XIV CONGRESSO NAZIONALE
MILANO
29-30-31 ottobre 2025
PREVENZIONE E CURA DELLE DIPENDENZE
Traguardi raggiunti e nuove prospettive di intervento e di ricerca
Centro Congressi QUARK Hotel Milano
FeDerSerD
Federazione Italiana degli Operatori dei Dipartimenti e dei Servizi delle Dipendenze

Epatiti e comorbilità internistiche

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Epatiti e comorbilità internistiche

Comorbilità internistiche

- Coesistenza di malattie croniche con impatto reciproco
- Nei pazienti con epatite cronica:

  Rischio aumentato di malattie metaboliche, cardiovascolari, renali

  Necessità di monitoraggio multidisciplinare
- Le comorbilità influenzano la progressione della malattia epatica e la risposta terapeutica

Studio Osservazionale multicentRico sulla PREsentazione clinica della cirroSi in ItAlia nel 2024 (Studio SORPRESA)

PAZIENTI	EZIOLOGIA	NUMERO PAZIENTI (%)
215 (34.3%)	ALD	71 (33%)
	MetALD	62 (28.8%)
	MASLD	91 (42.3%)
	Virus	23 (10.7%)
	Autoimmuni	12 (5.6%)
	Altre eziologie	6 (2.8%)

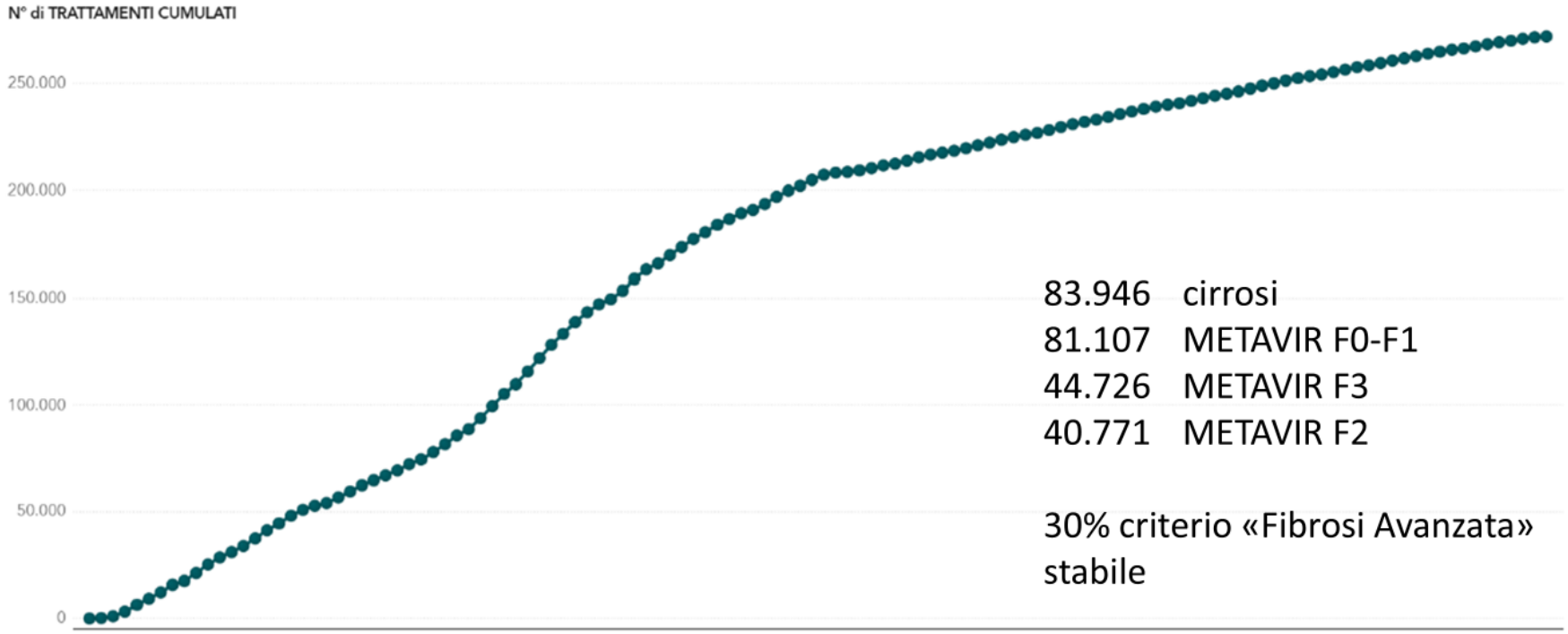
PAZIENTI	EZIOLOGIA	NUMERO PAZIENTI (%)
411 (65.7%)	ALD	94 (22.8%)
	MetALD	31 (7.5%)
	MASLD	121 (29.4%)
	Virus	121 (29.4%)
	Autoimmuni	24 (5.8%)
	Altre eziologie	20 (4.8%)

Epatiti e comorbilità internistiche

HCV

AIFA Agenzia Italiana del Farmaco

Trend cumulativo dei trattamenti avviati



83.946 cirrosi
81.107 METAVIR F0-F1
44.726 METAVIR F3
40.771 METAVIR F2

30% criterio «Fibrosi Avanzata» stabile

272.101 «avviati» sono i trattamenti (solo pazienti eleggibili) con almeno una scheda di dispensazione farmaco

31 marzo 2025 update

Epatiti e comorbilità internistiche

PATIENTS LIVING IN ITALY WITH CHRONIC HBV OR HDV IN 2024

Official Data from Local Health Authorities (including regularly residing foreign nationals)

50,040,752 adult residents in Italy on 1st January 2024

67,514 exemptions for HBV
0.13% of residents

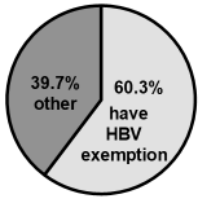
5,216 exemptions for HDV
0.010% of residents

Only individuals who are regular residents are eligible for exemption

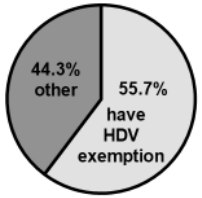
Some patients already have exemptions for other conditions and do not receive the one for HBV or HDV

