ACG Clinical Guideline: Alcohol-Associated Liver Disease (ALD)

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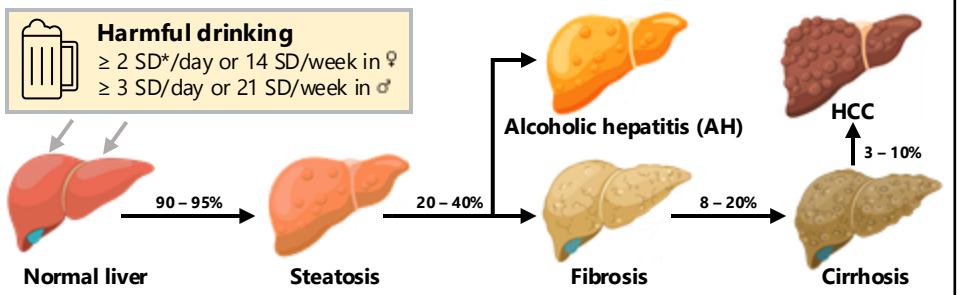
ALD disease spectrum



*1 Standard drink (SD) = 14 g of alcohol.


12 oz Beer (5%ABV)


5 oz Wine (12%ABV)


1.5 oz Liquor (40%ABV)

Epidemiology and disease burden

ALD is a major cause of advanced liver disease and liver-related mortality globally. ↑Prevalence among younger adults, women, and minorities.

Patients w/ ALD often present at an advanced stage w/ cirrhosis complications, progress faster than other liver diseases, and rarely received AUD treatment.

Risk factors for ALD

Risk factors: ↑amount/duration of EtOH use, daily use & binge drinking in those w/ liver disease, ♀ sex, drinking outside of meals, liquor, genetic variants (α-1 antitrypsin, PNPLA3, TM6SF2, and MBOAT7), obesity, metabolic syndrome, gastric bypass anatomy, & chronic hepatitis viral infection

Recommend **tobacco cessation** for patients w/ heavy alcohol use due to ↑risk of cirrhosis.

Recommend patients w/ obesity, type 2 diabetes, a history or planned gastric bypass surgery, or chronic HBV/HCV infection to **avoid alcohol consumption.**

Diagnosis and management of alcohol use disorder (AUD) in patients with ALD

Screen for AUD w/ **AUDIT-C** at every medical encounter. Consider using alcohol biomarkers for patients w/ altered mental status or unreliable alcohol history.

Non-pharmacologic Tx: **brief motivational intervention** (5"A" model; ask, advice, assess, assist, & arrange).

Pharmacologic Tx for compensated ALD:
✅ Recommend **Baclofen** (titrate from 5 mg PO TID to 15 mg PO TID).
✅ Suggest **Acamprosate** (avoid if GFR < 30), **Naltrexone**, **Gabapentin**, or **Topiramate**
❌ **Disulfiram** due to its ineffectiveness and idiosyncratic hepatotoxicity

Address and manage alcohol withdrawal syndrome using the CIWA protocol. U**se benzodiazepines cautiously**, w/ careful monitoring to avoid precipitating coexisting hepatic encephalopathy. Lorazepam and oxazepam are preferred over diazepam or chlordiazepoxide in patients w/ poor liver function due to their shorter t1/2 & different metabolic pathways.

ALD screening

Screen individuals w/ harmful drinking using cost-effective NITs (FIB-4 ± FibroScan) for early detection and assessment of fibrosis severity in asymptomatic ALD. Reserve liver biopsy for cases where NITs are inconclusive.

Counsel patients w/ heavy drinking and ALD on the risk of progressive liver disease with continued alcohol consumption, and refer them to a hepatologist.

Management of ALD

Absolute alcohol abstinence. Treat AUD w/ behavioral Tx ± medication managed by an **integrated multidisciplinary team** including a hepatologist and addiction specialist.

General care for cirrhosis.

Liver transplant (LT) referral for patients w/ ALD cirrhosis complications.

