

roshapharma

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What is MASLD?

Metabolic dysfunction–associated steatotic liver disease



1 **MASLD is a liver disease characterized by hepatic steatosis plus at least one cardiometabolic risk factor.**

2 **It is closely linked to obesity, type 2 diabetes, and other metabolic disorders.**



Obesity

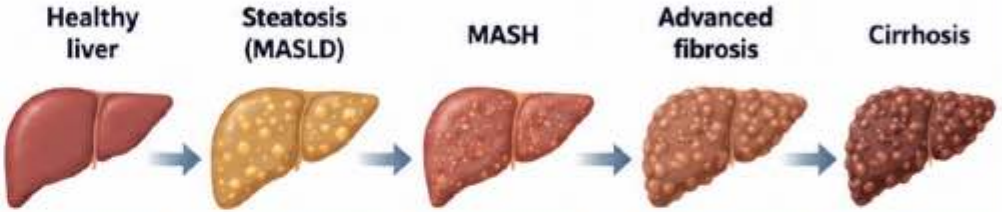


Type 2 diabetes



Other metabolic disorders

3 **MASLD spans a spectrum from simple steatosis to MASH, advanced fibrosis, and cirrhosis.**

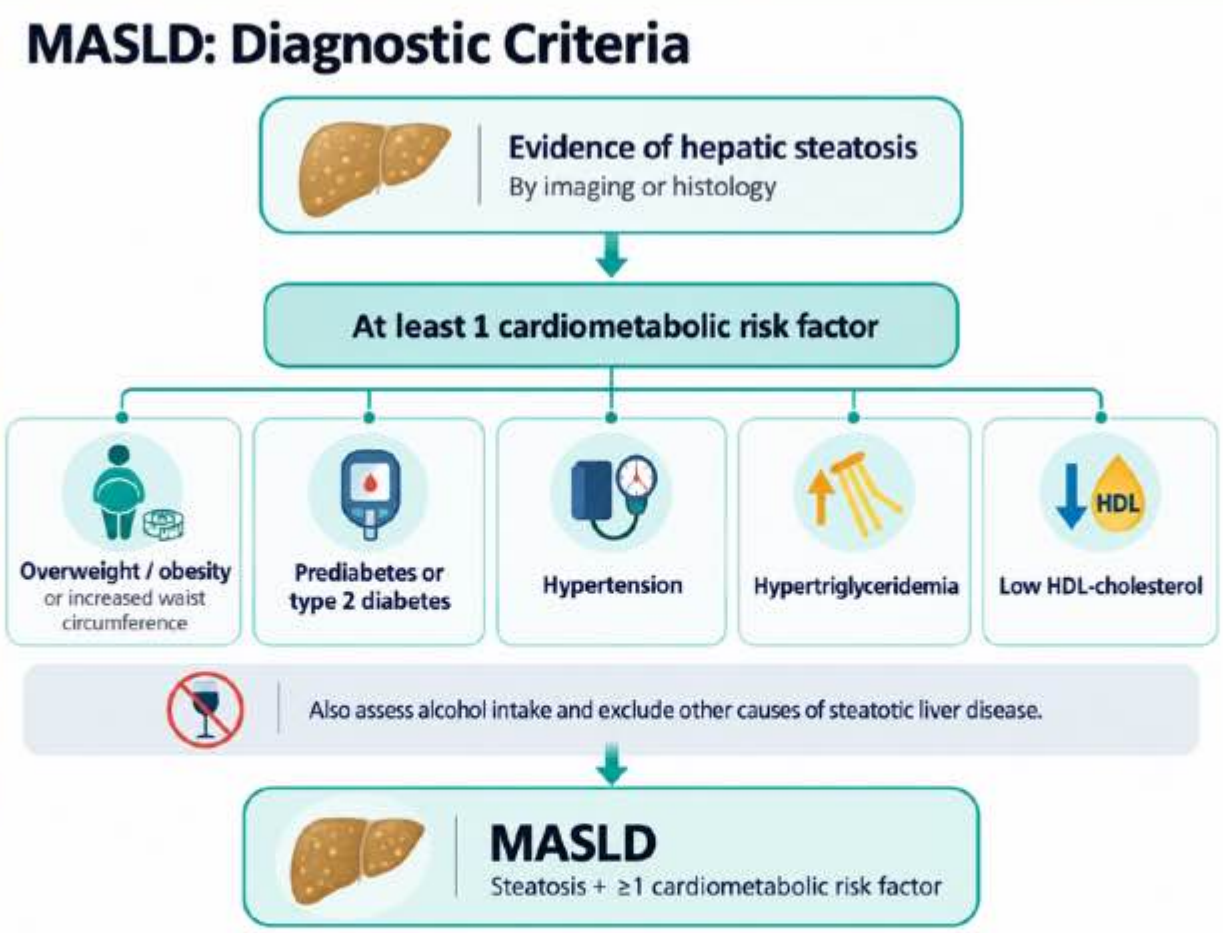


Healthy liver	Steatosis (MASLD)	MASH	Advanced fibrosis	Cirrhosis
< 5% fat in hepatocytes	Hepatic steatosis (≥ 5% fat)	Steatosis + inflammation ± ballooning	Progressive fibrosis (stages F2–F3)	Cirrhosis (stage F4)

A multisystem metabolic liver disease with a broad clinical spectrum.

