Biomarcadores en NASH
¿Cuáles son de aplicación en la práctica clínica diaria?

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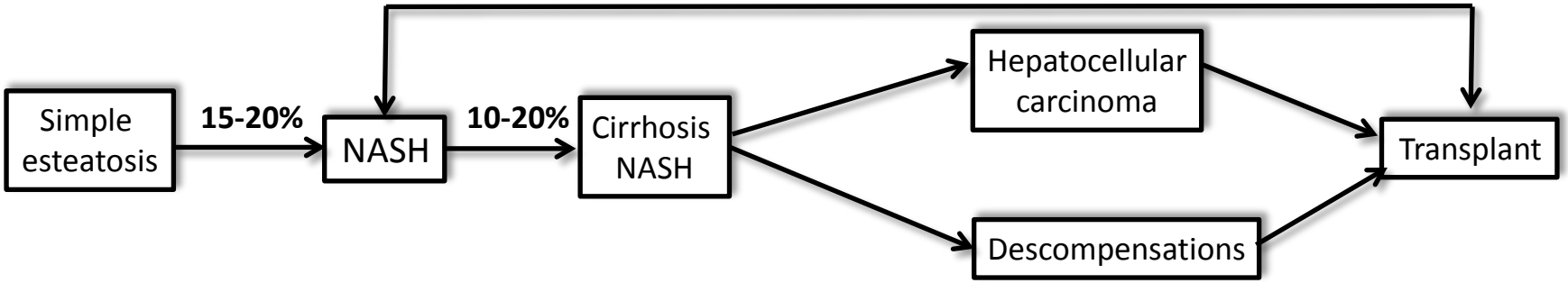
SeLiver Group-Instituto de Biomedicina de Sevilla (IBiS)
Hospital Universitario Virgen del Rocío

Background **NAFLD spectrum**



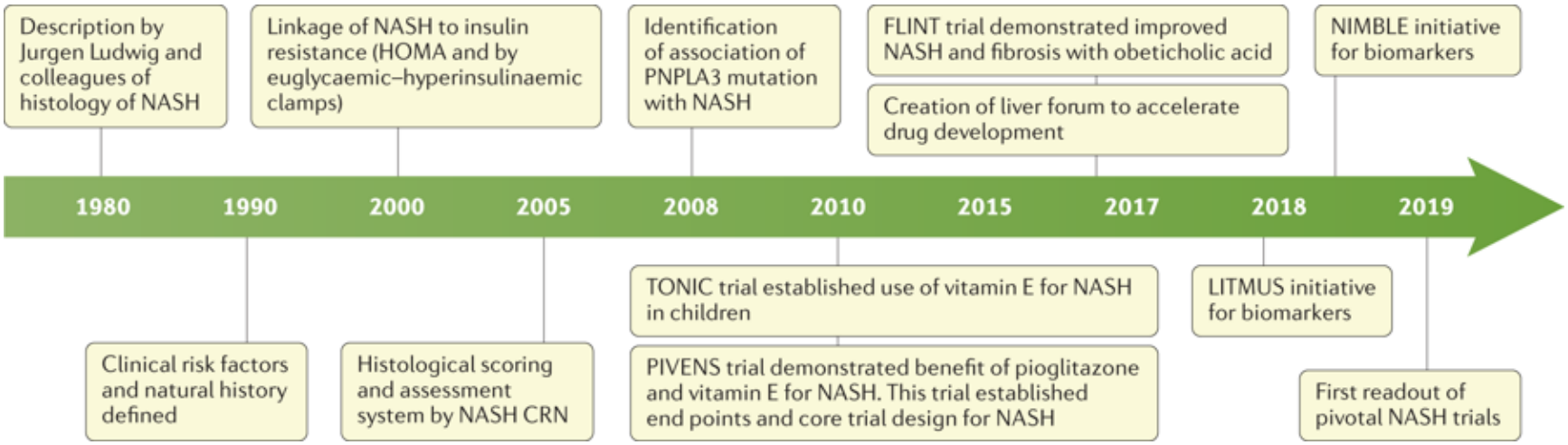
NAFLD patients have an increased risk of mortality, related to both liver and cardiovascular diseases, with hepatic fibrosis being the best predictor of mortality.

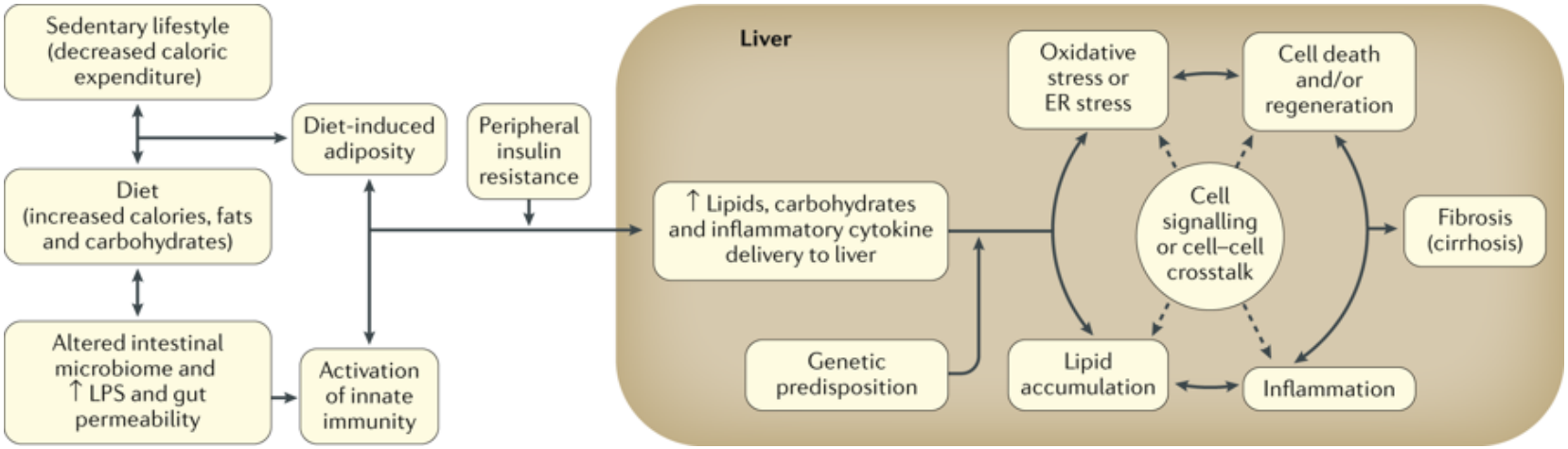
NASH is currently the second leading cause of liver transplant worldwide, and the number of receptors has tripled since 2004.

