Alcohol-Associated Liver Disease ACG Clinical Guideline 2023 and NIAAA Alcoholic Hepatitis Consortia-NIH Sponsored 2016 Recommendations

Alcoholic-associated liver disease (ALD): comprises a broad spectrum of diseases ranging from:

- **Alcoholic fatty liver disease**
  - Alcoholic associated steatosis or fatty liver
  - Alcoholic associated steatohepatitis (ASH)
- **Alcoholic associated hepatitis (AH**)
  - **S**evere form of ASH
- **Cirrhosis and its complications**
  - Ascites
  - Portal hypertension-related bleeding
  - Hepatic encephalopathy
  - HCC

Harmful drinking: >4 drinks on any day or >14 drinks per wk for man and >3 drinks a day or >7 drinks a wk for woman.

- Noninvasive blood and/or radiological tests (NITs) should be used to assess the severity of fibrosis in persons with asymptomatic alcohol-associated liver disease.
- Fibrosis-4 (FIB-4) score (age, AST, ALT, platelets) and hepatic transient elastography are best NITs for fibrosis detection among persons with ALD.
- Liver biopsy is not required for staging of fibrosis but may be needed if there is diagnostic uncertainty based on noninvasive assessment.

Clinical diagnosis of alcoholic steatosis

- Patient with alcohol use disorder (AUD) with hepatic steatosis on ultrasound or CT abdomen
- Absence of other causes of liver disease

Clinical diagnosis of steatohepatitis

- Patient with alcohol use disorder (AUD) with hepatic steatosis on ultrasound or CT abdomen
- Elevation in liver enzymes (aspartate aminotransferase (AST)>alanine aminotransferase (ALT), serum bilirubin<3 mg/dL
- Absence of other causes of liver disease

Clinical diagnosis of alcohol associated hepatitis (AH) see figure 1:

The NIAAA-funded Alcoholic Hepatitis Consortia proposed criteria to clinically define alcohol-associated hepatitis:

- Ongoing consumption of more than 3 drinks per day for women and 4 drinks per day for men for 6 months or more, with less than 60 days of abstinence before the onset of jaundice.
- Onset of jaundice within the previous 8 weeks.
- A total serum bilirubin level of more than 3 mg/dl.
- AST level of more than 50 IU per liter, and a ratio of AST to ALT of more than 1.5, with both values less than 400 IU per liter.
- Exclusion of other causes of jaundice

- ❖ Ischemic hepatitis: Presence of hypotension, sepsis, massive bleeding, or recent cocaine use
- ❖ Viral hepatitis: Viral serology
- ❖ Drug-induced liver injury: Review detailed history
- ❖ Autoimmune hepatitis: ANA, SMA, IgG
- ❖ Mechanical obstruction (biliary obstruction/Budd-Chiari/HCC): US and/or MRI

Possible AH

- Clinically diagnosed AH but with potential confounding factors.
- Transjugular liver biopsy is recommended, especially if specific pharmacologic interventions are proposed.

Probable AH

- Clinically diagnosed AH without confounding factors
- Transjugular liver biopsy is not necessary

Definite AH

- Requires histological confirmation with transjugular liver biopsy

Confounding factors:

- Sepsis, shock, cocaine use within 7 days, or recent use of a drug with potential liver injury (DILI) within 30 days
- Uncertain alcohol use assessment
- Atypical laboratory tests (e.g., AST < 50 IU/mL or > 400 IU/mL, AST/ALT ratio < 1.5), antinuclear antibody > 1:160 or SMA > 1:80

