Diabete e steatosi epatica: luci e ombre

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Honorarium as a speaker in Scientific Events

Sigma-Tau, Lilly, AstraZeneca, Takeda, Janssen, Boheringer Ingelheim, Sanofi Menarini Diag, MSD, Novo Nordisk, Roche Diag, Novartis, Servier, Bayer

CoI

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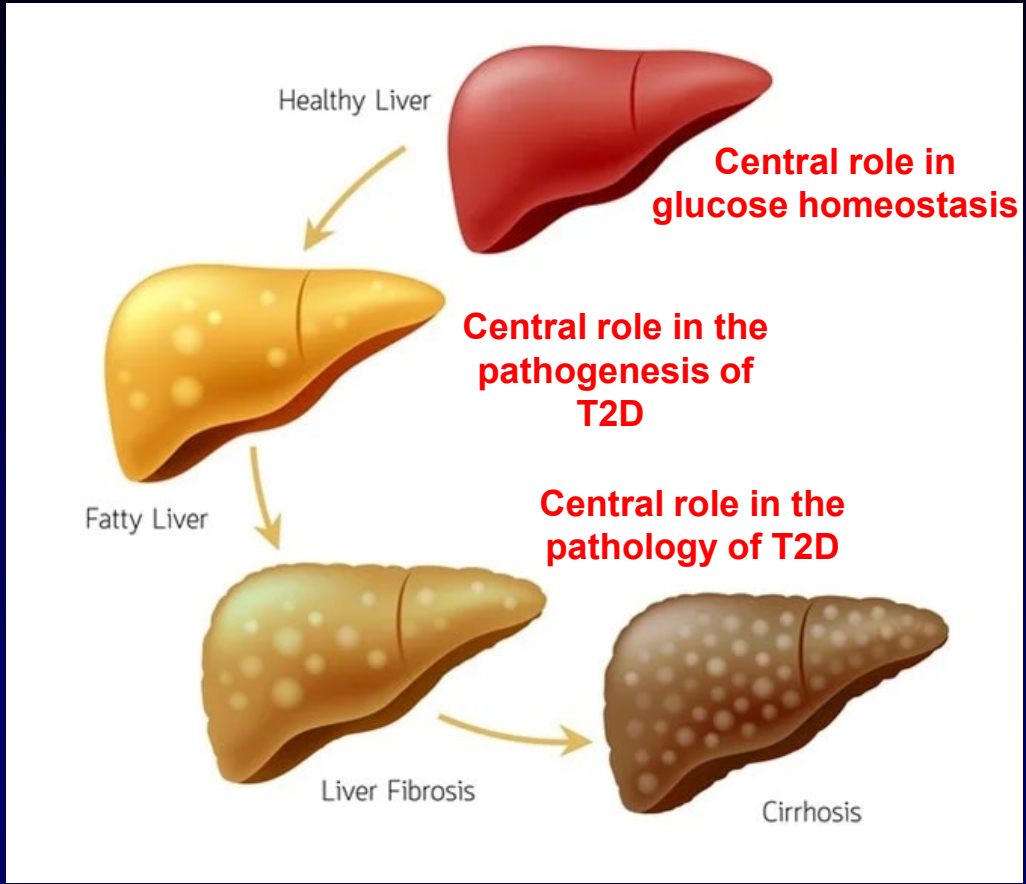
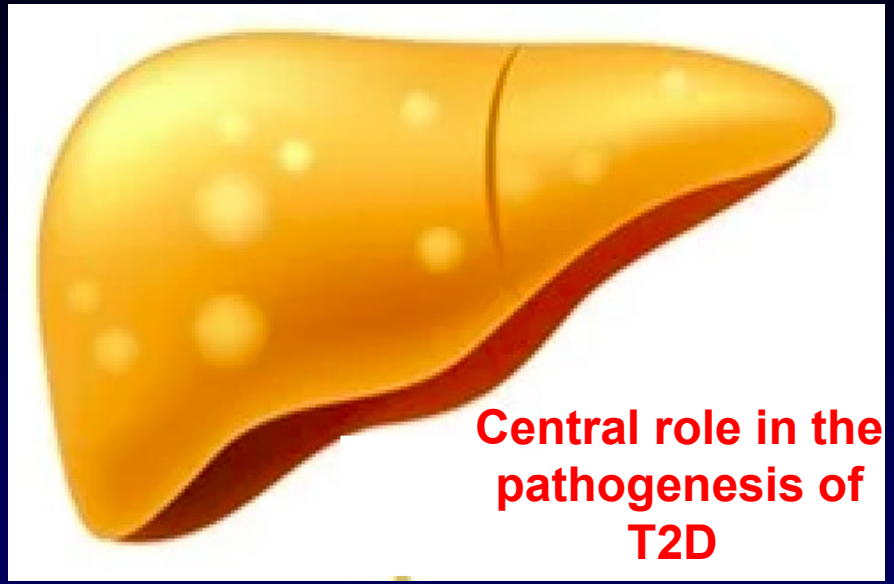
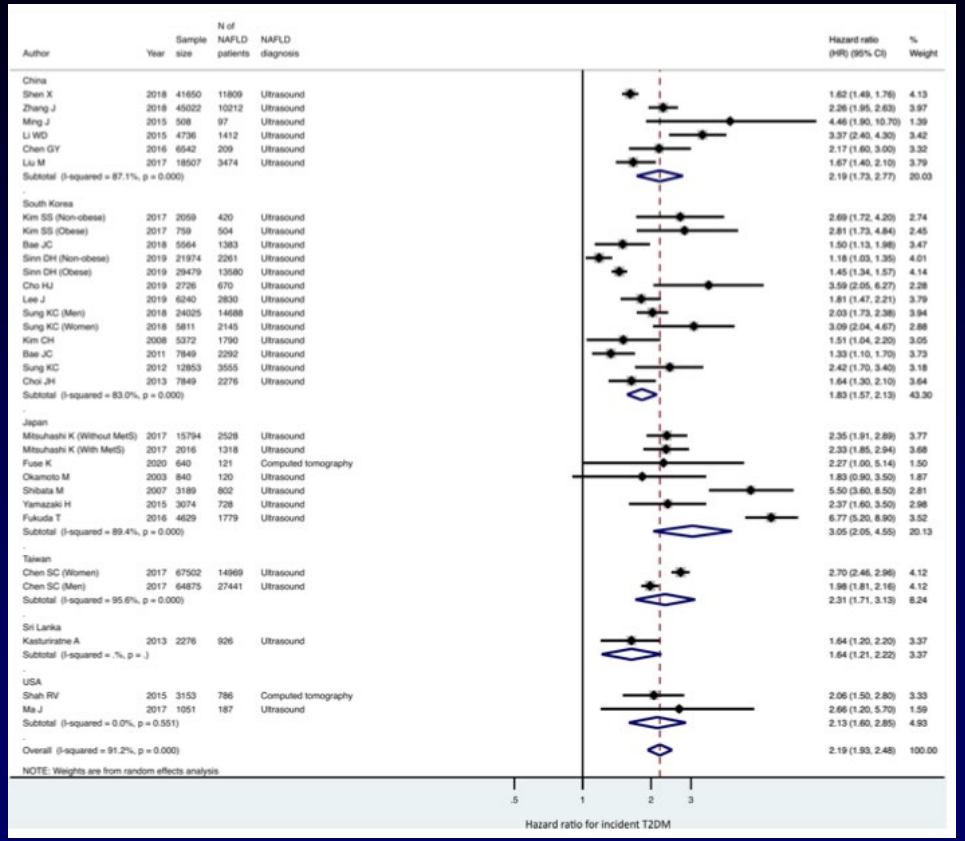
la presentazione non contiene discussione di farmaci in studio o ad uso off-label