Exemption held in 2024, Survey from 30 Centers

Out of 6,775 HBV patients



Out of 504 HDV patients

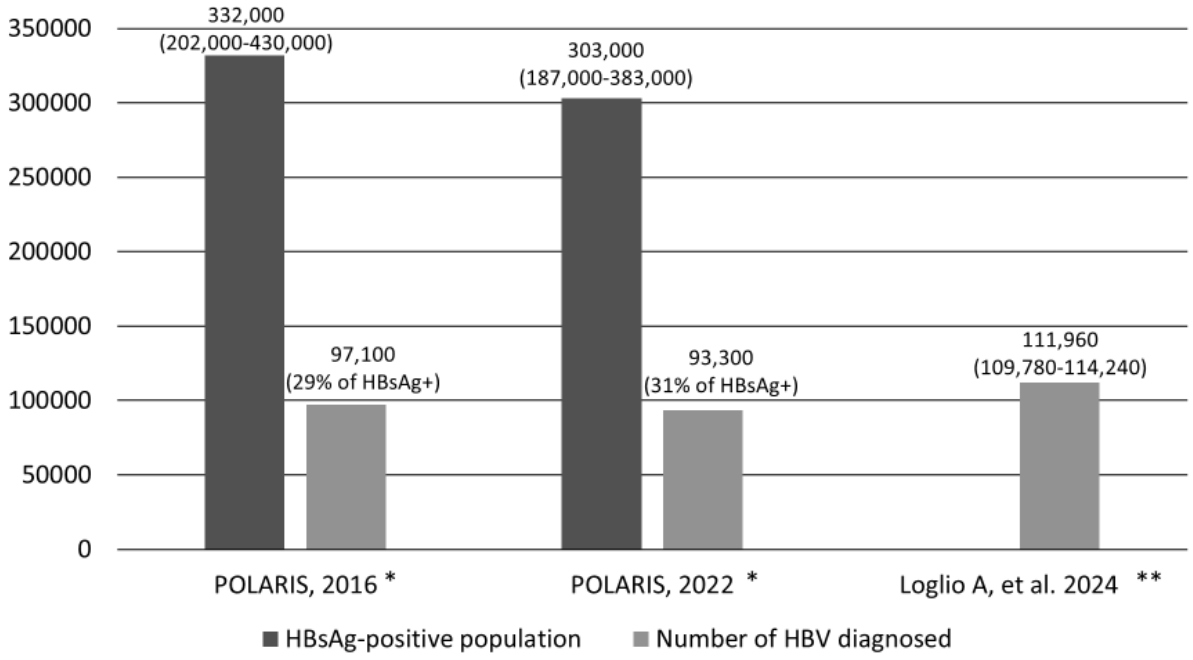


New data on patients with a diagnosed liver condition in Italy

111,960 HBV
(95%CI: 109,780-114,240)
0.22% of adult residents

9,360 HDV
(95%CI: 8,690-10,150)
0.019% of adult residents

HBV population in Italy according to different period of time and study type



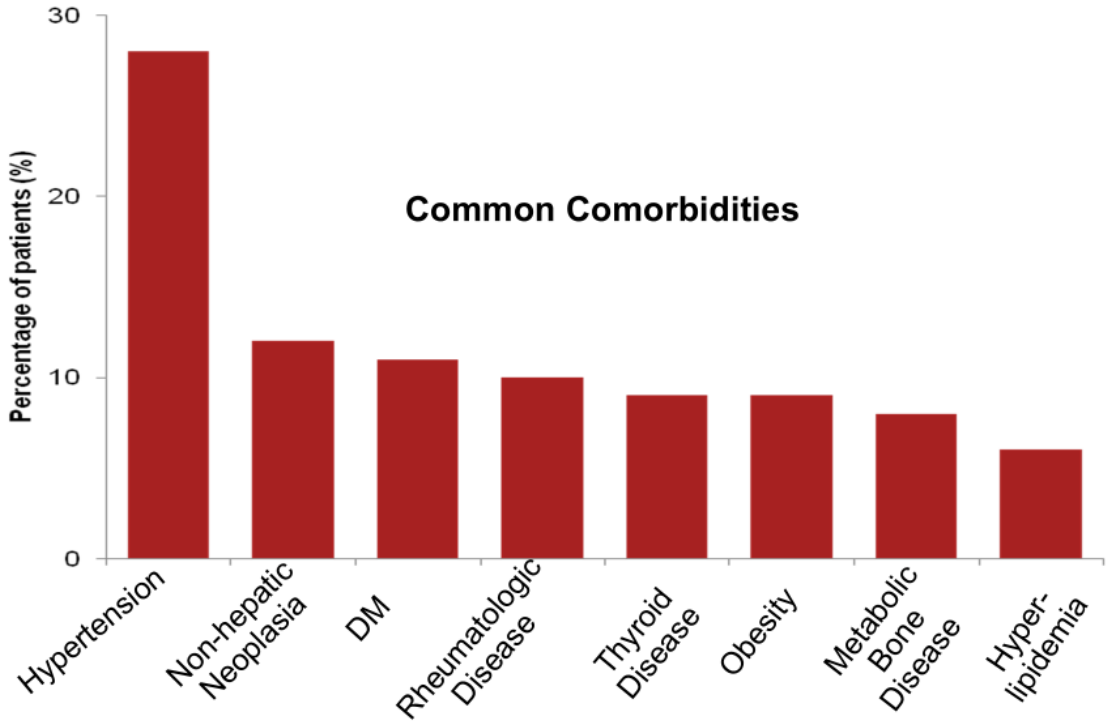
*estimates according to mathematic models and previous literature; **real-data

Loglio A et al, Liver Int 2025

Comorbidities in CHB patients

Multicenter assessment of 500 consecutive CHB patients receiving long-term NUCs at outpatient liver clinics of 5 tertiary Greek hepatology centers

	N=500
Age, years	57.7±14.9
Male, n (%)	329 (66)
Alcohol abuse, n (%)	20 (4)
Former or current smoker, n (%)	147 (29)
Current NUC, n (%) TDF ETV Combination	 301 (60) 185 (37) 14 (3)
HCC development under treatment, n (%)	21 (4)
Decompensated cirrhosis, n (%)	48 (10)
Previous antiviral treatment	213 (43)
Total Rx duration, mean±SD (range), months	72 ± 58 (1-212)
LAM-experienced, n (%)	156 (31.1)
LAM-resistant, n (%)	104 (21)



CHB patients are of older age and have multiple comorbidities

Siakavellas, EASL2018, FRI-292

OS-016 Cirrhosis death rates are increasing rapidly among young Americans – analysis of national death certificate data

Background & Aims

- In the United States (US), there has been a concerning increase in the prevalence of obesity, diabetes, unhealthy alcohol use, and incident chronic hepatitis C virus infections among younger individuals.

Aim: To assess trends in cirrhosis mortality among Americans younger than 35 years old.

Methods

Database

National Vital Statistics System: vital statistics based on death certificates from the entire US.

Data selection

- Underlying cause from cirrhosis (K70.3, K71.7, K72.9, K74.3, K74.4, K74.5, K74.6) or
- Complications of cirrhosis (I85.0, I86.4, K76.6, K76.7, R18).
- Individuals younger than 35 from 1999-2023.

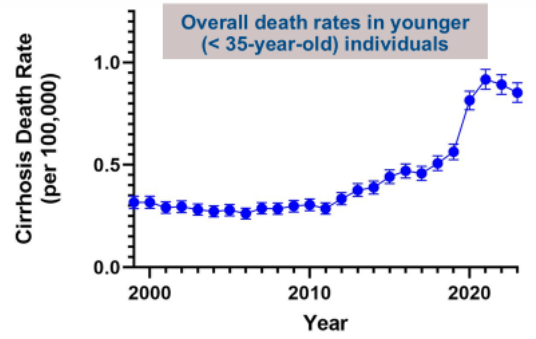
Data analysis

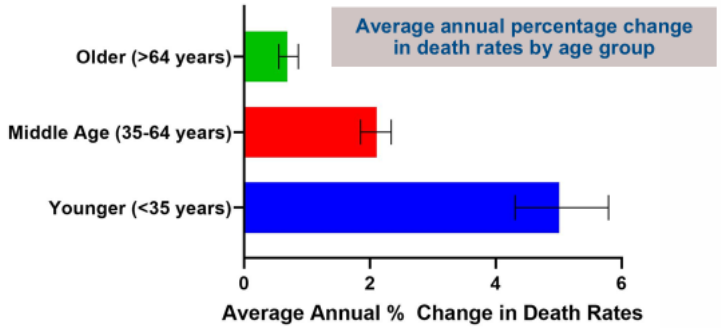
- Extraction of the number of deaths and calculation of annual mortality rates overall and stratified by gender.
- Deaths among younger individuals (<35 years) were compared to middle age (35-64) and older (>64) individuals.
- Examination of trends in cirrhosis deaths with a contributing cause from ALD, MASLD, and viral hepatitis.
- Use of the NCI Joinpoint program for evaluation of statistically significant changes in APC and overall AAPC in death rates.

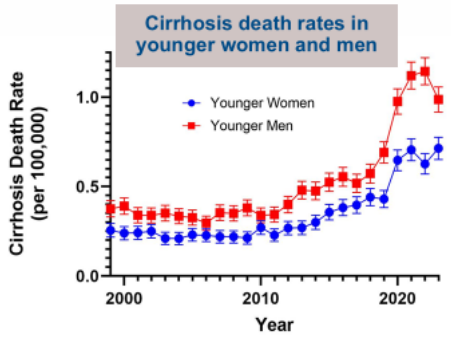
Moon A, et al. EASL ILC 2025

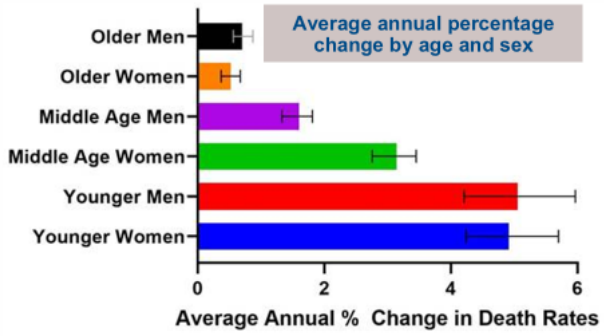
OS-016 Cirrhosis death rates are increasing rapidly among young Americans – analysis of national death certificate data

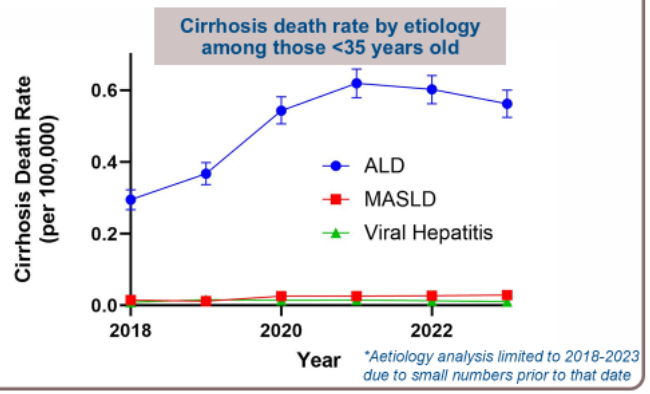
Results











Conclusion

Cirrhosis death rates have increased more rapidly among younger individuals and these increases accelerated from 2018-2023, particularly among younger males. Increased alcohol use in recent years has likely contributed to recent rises in cirrhosis death rates among Americans under age 35.

Moon A, et al. EASL ILC 2025

Epatiti e comorbilità internistiche

LB2553 High prevalence of undiagnosed liver fibrosis in the adult European population driven by metabolic risk factors and alcohol consumption. results from the prospective liverscreen cohort in 30,541 subjects

Background & Aims

- Findings from small-scale, single-country cohorts suggest that undiagnosed liver fibrosis resulting from chronic liver disease is common in the general population.
- However, the exact prevalence and main risk factors remain incompletely understood.

Aim: To investigate the prevalence of undiagnosed liver fibrosis in a prospective large-scale multi-national European cohort and determine the association between liver fibrosis and metabolic risk factors and/or alcohol consumption.