Metabolic status has been recently proven to impact further on NASH development, as well as on significant fibrosis, renal disfunction and atherogenic profile than obesity *per se*.

Wong et al, Gastroenterology 2015 Ekstedt et al, Hepatology 2015 Ampuero et al, AP&T 2018

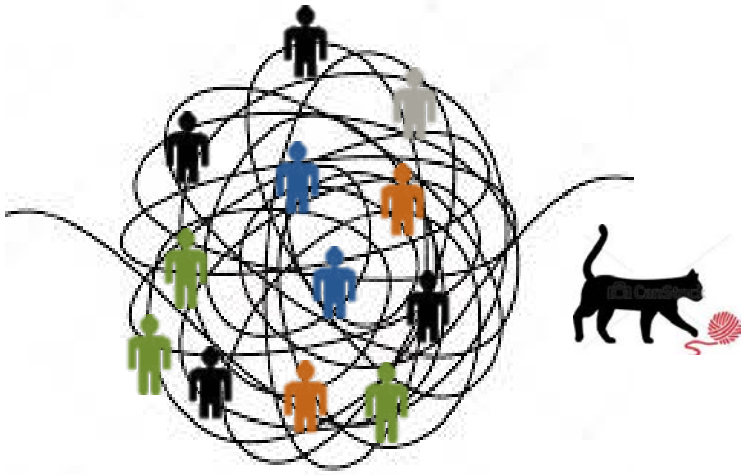
Background NAFLD history evolution





Sanyal et al, Nat Rev in Gastroenterol & Hepatol 2019

Background Phenotype definition



Healthy

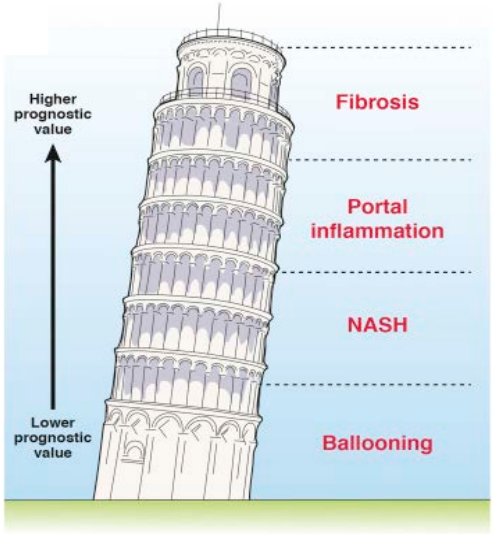
Simple steatosis

NASH w/o liver fibrosis

Advanced fibrosis/cirrhosis

Liver disease unrelated to NAFLD

Disease heterogeneity = No NASH phenotype definition



Reflection of underlying disease pathways

- Hepatocellular apoptosis
- Inflammation
- Oxidative stress
- Abnormal adipokine signalling

Loomba, Gastroenterology 2015

Background Liver biopsy assessment

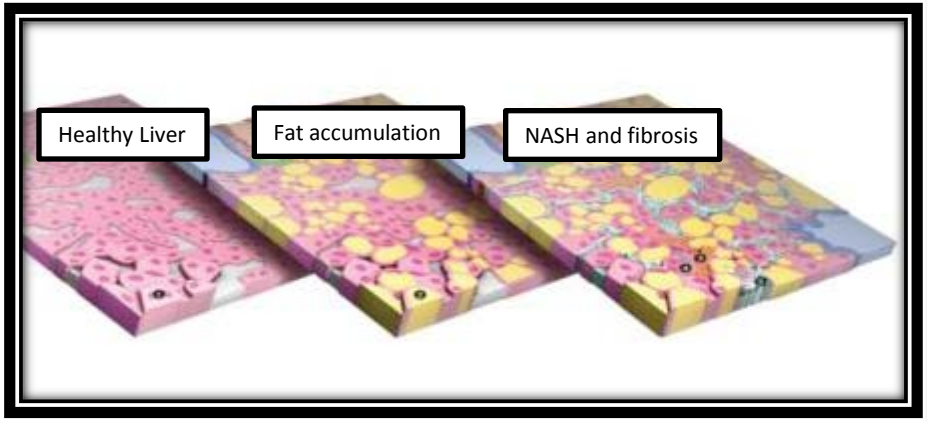
ADVANTAGES

- Validated scores
- Widespread

DRAWBACKS

- Discomfort
- Cost
- Sample variability
- Morbi-mortality

- Diagnostic criteria for NASH
- Overlap between inflammation & fibrosis
- Stabilisation over time



Leslie, Science 2015

Background CPG recommendations

Clinical Practice Guidelines

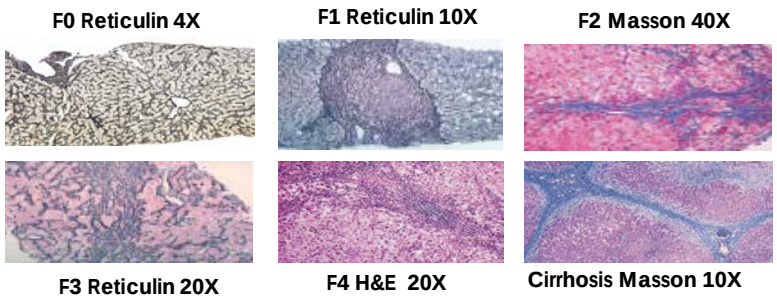
CrossMark

EASL 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)

- Primary care settings: To identify the risk of NAFLD among individuals with increased metabolic risk
- Secondary and tertiary care settings:
  - To identify those with worse prognosis
  - To monitor disease progression
  - To predict response to therapeutic intervention



EASL Clinical Practice Guidelines, J Hepatol 2016

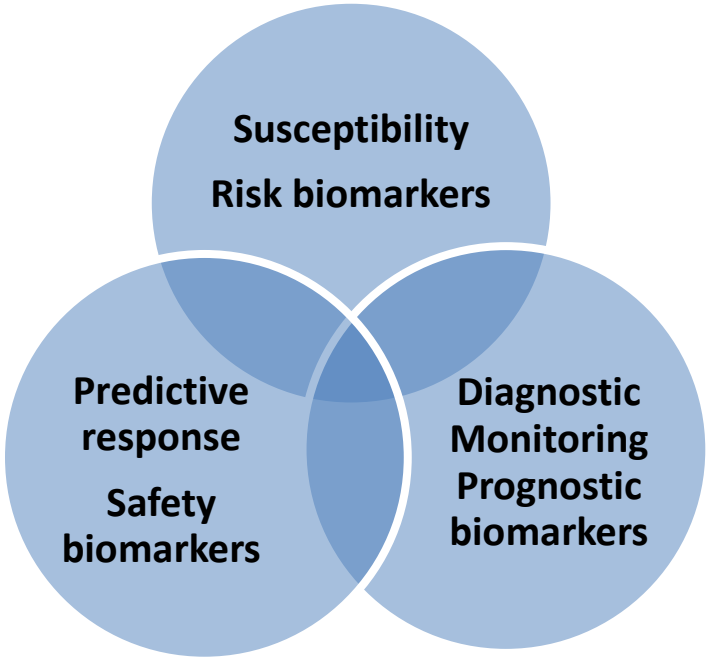
Background **Biomarker definition**

✓ **Biological characteristic that can be objectively measured and evaluated as an indicator of pathogenic processes from susceptibility to disease and therapeutic response.**