3 topics for the diabetologist




Central role in the
pathogenesis of
T2D

NAFLD and incident T2DM



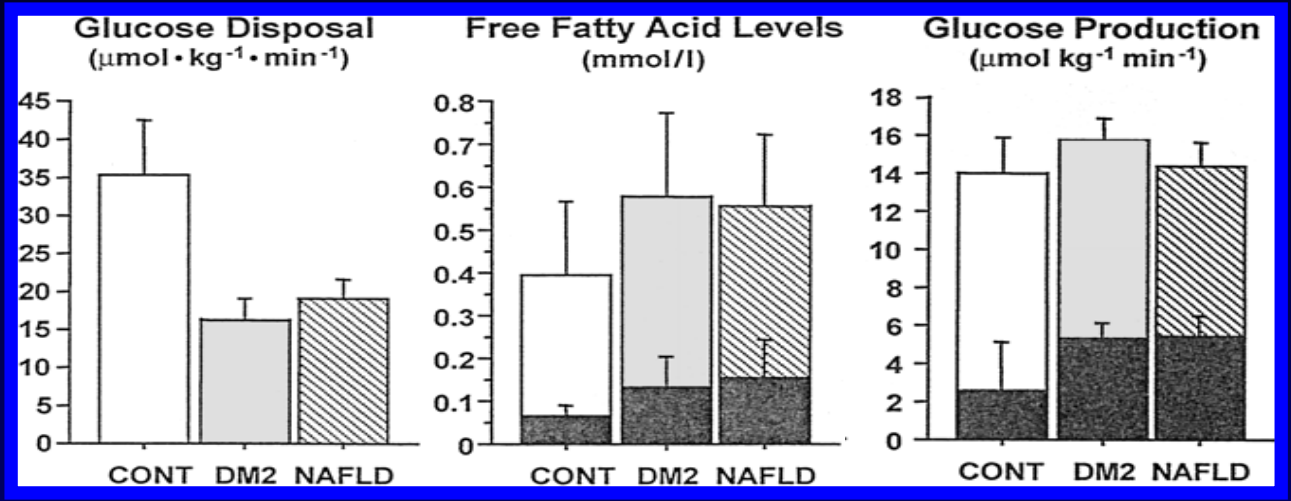
A) ultrasonography

B) Liver biopsy

Related to the severity of fibrosis

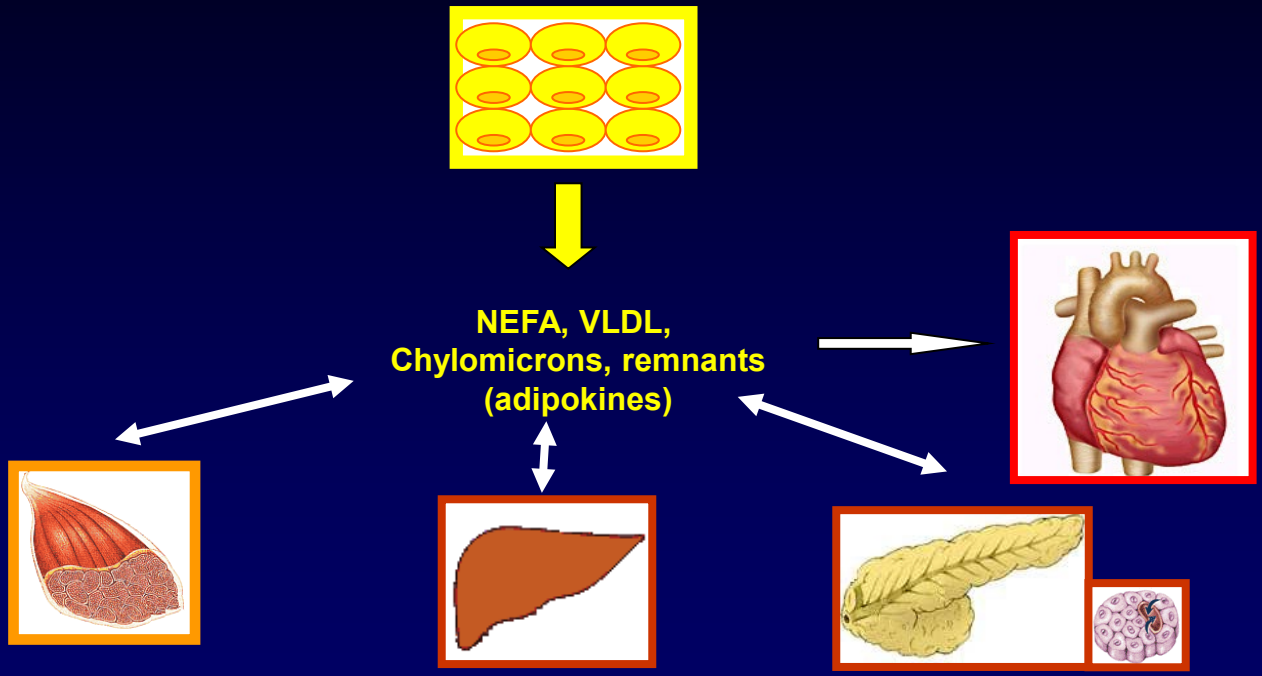
Mantovani A et al, Gut, 2020

NAFLD & Insulin resistance



Marchesini G et al Diabetes, 2001

