibrosis stage. (B) Between fibrosis stage and activity grade.



Bedossa P et al. Hepatology 2012;56:1751

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Histological features in liver biopsy as gold standard:

Steatosis >> Steatohepatitis >> Fibrosis

c) Sampling variability[1]

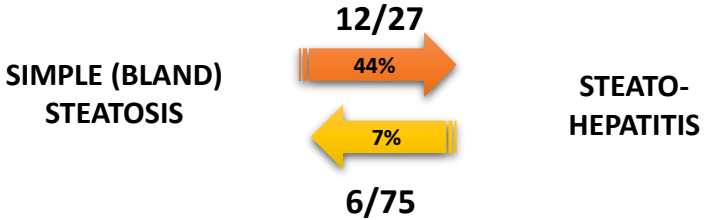
Diagnostic accuracy of 2nd biopsy:
NASH: 0.81 (0.65–0.90)
F3-F4: 0.87 (0.7–0.95)
Ballooning: 0.66 (0.57–0.73)

N=51 NAFLD (2 samples of liver biopsy)

NPV NASH: 74%
≥1 Fibrosis stage: 41%
Bridging fibrosis in just 1 biopsy 35%

d) Progression over time[2]

Evidence of NAFLD progression from steatosis to fibrosing-steatohepatitis…
N=108 mean follow-up 6.6 years



1. *Ratziu V, et al. Gastroenterology 2005;128:1898*
2. *McPherson S, et al. J Hepatol 2015;62:1148*

Clinical end-points:

Liver-related outcomes: Fibrosis progression to cirrhosis >> Cirrhosis decompensation >> Liver cancer

Extrahepatic outcomes: CV events >> extrahepatic neoplasms

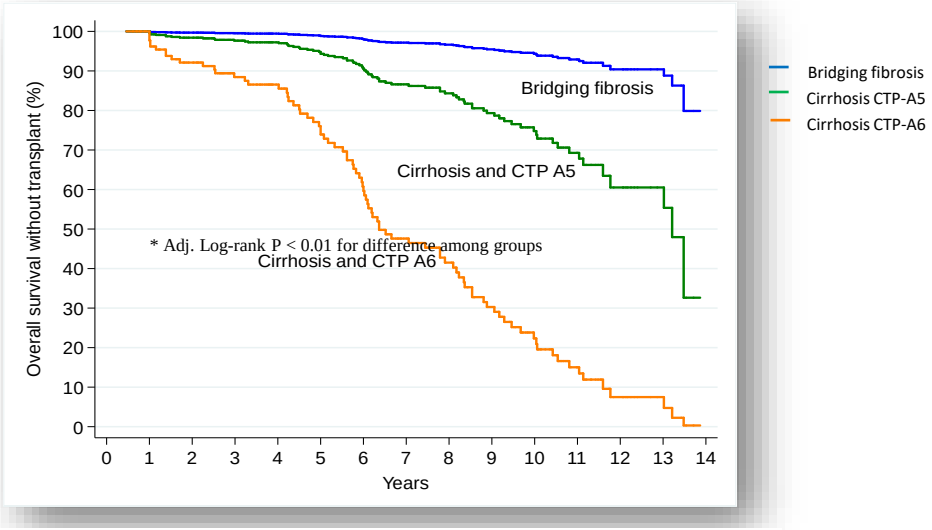
Survival

The Long-Term Clinical Course of Histologically Advanced NAFLD. Impact of Fibrosis Severity on Major Clinical Outcomes.

N=458

Transplant-Free Survival

Stratified analysis by fibrosis and CTP classes



(Adjusted analysis by center, race/ethnicity, age and gender*)

Vilar-Gómez et al. Gastroenterology 2018

Clinical case

Female 58 yo old with metabolic syndrome & steatosis

Patient attended out patient office at primary care due to hyperecogenicity of the liver in abdominal ultrasound.

Personal history

- No drug allergies.
- Never smoked.
- No alcohol consumption.
- Menopause at 47 years old.
- Arterial hypertension.

Family history

- Father died due to lung cancer.
- Mother alive at 76 years old suffering from type 2 diabetes.
- Two brothers with arterial hypertension.
- No cardiovascular events in the family.

Physical exploration

Systolic arterial pressure: 150 mmHg; **Diastolic arterial pression: 85 mmHg;** Weight: 83 kg; Height: 166 cms; **Body mass index: 30.6 kg/m2 (Obesity degree 1);** **a**cantosis nigricans. Waist perimeter: 100 cms; Abdomen and cardiorespiratory exploration without alterations.