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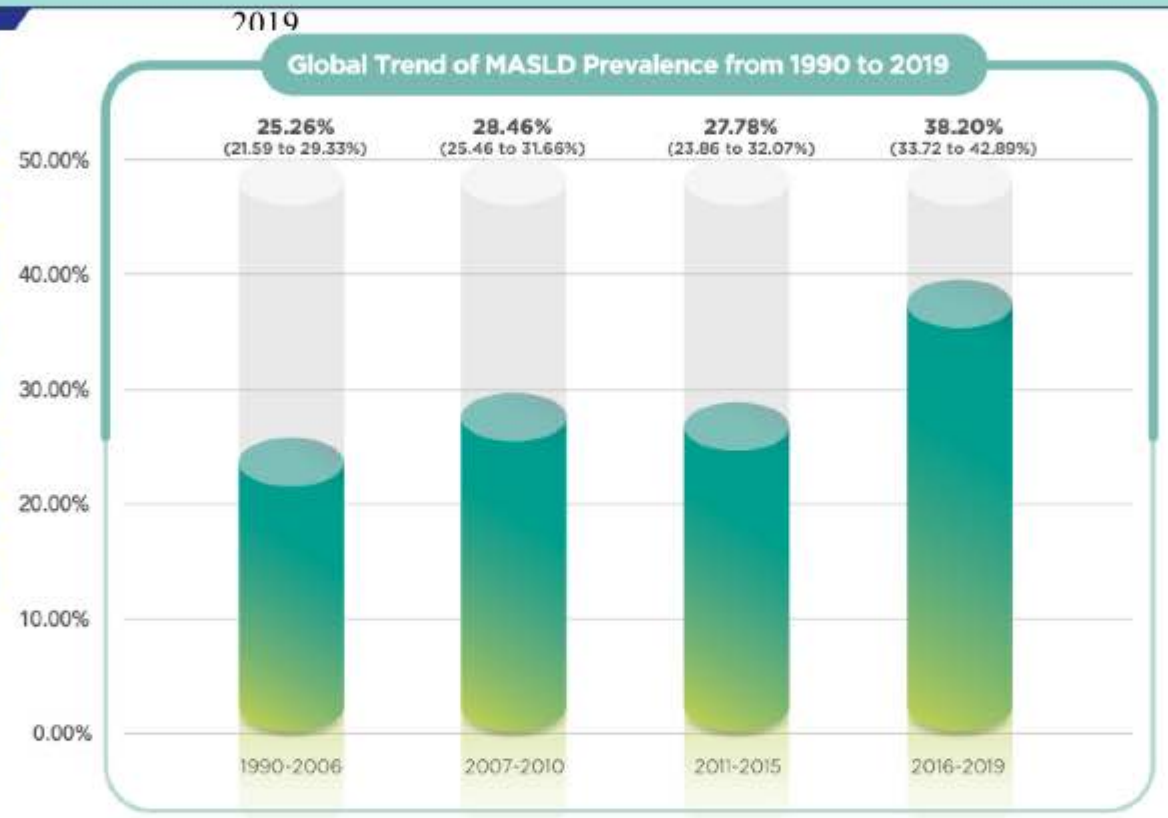
MASLD is characterized by hepatic steatosis in the presence of at least one cardiometabolic risk factor.



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MASLD/MASH; An Uprising Global Health Challenge