Methods

Population

30,541 participants:
- May 2018 - December 2024
- Older than 40 years
- Without known liver disease
- From the general population in 9 European countries

Data collection
- Demographic data
- Clinical data
- Standard lab parameters

+

Liver fibrosis

Assessed by liver stiffness measurement (LSM) using vibration controlled transient elastography (Fibroscan®).

Subjects' selection

Since LSM < 8kPa rules out significant fibrosis, only subjects with LSM ≥ 8kPa, and/or ALT ≥ 1.5.

Evaluation of liver disease

Primary outcome
- Prevalence of LSM ≥ 8kPa.

Graupera I, et al. EASL ILC 2025

Epatiti e comorbilità internistiche

LB2553 High prevalence of undiagnosed liver fibrosis in the adult European population driven by metabolic risk factors and alcohol consumption. results from the prospective liverscreen cohort in 30,541 subjects

Results

Demographics

Mean age	58 years
Female	57%
Caucasian	89%

Metabolic risk factors and alcohol use

Metabolic risk factors	
Overweight / Obesity	40% / 26%
Dyslipidemia	53%
Arterial hypertension	35%
Type 2 diabetes (T2D)	10%
Alcohol use	
Hazardous consumption (SDU ≥14-21/w or AUDIT-C≥5)	18%
High-risk consumption (SDU≥35-42/w or AUDIT-C≥8)	3.4%

Prevalence and predictors of liver fibrosis

Liver stiffness measurement (LSM)	
Prevalence of LSM ≥ 8kPa	4.6%
Prevalence of LSM ≥ 10 kPa / ≥ 15 kPa	2.5% / 0.8%
Prevalence of LSM ≥ 8kPa according to the number of metabolic risk factors (MRF)	1.3% (0 MRF), 2.3% (1 MRF), 5.2% (2 MRF), 9.8% (3 MRF) and 21.6% (4 MRF)
Prevalence of LSM ≥ 8kPa according to the number of metabolic risk factors (MRF) + hazardous alcohol use	1.7% (0 MRF + alcohol), 4.5% (1 MRF + alcohol), 8.1% (2 MRF + alcohol), 14.9% (3 MRF + alcohol) and 28.5% (4 MRF + alcohol)
Strongest predictors of LSM ≥ 8 kPa	Obesity (OR 3.8), T2D (OR 3.0), high-risk alcohol (OR 2.5)
Steatosis (CAP ≥ 275 dB/m)	32%
LSM ≥ 8 kPa with / without steatosis	8.8% vs 2.6%
Chronic liver disease diagnosis	Confirmed in 31% of referred subjects (67% via biopsy)
Main etiologies	MASLD, ALD, MetALD

Conclusion

In this large-scale European cohort, we found a remarkably high prevalence of undiagnosed liver fibrosis mainly related to steatotic liver disease driven by metabolic risk factors and/or high-risk alcohol consumption. Efforts should be made to identify liver fibrosis early to apply specific therapies that could reverse liver fibrosis.

Epatiti e comorbilità internistiche

OS-030-YI Discrepancies between self-reported alcohol intake and phosphatidylethanol in 2,924 individuals at risk of steatotic liver disease

Background & Aims

- In the presence of hepatic steatosis and cardiometabolic risk factors, alcohol intake defines the subtypes of steatotic liver disease (SLD). However, self-reported alcohol intake is prone to recall bias and underestimation.
- The blood-based biomarker phosphatidylethanol (PEth) provides an objective measure of past two to four weeks' alcohol intake but has primarily been used to monitor abstinence or heavy drinking in alcohol use disorder studies.

Aim: To compare the correlation between PEth and self-reported alcohol intake in a screening cohort of people at risk of SLD.

Methods

Population

Prospective, single center screening study with two recruitment groups:
- **Alcohol group**: current/prior harmful alcohol use.
- **Metabolic group**: obesity (BMI > 30) or type 2 diabetes.

Investigations

- Medical history and objective measures.
- PEth measured from whole blood.
- Self-reported alcohol intake by questionnaire: a) past week, b) average intake the past three months, c) AUDIT-C.
- Liver stiffness measurements (LSM) by transient elastography.

Classifications

- PEth drinking groups: < 20, 20-79, 80-199, > 200 ng/mL.
- AUDIT-C risk groups: < 3/4 (f/m), 3-7/4-7, > 8.
- SLD classification based on a) CAP > 248 dB/m or LSM > 8 kPa, b) cardiometabolic risk factors, c) self-reported 3 months' average alcohol intake, thresholds according to nomenclature.

Bech K, et al. EASL ILC 2025

OS-030-YI Discrepancies between self-reported alcohol intake and phosphatidylethanol in 2,924 individuals at risk of steatotic liver disease

Results

Baseline characteristics

	Alcohol group	Metabolic group
n	1,482	1,442
Male sex	65%	36%
Age, years	59 (52-65)	56 (50-62)
BMI ≥ 30 kg/m²	26%	79%
Prediabetes or type 2 diabetes	54%	60%
LSM ≥ 8 kPa	9.8%	8.8%
CAP ≥ 248 dB/m	63%	77%
PEth, ng/mL	172 (45-434)	11 (5-37)
Alcohol intake past week, g/day	17 (0-41)	2 (0-7)
Alcohol intake past 3 months, g/day	31 (9-48)	3 (2-9)
AUDIT-C, points	7 (5-9)	3 (2-4)

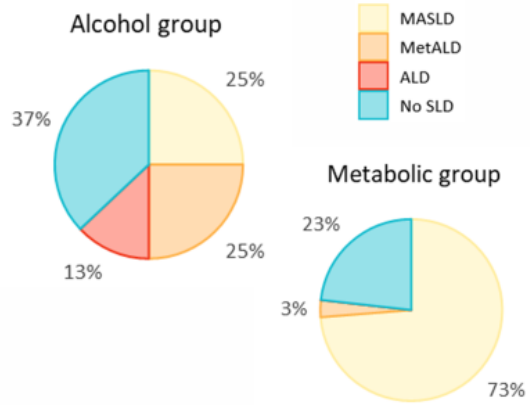
Correlation coefficients

	Alcohol group	Metabolic group
Correlation PEth vs. Alcohol intake past week, ρ	0.638	0.655
Correlation PEth vs. Alcohol intake past 3 months, ρ	0.627	0.725

Concordance between PEth and self-reported alcohol intake

Self-reported alcohol intake (3 months' average) (g/day)	PEth (ng/mL)			
Alcohol group (n=1,482)	<20	20-79	80-199	≥200
<20/30	17%	10%	8%	8%
20-50/30-60	1%	3%	12%	23%
≥50/60	1%	1%	2%	14%
Metabolic group (n=1,442)				
<20/30	64%	22%	7%	3%
20-50/30-60	<1%	1%	1%	1%
≥50/60	<1%	<1%	<1%	<1%

SLD classification according to self-reported alcohol intake the past 3 months, stratified by recruitment group



- Red highlights: significant underreporting.
- Yellow highlights: additional underreporting according to current PEth thresholds (< 20 and > 200 ng/mL).

Conclusion

This study demonstrates a monotonic correlation between PEth and self-reported alcohol intake, however with PEth revealing substantial underreporting, particularly among individuals with a history of alcohol overuse. At current recommended thresholds, up to one third of individuals with MASLD may be reclassified as MetALD or ALD. Integrating PEth into SLD diagnostic algorithms may therefore improve patient subclassification.

Epatiti e comorbilità internistiche

Clinical utility of phosphatidyl-ethanol to detect underreported alcohol use and enhance steatotic liver disease subclassification

