Alcohol-Associated Steatosis

Diagnosis & Management

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Introduction to ALD

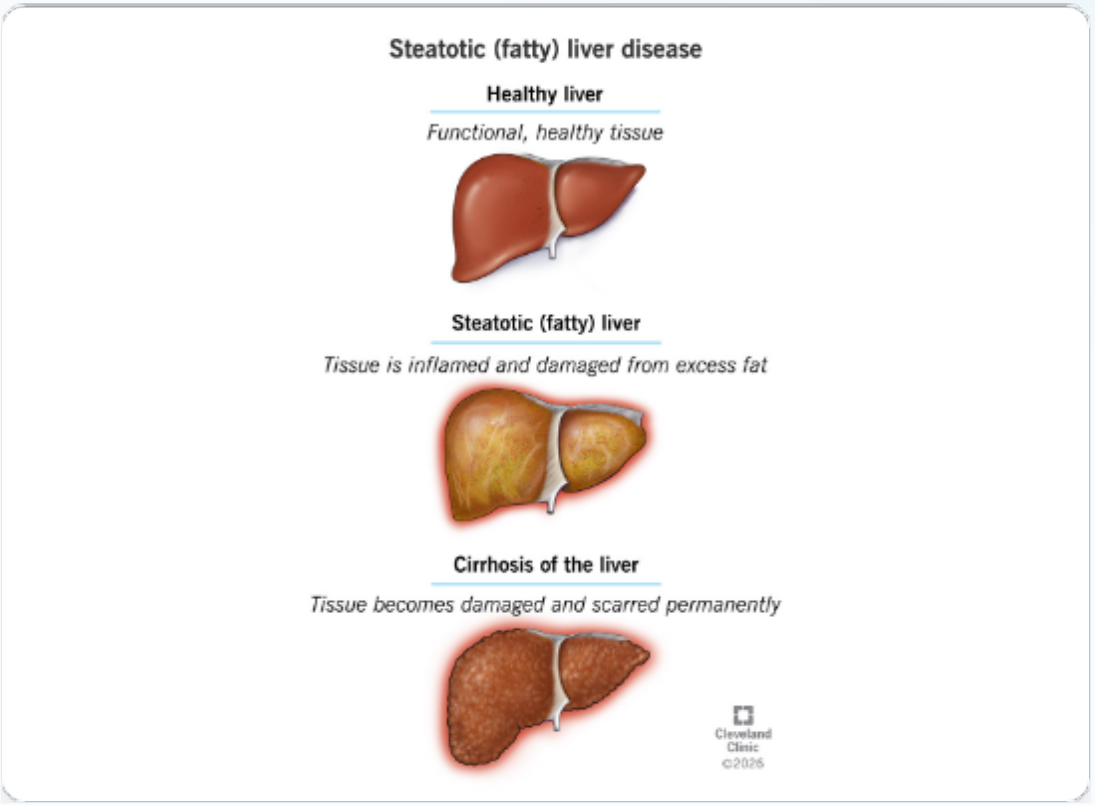
→ Spectrum of **liver disease** from **harmful alcohol use**