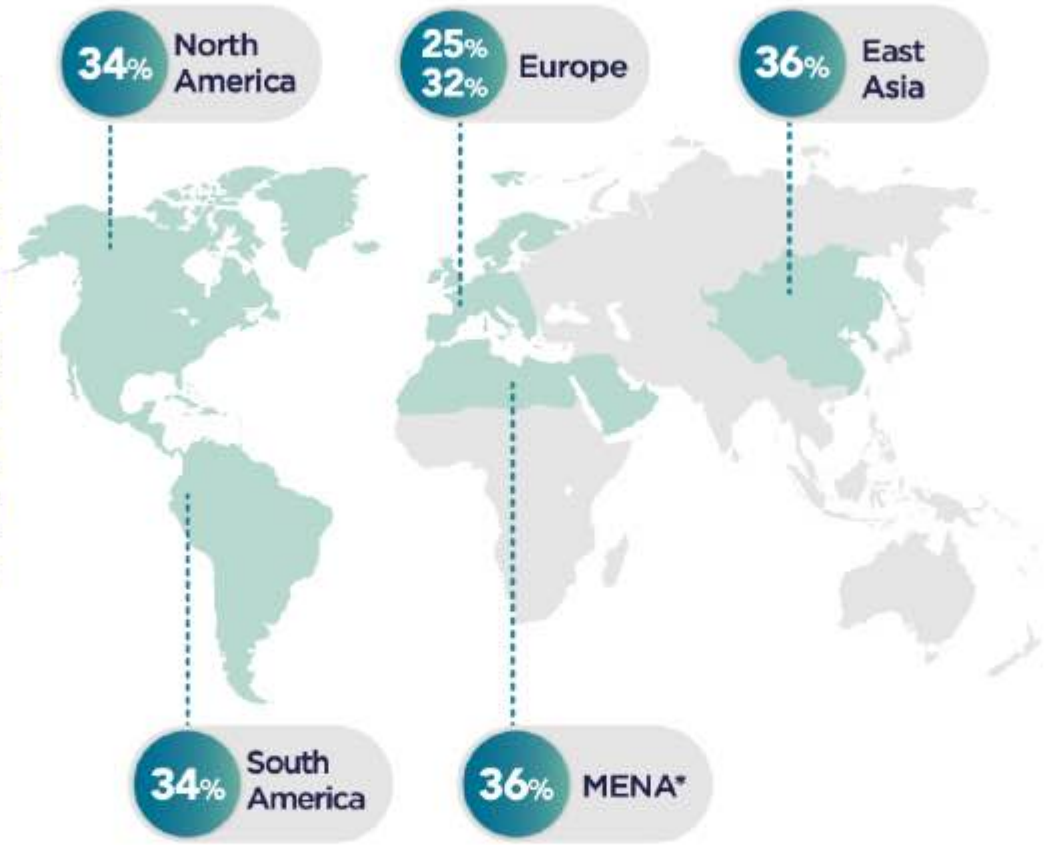
Global MASLD prevalence increased from 25.26% in 1990 to 38.20% in 2019 (p<0.001), expecting it to reach 55.4% by 2040.



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MASLD/MASH; An Uprising Global Health Challenge

Prevalence of MASLD estimations around the world

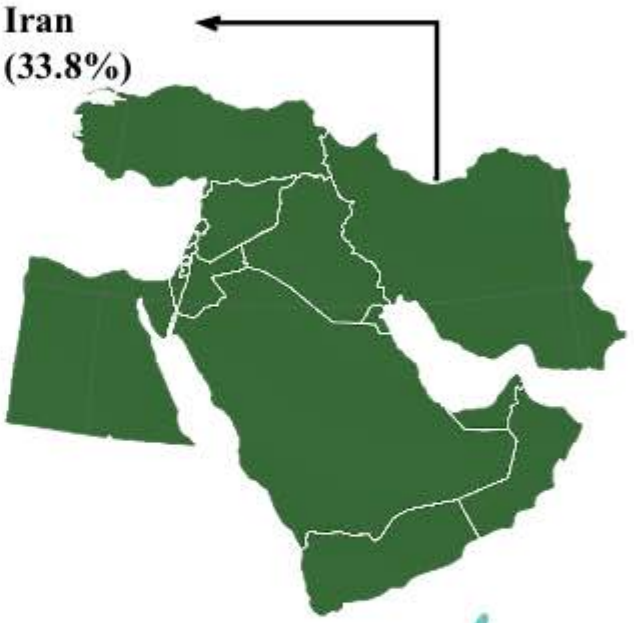


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MASLD/MASH; An Uprising Global Health Challenge

Prevalence of MASLD in Iranian population

- The MENA countries expected to have the highest number of MASLD cases are Egypt, followed by Türkiye and **Iran (33.8%)**.

