

ECHO IDAHO

Diabetes and Metabolic Conditions

MASLD Testing and Management for Patients with Diabetes

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Learning Objectives

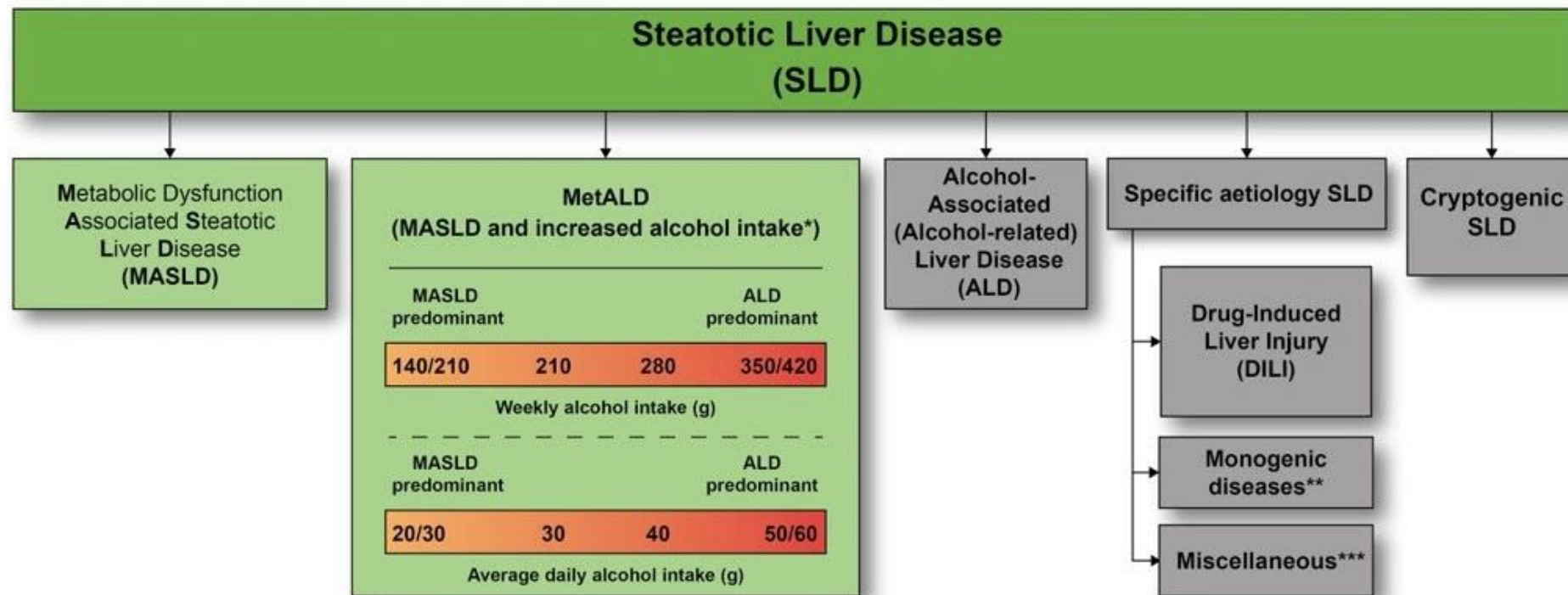
- Identify patients with MASLD
- Know how to risk stratify patients
- Know what MASLD specific treatments are available

Outline

- Nomenclature
- Diagnosis
- Staging
 - Elastography
 - Blood based fibrosis testing
- Management

Fatty liver → Steatotic liver disease

- MASLD, MASH (formerly NAFLD and NASH)



*Weekly intake 140-350g female, 210-420g male (average daily 20-50g female, 30-60g male)

**e.g. Lysosomal Acid Lipase Deficiency (LALD), Wilson disease, hypobetalipoproteinemia, inborn errors of metabolism

***e.g. Hepatitis C virus (HCV), malnutrition, celiac disease

How do you diagnose MASLD?