SURROGATE ENDPOINTS

TO BE CONSIDERED [A to F]:

- Availability and acceptability
- Bias of process
- Cost
- Diagnostic accuracy
- Errors of measurement
- Feasibility



U.S. Food and Drug Administration
Protecting and Promoting Your Health

Food and Drug Administration (FDA) 2017

Non-invasive diagnosis of NAFLD

Simple steatosis

Blood biomarkers & Panels

- HSI
- FLI
- Steatotest
- NAFLD Liver Fat Score

Imaging Biomarkers

- Ultrasound
- CAP
- MRI-PDFF
- MRS

NASH

Blood biomarkers & Panels

- Apoptosis & Inflammatory
- Cytokines & Hormones
- NASHTest
- OWLiver

Imaging Biomarkers

- DEMILI (NASH-MRI)

Fibrosis

Blood biomarkers & Panels

- NFS
- FIB-4
- HFS

Imaging Biomarkers

- FibroScan
- MRE
- DEMILI (FibroMRI)

Simple steatosis **Imaging biomarkers**

Test	Description	Accuracy	Reproducibility	Feasibility	Limitations
Ultrasonography	Echogenicity or brightness of the tissue depends on the degree of scattering	0.93	Kappa ranging from 0.54 to 0.92 for intraop & 0.44-1.00 for interop reliability	Easy, no radiation, widely available, low cost	Low sensitivity for mild steatosis, operat-dependent & reduction in Se-Sp when obese or advanced fibrosis
Controlled Attenuation Parameter (CAP)	Degree of US attenuation by hepatic fat using a simultaneous TE	0.82 for any steatosis, increases with steatosis degree	Concordance correlation coefficient 0.82	Inmediate assessment of steatosis, ambulatory clinic assessment, simultaneous liver stiffness, failure rate<10%	Lower reliability when differentiating between steatosis grades.
MRI-PDFF	Should be added to MRI scanners to quantitatively assess steatosis	0.99 to diagnose any steatosis	ICC>0.90	Not affected by obesity, simultaneous MRI for liver architecture & HCC	Cost, time-consuming, requires MRI equipment, inaccurate when acute inflammation or iron overload
MRS	Evaluates liver triglyceride content, requires a proper acquisition technique	0.89	ICC>99%	Absolute liver fat can be measured & 0.5% fat is detected	Complex analysis, time-consuming, sampling error

Karlas et al, J Hepatol 2017 Park et al, Gastroenterol 2017 EASL –ALEH CPG, J Hepatol 2015 Hernaez et al, Hepatology 2011

Simple steatosis **Imaging biomarkers**

HEPATOLOGY AASLD

Original Article | Full Access

Unexpected Rapid Increase in the Burden of Nonalcoholic Fatty Liver Disease in China From 2008 to 2018: A Systematic Review and Meta-Analysis

Feng Zhou, Jianghua Zhou, Wenxin Wang, Xiao-Jing Zhang, Yan-Xiao Ji, Peng Zhang, Zhi-Gang She, Lihua Zhu, Jingjing Cai, Hongliang Li

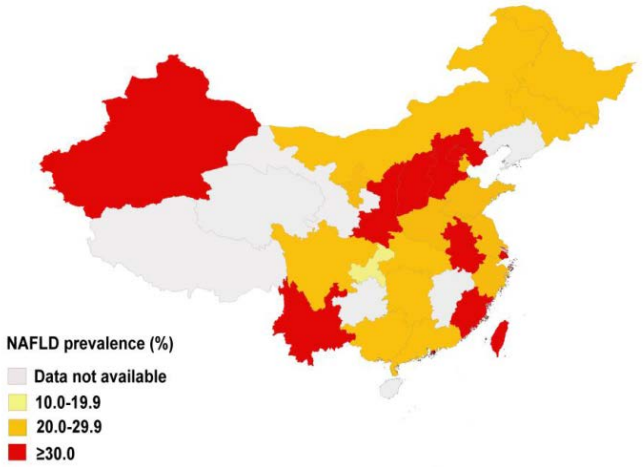
First published: 09 May 2019 | https://doi.org/10.1002/hep.30702

Diagnostic Approach	Capability of Diagnosis	Number of Studies	Total Sample Size	Proportion in the Included Studies
Fatty liver index	Steatosis	1	2,054	0.26%
Ultrasound	Steatosis	355	2,041,444	90.56%
MRI/MRS	Steatosis	10	5,288	2.55%
CT	Steatosis	4	1,251	1.02%
FibroScan	Steatosis	1	836	0.26%
Biopsy	Steatosis	7	2,001	1.79%
	NASH	10	1,054	2.60%
	Fibrosis	4	626	1.02%
Total	-	392	2,054,554	100%

- 392 studies
- 2.054.554 patients included
- Assessment:
  - Epidemiology
  - Risk factors
  - Complications
  - Management

KEY FINDINGS

- National prevalence 29.2%
- Disease burden: middle-aged, males, GDP>100,000 yuan, Northwest China
- US primary imaging tool



Zhou et al, Hepatology 2019, in press

Simple steatosis **Imaging biomarkers**

Gastroenterology 2019;156:1717–1730

Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease

Peter J. Eddowes,[1,2,3,4] Magali Sasso,[5] Michael Allison,[6] Emmanouil Tsochatzis,[7] Quentin M. Anstee,[8] David Sheridan,[9] Indra N. Guha,[4] Jeremy F. Cobbold,[10] Jonathan J. Deeks,[11] Valérie Paradis,[12] Pierre Bedossa,[12] and Philip N. Newsome[1,2,3]

KEY FINDINGS

- CAP & TE by FibroScan are reliable biomarkers to non-invasively assess liver steatosis & fibrosis in NAFLD

> Underwent liver biopsy within 2 weeks of FibroScan
(M or XL probe according to the automatic probe recommendation tool)