Blood test

Biochemistry	**Glucose 116 mg/dL Urea 48 mg/dL Creatinine 0,76 mg/dL ; Uric acid 5,4 mg/dL; Lipids: Total Cholesterol: 226 mg/dL; HDL: 34 mg/dL; LDL: 146 mg/dL; Triglycerides: 194 mg/dL; LFT: Total bilirubin 1.31 mg/dL; AST: 35 U/L; ALT: 32 U/L; GGT: 77 U/L; AP: 110 U/L; LDH 207 U/L, total proteins: 7.2 g/dL; Albumin: 4.6 g/dL; Iron metabolism: Iron in blood: 118 µg/dL; TSI: 31 %; ferritin: 507 ng/mL**
Coagulation	**Haemoglobin: 15 g/dL, Platelets: 195 x 10^9/L; INR: 1.03**
Autoimmunity	**Immunoglobulins A, M and G normal; ANA, AMA, SMA, antiLKM, antiTGA: negatives**
Virus	**Hepatitis B, C, E negatives**
Metabolic	**Baseline Insulin: 48.3 µU/mL; HOMA: 13,8; HbA1c 6.5 %; Ceruloplasmine: 31 mg/dl; TSH 6.37 µUI/ml, T4-L 1.06 ng/dl; A1AT: 145 mg/dl**