Study cohort: San Diego Liver Study

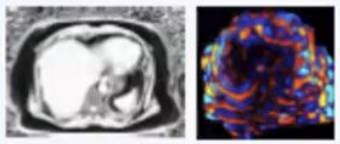
556 adults with overweight/obesity

391 (73%) with SLD

Alcohol use assessment

Standardized questionnaires
DSM-V criteria
PEth testing

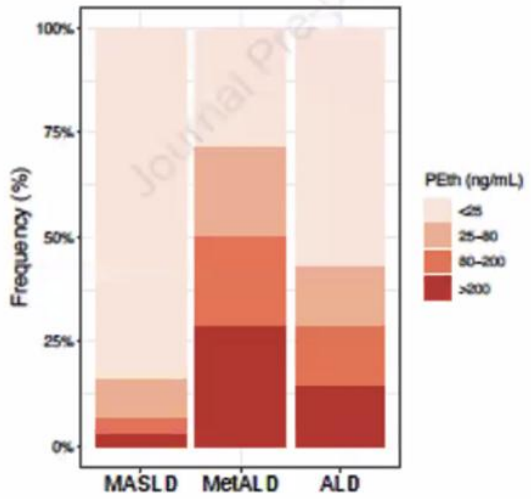
Liver disease phenotyping

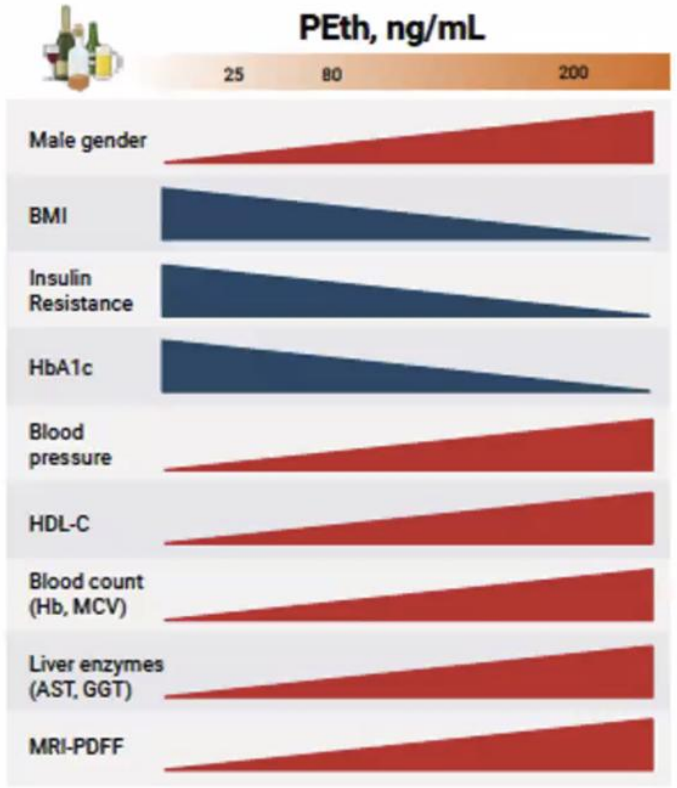


MRI-PDFF
MRE

PEth + Self-reported alcohol use

16% underreported alcohol use in SLD
↑4-fold increase in MetALD diagnoses
↑3-fold increase in ALD diagnoses

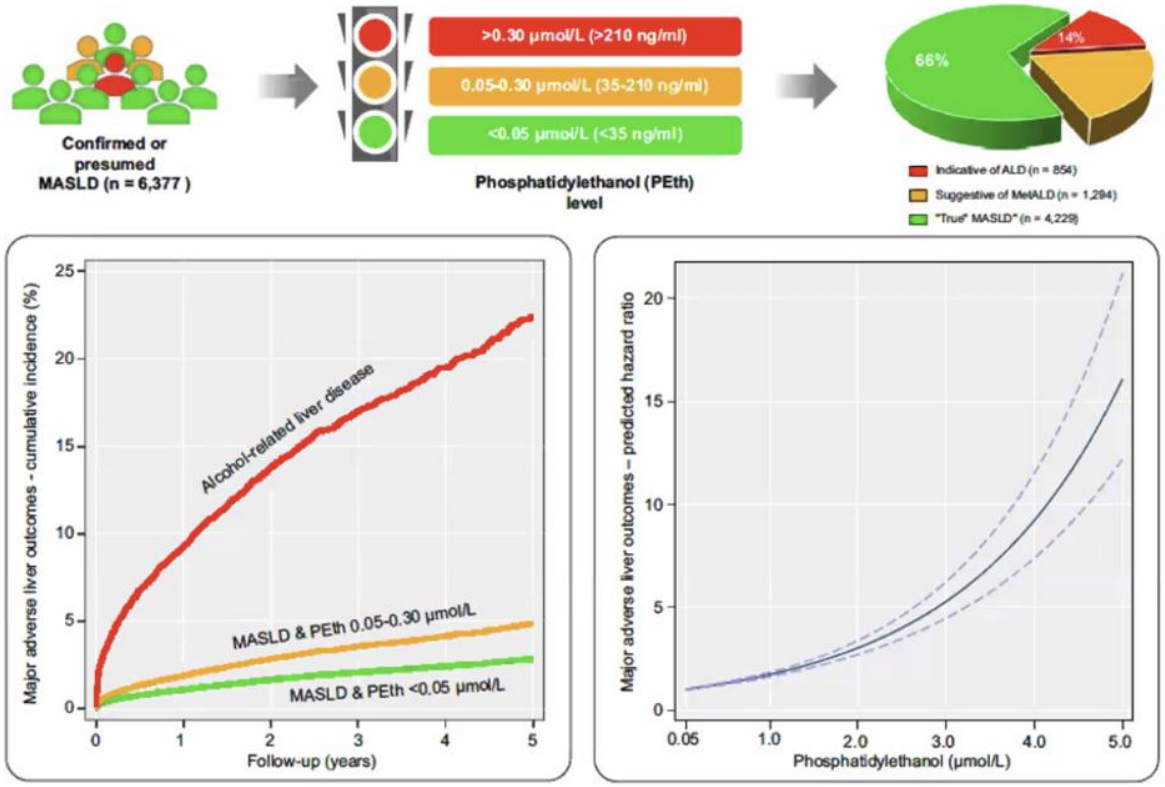




Tavaglione. J Hepatol 2025

Epatiti e comorbilità internistiche

Phosphatidylethanol levels distinguish steatotic liver disease subgroups and are associated with risk of major liver outcomes

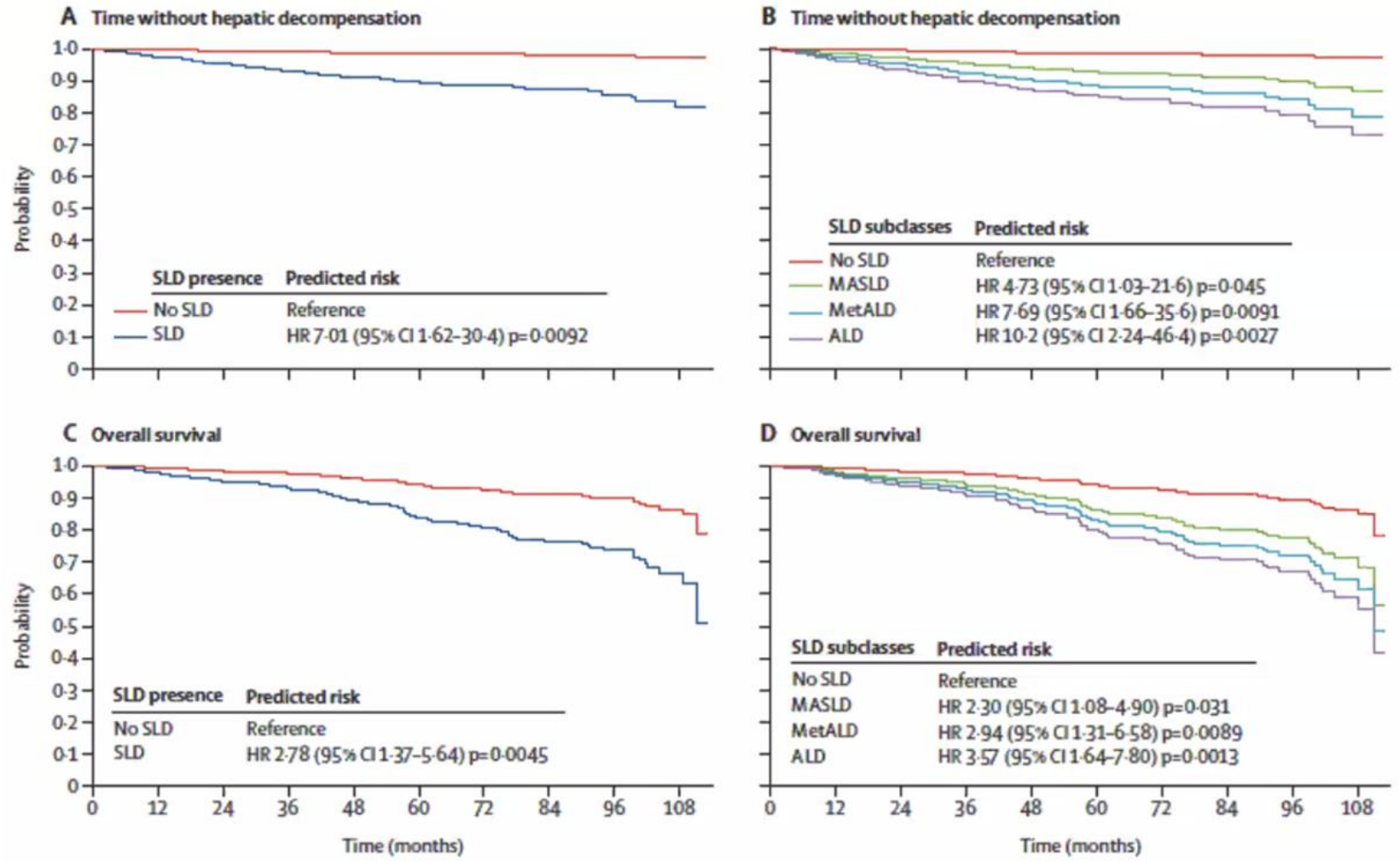


6,377 patients with presumed MASLD
Sweden 2012 - 2020

- 20% of patients with presumed MASLD had PEth levels between 35–210 ng/ml, suggestive of MetALD.
- 13% had PEth >210 ng/ml, indicative of ALD.
- Higher PEth was linked to an increased rate of MALOs in patients without cirrhosis and after adjusting for confounders.
- Patients with ALD had the highest PEth levels and poorest prognosis.

