Acute-on-chronic liver failure (ACLF)

February 14, 2021 by Josh Farkas

![Image](https://emcrit.org/ibcc/aclf/attachment/aclftop/)

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**definitions**

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**decompensated cirrhosis**

- This is defined roughly as the new onset of ascites, hepatic encephalopathy, gastrointestinal hemorrhage, or hepatorenal syndrome in a patient with cirrhosis.
  - Organ failure may or may not occur.
  - Patients may or may not require hospital admission.

**acute-on-chronic liver failure (ACLF)**

[https://emcrit.org/ibcc/aclf?preview_id=445786&preview_nonce=fdd81679044&_thumbnail_id=1&preview=true](https://emcrit.org/ibcc/aclf?preview_id=445786&preview_nonce=fdd81679044&_thumbnail_id=1&preview=true)
• ACLF refers to the *most severe subset* of patients with acutely decompensated cirrhosis, who are at higher risk of short-term mortality.
• There is disagreement about the precise definition of ACLF. Regardless, the crux of the definition involves failure of two or more nonhepatic organs (e.g., renal failure, severe encephalopathy, respiratory failure, shock, or severe coagulation abnormalities) in combination with worsened hepatic function.
  • ACLF is essentially *decompensated cirrhosis causing multiorgan failure*.

pathophysiology

underlying hepatorenal physiology • inflammatory triggers

• Cirrhosis causes systemic vasodilation, with reflex vasoconstriction of the renal vasculature (sometimes referred to as "hepatorenal physiology," more on this [here](https://emcrit.org/ibcc/hrs/)).
• Chronic vasodilation renders patients vulnerable to any hemodynamic insult. Additional sources of inflammation may promote *further* vasodilation, leading to profound vasodilation and hypoperfusion. Overall, this process has several parallels to septic shock.
  • Sepsis itself is a common source of inflammation and thus a common trigger of ACLF.
  • Sterile inflammation may also trigger ACLF (e.g., alcoholic hepatitis, or translocation of bacterial lipopolysaccharide from the gut).

common causes of ACLF

• **Infection** (including spontaneous bacterial peritonitis, urosepsis, pneumonia, and cellulitis).
• **Hemorrhage** (e.g., variceal bleeding, portal gastropathy, peptic ulceration)
• **Thrombosis** (e.g., portal vein thrombosis, hepatic vein thrombosis a.k.a. Budd-Chiari syndrome)
• Hepatic insult:
  • **Alcoholic hepatitis** (very common cause of ACLF).
  • **Drug-induced liver injury** (especially acetaminophen toxicity).
  • Viral infection: acquisition of new viral infection or flare of chronic viral hepatitis.
  • Biliary obstruction.
• Hemodynamic abnormalities:
  • Hypovolemia (e.g., due to excess diuretic or poor PO intake).
  • Hypervolemia (e.g., due to cirrhosis with volume retention).
  • Pulmonary hypertension (typically portopulmonary hypertension caused by cirrhosis).
  • Medications (e.g., antihypertensives, vasodilators, nephrotoxins).
• Iatrogenic (e.g., hepatic resection, ablation of hepatocellular carcinoma, abdominal surgery).

evaluation of ACLF

history

• Focus on alcohol use and other potential hepatotoxic drugs (especially acetaminophen), herbal medications, or dietary supplements.
• Evaluate volume status (e.g., history of fluid intake, edema, diarrhea, and weight changes).
• Evaluate for recent changes in diuretic or hemodynamic medications (e.g., beta-blocker escalation).
• Review recent procedures or other iatrogenic exposures (e.g., inhalational anesthetics can injure the liver or use of chemotherapeutic agents in patients with chronic hepatitis).

labs

• Electrolytes, including magnesium and phosphate.
• Liver function tests.
• Coagulation tests.
• Complete blood count.
Infection is the most common cause of ACLF. Cirrhotic patients may not mount a fever, so there should be a very low threshold for an infection workup (e.g., blood cultures, urinalysis with culture PRN, chest X-ray).

- Acetaminophen level.
- Depending on exposure history, investigation may be warranted to exclude acute superimposed viral hepatitis.

**imaging**

- Echocardiography at bedside to evaluate hemodynamics.
- Formal RUQ ultrasonography with Doppler, to evaluate for portal or hepatic vein thrombosis.
- Chest X-ray, if there is any concern regarding infection or respiratory failure.

**procedures**

- Paracentesis if a substantial volume ascites is present, to exclude spontaneous bacterial peritonitis.
  - (More on paracentesis to exclude spontaneous bacterial peritonitis [here](https://emcrit.org/ibcc/sbp/#paracentesis).)

