



Top 10 Management Tips for the Patient with Acute on Chronic Liver Failure

Key Article

- Fuhrmann V, Whitehouse T, Wendon J. The ten tips to manage critically ill patients with acute-on-chronic liver failure. *Intensive Care Med.* 2018.

Background

- Chronic liver disease is the fifth leading cause of death worldwide.
- Major causes of liver disease & cirrhosis include viral hepatitis, alcohol, and nonalcoholic fatty liver disease, where progressive liver disease results in eventual multisystem organ failure.
- Cirrhosis is a progressive disease in most cases and results in death in the absence of transplant.
- Acute-on-chronic liver failure is a unique clinical entity that differs from cirrhosis in that it is potentially reversible.

How do you Define Acute on Chronic Liver Failure (ACLF)?

- Decompensation often recognized by new onset ascites, hepatic encephalopathy, GI bleeding, or certain bacterial infections such as spontaneous bacterial peritonitis (SBP), spontaneous bacterial empyema (SBE).
- SBP and SBE are often caused by gut bacterial translocation into adjacent fluid (ascites)
- ACLF is the progression of the decompensated patient, with new onset organ failure.

Should we fluid resuscitate ACLF patients with crystalloid or albumin?

- Liver failure is a hyperdynamic state, characterized by a decrease in systemic vascular resistance and an increase in both cardiac output and heart rate.
- The drop in SVR is usually caused by overproduction of nitric oxide, endogenous vasoactive substances.
- A decreased intravascular oncotic pressure can lead to excessive 3rd spacing and intravascular volume loss.
- Crystalloids are preferred for fluid resuscitation in most patients with ACLF, except for a few circumstances – such as hepatorenal syndrome, hypotension after large-volume paracentesis, and in patients with spontaneous bacterial peritonitis.

When and what vasopressor should we use in patients with ACLF?

- An initial MAP target of ≥ 60 mmHg is reasonable in most patients with ACLF
- This target may be decreased over time, but it is often unclear early in the resuscitation phase.
- Norepinephrine is usually appropriate as a first-line vasopressor

- Vasopressin is an appropriate second-line vasopressor in patients with catecholamine refractory shock, but should be used with caution – as it can cause excessive splanchnic vasoconstriction leading to worsening gut ischemia and lactic acidosis.
- In patients with GI bleeding and hepatorenal syndrome, terlipressin (a vasopressin analog) has been found to improve outcomes

What are some clinical pearls for managing Acute Kidney Injury (AKI) in patients with ACLF?

- First, look for usual suspects of AKI and address hypotension, infection, and other causes of kidney injury.
- Early interventions that may improve renal perfusion include reducing excessive intra-abdominal pressure with paracentesis, transfusion of packed red blood cells to achieve a hemoglobin > 7 mg/dL
- Hepatorenal syndrome (HRS) occurs in approximately 20% of patients with advanced cirrhosis during the first year after diagnosis, and in up to 40% during the first 5 years after diagnosis
- If hepatorenal syndrome is suspected, early administration of albumin and vasopressin should be administered to achieve a MAP goal > 60 mmHg.
- **OPTIONAL Discussion Point: Diagnosis of HRS**
 - **Major criteria**
 - Advanced hepatic failure with portal hypertension
 - **Serum Cr > 1.5 mg/dL, that does not improve with resuscitation**
 - **Absence of shock**
 - **Proteinuria < 500 mg/dL**
 - No obstructive uropathy or parenchymal renal disease
 - Additional criteria
 - Urine volume less than 500 mL/d.
 - **Urine Na⁺ of less than 10 mmol/L. Urine osmolality greater than plasma osmolality.**
 - Urine red blood cells less than 50 per high-power field.
 - **Serum Na⁺ concentration of less than 130 mmol/L.**

How should we approach bleeding and anticoagulation in ACLF patients?

- Clotting factors and endogenous anticoagulants are typically equally reduced leading to rebalanced hemostasis
- **Routine blood tests such as INR do not accurately reflect coagulation performance, but are helpful in establishing liver synthetic function**
- The best predictors of bleeding are **platelet count and fibrinogen level.**
- **In case of active bleeding, target a platelet count > 50k/dL and fibrinogen > 150 mg/dL**

Is there a need to aggressively fix coagulopathy prior to procedures?

- In general, before routine procedures such as arterial line placement, central line placement, or paracentesis there is no need to emergently reverse INR with FFP, vitamin K, or other factor containing treatments.

- We now know that the PTT and INR only measure the procoagulant pathway and do not detect the defects in the anticoagulant pathway.
- Targeting the INR or the prothrombin time alone leads to unnecessary volume expansion and especially overuse of plasma.
- Again, a platelet count > 50K and fibrinogen level > 150 should be able to ensure the patient can form an adequate clot.

How should we manage patients with hepatic encephalopathy?

- Brain dysfunction caused by liver insufficiency and or portosystemic shunt leading to decreased cerebral perfusion and cerebral edema
- Patients often present with elevated ammonia levels
- Oral lactulose can and rifaximin can help reduce ammonia by reducing colonic reabsorption and production
- Airway protection is a major concern, so intubate if necessary. Propofol and fentanyl are reasonable analgesedation choices. **Benzodiazepines should be avoided** as they can accumulate secondary to poor liver function and clearance.

Are there any special considerations for managing respiratory insufficiency in ACLF?

- In general, lung protective ventilation strategies should be employed if the patient requires mechanical ventilation
- **PEARL: If concerned for upper GIB, I'll often place an NG tube prior to intubation**
 - Pushing a paralytic in RSI will reduce lower esophageal sphincter tone, increasing risk for a bloody airway!!

Are nasogastric tubes safe in patients with esophageal varices?

- Yes
- The only relative contraindication for nasogastric tube placement would be recent variceal banding, and should probably be discussed with GI specialist prior to placement

Should I place a chest tube in the patient with hepatic hydrothorax?

- Probably not. Chest tube insertion in patients with cirrhosis is fraught with complications including pneumothorax, hemothorax, empyema, electrolyte abnormalities, and renal failure
- Medical management aimed to reduce ascites are largely preferred, as risk of complication >>> benefit.
- Consider a diagnostic thoracentesis if concerned for infection, as spontaneous bacterial empyema can occur and can be an unrecognized cause of occult infection.