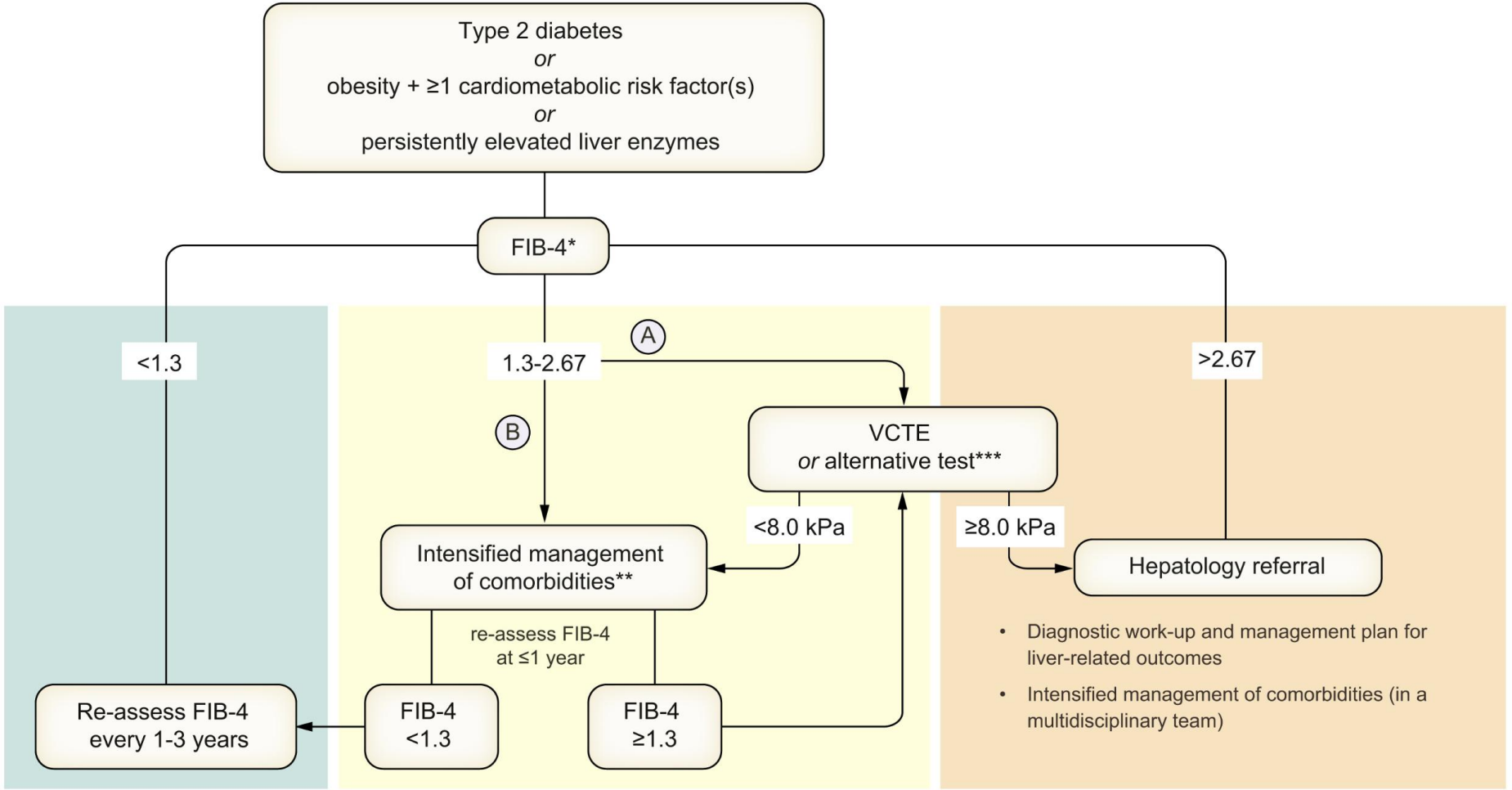
Vaz. J Hepatol 2025

Overall survival and hepatic decompesation across the spectrum of SLD



Israelsen. Lancet 2024

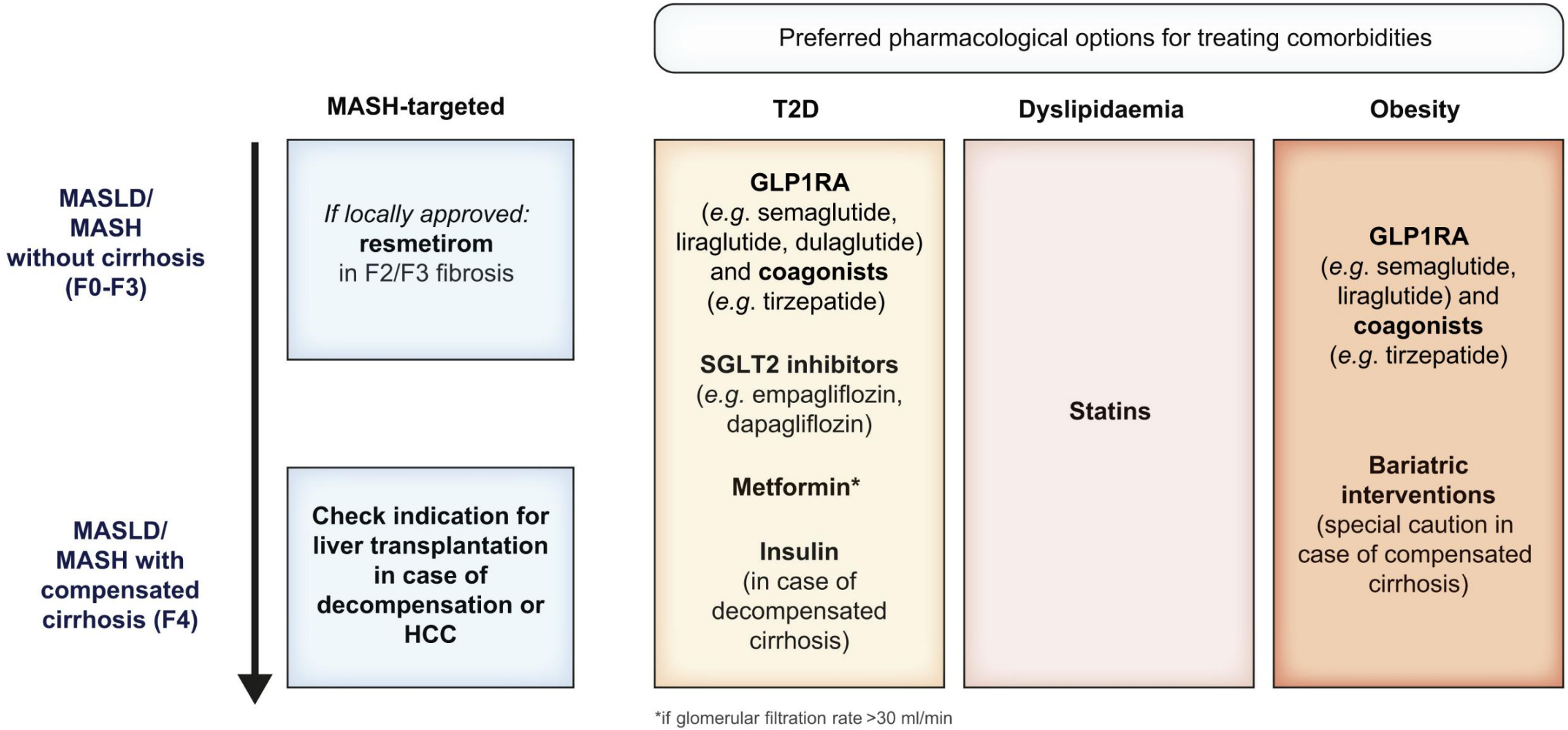
Epatiti e comorbilità internistiche



* FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cut-off is 2.0)
** *e.g.* lifestyle intervention, treatment of comorbidities (*e.g.* GLP1RA), bariatric procedures
*** *e.g.* MRE, SWE, ELF, with adapted thresholds
Ⓐ and Ⓑ are options, depending on medical history, clinical context and local resources

EASL-EASD-EASO. J Hepatol 2024

Epatiti e comorbilità internistiche



EASL-EASD-EASO. J Hepatol 2024

LB2593 Treatment with resmetirom for up to two years led to improvement in liver stiffness, fibrosis biomarkers, fibrosis scores and portal hypertension risk in 122 patients with compensated MASH cirrhosis

Results

Baseline

Age (mean ± SD)	61.3 ± 9.1 years
Female	56%
Hispanic	27%
BMI (mean ± SD)	35.3 ± 7.6 kg/m²
Type 2 Diabetes (T2D)	65%
VCTE (kPa)	20.1 (17.1, 31.3)
CAP (dB/m)	327 (292, 370)
FIB-4	2.4 (1.7, 3.8)
MRE (kPa)	5.2 (4.4, 6.3)
ELF	10.7 (10.0, 11.5)
MRI-PDFF (%)	8.6 (6, 11.5)
Agile 3+	0.96 (0.89, 0.93)
Agile 4	0.64 (0.40, 0.84)

median, (Q1,Q3)

Treatment

Resmetirom statistically significantly improved:

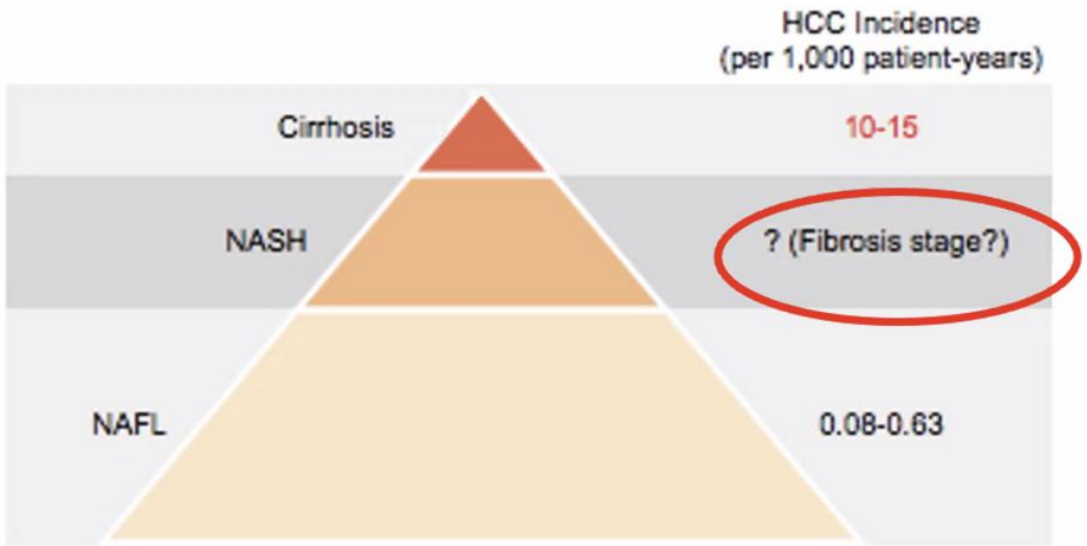
VCTE (mean change, year 1/2)	-6.1 (1.4) / -6.7 (1.3) kPa
MRE (mean change, year 2)	-0.57 (0.14) kPa
P3NP (mean change, year 2)	-1.6 (0.57) ng/mL
Agile 3+ / Agile 4	-0.06 (0.01) / -0.09 (0.02)
MRI-PDFF (% change)	-33%
ALT / AST / GGT (% change)	-25% / -21% / -45%
LDL / ApoB / Triglycerides (%)	-20% / -22% / -30%
VCTE response rates	
≥25% decrease (year 1 / 2)	46% / 52%
≥25% increase (year 1 / 2)	12% / 9%

CSPH (Baveno VII Criteria)	
Baseline CSPH (probable/definitive)	63%
Reversion from CSPH (year 1 / 2)	20% / 28% of CSPH+ no longer met criteria
Fibrosis reversion	
F4 to F3 transition at year 2	35% (of patients with confirmed F4 at baseline)

Conclusion

At 2 years of treatment, resmetirom demonstrated significant improvements in non-invasive biomarkers, liver stiffness on imaging and portal hypertension risk in patients with MASH cirrhosis. Resmetirom was safe and well-tolerated in this population. These findings highlight the potential of resmetirom to demonstrate clinical benefit in MAESTRO-NASH OUTCOMES, an ongoing 845 MASH cirrhosis patient clinical outcome study.

Epidemiology of HCC in MASLD - RWD



HCC incidence in patients with NAFLD based on histological stage

The **annual incidence** rates of HCC in:

- MASLD-related **cirrhosis** range from 10 to 15 per 1,000 Patient Year
- MASLD **without cirrhosis** range from 0.03 to 0.63 per 1,000 Patient Year

Steatosis alone does not define MASLD risk; fibrosis stage is key

Iaonnu. J Hepatol 2021

Epatiti e comorbilità internistiche

TOP-107
Machine learning approaches for hepatocellular carcinoma risk stratification across various aetiologies

Background and Aims

New tools for HCC early detection are only cost-effective for patients with a high annual incidence exceeding 2%.

Aim: To develop Machine Learning (ML) models for risk stratification of HCC in prospective cohorts of patients with compensated cirrhosis and to compare their performance to traditional scoring systems.

Methods

Data collected from the HCC 2000 trial, the ANRS CO12 CirVir and CO22 Hepather cohorts, and CIRRAL cohort.

3671 patients either non-viral cirrhosis or cirrhosis related to resolved HCV or controlled HBV) who had undergone semiannual ultrasound surveillance.

- Training Group (n = 2447)
- Validation Group (n = 1224)

- **Cumulative incidence of HCC** estimated within a competitive risk framework
- **Fine-Gray regression model** Constructed as a reference for comparison with the ML models, FASTRAK and aMAP scores
- **A Single Tree (ST) model** Developed using conditional decision tree methodology.

Prognostic algorithms were derived using a Random Forest (RF) approach

Discrimination performance of the models was assessed in the validation set using the C-Index, and calibration curves were generated.

Nahon P, et al. EASL ILC 2025

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TOP-107
Machine learning approaches for hepatocellular carcinoma risk stratification across various aetiologies

Results

RF vs Traditional

No significant advantage for the ML models over traditional short-term scores, although there appeared to be an improvement in long-term prediction.

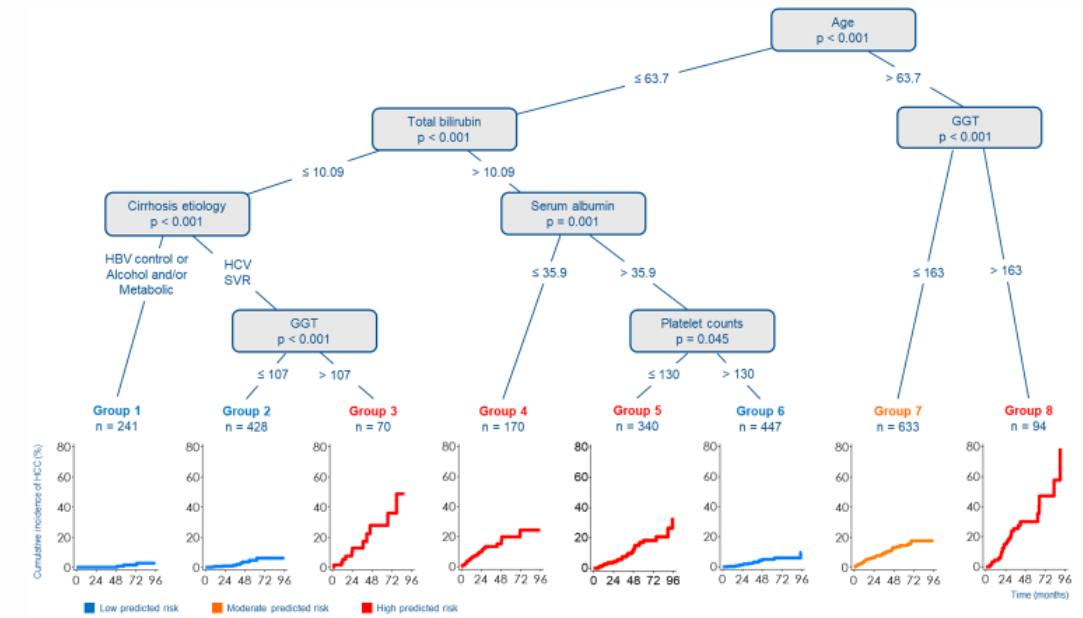
Model	5-year C-index
RF (ML)	0.76
FASTRAK	0.75
aMAP	0.75

ST approach

Six main predictors, generating **eight groups** based on various combinations of these predictors, each with contrasting HCC risks.

Main Split: Age
↳ **Younger** patients:
- Normal liver function → **Low Risk**
- Slightly impaired function → **Moderate Risk**
- Resolved HCV + ↑GGT → **High Risk**