Lipids in the wrong place: visceral fat and nonalcoholic fatty liver disease



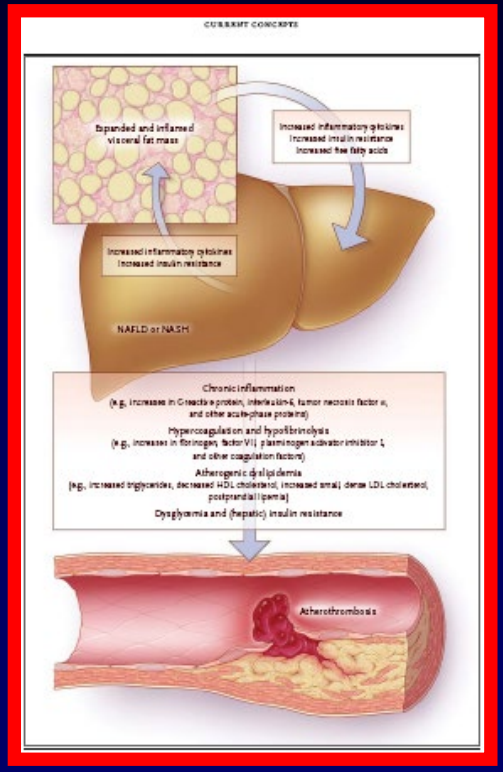
Perseghin G Diabetes Care, 2011

CURRENT CONCEPTS

Risk of Cardiovascular Disease in Patients with Nonalcoholic Fatty Liver Disease

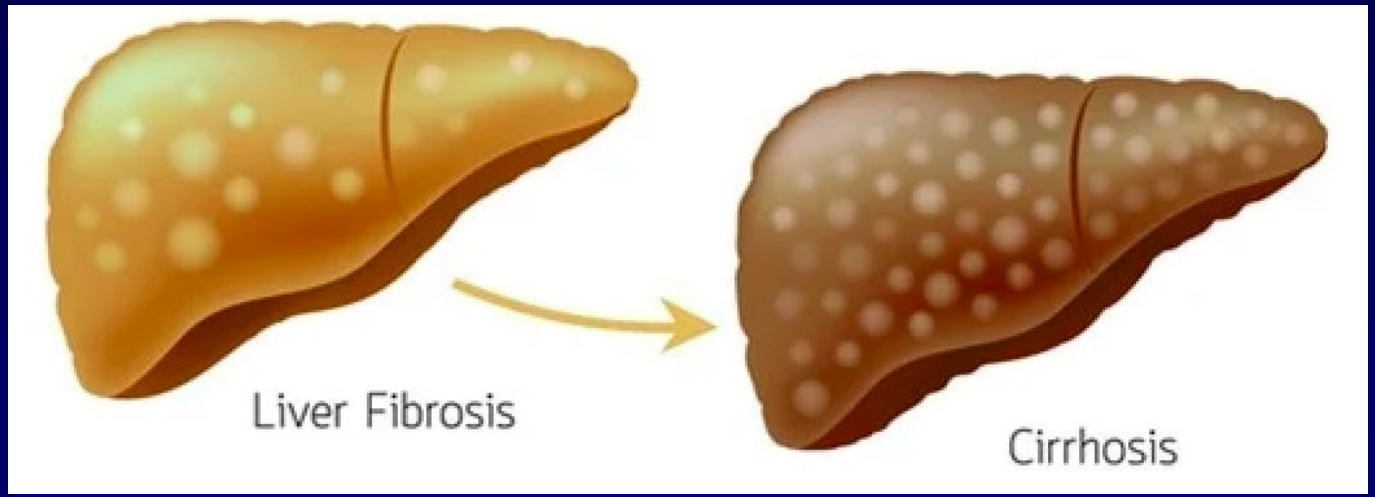
Giovanni Targher, M.D., Christopher P. Day, M.D., Ph.D., and Enzo Bonora, M.D., Ph.D.