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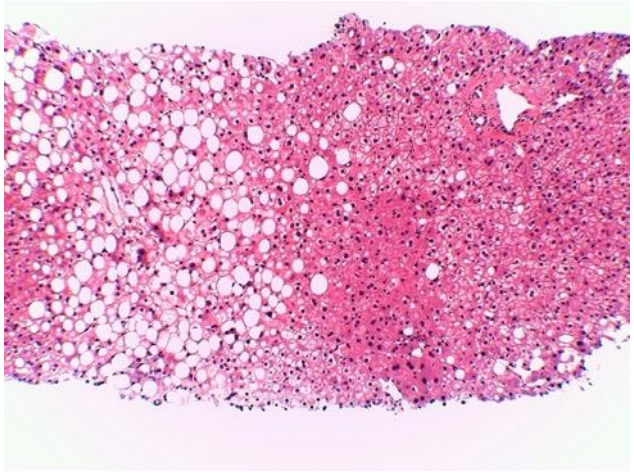
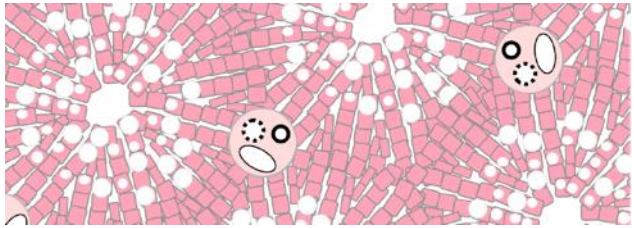