- Risk factors
 - BMI > 25 (23 if Asian), HTN, Dyslipidemia, T2DM
- Labs
 - Mild to moderate AST and ALT elevations (AST < ALT), sometimes Alk phos elevation
 - Low platelet count concerning for cirrhosis
- Imaging
 - US, CT, MRI can also suggest steatosis/fatty infiltration
- Rule out other causes of liver disease
 - ETOH, Medications, viral hepatitis, iron overload
 - Autoimmune liver disease (AMA, IgG, ANA, ASMA, ceruloplasmin, A1AT, TTG, IgA)
- Liver biopsy - only if alternative etiology is suspected or unable to stage noninvasively

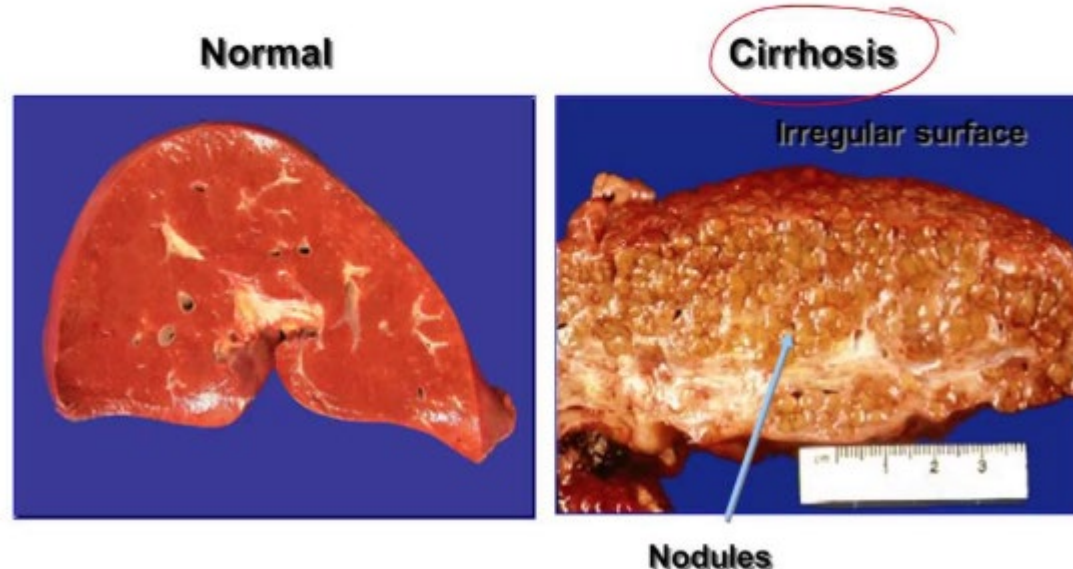
Staging MASLD

- Blood based fibrosis testing
- US based techniques
 - Vibration-controlled transient elastography (Fibroscan)- specialty clinics
 - 2D-SWE and ARFI – performed by radiology departments, usually more \$\$
- MR Elastography
 - More accurate than US based techniques but \$\$\$
- Liver biopsy

What is Fibroscan?

- Non invasive fibrosis testing
 - 80% sensitivity for detecting advanced fibrosis (F3) or cirrhosis (F4)
- Measures liver density

GROSS IMAGE OF A NORMAL AND A CIRRHOTIC LIVER



Density measurement (kPa)

- In soft tissues, stiffness is related to the velocity of elastic waves called **shear waves**.
- The faster the shear waves, the stiffer the medium.



$$\text{Stiffness (E)} \sim 3 \times (\text{shear wave speed})^2$$

1. Generate a shear wave in the liver

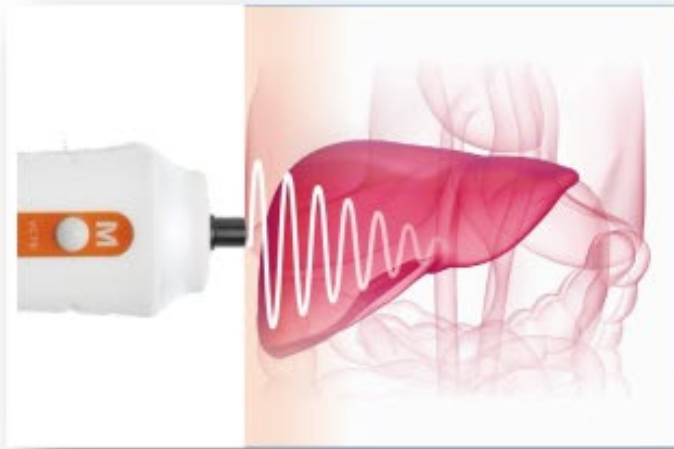
2. Uses ultrasound to measure shear wave speed V_s (m/s)