Cardiovascular Features



N Engl J Med 2010;363:1341-50.

Central role in the pathology of T2D



Do patients with diabetes have a poor hepatic-related prognosis?

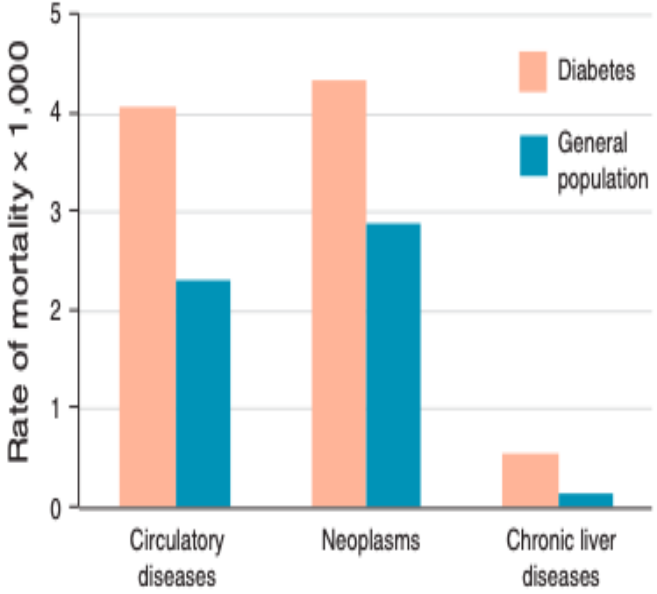


Figure 2. Age-standardized mortality rates (standard European population) for circulatory diseases, neoplasms, and chronic liver diseases among diabetics and the general population of the Veneto region aged 30–89 years.

Table 3. SMRs for CLDs reported as either the underlying or the contributing causes of death of 167,621 diabetic patients followed-up for 3 years

	Number of deaths	SMR	95% CIs
All CLD	1,183	2.55	2.41–2.70
Virus-related CLD[a]	234	2.17	1.90–2.47
Alcohol-related CLD[a]	260	2.25	1.98–2.54
NVNA-related CLD	707	2.86	2.65–3.08

CI, confidence interval; CLD, chronic liver disease; NVNA, non-viral non-alcohol; SMR, standardized mortality ratio.

[a]18 CLD deaths were classified as related to both alcohol and viral hepatitis.

Zoppini G et al
Am J Gastroenterol, 2014

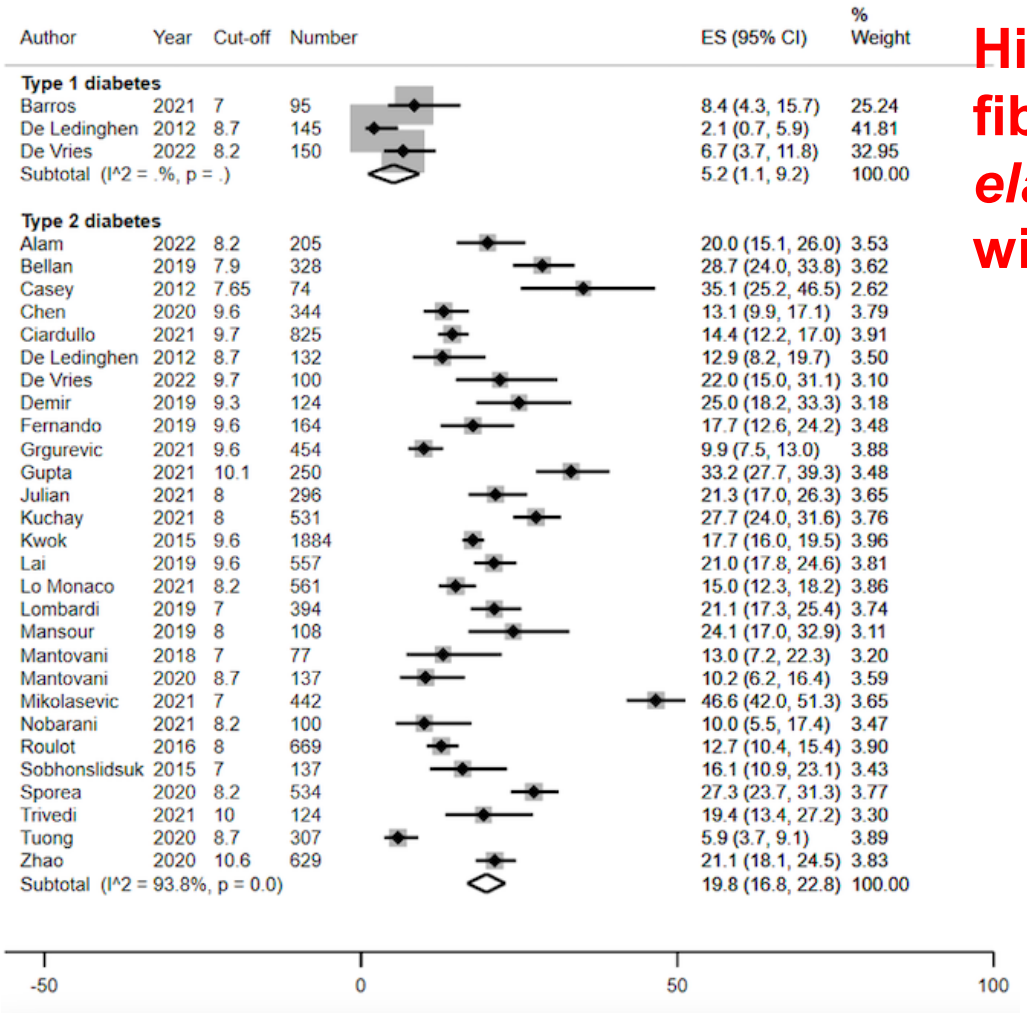
High prevalence of advanced liver fibrosis assessed by *transient elastography* among US adults with type 2 diabetes