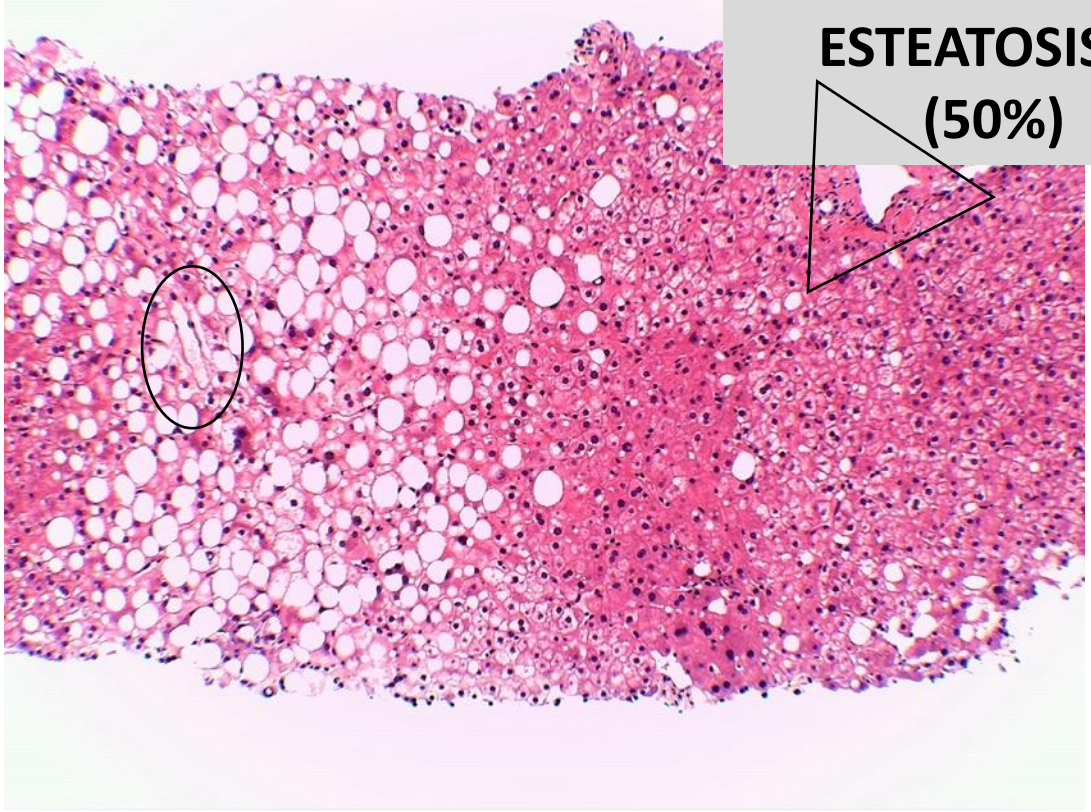
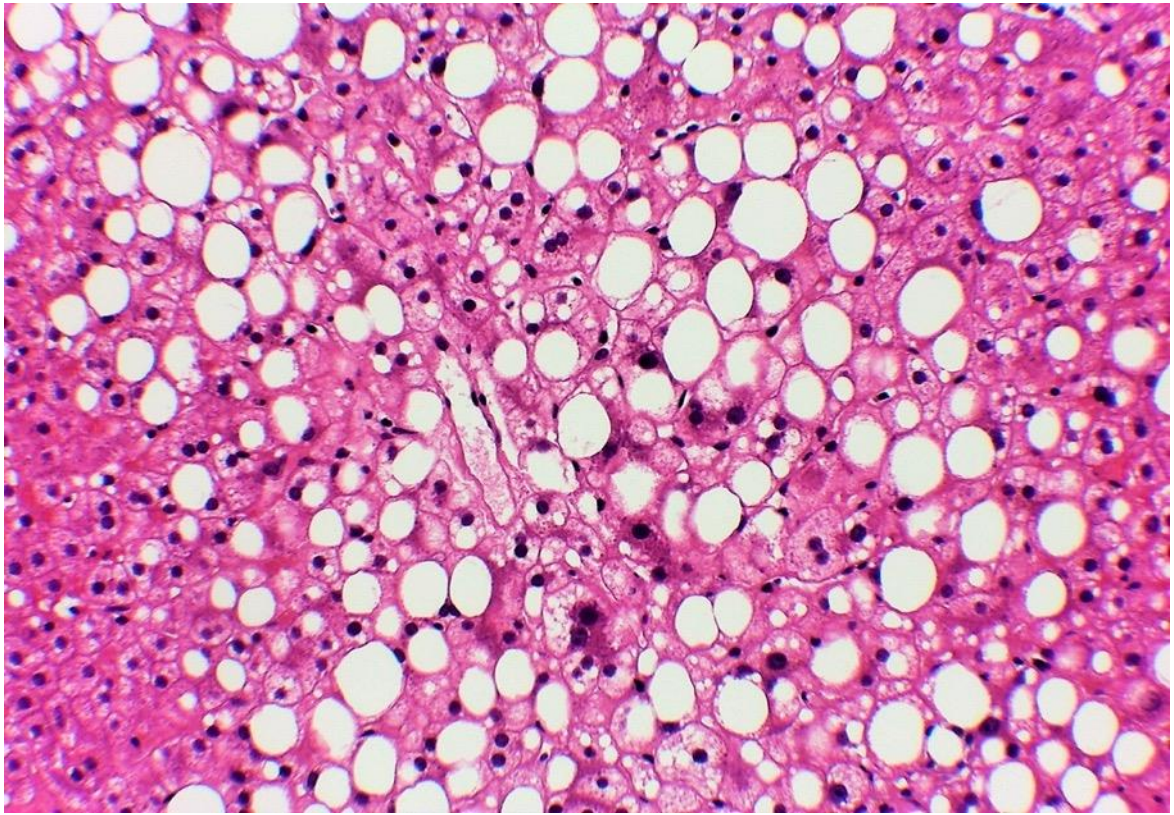
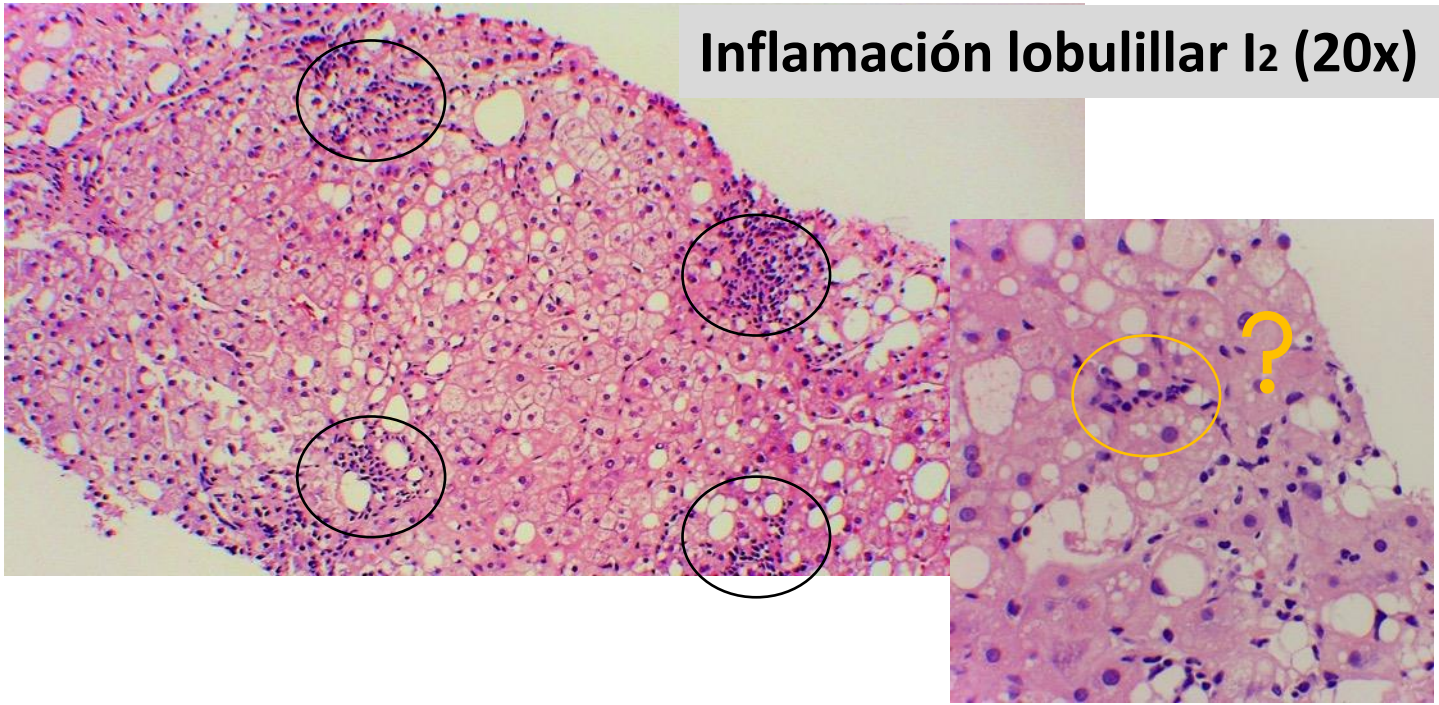