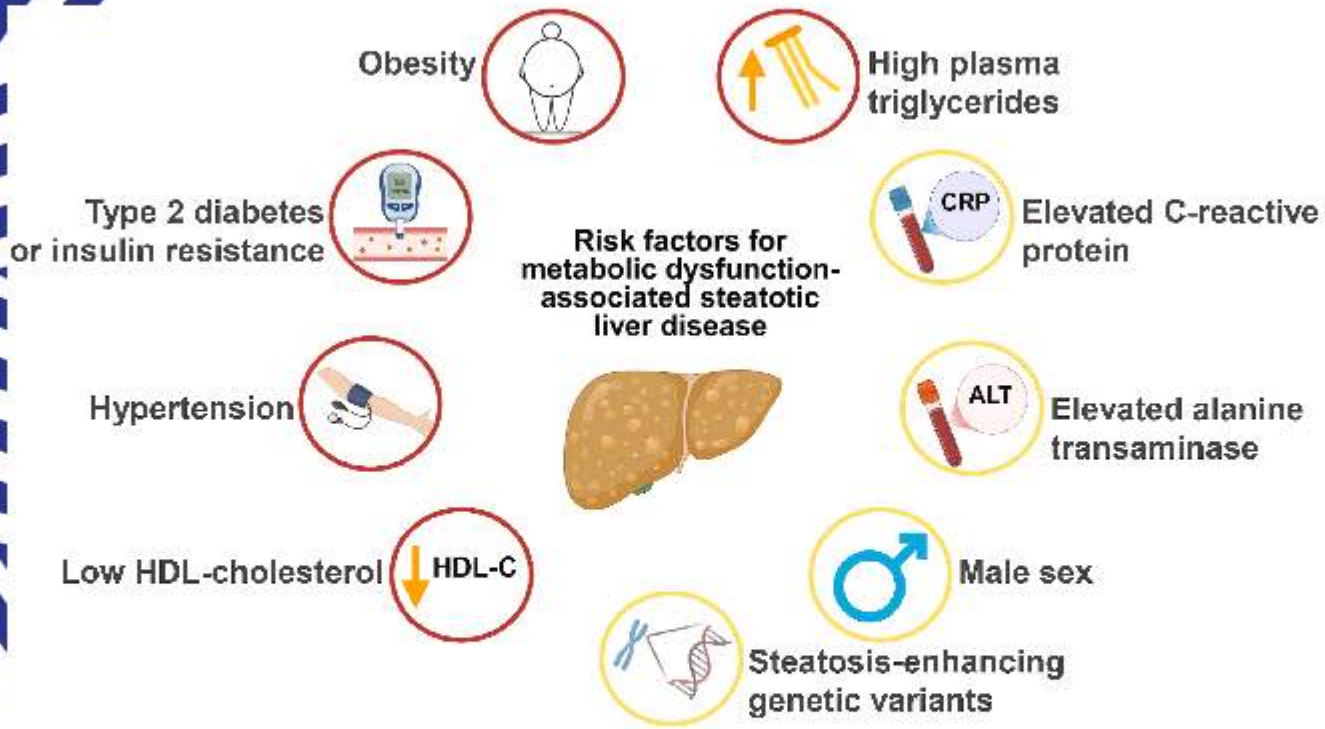


The **global disease burden** paired with the **public health impact** from clinical outcomes highlights the critical need for the development of highly effective, well-tolerated, and safe pharmacotherapy.

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MASLD and Cardiometabolic Risk

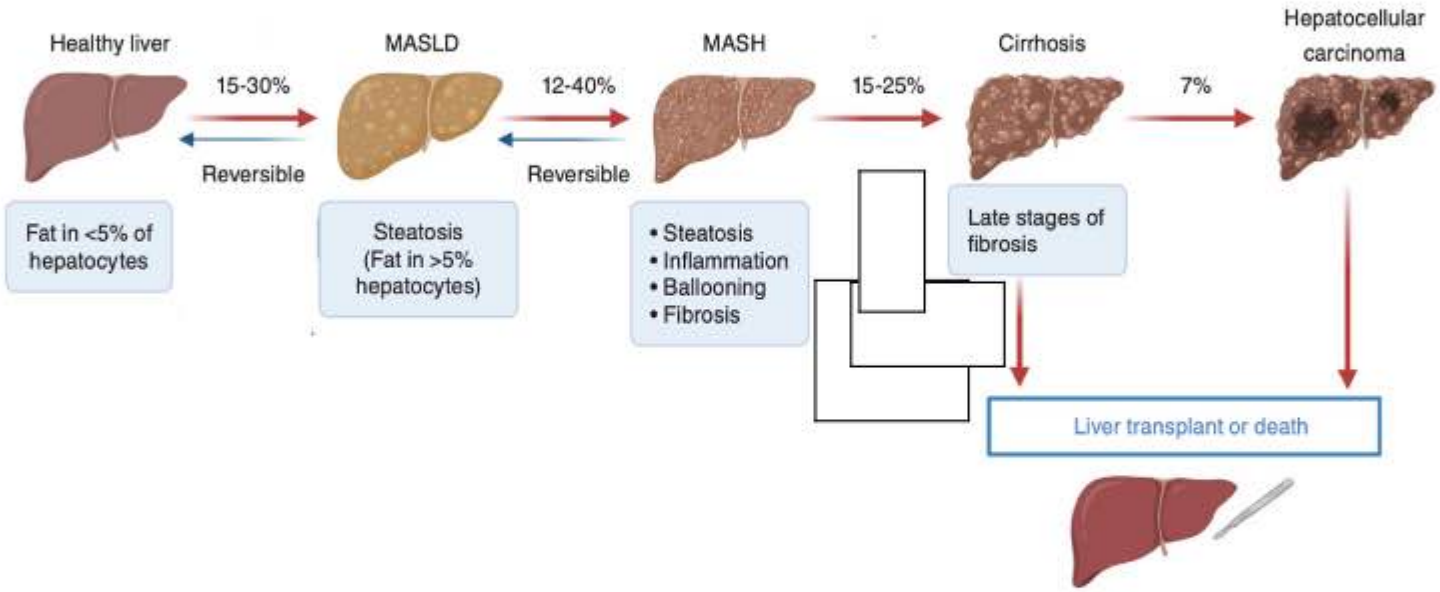
MASLD is a multi-system metabolic disease, closely linked to obesity, type 2 diabetes, hypertension, and other metabolic disorders.