→ Progression: **steatosis** (fatty changes) → **inflammation**

→ **Harmful alcohol use** = major **risk factor** for **injury**

→ Scope: strict focus on **diagnosis** & **management** of **steatosis**

→ Goal: intervene before **irreversible changes** occur



Terminology & Classification

Steatotic Liver Disease

→ Umbrella term for **hepatic steatosis**

→ Diagnosed via radiologic **imaging** or **liver biopsy**

Alcohol-Associated Steatosis

→ Specific **classification** of **ALD**

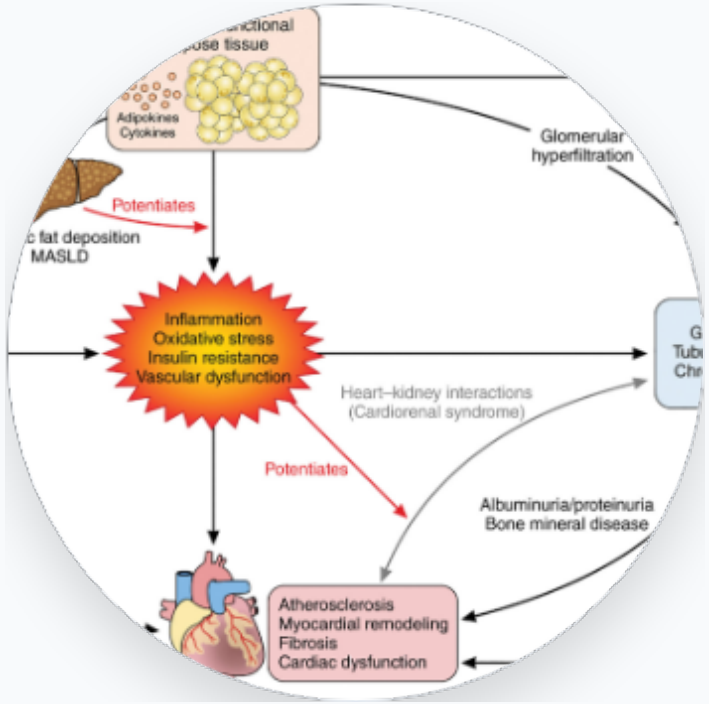
→ **Steatosis** present without **fibrosis** or **cirrhosis**

Alcohol-Associated Steatohepatitis

→ **Macrovesicular steatosis** present

→ Requires + **neutrophil infiltration**, **hepatocyte ballooning**, &/or **Mallory-Denk bodies**

The MetALD Spectrum



Metabolic Dysfunction & Alcohol (MetALD)

→ Dual etiology: **metabolic dysfunction** + **alcohol consumption**

Diagnostic Criteria:

→ Presence of **liver steatosis**

→ ≥1 **metabolic risk factor** (e.g., **overweight**, **dysglycemia**, **HTN**)

→ **Moderate alcohol** intake parameters met

→ **20-50g/day (Females)** & **30-60g/day (Males)**

Epidemiology

Prevalence

→ **Alcohol Use Disorder (AUD)** lifetime prevalence ~**18%** in US

→ Overall **ALD prevalence** in US adults ~**4%**

Geographic Variance

→ **ALD rates** correlate w/ **per capita alcohol consumption**

→ Hotspots: **Eastern Europe**, **Southern Europe**, & **UK**

→ Linked to **colder climates** & ↓ **sunlight hours**

Primary Risk Factors

Consumption Thresholds

→ Primary risk: **alcohol consumption** > **safety thresholds**

→ **High-risk alcohol use** defined as:

→ **>50 g/day (Females)**

→ **>60 g/day (Males)**

→ 1 **standard US drink** = **~14 g alcohol**

→ Examples: **12oz beer**, **5oz wine**, **1.5oz spirits**

→ **Liver injury** possible at ↓ volumes (esp. in **females**)



Additional Risk Factors

→ **Tobacco Use**: ↑ risk of **alcohol-associated liver injury**

→ **Binge Drinking**: drinking pattern impacts **disease risk** independently

→ **Metabolic Factors**: ↑ **BMI**, **diabetes**, & **hypertension** compound injury

→ **Coexisting Conditions**: synergistic acceleration w/ chronic **viral hepatitis**

→ **Genetic Polymorphisms**: mutations in **PNPLA3**, **MBOAT7**, **TM6SF2**, **HSD17B13** strongly predispose to progression



Diagnostic Evaluation

→ **Clinical Suspicion, Labs, & Imaging**

When to Suspect ALD

>50 g

DAILY INTAKE (FEMALES)

>2

AST:ALT RATIO

Clinical Suspicion Criteria

→ Suspect w/ history of **heavy alcohol use**

→ Thresholds: **>50 g/day (F)** & **>60 g/day (M)**

→ Must have ↑ **serum aminotransferases** &/or confirmed **liver steatosis**

→ **Aminotransferases** typically **<400 IU/L**

→ Disproportionate **AST elevation** typical

→ **AST:ALT ratio >1** (frequently **>2**) highly characteristic of **alcohol etiology**