Table 2 Features of the study population according to liver stiffness measurement (LSM) values

	<8 KPa	8-9.5 KPa	9.6-13 KPa	≥13 KPa	P
N (%)	636 (74.7)	63 (7.5)	68 (7.9)	58 (9.9)	0.627
Male participants (%)	48.6±7.26	41.1±8.36	49.1±10.35	55.5±3.57	
Age (years)	60.9 ±1.00	59.3 ±2.57	61.5 ±2.97	57.8 ±1.39	0.082
Disease duration (years)	9.6 ±0.66	8.8 ±1.79	12.4 ±2.98	10.3 ±2.75	0.716
BMI (Kg/m^2)	31.9 ±0.56	35.7 ±0.86	36.9 ±1.37	39.4 ±1.47	<0.001
Obesity (%)	57.5 ±3.41	81.5 ±3.55	81.5 ±7.23	88.9 ±4.93	<0.001
Waist circumference (cm)	108.6 ±0.96	118.5±2.24	120.6 ±3.26	128.1 ±4.23	<0.001

Data are expressed as weighted proportions (± Standard Error (SE)) for categorical variables and as weighted means ± SE for continuous variables. One-way ANOVA and Rao-Scott chi-square test were used to compare groups.

Ciardullo S et al Diabetes Care, 2021



High prevalence of liver fibrosis assessed by *transient elastography* among patients with type 2 diabetes

Ciardullo S et al
Diabetes Res Clin Pract, 2022

Prevalence of Liver Steatosis and Fibrosis Detected by *Transient Elastography* in Adolescents in the 2017–2018 NHANES

4.4%
95% CI, 2.51–6.33

Table 3. Features of the Study Population Segregated by the Degree of Estimated Liver Fibrosis

	F0–F1 (n = 816)	≥F2 (n = 51)	*P* Value
Female/male	816 (398/418)	51 (18/33)	.06
Age, y	15.0 ± 0.1	15.6 ± 0.4	.33
BMI category, %			<.01
<5th percentile	4.0 ± 1.3	1.2 ± 1.2	
5th–84.9th percentile	59.6 ± 1.4	35.0 ± 8.5	
85th–95th percentile	16.9 ± 1.7	5.0 ± 3.5	
≥95th percentile	19.5 ± 1.4	58.8 ± 8.3	

Table 4. Characteristics Associated With the Presence of Significant Fibrosis in a Multivariate Logistic Regression Model

Predictor	OR (95% CI)	*P* Value
BMI(per unit increase)	1.10 (1.03–1.18)	<.01
Age (per unit increase)	1.08 (0.79–1.48)	.59
Sex		
Male	Reference	
Female	0.44 (0.17–1.18)	.10
Race/ethnicity		
Non-Hispanic White	Reference	
Non-Hispanic Black	3.96 (1.19–13.18)	.03
Hispanic	1.41 (0.36–5.58)	.60
Other	1.25 (0.32–4.90)	.74
Blood pressure status		
Normal	Reference	
Elevated	1.12 (0.27–4.66)	.87
Hypertension	2.42 (0.82–7.12)	.10

BMI, body mass index; CI, confidence interval; OR, odds ratio.

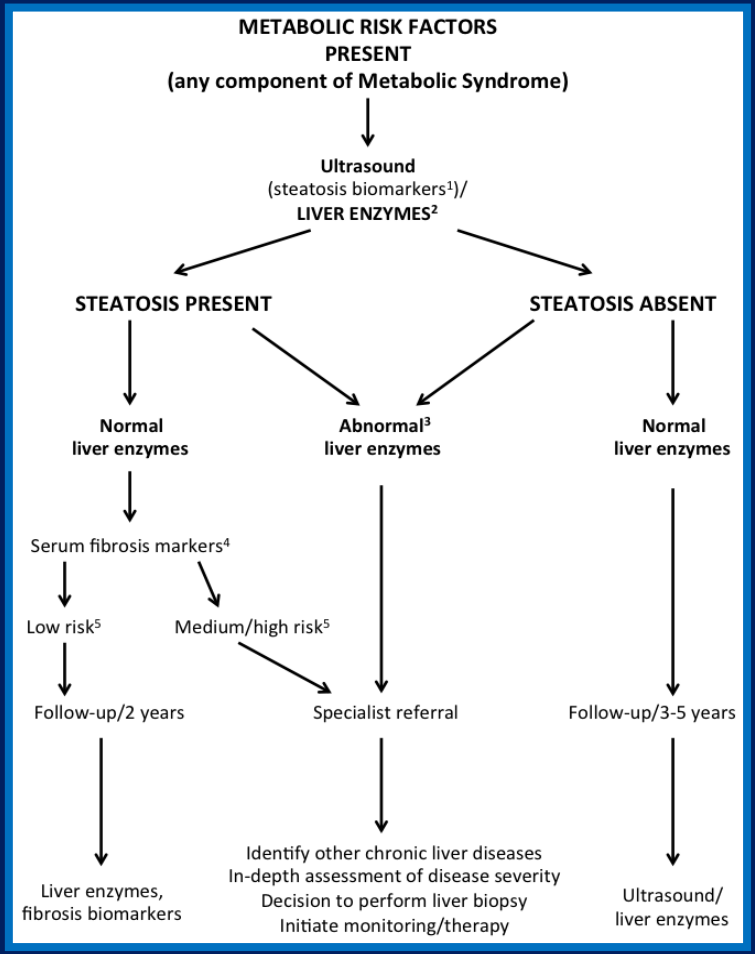
Ciardullo S et al Clin Gastroenterol Hepatol, 2021