Alcohol biomarkers

Test	Source	Window	Sens (%)	Spec (%)
EtOH	Blood	12 – 24 h	30 – 50	95
EtG	Urine	3 – 7 d	70 – 76	93 – 99
EtS	Urine	3 – 7 d	73 – 82	86 – 89
CDT	Blood	2 – 4 wk	25 – 100	57 – 100
PEth	Blood	30 d	73 – 100	66 – 96
EtG	Hair	3 – 6 mo	58 – 100	66 – 100

EtOH: ethanol, EtG: ethyl glucuronide, EtS: ethyl sulfate, CDT: carbohydrate-deficient transferrin, PEth: phosphatidylethanol

ABV: alcohol by volume, AUDIT-C: alcohol use disorders identification test-consumption tool, CIWA: clinical institute withdrawal assessment, NITs: non-invasive tests

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Alcoholic hepatitis (AH) is a severe form of ALD

NIAAA diagnostic criteria for AH

Probable AH

Onset of jaundice ≤ 60 d of heavy alcohol use (≥ 3 SD/d in ♀ or ≥ 4 SD/d in ♂) for ≥ 6 months.*

Serum bilirubin > 3 mg/dL, ↑AST of 50 – 400 U/L, ↑ AST/ALT ratio > 1.5.

Absence of other causes†

Possible AH

Clinical diagnosed AH w/ confounding etiology or unclear h/o alcohol consumption.

Transjugular liver biopsy

Definite AH

Biopsy proven AH.

Stratify disease severity & determine eligibility for steroid treatment

MELD‡ ≤ 20
moderate AH

Outpatient hepatology care
Enroll in clinical trials

MELD > 20
severe AH, ↑↑ short-term mortality

Other management
- ✅ Hospitalization
- ✅ 5-day **NAC** as an adjuvant to steroid
- ✅ Nutrition: **oral/enteral**/parenteral **nutritional supplements** if malnourished or unable to meet caloric requirements§ (< 21 kcal/kg/d) + vitamin B1, B12, and zinc
- ✅ Sustained alcohol abstinence
- ❌ Universal **prophylactic antibiotics** and **pentoxifylline**
- ❓ **G-CSF** and **microbiome**-based therapies

Contraindication to steroid
- Untreated infection (especially HBV)
- Uncontrolled DM
- GI bleeding
- Severe renal failure
- MELD > 50 (use steroid carefully)

Yes

No

Prednisolone 40 mg PO daily¶ or
Prednisone 40 mg PO daily or
Methylprednisolone 32 mg IV daily

@ day 4 or 7 Lille

≤ 0.45

Responder
Continue steroids for 28 days

> 0.45

Non-responder
Discontinue steroids

‡ Original MELD and not MELD-Na or MELD 3.0 calculation.
§ Caloric intake goal for patients w/ cirrhosis or AH is 35 kcal/kg/d w/ 1.2 – 1.5 g/kg/d of protein.

Liver transplant (LT)/ palliative care

Consider **early LT** for highly selected patients w/ severe AH unresponsive to medical management & at high risk of death.

Selection for LT shouldn't be based on a certain duration of sobriety but a comprehensive psychosocial evaluation by a social worker and an addiction specialist in addition to validated assessment tools.

Factors that predict alcohol use after LT
- Length of abstinence prior to LT
- H/O legal consequences of alcohol use
- Lack of willingness to engage in AUD treatment
- Multiple prior failed rehabilitation attempts
- Untreated psychiatric disease
- H/O polysubstance abuse
- Lack of insight
- Lack of social support

Early/heavy alcohol use ↑ graft loss and long-term mortality in LT recipients (~30% relapse within 2 years) highlighting the need for early detection and management through self-report tools ± alcohol biomarkers and a multidisciplinary integrated care model.

Consider palliative care for patients w/ severe AH unresponsive to steroid, ineligible for LT, and have ≥ 4 organ failures.

Public policy and prevention

Goal: ↓ alcohol use. ↓ burden of ALD-related complications, morbidity, and mortality.

Interventions ex. ↑ alcohol excise taxes, restrict alcohol marketing, raise the legal age for alcohol purchases, stricter legal consequences for DUI and public drinking, education, etc.

* Often w/ malaise, tender hepatomegaly, and decompensation (ascites, encephalopathy, bacterial infection, and variceal bleeding) as the inflammation and steatosis of AH may promote de novo onset of portal hypertension in patients w/ minimal pre-existing liver disease and those w/ previously compensated cirrhosis.
† Mechanical obstruction: liver imaging to r/o HCC and biliary obstruction & Doppler US to r/o portal v thrombosis and Budd Chiari syndrome. Drug-induced liver injury: review medications/supplements using LiverTox database. Viral hepatitis: HAV, HBV, HCV, & HEV serology. Autoimmune: ANA, ASMA, IgG, & AMA. Wilson: ceruloplasmin & 24 h urine copper. Ischemic hepatitis: H/O shock or recent cocaine use.
¶ Prednisolone has been more extensively studied and is generally used over prednisone. IV Methylprednisolone is an alternative for those unable to take PO.

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