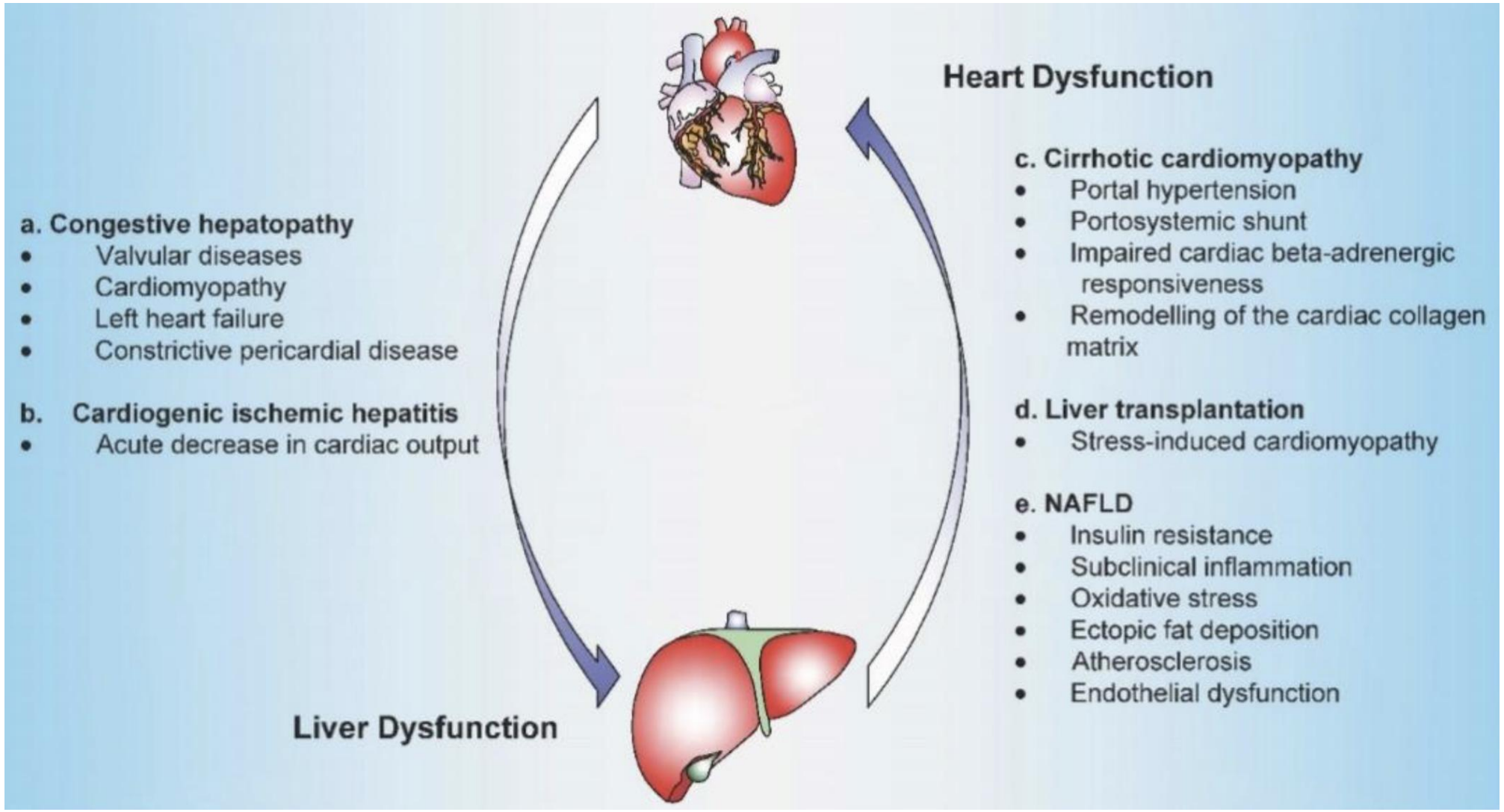
Key predictors identified by ML



Conclusion

ML algorithms highlight interactions between variables, aid in identifying patient clusters defined by varying risk levels, and highlight “extreme phenotypes” of patients with particularly high risks of HCC.

Epatiti e comorbilità internistiche



El Hadi H, Cells 2020

Cardiometabolic risk and physical activity

Clinical Practice Guidelines

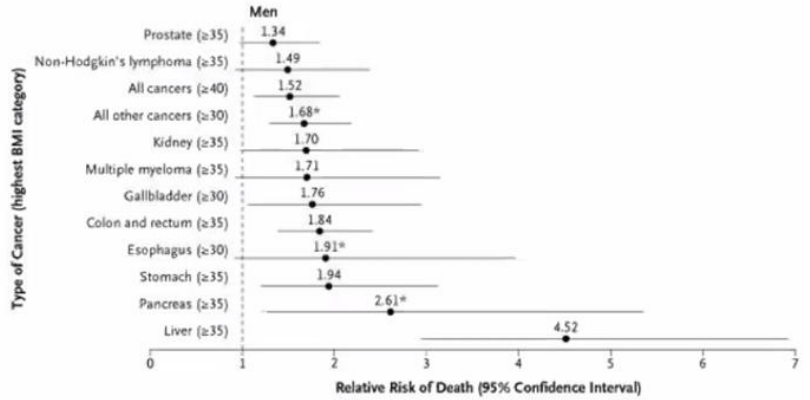
JOURNAL OF HEPATOLOGY

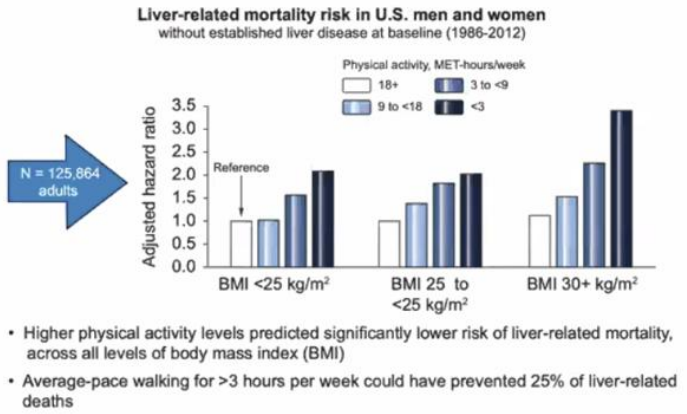
EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD)☆

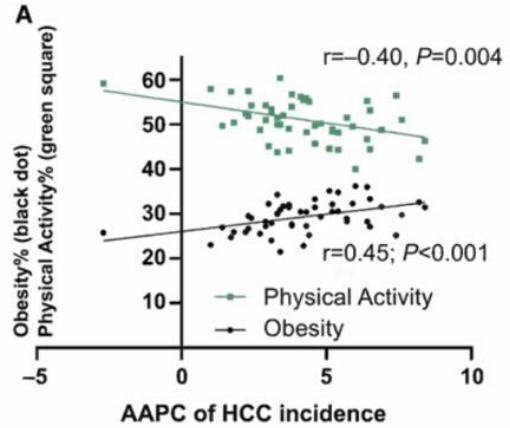
European Association for the Study of the Liver (EASL)*, European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO)

Statements

- Type 2 diabetes and obesity (particularly abdominal obesity) are the metabolic diseases with the strongest impact on the natural history of MASLD, including progression to MASLD/MASH-related advanced fibrosis, cirrhosis and hepatocellular carcinoma (**LoE 2, strong consensus**).
- Males aged >50 years, postmenopausal women, and individuals with multiple cardiometabolic risk factors are at increased risk of progressive fibrosis and the development of cirrhosis and its complications (**LoE 2, strong consensus**).