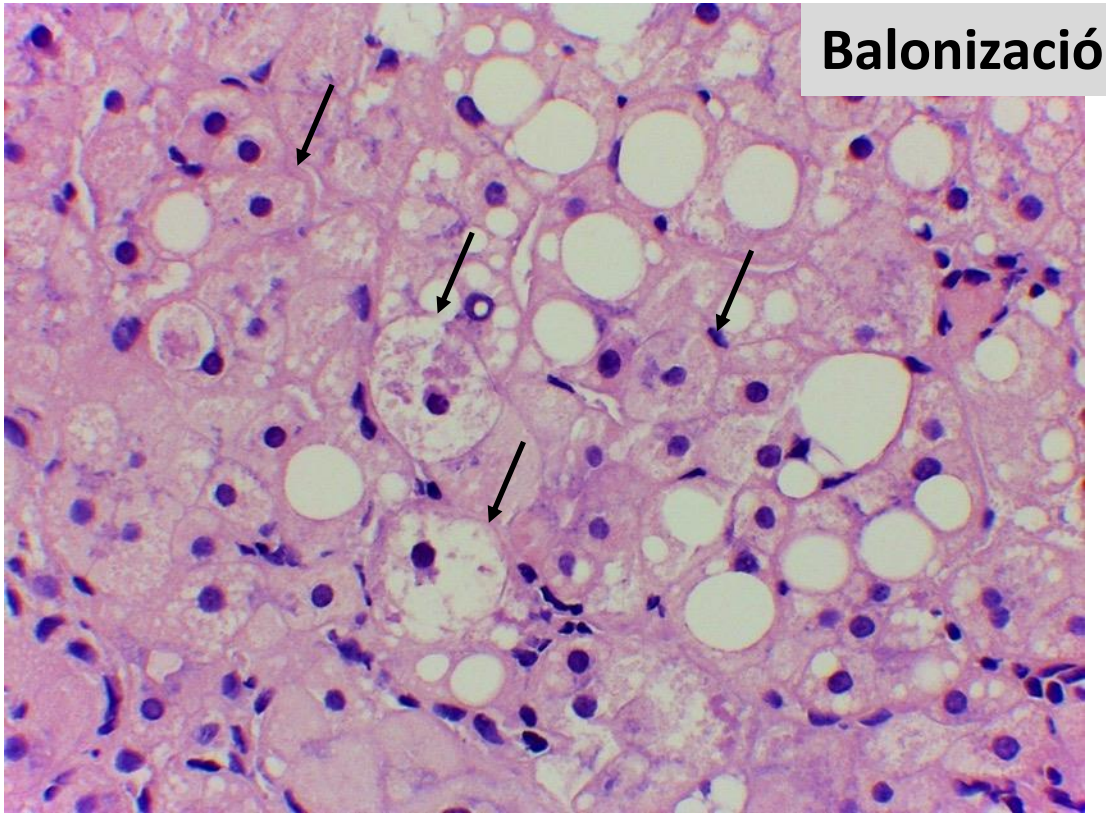

ESTEATOSIS S2
(50%)



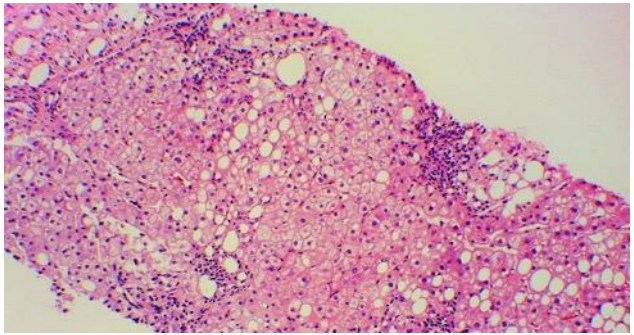
Inflamación lobulillar I_2 (20x)