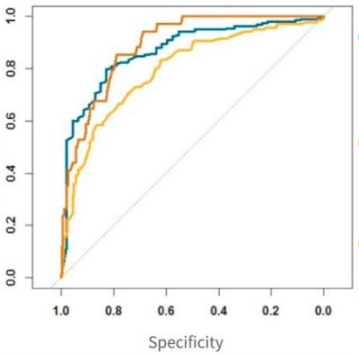
Steatosis

Fibrosis

CAP (dB/m)

LSM (kPa)

> Results and conclusions



CAP for steatosis (S≥1):
> AUC = 0.87 (0.82-0.92)

LSM for advanced fibrosis (F≥3):
> AUC = 0.80 (0.75-0.84)

LSM for cirrhosis (F=4):
> AUC = 0.89 (0.84-0.93)

> Steatosis or probe type had no impact on LSM (multivariable analysis)

Eddowes et al, Gastroenterology 2019

Simple steatosis **Blood biomarkers & panels**

Test	Description	Accuracy	Reproducibility	Feasibility	Limitations
Fatty Liver Index (FLI)	BMI, WC, Tryglicerides & GGT	0.84	Not tested yet	High	Suboptimal gold standard (US). Steatosis grades.
Hepatic Steatosis Index (HSI)	AST:ALT ratio, BMI, female sex & DM2	0.81	Reproducible	High	Suboptimal gold standard (US). Steatosis grades.
NAFLD Liver fat score	MetS, DM2, insulin, AST:ALT ratio	0.86	Reproducible	Intermediate	Fasting insulin.
SteatoTest	FibroTest + BMI, Cholesterol, tryglicerides & glucose	0.80	Reproducible	Intermediate (formula)	High cost

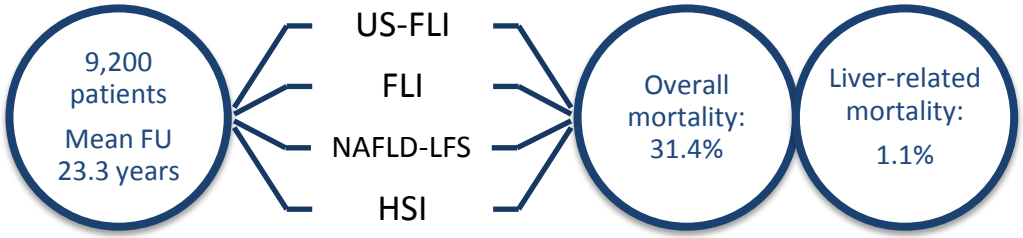
Lee et al, Dig Liver Dis 2010 Kotronen et al, Gastroenterol 2009 Poynard et al, Comp Hepatol 2005 Bedogni et al, BMC Gastroenterol 2006

Simple steatosis **Blood biomarkers & panels**

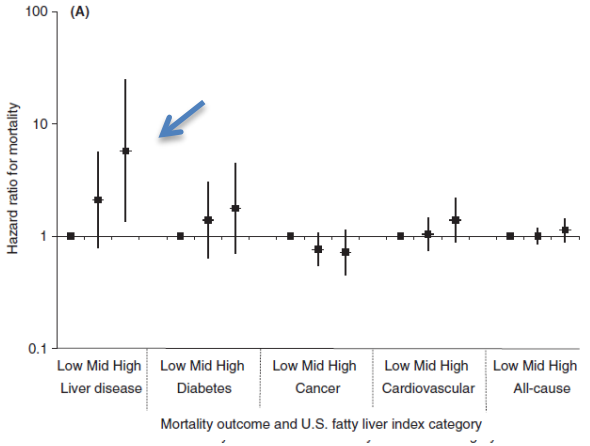
WILEY AP&T Alimentary Pharmacology & Therapeutics

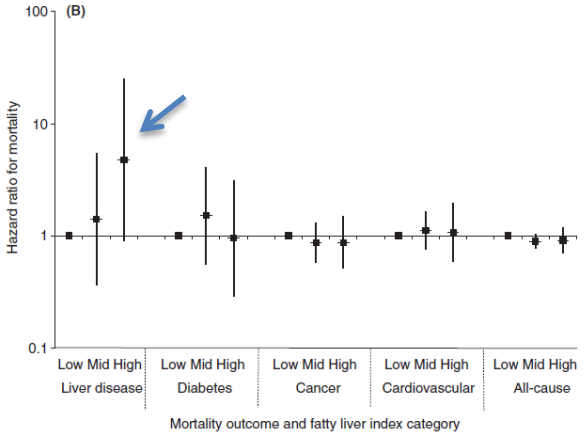
Liver fat scores predict liver disease mortality in the United States population

Aynur Unalp-Arida[1] | Constance E. Ruhl[2]



Score Characteristic	Fat probability Low	Intermediate	High
US fatty liver index			
Cut-points	<10	10-<30	≥30
Number	2548	2613	1769
Per cent	42.8	36.8	20.4
Median (inter-quartile range)	5.3 (3.5, 7.3)	17.2 (13.0, 22.1)	44.9 (36.9, 60.6)
Fatty liver index			
Cut-points	<30	30 to <60	≥60
Number	2796	1649	2483
Per cent	45.7	23.4	30.9
Median (inter-quartile range)	10.4 (5.1, 18.3)	44.0 (36.8, 52.3)	83.4 (71.5, 92.7)
NAFLD liver fat score			
Cut-points	≤−1.41	>−1.41 to <1.26	≥1.26
Number	5254	2891	845
Per cent	63.7	28.9	7.4
Median (inter-quartile range)	−2.5 (−2.9, −2.0)	−0.5 (−1.0, 0.2)	2.4 (1.7, 3.7)
Hepatic steatosis index			
Cut-points	<30	30-36	>36
Number	2495	3376	3352
Per cent	29.8	37.5	32.7
Median (inter-quartile range)	27.7 (26.2, 28.8)	32.7 (31.4, 34.3)	40.4 (37.9, 44.2)





KEY FINDINGS

- Elevated liver disease mortality associated with high US-FLI or intermediate or high NAFLD-LFS
- Overall and CVD not associated with high fat scores

Unalp-Arida, AP&T 2018

Non-invasive diagnosis of NAFLD

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- HFS

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NASH Blood biomarkers & panels

Blood biomarkers & panels	Candidates	Advantages	Disadvantages
Apoptosis markers	CK18 fragments	CK18 is the most well-validated blood biomarker. Commercially available	Uncertain optimal cut-offs
Inflammatory markers	CRP, TNF, IL-8, CXCL10	Correlation with inflammatory activity in NASH. Commercially available.	Not validated, might be influenced by systemic inflammation.
Adipocytokines & hormones	Adiponectin, leptin, resistin, visfatin, FGF21	Coomercially available. FGF21 dynamic to changes in NAFLD over time.	Limited accuracy in isolation, mostly validated in bariatric populations.
Combined panels	NASHTest	Reliable, moderate to high degree of accuracy, commercially available	High cost Dynamic changes not evaluated yet
OWLiver	Serum metabolites analysed by	High diagnostic accuracy in both estimation & validation sets	Cost

