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Diagnosing, Staging, and Treating Patients in an Advancing Field

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Strengthening Your Diagnostic and Management Muscles

Our Clinical Resource Center on MASH
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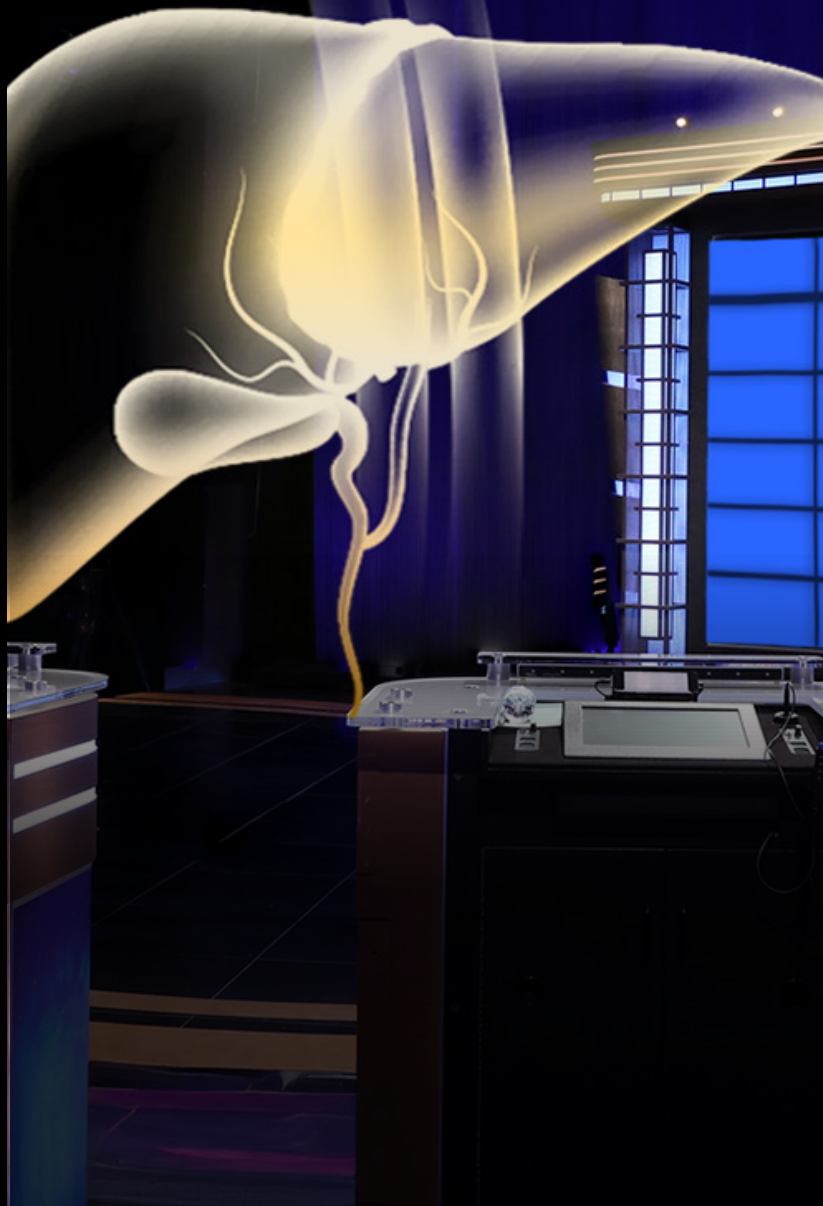
INTEGRITAS COMMUNICATIONS

CAN YOU MASTER MASH DIAGNOSIS AND MANAGEMENT?



A Clinician's Pocket Guide to MASH Diagnosis and Management

Who Should Be Screened for MASLD?

- **All patients** with hepatic steatosis or clinically suspected MASLD based on obesity and metabolic risk factors should undergo primary risk assessment with FIB-4
- **In patients** with T2D/pre-T2D or ≥2 metabolic risk factors (or imaging evidence of hepatic steatosis), FIB-4 should be repeated every 1 to 2 years if initial score is below cutoff for indeterminant fibrosis
- **In patients** with <2 metabolic risk factors, FIB-4 should be repeated every 2 to 3 years if initial score is below cutoff for indeterminant fibrosis
- **High-risk individuals**, such as those with T2D, medically complicated obesity, family history of cirrhosis, or more than mild alcohol consumption, should be screened for advanced fibrosis using ELF, TE, or other imaging measures

Hepatic Indications for MASH

- ≥5% of hepatocytes display macrovesicular steatosis
- Presence of inflammation and cellular injury (ballooning), with or without fibrosis

LABORATORY-, SERUM-, OR IMAGING-BASED NITS CAN BE USED TO ESTIMATE FIBROSIS LEVELS AND STEATOSIS FOR PRESUMED MASLD/MASH DIAGNOSIS.

FIB-4 Cutoff Values

Score for Age <65 Years	Score for Age ≥65 Years	Risk Category for Advanced Fibrosis
<1.3	<2.0	Low risk
1.3-2.67	2-2.67	Intermediate risk
>2.67	>2.67	HIGH RISK

Initial Screening for Risk of Advanced Fibrosis

FIB-4 ≥1.3

NO

Reassess periodically

- FIB-4 every 1-2 years if T2D/pre-T2D or ≥2 metabolic risk factors
- FIB-4 every 2-3 years if no T2D and <2 metabolic risk factors

YES

FIB-4 >2.67

- Perform secondary assessment and evaluate for pharmacotherapy

Secondary Risk Assessment

Risk Level	TE, kPa	ELF
Low	<8	<7.7
Intermediate	8-12	7.7-9.8
High	>12	>9.8

Consider additional stratification with MRE or cT1.