Initial Clinical History

- **Symptom Review**: assess for non-specific sx (e.g., **fatigue**); **steatosis** often **asymptomatic**
- **Medication Hx**: document **herbal supplements** & **OTC drugs** to rule out **drug-induced steatosis**
- **Risk Factor Assessment**: evaluate exposures to **viral hepatitis**, **metabolic conditions** (**T2DM**), & **family hx**
- **Alcohol Documentation**: detail type, amount, pattern, & duration of **alcohol use**

Liver Biochemistries

Aminotransferases

→ **Serum levels** normal or moderately ↑

→ **AST** typically **<8x ULN** & **ALT <5x ULN**

→ **AST:ALT ratio >1** common; **ratio >2** strongly implies **ALD**

→ Lower **ALT** driven by hepatic deficiency of **pyridoxal 5'-phosphate** (**ALT cofactor**)

Other Liver Tests

→ **Gamma-glutamyl transpeptidase (GGT)** frequently ↑ (~**8-10x ULN**)

→ **GGT** may remain ↑ for weeks post-**abstinence**

→ Evaluate **total bilirubin** & **alkaline phosphatase** for overall **liver inflammation**

→ Normalizes/rules out **biliary pathology**



Additional Laboratory Evaluation

Synthetic Function

→ Obtain **prothrombin time (PT)** & **international normalized ratio (INR)**

→ Obtain **serum albumin**

→ Standard measures of hepatic **synthetic capacity**

Basic Hematology

→ Obtain **complete blood count (CBC)** w/ **platelets**

→ Provides baseline assessment for **overall health**

→ Used in broader screening/ruling out **alternate etiologies**



Excluding Other Etiologies

Viral Hepatitis

→ Screen **HBV**: **HBsAg**, **anti-HBs**, **total anti-HBc**

→ Screen **HCV**: **anti-HCV antibody**
→ reflex to **viral RNA**

Autoimmune Panels

→ Assess **IgG levels**, **ANA**, **anti-SMA**, **anti-LKM-1**

→ Excludes **autoimmune hepatitis**

Metabolic / Genetic

→ Check **Alpha-1 antitrypsin** & **iron studies** (**ferritin/TIBC**)

→ Consider **ceruloplasmin** (age **<40**) for **Wilson disease**

Biomarkers of Alcohol Use

→ Routine **blood biomarkers** not mandatory

→ Highly useful for **underreported consumption**

→ **Phosphatidylethanol (PEth)**: most widely used & specific **biomarker**

→ **PEth** provides strong evidence for **alcohol consumption** in prior **2-3 weeks**

→ **PEth <20 ng/mL** = minimal/no **alcohol consumption**

→ **Carbohydrate-deficient transferrin (CDT)**: not routinely measured (risk of **false positives**)



Diagnostic Imaging: Ultrasound

Initial Imaging Approach

→ **Transabdominal ultrasound (US)** = initial test of choice (if no imaging in **<12 months**)