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The Spectrum of

MASLD encompasses a broad spectrum ranging from simple steatosis to MASH, advanced liver fibrosis, cirrhosis, liver transplantation, and liver-related mortality.

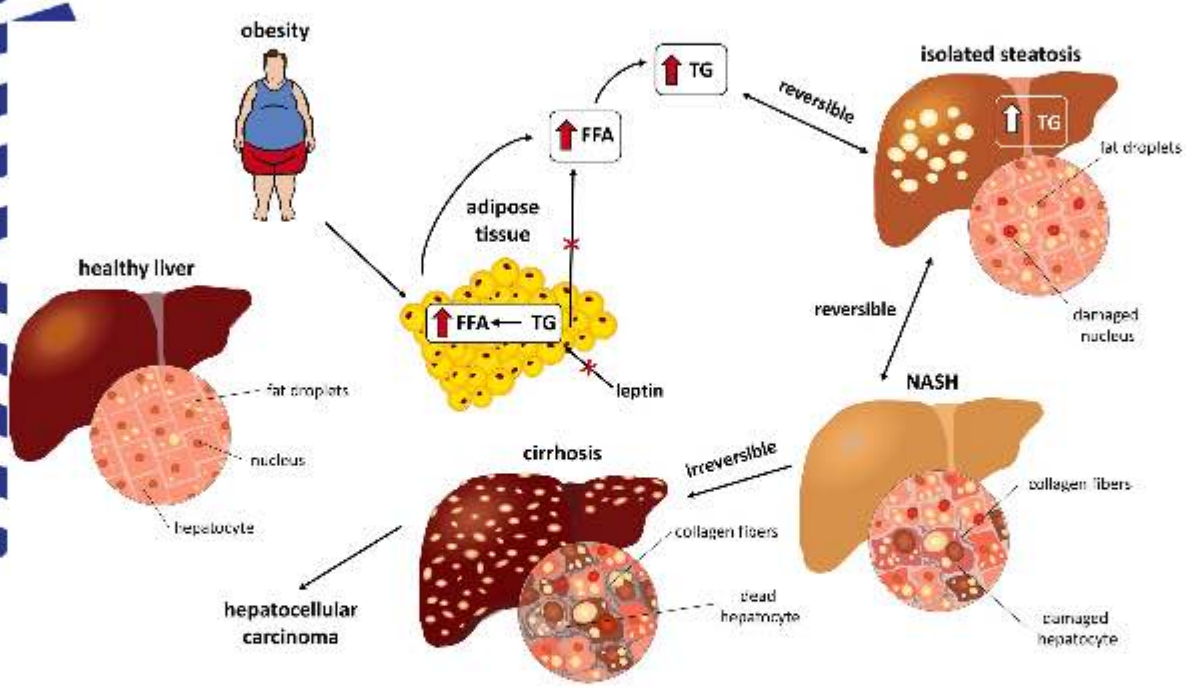


Current understanding of the progression and regression of MASLD

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MASLD/MASH Pathophysiology

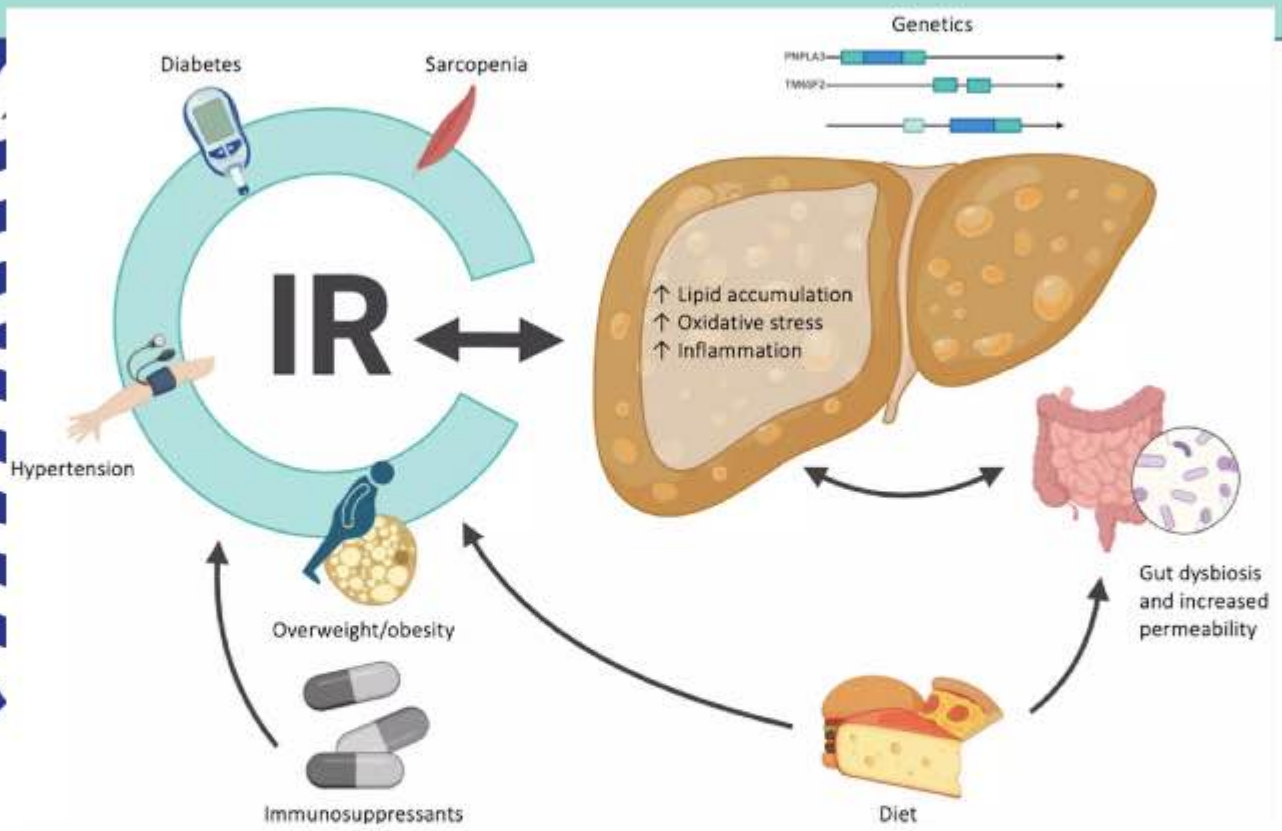
- MASLD originates from underlying metabolic dysfunction and insulin resistance, driving excess fat accumulation in the liver.
- As the disease advances, lipotoxicity triggers persistent inflammation and hepatocellular injury, paving the way toward MASH and progressive fibrosis.



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Multifactorial Pathogenesis of

- Insulin resistance acts as a central driver linking cardiometabolic risk factors, obesity, sarcopenia, genetic



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MASLD/MASH; A Massive Burden on Healthcare System

MASLD progresses to metabolic dysfunction-associated steatohepatitis (MASH) at a rate of 12-40% with a significant risk of:



Cirrhosis



Hepatocellular carcinoma (HCC)