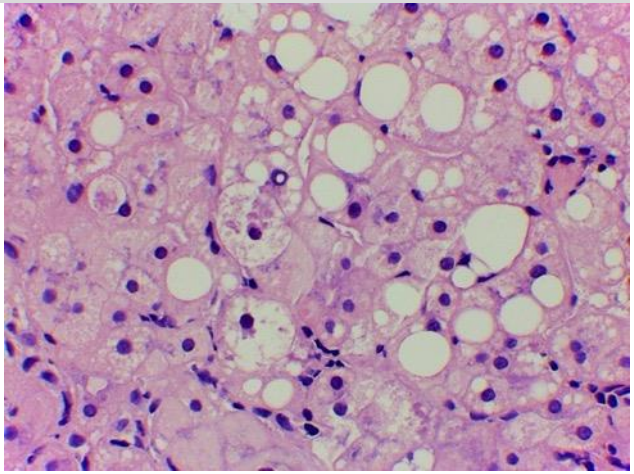


Balonización B2

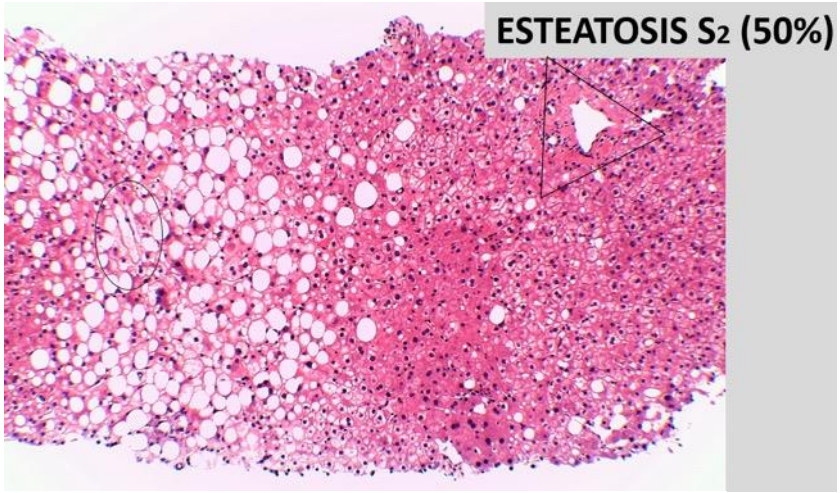


Inflamación lobulillar (20x) I_2 + Balonización B_2= A_4

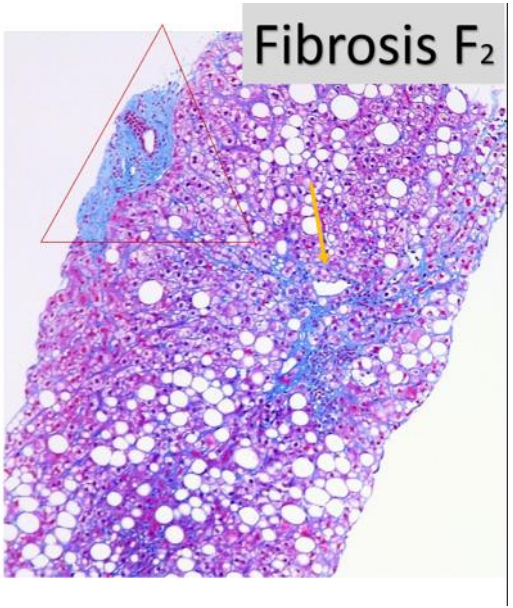




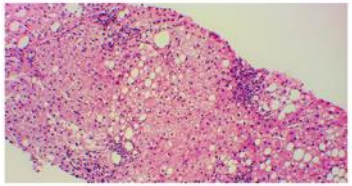
ESTEATOSIS S_2 (50%)

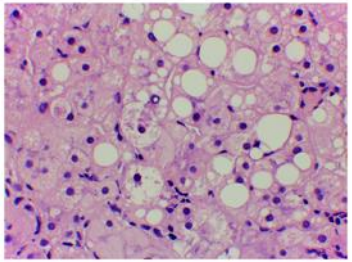


Fibrosis F_2



Inflamación lobulillar (20x) I_2 + Balonización B_2= A_4





$S_2A_4F_2$

Take home messages

Hepamet Fibrosis score is superior to other fNITs in screening NAFLD-Fibrosis in primary care.
Ultrasonography could detect steatosis when higher than 12.5% if using 5 US criteria.
Imaging biomarkers (transient elastography and shear-wave) plus MRI techniques allow assessment of liver damage in NAFLD with high diagnostic accuracy:

1. **Transient Elastography should add metabolic status of the liver to the interpretation of stiffness (HFS+FS).**
2. **MR Elastography** correctly classify across fibrosis stages
3. **Proton-Density Fat Fraction** accurately quantify fat accumulation in the liver
4. **Liver-multiscan** could predict liver injury combining inflammation and fibrosis
5. **DeMILI** showed the best diagnostic accuracy for NASH

"tunnel of MRI-based NASH & Fibrosis diagnosis"
PDFF >> MRI (LMS + DeMILI) >> MRE

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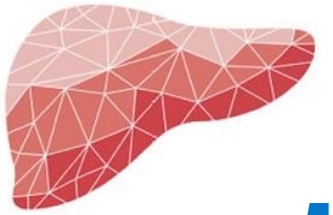
@sapdes
@AEEH_Liver
@SEPDigestivas

Prof. Manuel Romero-Gómez
Virgen del Rocio University Hospital. Institute of Biomedicine of Seville. University of Seville.



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