**management of inciting cause**

- If a cause of decompensation is discovered, it should be immediately addressed.
- Whether or not a cause is found, **aggressive multiorgan support** should be provided as outlined in the next section. This aims at **treatment or prevention** of common problems encountered in ACLF (e.g., hepatic encephalopathy, malnutrition, infection, and hepatorenal syndrome).

**nonspecific management – cirrhosis support package**

**cardiovascular**

- If hypovolemic, 5% albumin might be a preferred fluid. The recent ATTIRE trial demonstrated that administration of albumin to target an albumin level >3 g/dL was nonbeneficial – this demonstrates that fluids should be titrated to optimize hemodynamics, rather than albumin levels.
- Consider targeting a high Bp (e.g., MAP>80 mm) if hepatorenal syndrome is probable.
- There may be a relatively low threshold for **stress-dose steroids** to treat shock or alcoholic hepatitis, given a high prevalence of relative adrenal insufficiency in advanced cirrhosis (31589973, 31977332).
- There should be a low threshold to **discontinue antihypertensives and diuretics**.
- **Continue midodrine** if the patient is on it chronically.

**gastrointestinal**

- Avoid constipation, with an extremely low threshold to initiate lactulose as the cathartic agent of choice.
- **Stress ulcer prophylaxis** should be considered, even in non-intubated patients (e.g., patients who are on steroid and have a history of gastrointestinal hemorrhage).
- GI hemorrhage should be suspected and treatment initiated early (e.g., in patients with falling hemoglobin). More on the management of GI bleeding [here](https://emcrit.org/ibcc/gi-bleeding/).

**hepatology**

- Consider prednisolone for alcoholic hepatitis (more on this [here](https://emcrit.org/ibcc/alcoholic-hepatitis/)).
- HBV: Consult with infectious diseases and/or hepatology, consider immediate therapy.

**nutritional**

- In severe alcoholism:
If poor baseline oral intake, gradually advance diet while following phosphate for evidence of refeeding syndrome. If altered mental status with possible Wernicke's encephalopathy.

Thiamine 100 mg IV daily for most patients. High-dose thiamine (500 mg IV q8hr) if vascular collapse with possible Wernicke's encephalopathy.

Vitamin B6 (pyridoxine) supplementation might be considered, to reduce the seizure threshold.

Full nutritional support should generally be provided to most patients (i.e., protein should not be restricted).

Avoid nephrotoxins.

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Treat electrolyte abnormalities (especially hypokalemia or sodium abnormalities, if they seem to be contributing to encephalopathy).

Treat acute kidney injury early (defined as a creatinine rise by 0.3 mg/dL, or 1.5 times baseline):

- Consider empiric therapy for hepatorenal syndrome, including albumin and vaspressors (more on this here).
- Consider therapeutic paracentesis, if the patient has tense ascites (with 8 grams/liter of 20% albumin replacement).

Infectious diseases

Empiric antibiotics may be indicated in gastrointestinal hemorrhage, suspected septic shock, or a known site of infection (e.g., pneumonia).

Hematology

If the INR is elevated:

- DVT prophylaxis is still indicated (when in doubt, thromboelastography may help clarify whether there is true enzymatic hypocoagulation).
- Consider 10 mg vitamin K intravenously (to exclude vitamin K deficiency and thereby promote accurate prognostication).

Endocrine

Avoid hypoglycemia (the liver's ability to release glucose is often impaired).

- Follow glucose levels, especially if patients are NPO.
- Don't aggressively control hyperglycemia.

Neurology

Hepatic encephalopathy (full chapter here).

- There should be a very low threshold to initiate lactulose +/- rifaximin for delirium (in addition to investigating and treating any additional contributory factors; more on delirium here).
- For intubated patients with hepatic encephalopathy and ACLF, whole-bowel lavage with polyethylene glycol may be considered (to expedite management of encephalopathy and reduce bacterial translocation).
- Avoid sedatives & deliriogenic medications.

Avoid empiric diagnosis and subsequent aggressive therapy for “alcohol withdrawal.” Delirious patients often have hepatic encephalopathy or multifactorial ICU delirium, rather than alcohol withdrawal; benzodiazepines or barbiturates will only exacerbate these conditions.

Transplantation vs. palliation

Consider candidacy for liver transplantation and discuss with a liver transplant service or center if this is a possibility.

If not a candidate for transplantation, consider palliative care consultation.
Failure to aggressively address all of the failing organs involved in ACLF (the key to treatment is often prompt and simultaneous support of multiple organ systems). In particular, if renal dysfunction occurs, this should be rapidly managed (often in a fashion similar to hepatorenal syndrome).

Excluding the possibility of infection based on a lack of fever (patients with advanced cirrhosis may fail to mount a fever).

references


The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.