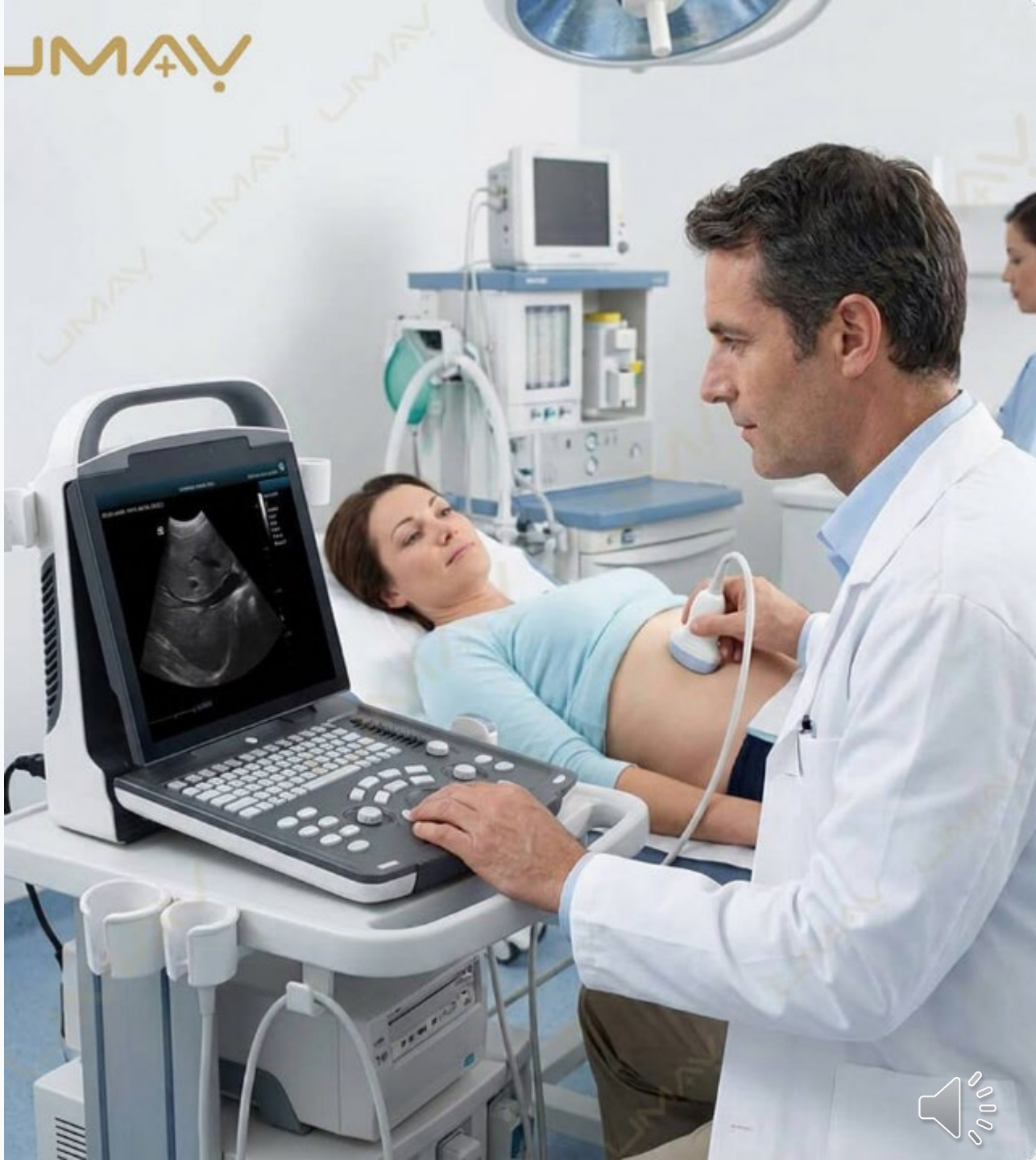
Findings in early ALD:

→ Diffuse, **hyperechoic texture** (**bright liver**) indicates **steatosis**

→ Confirms **homogeneity** & excludes **biliary obstruction** or **masses**

Diagnostic Accuracy:

→ Sensitivity **60-94%** & Specificity **88-95%**
→ ↓ accuracy if **steatosis burden <30%**



Advanced Imaging: CT & MRI

Computed Tomography (CT)

→ Detects **steatosis** via ↓ **liver attenuation** relative to **spleen**

→ Requires **non-contrast** images (contrast alters densities)

→ Criteria: Liver attenuation **<40 HU** or **≥10 HU** less than spleen

→ **Liver-to-spleen ratio <0.8** = **100% specificity** for **steatosis**

Magnetic Resonance (MRI)