3. Compute the corresponding stiffness (E) in kPa



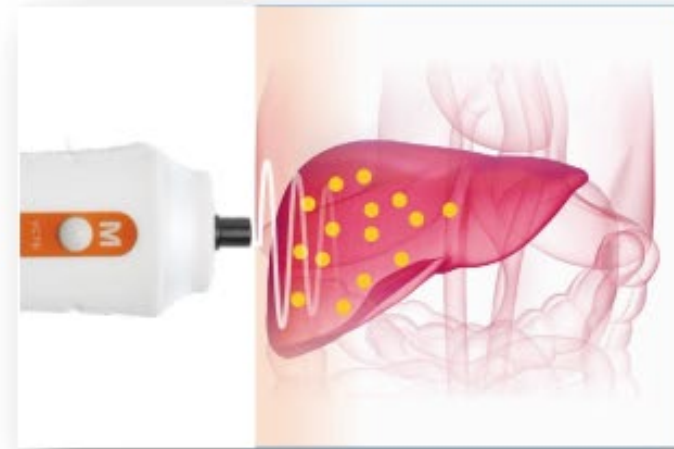
CAP (Ultrasound attenuation Rate)

CAP (dB/m) is measured by sending ultrasound waves into the liver and then measuring how much of the signal was attenuated.



Liver without Steatosis

- Low Ultrasound attenuation rate
- Low CAP value (dB/m)



Liver with Steatosis

- High Ultrasound attenuation rate
- Elevated CAP value (dB/m)

Confounding factors

(aka other things that make the liver seem dense)

- Alcohol
- Inflammation
- Hepatic Congestion (R heart failure)
- Cholestasis

- Not fasting
- Operator Error

- These factors falsely INCREASE results. Hard to have false negative or decrease kPa

How to use Fibroscan

1) Staging Liver Disease

- Prognosis based on fibrosis stage >> steatosis
- If F2 or F3, then qualify for MASLD specific medications
- If F4, standard cirrhosis protocol for HCC screening with US and AFP q6 months

2) Evaluate for steatosis

- !!!! Does NOT replace standard US in the workup of abnormal LFTs because we are not looking for structural/biliary changes
- Less of a reliable measurement for grading steatosis

Blood based fibrosis testing

- Free “tests”
 - Fib 4 – Age, AST, ALT, platelet count
 - Good at ruling OUT advanced fibrosis (90% NPV for if score < 1.3)
 - APRI – AST to platelet ratio
 - NFS (NAFLD fibrosis score) – age, BMI, DM, AST, ALT, Plt count, albumin
- Proprietary panels -not recommended in AASLD guidelines
 - ELF – can be used to get insurance prior authorization for MASH specific medications
 - FibroSure/FibroTest, FibroSpect, etc