Cardiometabolic Criteria for MASLD

	Adult Criteria (at least 1 of 5)	Pediatric Criteria (at least 1 of 5)
Overweight/ Obesity	• BMI ≥25 kg/m2 (23 Asia) ***OR*** • Waist circumference >94 cm (men) or 80 cm (women) ***OR*** ethnicity-adjusted equivalent	• BMI ≥85th percentile for age/sex (BMI z score ≥+1) ***OR*** • Waist circumference >95th percentile ***OR*** ethnicity-adjusted equivalent
Impaired Glucose	• Fasting serum glucose ≥100 mg/dL ***OR*** • 2-hour post-load glucose level ≥140 mg/dL ***OR*** • HbA1c ≥5.7% ***OR*** • T2D OR treatment for T2D	• Fasting serum glucose ≥100 mg/dL ***OR*** serum glucose ≥200 mg/dL OR • 2-hour post-load glucose level ≥140 mg/dL ***OR*** • HbA1c ≥5.7% ***OR*** • T2D OR treatment for T2D
Hypertension	• BP ≥130/85 mm Hg ***OR*** • Antihypertensive drug treatment	• Age <13 years: ≥95th percentile ***OR*** ≥130/85 mm Hg • Age ≥13 years: 130/85 mm Hg ***OR*** antihypertensive drug treatment
Impaired HDL-C	• Plasma HDL-C ≤40 mg/dL for men and ≤50 mg/dL for women ***OR*** • Lipid-lowering treatment	• Plasma HDL-C ≤40 mg/dL ***OR*** • Lipid-lowering therapy
Triglycerides	• Plasma triglycerides ≥150 mg/dL ***OR*** • Lipid-lowering treatment	• Age <10 years: plasma triglycerides ≥100 mg/dL • Age ≥10 years: plasma triglycerides ≥150 mg/dL ***OR*** lipid-lowering therapy

Patients must meet ≥1 cardiometabolic criteria, in addition to steatosis, to be diagnosed with MASLD.

References

- Chen VL, et al. *Hepatology.* 2025;81(1):312-320.
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- Rinella ME, et al. *Hepatology.* 2023;77(5):1797-1835.
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- Whelton PK, et al. *J Am Coll Cardiol.* 2018;71(19):e127-e248.

ACE, angiotensin-converting enzyme; ALT, alanine aminotransferase; ARB, angiotensin receptor blocker; AST, aspartate aminotransferase; BP, blood pressure; BMI, body mass index; CT1, iron-corrected T1 mapping; DILI, drug-induced liver injury; ELF, Enhanced Liver Fibrosis; F, fibrosis; FAST, FibroScan-AST; FIB-4, Fibrosis-4; GLP-1, glucagon-like peptide 1; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LSM, liver stiffness measure; MASH, metabolic dysfunction–associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease; MAST, MRI-AST; MEFIB, MRI plus FIB-4; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; NIT, noninvasive test; PPAR, peroxisome proliferator-activated receptor; T2D, type 2 diabetes; TE, transient elastography.

Patient Eligibility for Resmetirom

MASH with biopsy-proven F2 or F3 *OR*

- TE, 8-15 kPa
- MRE, 3.1-4.4 kPa
- ELF score, 9.2-9.7 (+ second NIT)
- ELF score, 9.8-11.3 (if in isolation)
- FAST, MAST, MEFIB

Start resmetirom if eligible

- 80 mg if <100 kg
- 100 mg if ≥100 kg

3 MONTHS — **Confirm safety**
(Routine DILI parameters and tolerability)

Treatment safety monitoring — **6 MONTHS**
(hepatic function, thyroid function, lipid profile)

EFFICACY AT 12 MONTHS

No response
- Worsening of NITs
- Consistent increase in ALT

→ **STOP**

Benefit uncertain
- **TE:** <25% or MRE <20% drop in LSM
- **ALT:** no significant improvement
- **MRI-PDFF:** <30 reduction

→ **Consider continuing, add-on, or alternate approach**

Beneficial response
- **ALT:** significant improvement or normalization
- **TE:** ≥25% or **MRE:** ≥20% drop in LSM

→ **Continue**

Addressing Cardiometabolic Comorbidities

GLP-1–targeting therapies, particularly semaglutide and tirzepatide, have demonstrated numerous extrahepatic benefits:

- Glycemic control
- Management of obesity
- Reduction in major adverse cardiovascular events

Addressing these comorbidities can reduce the risk of advanced fibrosis and disease progression!

American Association for the Study of Liver Diseases Practice Guidance

- Consider semaglutide or liraglutide in patients with MASH without cirrhosis due to benefits in T2D, obesity, and cardiovascular disease
- Tirzepatide may be used for patients with T2D and/or obesity with MASLD for its benefits in both T2D and obesity

Follow other guidelines for management of hypertension and dyslipidemia!

There is NO contraindication to statins; thus, use per lipid guidelines. If a fibrate is required, consider one with PPAR activity.

ACE inhibitors or ARBs may have beneficial effect on liver fibrosis, and hypertension treatment should be conducted according to guidelines.