Clinical Practice Guidelines

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)



Legend:

[1] Steatosis biomarkers: Fatty Liver Index, SteatoTest, NAFLD Fat score (see Tables)

[2] Liver tests: ALT AST, gGT

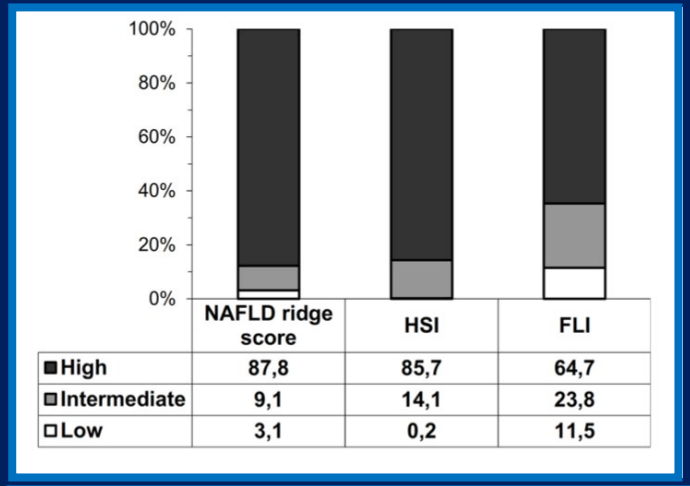
[3] Any increase in ALT, AST or gGT

[4] Serum fibrosis markers: NAFLD Fibrosis Score, FIB-4, Commercial tests (FibroTest, FibroMeter, ELF)

[5] Low risk: indicative of no/mild fibrosis; Medium/high risk: indicative of significant fibrosis or cirrhosis (see Tables)

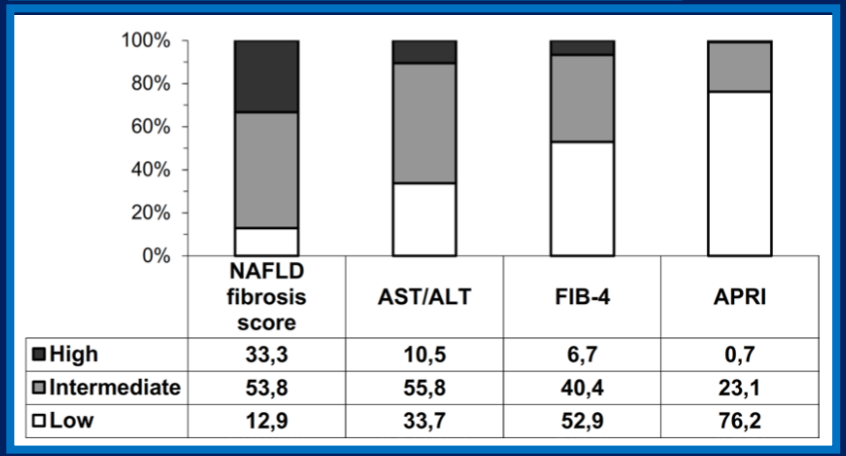
EASL, EASD, EASO, 2016

Findings in the Italian Real World



	NAFLD ridge score	HSI	FLI
High	87,8	85,7	64,7
Intermediate	9,1	14,1	23,8
Low	3,1	0,2	11,5

Steatosis

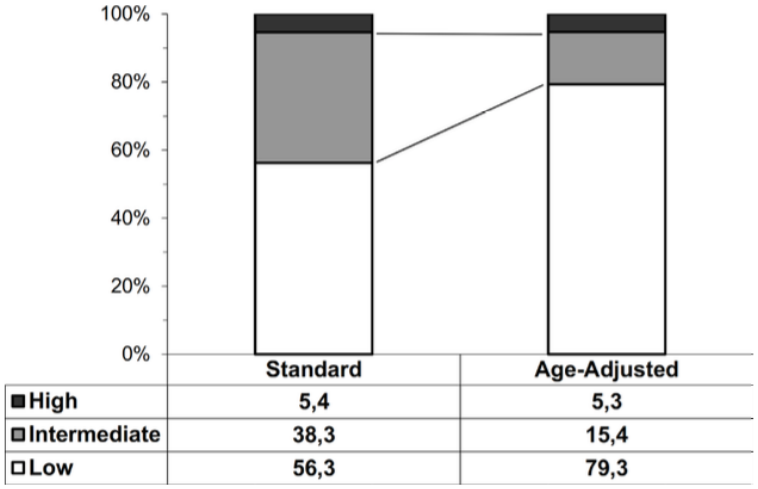


	NAFLD fibrosis score	AST/ALT	FIB-4	APRI
High	33,3	10,5	6,7	0,7
Intermediate	53,8	55,8	40,4	23,1
Low	12,9	33,7	52,9	76,2

Fibrosis

Ciardullo S et al
BMJ Open Diabetes Res Care, 2020

Findings in the Italian Real World



	Standard	Age-Adjusted
High	5,4	5,3
Intermediate	38,3	15,4
Low	56,3	79,3

Figure 2 Proportion of patients with low, intermediate and high FIB-4 scores using standard and age-adjusted cut-offs. White bars represent low probability of fibrosis, gray bars represent intermediate probability and black bars represent high probability. Data are referred to patients with FLI>60. FIB-4, fibrosis-4; FLI, Fatty Liver Index.