Adapted from Wong et al, Nature Rev in Gastroenterol & Hepatol

NASH Blood biomarkers & panels

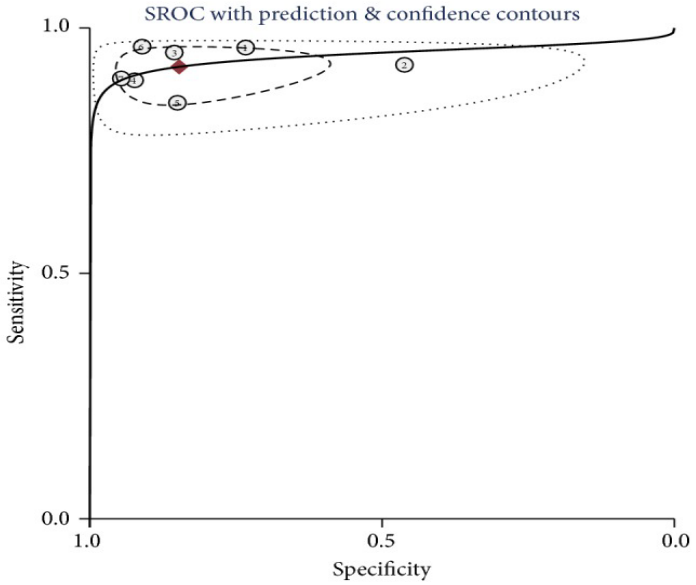
Review Article

Diagnostic Value of CK-18, FGF-21, and Related Biomarker Panel in Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis

Lei He,[1] Linfeng Deng,[1] Quan Zhang,[2] Jianli Guo,[3] Jinan Zhou,[1] Wenjian Song,[4] and Fahu Yuan[4]

- 25 studies
- All of them included at least CK18 (M30 or M65) & FGF21 plus other biomarkers (resistin, adiponectin)

Biomarker	Pooled Se	Pooled Sp
CK-18 M30	0.75	0.77
CK-18 M65	0.71	0.77
FGF21	0.62	0.78
CBP	0.92	0.85



AUROC 0.94 (CI95% 0.92-0.96)

KEY FINDINGS

- CK-18 & FGF-21 are associated with NASH but are not enough for the proper diagnosis
- The combination might be used as an accurate diagnostic tool

He et al, Biomed Res Int 2017

NASH Imaging biomarkers

Method	Steatosis	NASH	Fibrosis	Aspects
Abdominal Ultrasound	✔	✗	✗	+ First-line screening - Detects >30% fat
Computed Tomography	✔	✗	✗	- Radiation - Detects >30% fat
Magnetic Resonance	✔ [PDFF]	✗	✔	+ Validated & reliable - Cost
MR Elastography	✔	✗	✔	+ Diagnostic accuracy - Stratification
MR Spectroscopy	✔	✗	✔	- Availability - Stratification
Transient elastography	✔ [CAP]	✗	✔	+ Diagnostic accuracy - BIAS, i.e. obesity
ARFI	✗	✗	✔	- Narrow ranges of stratification

Park et al, Gastroenterol 2017 Saadeh et al, Gastroenterology 2002 Dulai et al, J Hepatol 2016 Schwenzer et al J Hepatol 2009

Non-invasive diagnosis of NAFLD

Simple steatosis

Blood biomarkers & Panels

- HSI
- FLI
- Steatotest
- NAFLD Liver Fat Score

Imaging Biomarkers

- Ultrasound
- CAP
- MRI-PDFF
- MRS

NASH

Blood biomarkers & Panels

- Apoptosis & Inflammatory
- Cytokines & Hormones
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- OWLiver

Imaging Biomarkers

- DEMILI (NASH-MRI)

Fibrosis

Blood biomarkers & Panels

- NFS
- FIB-4
- HFS

Imaging Biomarkers

- FibroScan
- MRE
- DEMILI (FibroMRI)

Fibrosis Blood biomarkers & panels

Test	Description	Accuracy	Reproducibility	Feasibility	Limitations
FIB-4 index	Age, AST, ALT, platelet count	AUROC 0.80 for F3 fibrosis	Not tested	High	None
NAFLD fibrosis score	Age, BMI, fasting glucose and/or DM2, AST, ALT, platelet count, albumin	AUROC 0.75-0.82 for F3 fibrosis	Not tested	High	Interpretation of BMI might differ across ehtnic groups
BARD score	AST, ALT, BMI, DM2	AUROC 0.69-0.81 for F3 fibrosis	Not tested	High	Interpretation of BMI might differ across ehtnic groups
FibroTest	GGT, Bilirubin, alpha2m, apolipoproteinA1 & haptoglobin	AUROC 0.88	Good	Useful in patients with chronic liver disease, accurate when obesity or overweight	Suboptimal for early-stage fibrosis; cost
FibroMeter NAFLD	Body weight, prothrombin index, AST, ALT, ferritin & fasting glucose	AUROC 0.76 for F2 6 0.77 for F3	Good	Accurate for severe fibrosis in different liver diseases	Cost
HEPAmet Fibrosis Score	Sex, age, DM2-HOMA, AST, Albumin, Platelets	AUROC 0.76-0.90	Good	High	None

Sterling et al, Hepatology 2006 Angulo et al, Hepatology 2007 Harrison et al, Gut 2008 nbert-Birmut et al, Lancet 2001 Boursier et al, J Hepatol 2017

Fibrosis Blood biomarkers & panels

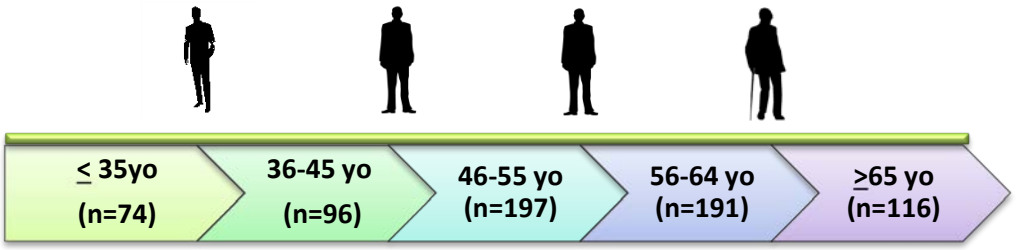
Open

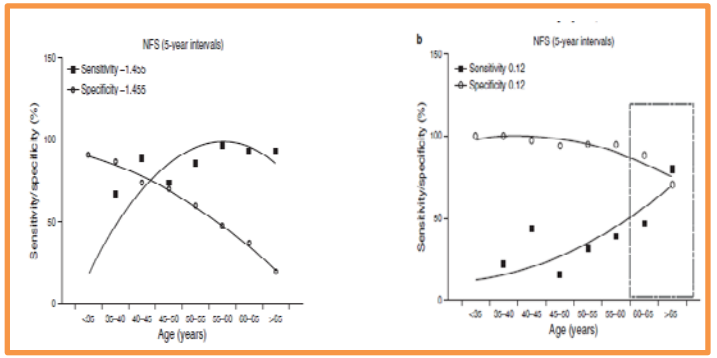
see related editorial on page 752

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]