→ **Gradient echo pulse** sequences highly sensitive

→ **Water** & **fat** imaged in & out of phase

→ **Intracellular fat** → ↓ signal intensity on **out-of-phase** images

→ Up to **95% sensitivity** & **98% specificity**



Liver Biopsy Indications

→ Clinical, lab, & imaging findings typically sufficient for **diagnosis**

→ Reserve **biopsy** strictly for cases of **uncertain diagnosis**

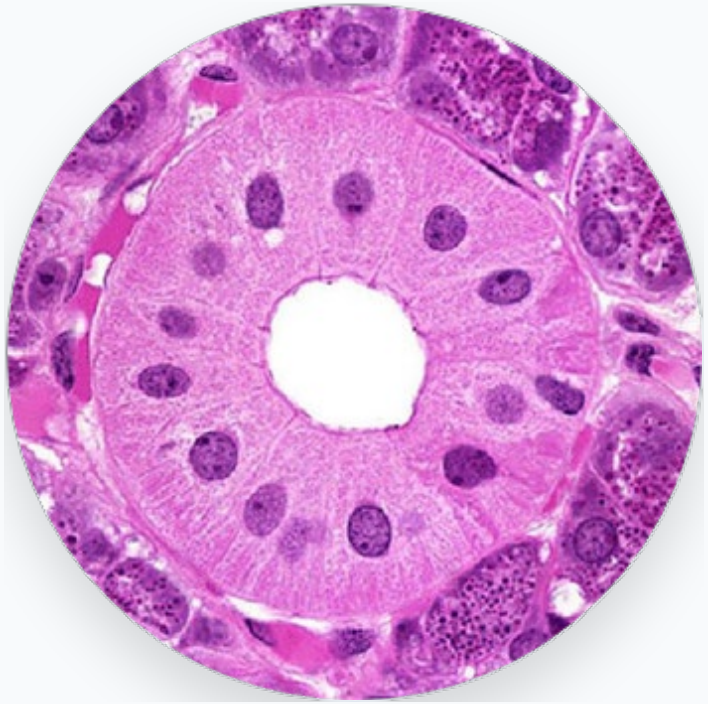
→ Indicated when alternate/co-existing **primary etiology** suspected (e.g., **MetALD overlaps**)

→ Consider for persistently ↑ **serum aminotransferases** (**>6 months**) despite strict **abstinence**

→ Utilized when noninvasive **testing** yields indeterminate/conflicting results



Histologic Findings



Cellular Pathology

→ Hallmark of **ALD steatosis** = **macrovesicular steatosis**

→ Single **large vacuole** (**fat droplet**) occupies entire **hepatocyte**

→ Pushes **nucleus** to cellular edge

Early Changes:

→ **Fat accumulation** easily seen via **light microscopy**

→ Minimal **inflammatory changes** at this stage

→ Occasional **lipogranulomas** in lobules or portal tracts

→ **Fat** primarily composed of **neutral triglycerides**

Differential Diagnosis

→ **MASLD**: highly similar histology (differentiate via strict **alcohol hx** or **PEth**)

→ **ALD specific histology**: **canalicular cholestasis**, marked **ductular reaction**, acute **portal inflammation**, **periportal fibrosis**

→ **Medications**: rule out **drug-induced steatosis** (e.g., **amiodarone**, **methotrexate**, **glucocorticoids**)

→ **Other Conditions**: exclude chronic **Hepatitis C** (**genotype 3**) & symptomatic **Wilson disease**

→ **Parenteral Nutrition**: linked to ↑ **liver enzymes** & **liver steatosis**



Management of Steatosis

→ **Abstinence**, **Nutritional Support**, & **Monitoring**

Abstinence & Nutrition

1. Abstinence

→ Absolute cornerstone of **management** for all **ALD**

→ Leads to rapid, complete resolution of **fatty infiltration** (**steatosis**)

→ Often resolves within **weeks** of **alcohol cessation**

→ Continued use → progression to **steatohepatitis** & **fibrosis**

2. Nutritional Support

→ Assess all patients for **protein calorie malnutrition** & **vitamin deficiencies**

→ Goal: **35 kcal/kg/day** total energy intake

→ Goal: **1.2 - 1.5g protein/kg/day**

→ Requires **multiple meals** daily (must include **breakfast** & **nighttime snack**)

Immunizations & Monitoring

Immunizations

→ Vaccinate for **Hepatitis A (HAV)** & **Hepatitis B (HBV)** if no immunity

→ Administer **pneumococcal vaccination**

→ Ensure standard general population immunizations (e.g., **influenza vaccine**)

Clinical Monitoring

→ Evaluate for symptoms of **disease progression**

→ Monitor **liver biochemical tests** & **platelet count** every **3 months**

→ Obtain **hepatology consultation** for persistently ↑ **liver biochemical tests** despite **abstinence**