Liver transplantation



And Liver-related death

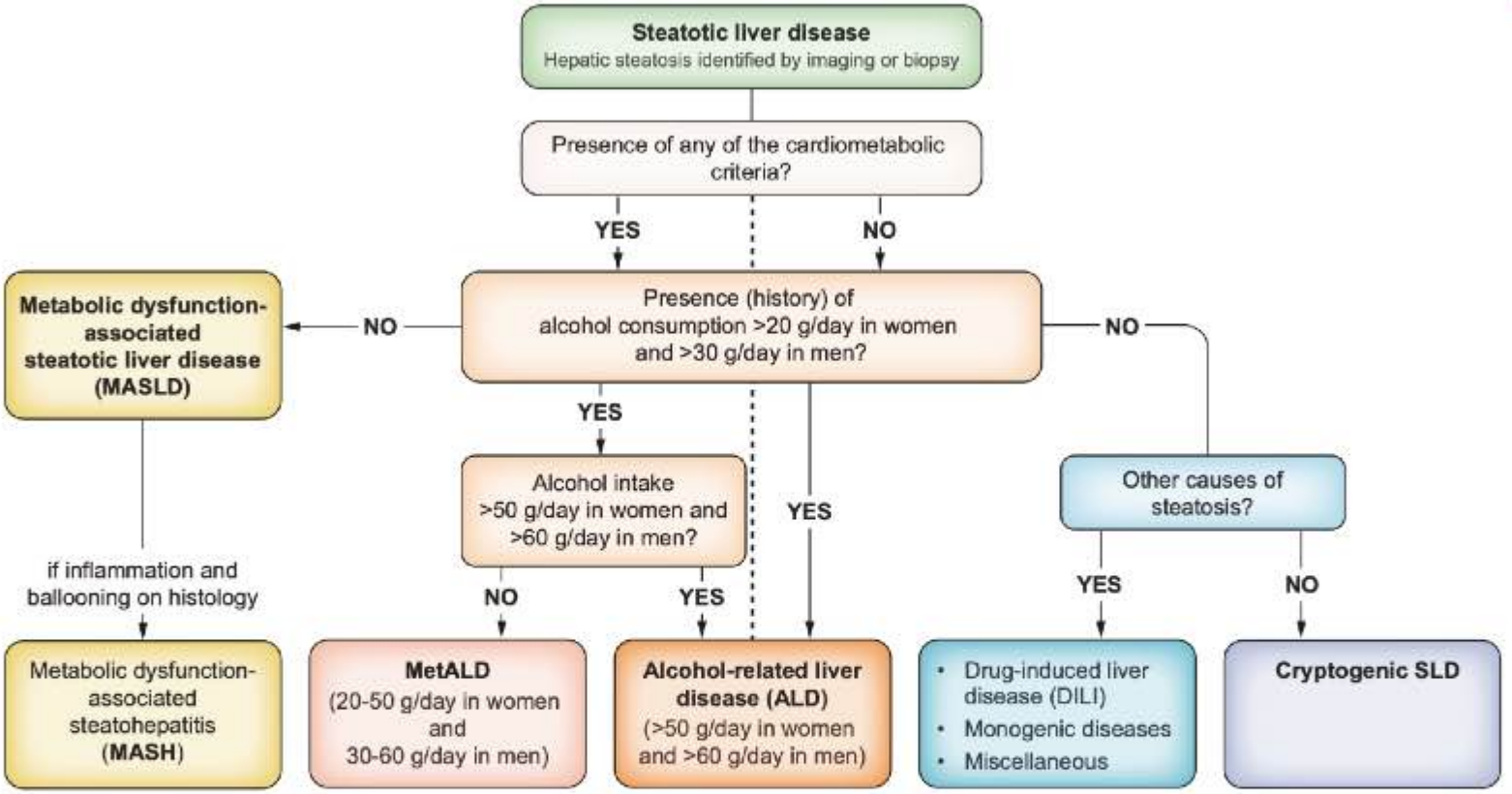


MASH is responsible for most liver-related morbidity, mortality and transplant demand, with prevalence rising alongside obesity and type 2 diabetes worldwide.[2,3]

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Excluding Other Liver Diseases

Appropriate consideration of alcohol intake and other causes of steatotic liver disease is required.



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Practical Diagnostic Workup in Suspected MASLD

Condition / cause	What to check
Alcohol-related liver disease	Detailed alcohol history; assess quantity and pattern of intake
Viral hepatitis	HBsAg, anti-HCV; if anti-HCV positive, check HCV RNA
Drug-induced steatosis / steatohepatitis	Review medications; examples: amiodarone, tamoxifen, corticosteroids
Hemochromatosis / iron overload	Ferritin and transferrin saturation
Autoimmune liver disease	If indicated: ANA, ASMA, and IgG
Wilson disease	Ceruloplasmin and further evaluation in selected younger patients
Alpha-1 antitrypsin deficiency	A1AT level and phenotype/genotype when suspected
Other selected causes	Consider celiac disease, severe malnutrition, and rare genetic disorders based on clinical clues

Diagnosis of MASLD requires steatosis + cardiometabolic risk, while other liver diseases should be actively assessed.

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Who should undergo fibrosis risk assessment in suspected MASLD?

1. **Type 2 diabetes**

2. **Overweight/obesity with ≥1 additional cardiometabolic risk factor**
   Prediabetes, dyslipidemia, hypertension, or metabolic syndrome