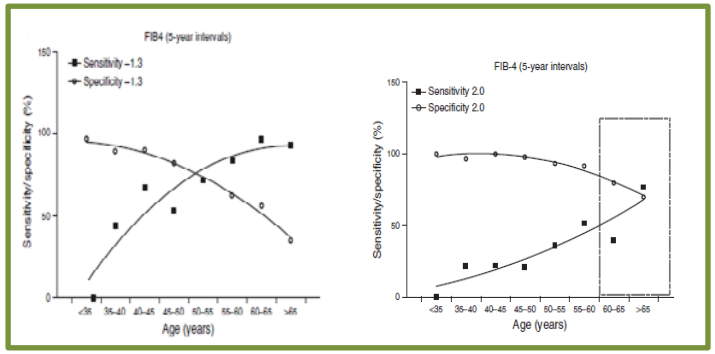
- N=640 patients
- Patients divided into 5 age-based groups
- AST/ALT ratio, FIB-4 & NFS were evaluated





KEY FINDINGS

- NFS & FIB-4 have similar accuracy for advanced fibrosis in patients aged >35 yo.
- Specificity is very low in patients >65 yo.
- New thresholds are proposed for patients >65 yo



McPherson et al, Am J Gastroenterol 2017

Fibrosis Blood biomarkers & panels

Registro HEPAmet

Cohorts	Estimation	Validation		
Variables	N=758	N=288	N=344	N=444
Male sex	44.9%	62.5%	42.2%	60.1%
Age	53.9 ± 12.4	46.2 ± 13.3	51.1 ± 12.1	54.2 ± 12.3
BMI	36.4 ± 10.1	29.9 ± 5	36 ± 8.3	31.4 ± 6.5
Obesity (BMI>30)	64.9%	44%	74.7%	50.7%
Type 2 DM	27.6%	21.5%	43.6%	45.9%
HOMA	4.73 ± 4.3	4.05 ± 3	7.1 ± 9.2	4.85 ± 5
AST (IU/mL)	35 ± 26	46 ± 31	44 ± 31	46 ± 30
Triglycerides (mg/dL)	155 ± 81	146 ± 78	174 ± 97	150 ± 93
Albumin (g/dL)	4.38 ± 0.40	4.60 ± 0.39	4.26 ± 0.5	4.38 ± 0.4
Platelets (x10⁹/L)	251 ± 73	232 ± 69	223 ± 68	228 ± 63
Significant Fibrosis	22%	46.9%	35.8%	52.3%
Advanced Fibrosis	12.1%	20.8%	25.3%	27.3%
Cirrhosis	2.9%	7.3%	11.3%	6.8%

- N=1834 patients
- NFS, FIB-4 & HFS evaluated

SPAIN (n=758)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,783	0,718	0,741
AUROC F3-F4	0,867	0,775	0,772
AUROC F4	0,933	0,834	0,88

ITALY (n=288)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,778	0,711	0,698
AUROC F3-F4	0,838	0,785	0,773
AUROC F4	0,86	0,85	0,83

CUBA (n=344)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,812	0,714	0,778
AUROC F3-F4	0,872	0,768	0,84
AUROC F4	0,924	0,918	0,92

FRANCE (n=444)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,719	0,7	0,679
AUROC F3-F4	0,81	0,779	0,765
AUROC F4	0,869	0,9	0,836

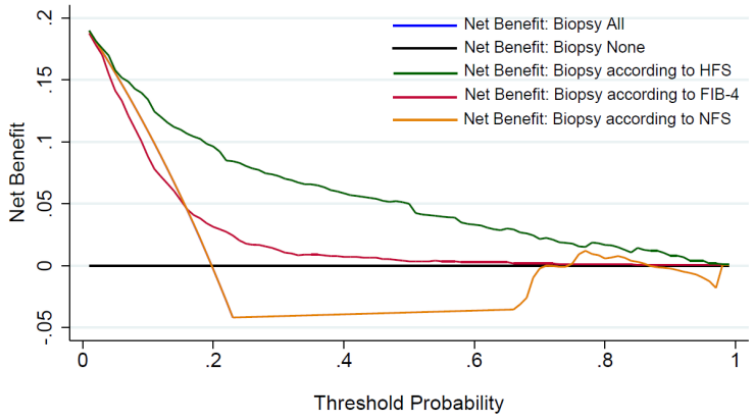
GLOBAL (n=1834)	Hepamet	NFS	FIB-4	
AUROC F2-F4	0,758	0,679	0,731	P=0.0001
AUROC F3-F4	0,847	0,767	0,797	P=0.0001
AUROC F4	0,902	0,863	0,875	P=0.0397

ESTIMATION (n=758)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,783	0,718	0,741
AUROC F3-F4	0,867	0,775	0,772
AUROC F4	0,933	0,834	0,88

VALIDATION (n=1076)	Hepamet	NFS	FIB-4
AUROC F2-F4	0,746	0,678	0,713
AUROC F3-F4	0,835	0,773	0,796
AUROC F4	0,888	0,875	0,863

KEY FINDINGS

- HFS improves the classification of liver fibrosis in NAFLD
- HFS decreases % of patients in the grey zone
- HFS does not require any age-adjusted cut-offs



Ampuero et al, manuscript submitted

Fibrosis Imaging biomarkers

Test	Description	Accuracy	Reproducibility	Feasibility	Limitations
FibroScan or Transient Elastography	Mechanically induced impulse. Two probes: M & XL	AUROC 0.84-0.95 depending on fibrosis stage and probe	ICC>0.90	Fast (<10min), ambulatory clinic setting, inmediacy of results	Requires fasting & dedicated device
MRE	Modified-phase contrast method to image the propagation of the shear wave in liver parenchima.	AUROC 0.86-0.97	ICC 0.83-0.96	Implemented on a regular MRI machine. Examines the whole liver.	Requires MRI facility, time-consuming and cost.
DEMILI-MRI	Optical analysis of MRI images using clinical protocols for MRI.	AUROC 0.83 for NASH & 0.85 for significant fibrosis	Under evaluation	Non-contrast enhanced needed, time <12 min, examines the whole liver, uses MRI regular machine. Evaluates both NASH and significant fibrosis simultaneously.	Requires MRI facility. Cost.