FIB-4

43.7% to **20.7%**

Ciardullo S et al
BMJ Open Diabetes Res Care, 2020

Findings in the US T2DM population

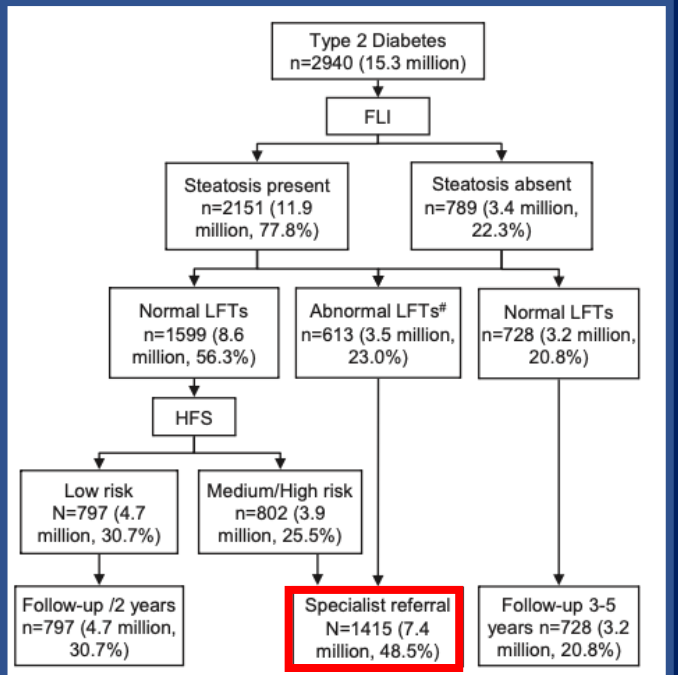


Fig. 1 – Application of the EASL-EASD-EASO guidelines flowchart using Hepamet Fibrosis Score (HFS). The results are presented as number of individuals (weighted number, weighted proportion). Abnormal liver enzymes were defined as AST > 40 U/L, ALT > 40 U/L or GGT > 50 U/L. Low risk of advanced fibrosis was defined as HFS < 0.12. FLI, Fatty Liver Index.

Insights from NHANES 2005–2016

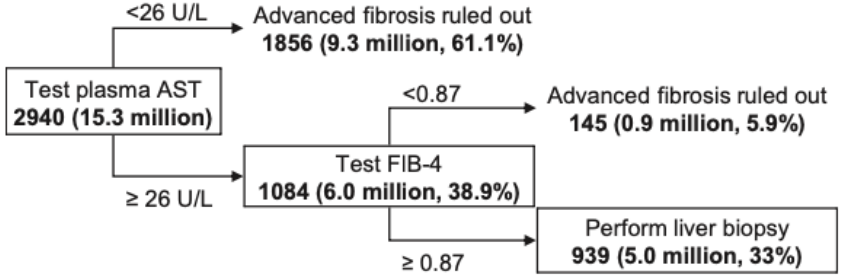


Fig. 2 – Sequential testing for the diagnosis of advanced fibrosis using a combination of AST and FIB-4. The results are presented as number of individuals (weighted number, weighted proportion).

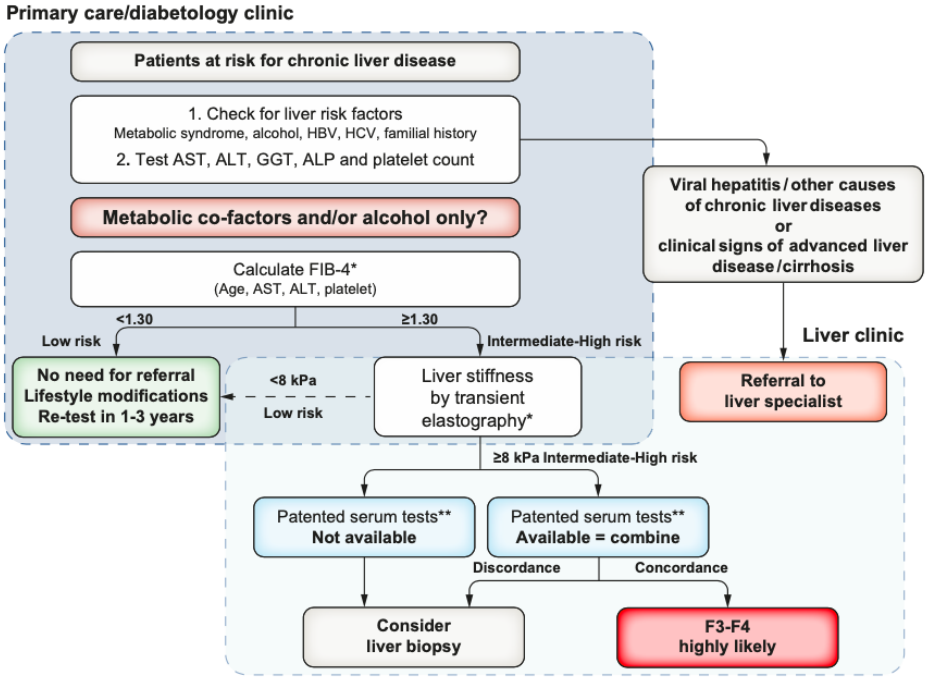
HFS

48.5%
7.4 million

Ciardullo S et al
Diabetes Res Clin Pract, 2020

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

European Association for the Study of the Liver*



Key message

NAFLD is largely prevalent in the diabetes clinic, may play a relevant pathogenic role but may also determine a poor prognosis