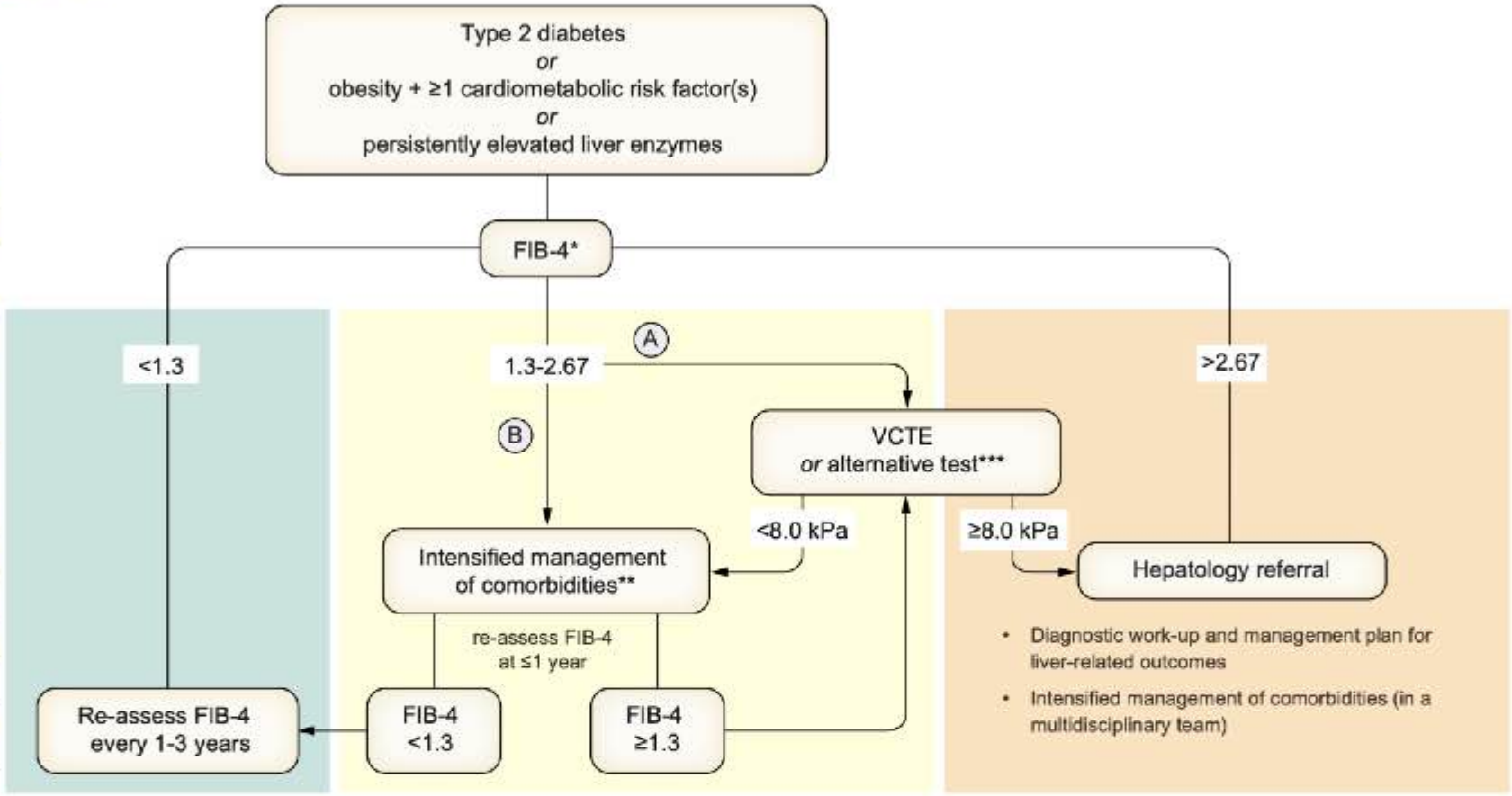
3. **Persistent unexplained elevation of ALT/AST**
   Abnormal liver enzymes without another clear cause

4. **Incidentally detected hepatic steatosis**
   Steatosis on ultrasound, CT, or MRI

5. **Established MASLD or lean individuals with metabolic disease**
   Consider assessment even with normal ALT when clinical suspicion is present

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Stepwise Risk Stratification of Liver Fibrosis in MASLD



* 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

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Limitations of FIB-4

Age-dependent performance
Lower accuracy in patients under 35; use adjusted cutoffs in older adults.

False negatives
A low FIB-4 does not completely exclude advanced fibrosis.

Reduced accuracy in T2D
Patients with type 2 diabetes may still have significant fibrosis despite a low score.

Indeterminate zone
Values between 1.3 and 2.67 often require second-line assessment such as VCTE.

Affected by acute illness
Transient changes in AST, ALT, or platelet count can distort the result.



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Key Takeaways

Identify at-risk patients
Screen individuals with MASLD and cardiometabolic risk factors (e.g. obesity, T2D, HTN, dyslipidemia).

Use FIB-4 as the initial assessment tool
FIB-4 is a simple, accessible, and validated tool to estimate the risk of advanced fibrosis.

Follow a stepwise approach
Patients with FIB-4 ≥1.3 should undergo second-line assessment (e.g. VCTE) or closer follow-up.

Recognize the limitations of FIB-4
Interpret FIB-4 with caution (age-dependent, risk of false negatives, reduced accuracy in T2D, indeterminate zone, and affected by acute illness).

Implement a comprehensive management plan
Address cardiometabolic risk factors and consider referral to a liver specialist for patients at increased risk of advanced fibrosis.

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Thank you!