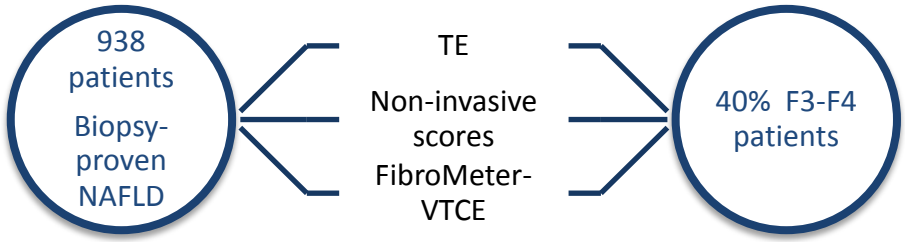
Adapted from Wong et al, Nature Rev in Gastroenterol & Hepatol

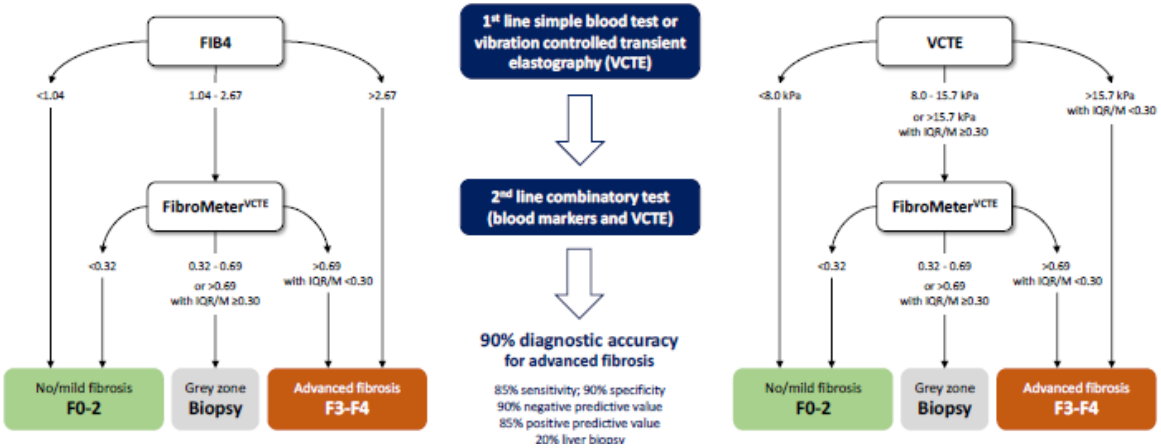
Fibrosis Imaging biomarkers

Accepted Manuscript

New sequential combinations of noninvasive fibrosis tests provide an accurate diagnosis of advanced fibrosis in NAFLD

Jérôme Boursier, Maeva Guillaume, Vincent Leroy, Marie Irlès, Marine Roux, Adrien Lannes, Juliette Foucher, Floraine Zuberbuhler, Cyrielle Delabaudière, Justine Barthelon, Sophie Michalak, Jean-Baptiste Hiriart, Jean-Marie Peron, Theophile Gerster, Brigitte Le Bail, Jeremie Riou, Gilles Hunault, Wassil Merrouche, Frederic Oberti, Laurence Pelade, Isabelle Fouchard, Christophe Bureau, Paul Calès, Victor de Ledinghen





Fibrosis Test	AUROC F≥2	AUROC F ≥3
NFS	0.71	0.72
FIB-4	0.71	0.76
FibroTest	0.70	0.74
Hepascore	0.71	0.76
FibroMeter	0.75	0.79
VCTE	0.83	0.84
FibroMeter-VCTE	0.83	0.87

KEY FINDINGS

- Sequential algorithms using FIB-4 or TE as a first-line procedure and FibroMeter-VCTE as a second-line well classifies 90% for advanced fibrosis, with a 20% of liver biopsy requirement

Boursier et al, J Hepatol 2019

Fibrosis Imaging biomarkers

SCIENTIFIC REPORTS

OPEN

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Published: 12 August 2016

Imaging biomarkers for steatohepatitis and fibrosis detection in non-alcoholic fatty liver disease

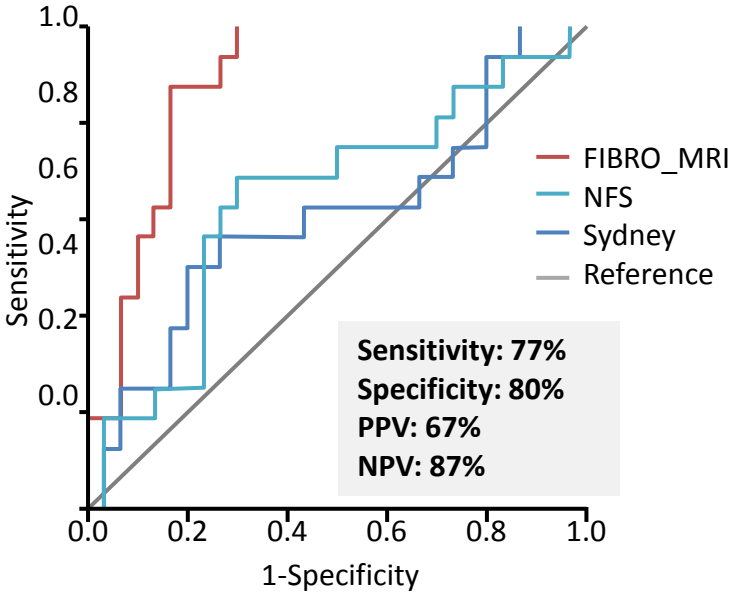
Rocío Gallego-Durán[1,2], Pablo Cerro-Salido[3], Emilio Gomez-Gonzalez[3], María Jesús Pareja[4], Javier Ampuero[1,2], María Carmen Rico[1,2], Rafael Aznar[5], Eduardo Vilar-Gomez[1,2], Elisabetta Bugianesi[6], Javier Crespo[7], Francisco José González-Sánchez[8], Reyes Aparcero[7], Inmaculada Moreno[10], Susana Soto[11], María Teresa Arias-Loste[9], Javier Abad[12], Isidora Ranchal[1,2], Raúl Jesús Andrade[10], Jose Luis Calleja[13], Miguel Pastrana[14], Oreste Lo Iacono[11] & Manuel Romero-Gómez[1,2]