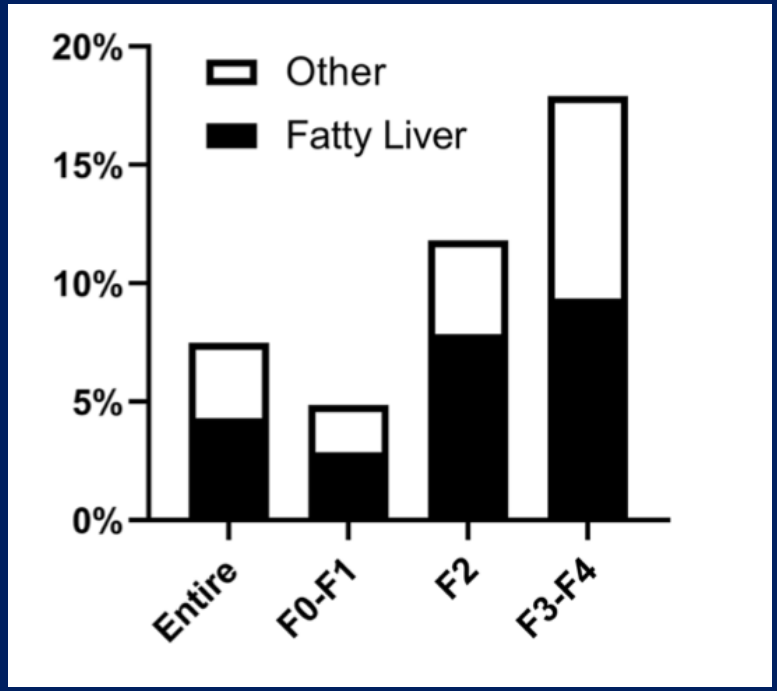
Much work is required to improve consciousness among HCP in the diabetes field for

1) Education and prevention

2) Better surveillance of the risk of potential gastro-enterologic complications in patients with T2DM

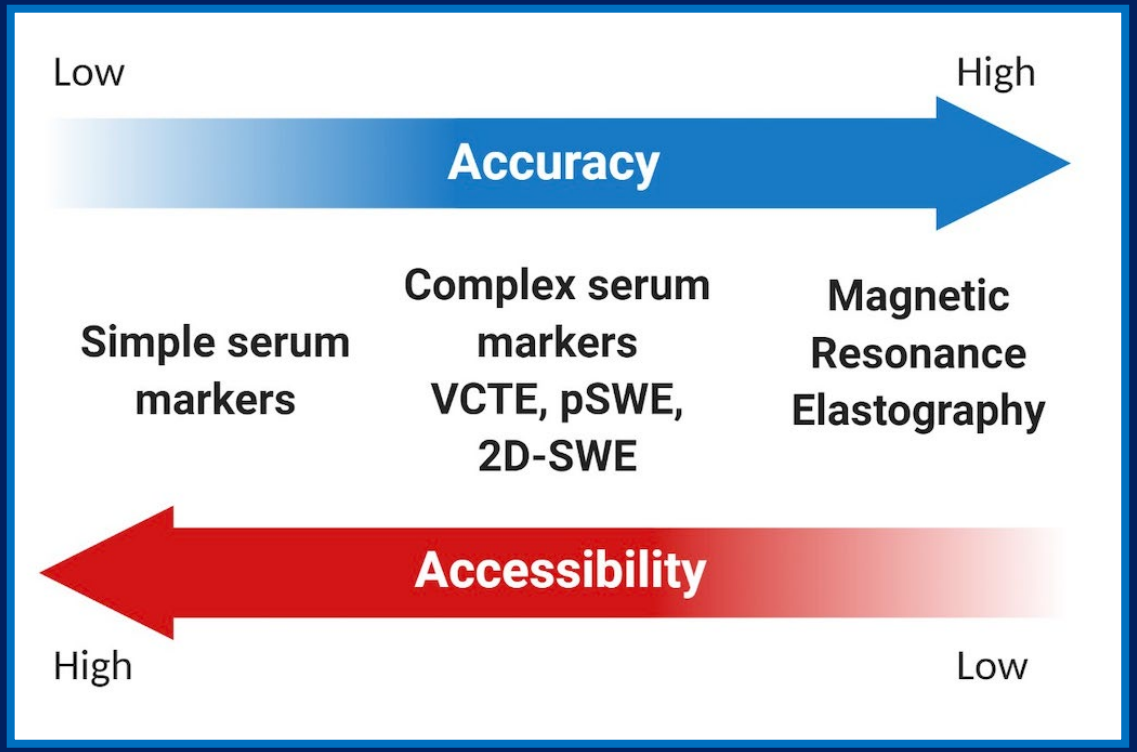
At this stage, we need to build a friendly, reliable and cost-effective screening process to be applied in the health care systems

“Ever told you had any liver condition?”



Ciardullo S et al Acta Diabetol, 2021

Personalization: patients and infrastructures



VCTE, vibration controlled transient elastography
pSWE, point shear-wave elastography
2D-SWE, 2 dimensional shear-wave elastography

Ciardullo S et al, Adv Clin Chem, 2022

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