Clinical presentation of AH

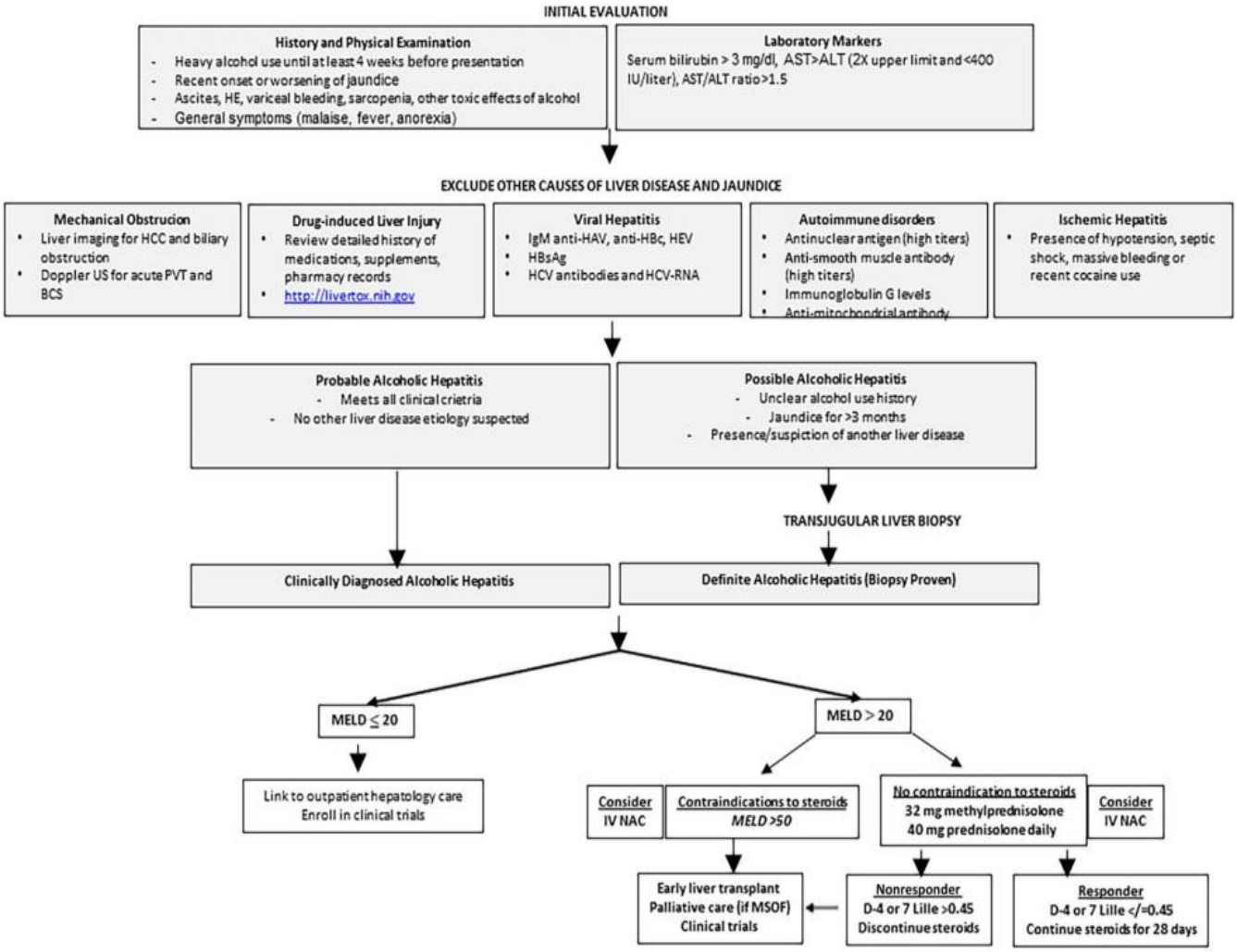
- SIRS and alcohol withdrawal symptoms
- Ascites, variceal bleeding, and hepatic encephalopathy may be present
- Patients may develop acute on chronic liver failure, which manifests with hepatic and extrahepatic organ failure which is associated with a poor prognosis
- Sepsis and malnutrition are common
- Infections are common: a comprehensive infectious screen is recommended as part of routine work-up.
- The majority of patients with severe AH have cirrhosis
- Although evidence of hepatic decompensation is not required to make the diagnosis of AH, physical examination signs may overlap with cirrhosis reflecting the presence of portal hypertension and its complications.
    - Furthermore, the inflammation and steatosis of AH may promote de novo onset of portal hypertension in patients with minimal pre-existing liver disease and those with previously compensated cirrhosis.

Treatment of AH:

- Nutritional supplementation, glucose control targeting levels <180 mg/dL, ulcer prophylaxis using proton pump inhibitors and RBC transfusion with the hemoglobin target of 7–8 g/dL, avoidance of nephrotoxic drugs, judicious use of diuretics, and low threshold for expanding circulating blood volume with albumin or crystalloids are recommended.
- Against universal administration of prophylactic antibiotics.

    - Because infections are common a comprehensive infectious screen is recommended and there should be a low threshold for diagnosis of infection and initiation of antibiotic therapy.
        - Piperacillin-tazobactam is generally the preferred drug used, although vancomycin and meropenem may be considered in patients with penicillin hypersensitivity.
- Corticosteroid therapy un patients with severe AH defined as MELD ≥20 and ≤50 if there are no contraindications.
    - Patients with MELD scores ranging from 25 to 39 derive the maximum benefit, limited benefit in the 40–50 range and no benefit with MELD scores above 50.
    - Prednisolone 40 mg/d for a total duration of 4 weeks.
        - Prednisolone is preferred over prednisone, as the latter requires conversion to prednisolone, which may be impaired in patients with impaired liver synthetic function. Methylprednisolone 32 mg/d IV is used for patients unable to take oral medications.
    - Assess response to corticosteroid treatment based on the Lille score at day 4 or day 7.
        - Among nonresponders (Lille score >0.45), corticosteroids should be discontinued.
- Use of intravenous N-acetyl cysteine as an adjuvant to corticosteroids.
    - Other society guidelines have not included such a recommendation
- Liver transplantation may be considered for highly selected patients with severe AH.
    - Referral to liver transplant center should be considered for patients with severe AH nonresponders to therapy for consideration of liver transplant or clinical trial.
    - Selection for LT in patients with ALD should not be based solely on an arbitrary duration of sobriety.
- Goals of care discussion with consideration for palliative care would be appropriate for patients with severe AH with 4 or more organ failures, who are nonresponsive to corticosteroids, and ineligible for early LT.

Figure 1: Evaluation and treatment alcohol associated hepatitis



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