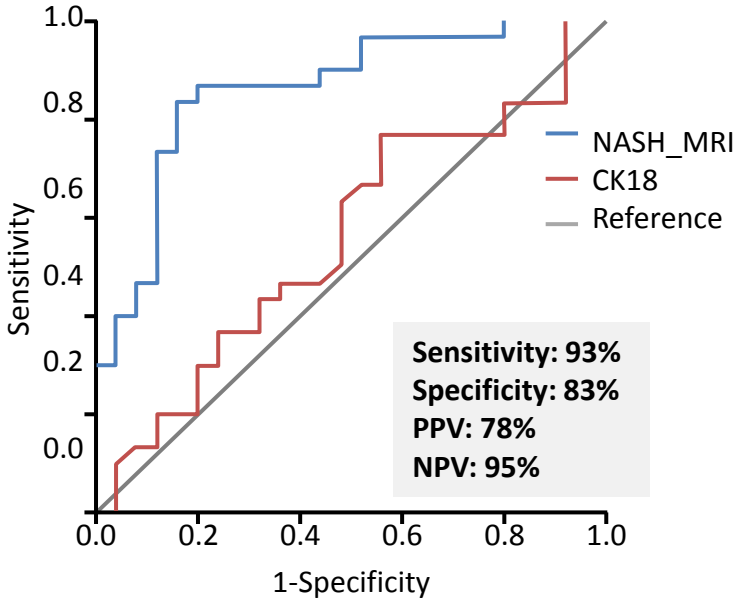
KEY FINDINGS

- DEMILI combining both NASHMRI & FibroMRI imaging biomarkers can accurately predict both NASH and significant fibrosis in NAFLD patients.

- ➢ N=126 biopsy proven NAFLD patients
- ➢ CK-18, Sydney index & NFS calculated

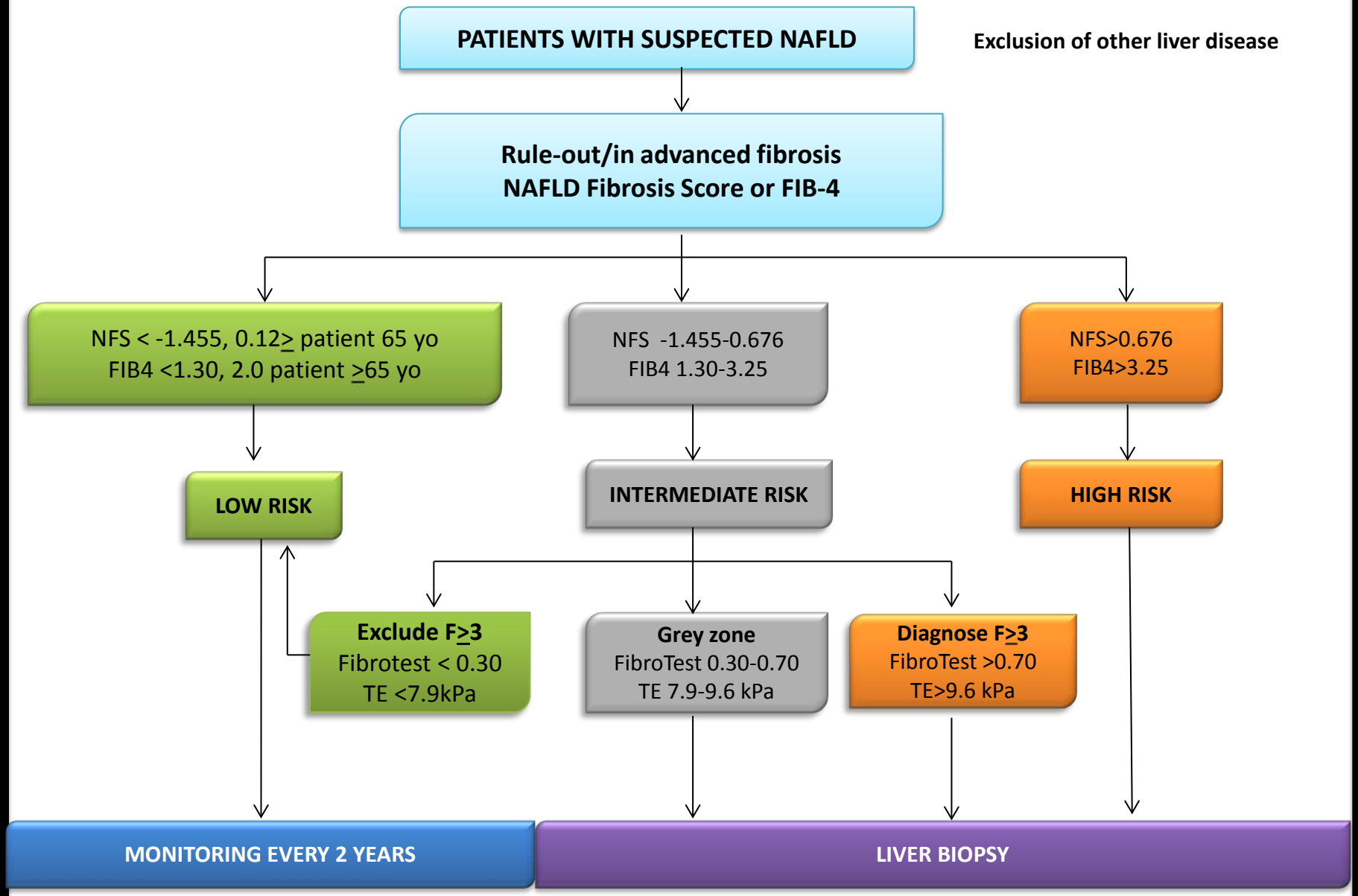
Test	AUROC
NFS	0.76
Sydney	0.69
CK-18	0.44
FibroMRI	0.85
NASHMRI	0.86





Gallego-Durán et al, Sci Rep 2016

Non-invasive algorithm



Modified from EASL CPG, J Hepatol 2016

Modified from Castera et al. Gastroenterol 2019

Take-home messages

- Use of non-invasive tests should be tailored according to the setting (primary health care, tertiary referral center, trial).
- For steatosis, ultrasound or CAP constitute the most common used methods due to their wide availability and low cost relative to others imaging methods.
- NASH biomarkers are lagged behind fibrosis or steatosis, partially due to the complex biology and dynamic activity of NASH. Future novel biomarkers are needed for NASH to select patients for clinical trials and to monitor the evolution of the disease.
- Performance of panel biomarkers are enough to rule out advanced fibrosis and can be used as a first-line screening and further combined with FibroScan.
- Novel algorithms including genetic and epigenetic biomarkers are really interesting but still need further evaluation.

¡Muchas gracias!

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AEEH ASOCIACIÓN ESPAÑOLA PARA EL ESTUDIO DEL HÍGADO