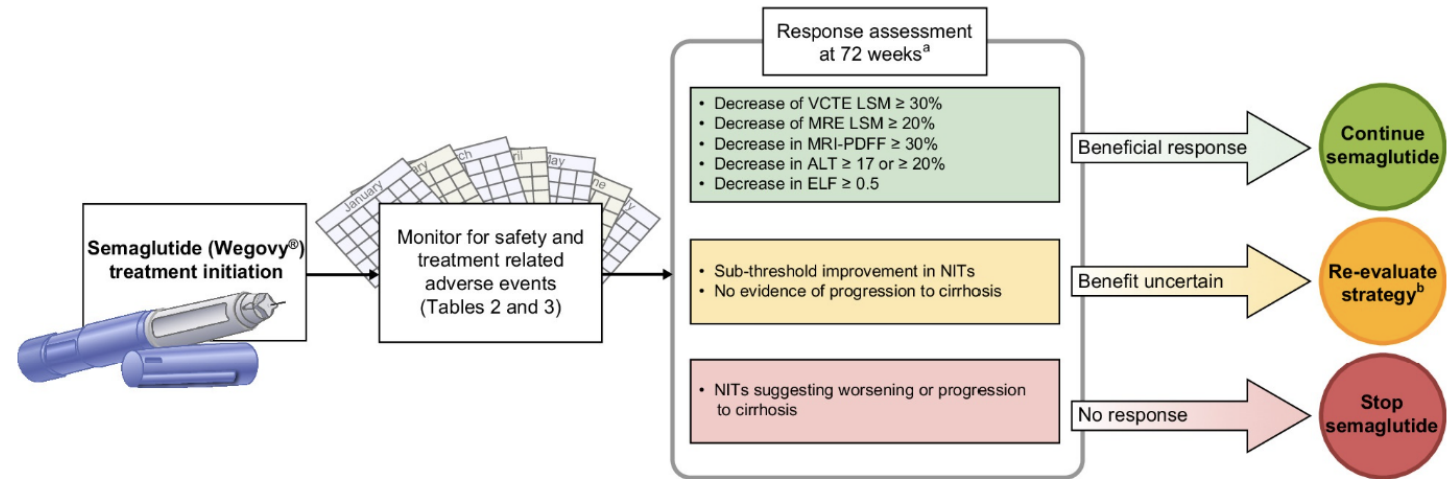
Management – non pharmacologic

- Weight loss – 10% total body weight reduction
 - Bariatric surgery
- Mediterranean Diet- consider referral to dietician
 - Other diets can work too but I generally don't recommend extreme diets like keto
 - 2 cups black coffee/day
- Physical Activity – 150 minutes/week
 - Beneficial even in absence of weight loss
- Avoid ETOH
- Immunizations for Hep A/B
- Optimize blood glucose and lipids

Management – pharmacologic

- GLP1 agonists
- Semaglutide (Wegovy)
 - FDA approved for MASH with F2 or F3 fibrosis – Fibroscan ~ 8-15 kPa
 - ESSENCE trial
 - Resolution of MASH without worsening of fibrosis (62.9% vs. 34.3% placebo, $p < 0.001$)
 - ≥ 1 stage reduction in liver fibrosis without worsening of MASH (36.8% vs. 22.4% placebo, $p < 0.001$)
- Tirzepatide and liraglutide – not FDA approved for MASH specifically but studies show effective

Assessment of safety and response to semaglutide (Wegovy®) for the treatment of MASH with moderate-to-advanced fibrosis (F2-F3)



^a Assess based on the same imaging-based or blood-based markers used to determine treatment eligibility.

^b Options may include re-optimizing lifestyle interventions and considering other therapy, with or without stopping semaglutide.

Management – pharmacologic

- Resmetirom (Rezdiffra)
 - FDA approved for MASH with F2 or F3 fibrosis
 - Thyroid receptor beta agonist
 - Promotes TG clearance reducing liver fat, reduces lipoproteins/lipotoxicity which decreases inflammation and fibrosis progression
 - Can be used first line (instead of GLP1)
 - Second line if cannot tolerate or do not achieve weight loss with GLP1
 - 52 week outcomes
 - MASH resolution ~25% vs 9% with placebo
 - Improvement of fibrosis by at least one stage 25% vs 14% with placebo

Management - pharmacologic

- Pioglitazone
 - Can be considered for patients with DM
 - 47% vs 21 % MASH resolution in PIVENS trial
 - Weight gain
- Vit E – guidelines say “select use” - I generally don't use

Key Points

- Diagnosed based on risk factors, imaging, labs and ruling out other causes of liver disease
- Staging is important for both prognosis and management including qualifications for MASH specific therapies
- Management includes both lifestyle changes and FDA approved medications including Semaglutide and Resmetiron

References

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