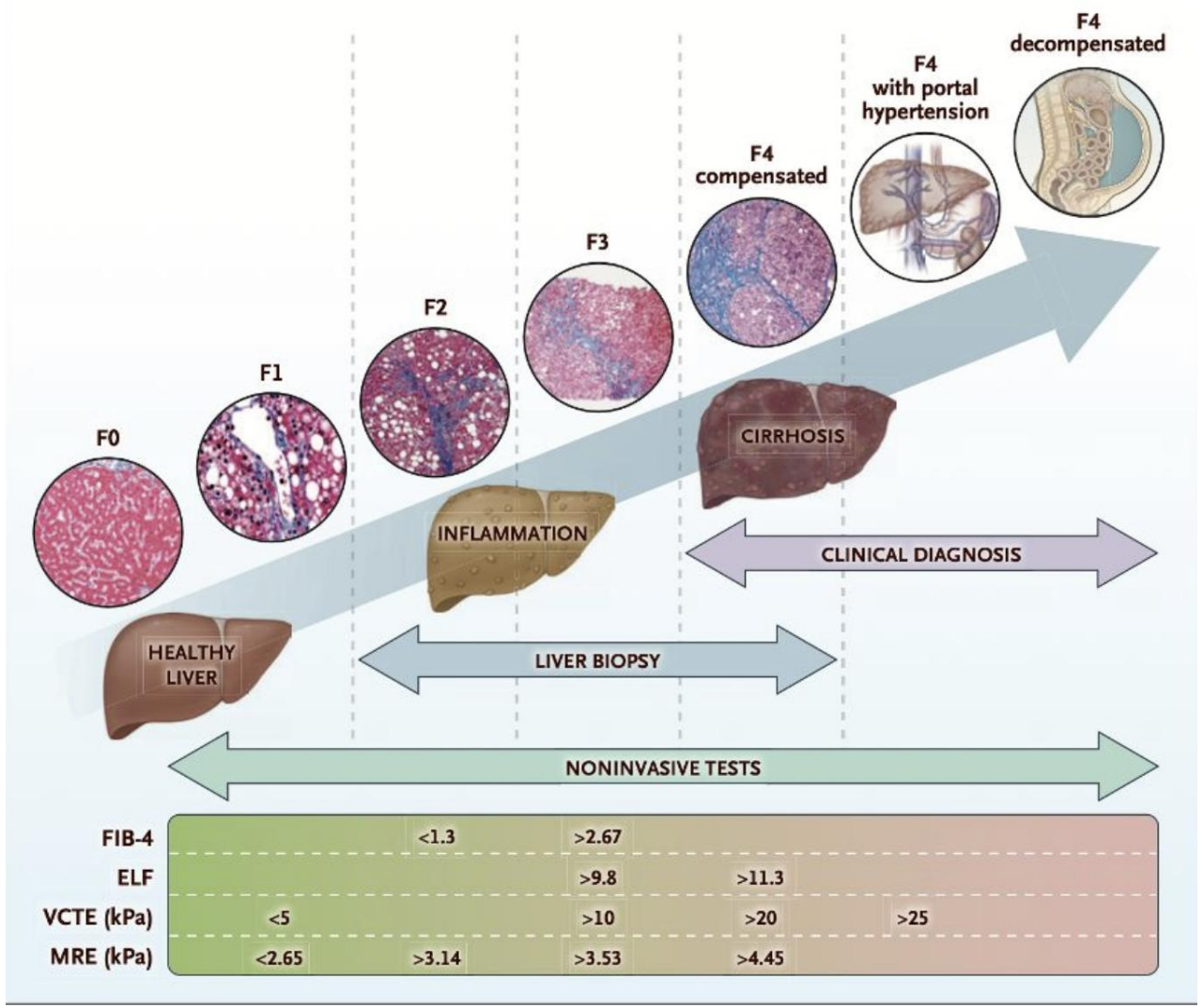






Calle et al. NEJM 2003; Simon et al. JHEP 2020; Lee et al. Hepatology 2021

Epatiti e comorbilità internistiche



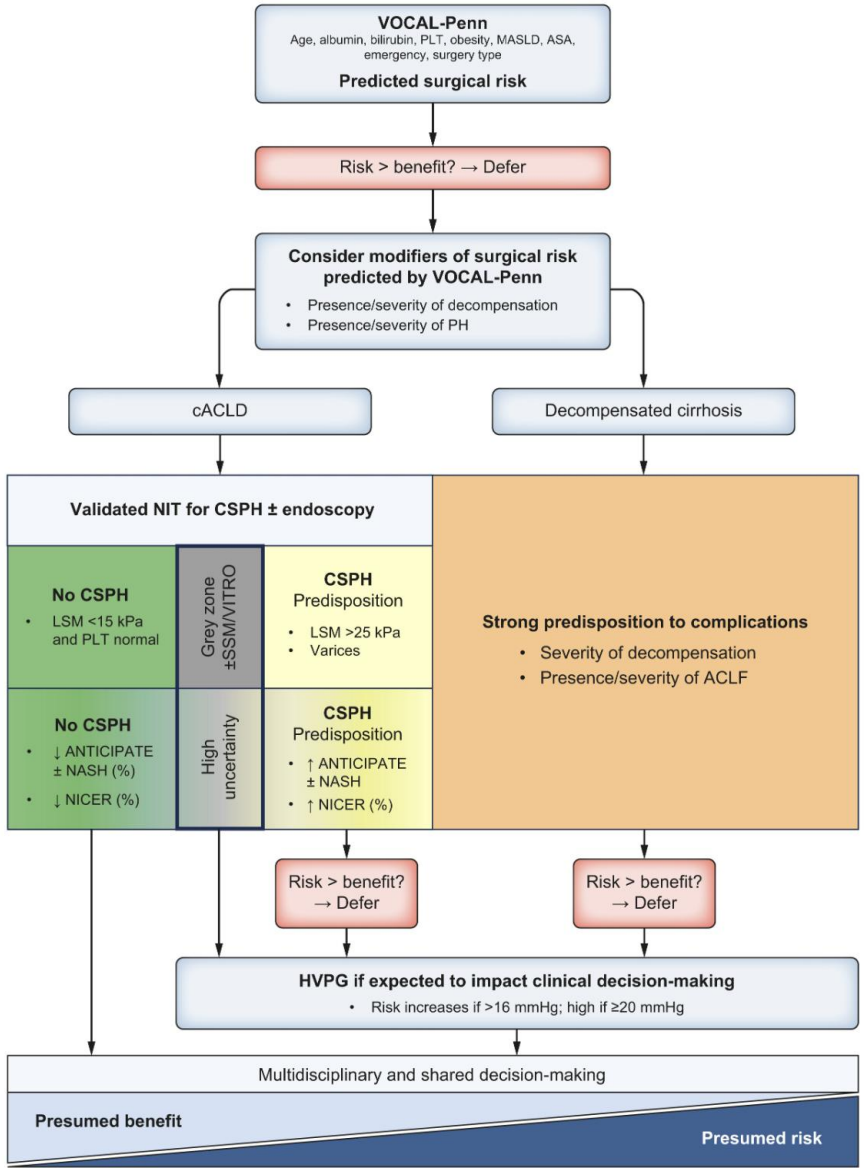
Castera L, Rinella ME, Tsochatzis EA. N Engl J Med. 2025

LSM <20 kPa AND PLT >150x10^9/L can be used to rule out high-risk varices in patients with HCV- and HBV cirrhosis

Baveno VII criteria

Epatiti e comorbilità internistiche

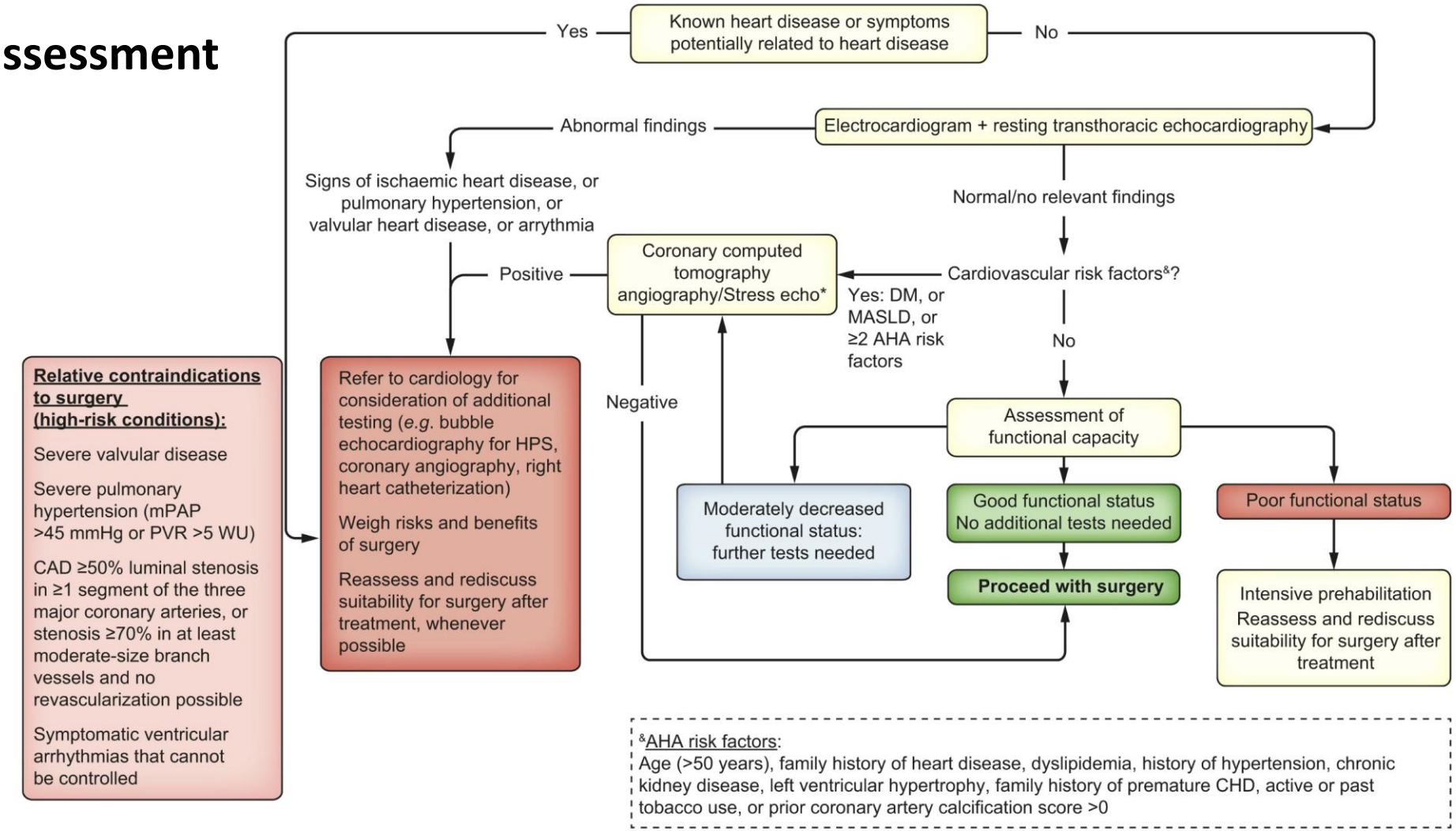
Cirrhosis and abdominal extrahepatic surgery risk



Thabut D, EASL CPG. J Hepatol 2025

Epatiti e comorbilità internistiche

Cardiac assessment



Thabut D, EASL CPG. J Hepatol 2025

Conclusioni

- Le epatiti croniche sono patologie sistemiche
- Le comorbilità internistiche influenzano prognosi e risposta terapeutica
- Approccio multidisciplinare è indispensabile / dipendenze
- Prevenzione, screening e follow-up continuo migliorano la sopravvivenza
- Referral

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PREVENZIONE E CURA DELLE DIPENDENZE
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Epatiti e comorbilità internistiche

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