WHAT'S NEW IN INTENSIVE CARE



The ten tips to manage critically ill patients with acute-on-chronic liver failure

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Patients with liver cirrhosis represent 2–5% of the intensive care unit (ICU) population [1, 2]; their admission is associated with a high mortality (36–86%) [3–5]. Acuteon-chronic liver failure (ACLF) is present in most of these patients. This article provides ten tips to support intensivists treating patients with ACLF.

1. What is hepatic decompensation and ACLF?

Acute hepatic decompensation (AD) is defined by new onset of ascites, hepatic encephalopathy (HE), gastrointestinal bleeding (GIB) or bacterial infections in chronic liver disease [3].

Acute-on-chronic liver failure is usually defined by the presence of AD with organ failure (as defined by the CLIF-SOFA-a modified SOFA score) [3]. Precipitating events may be extrahepatic (bacterial infections, GIB, etc.) or hepatic (alcohol, acute reactivation of hepatitis B, etc.) [3, 7]. The underlying cause of ACLF remains unknown in 20–45% [3, 7].

2. When should I administer albumin in ACLF?

Crystalloids are preferred for fluid resuscitation in most patients with ACLF. Hydroxyethyl starch should be avoided. Human albumin solution (HAS) has benefits in hepatorenal syndrome (HRS), large-volume paracentesis and spontaneous bacterial peritonitis (Fig. 1). It improves circulatory dysfunction because of its oncotic, antioxidant and antiinflammatory properties [8, 9]. HAS does not improve the incidence of acute kidney injury (AKI) or survival in cirrhosis and non-SBP-induced sepsis [8].

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3. Which kind of vasopressor should I use in patients with ACLF?

Patients with portal hypertension and cirrhosis are frequently vasodilated and have reduced blood volume. A mean arterial pressure (MAP) \geq 60 mmHg using fluids and norepinephrine as first-line vasopressor are usually appropriate where there is shock (although this MAP target is too ambitious in many patients) [8]. Vasopressin and terlipressin are appropriate second-line agents where hypotension persists but should be used with caution (potent constriction of the splanchnic circulation). Terlipressin is indicated in HRS and variceal hemorrhage as it reduces portal pressure, increases the systemic vascular resistance and improves outcomes [7–9].

4. What should I consider in treating AKI in ACLF?

Acute kidney injury occurs in <mark>> 50%</mark> of ICU cirrhosis and represents the most frequent organ failure in ACLF [3, 4]. Diuretics and nephrotoxic substances should be avoided. Underlying causes should be treated. Paracentesis is important for diagnosing SBP and avoiding abdominal compartment syndrome [9]. Adequate fluid resuscitation is warranted. Transfusion of packed red cells is recommended if hemoglobin < 7 g/dl. Where there is HRS, HAS and terlipressin or other vasoconstrictors should be administered to maintain a target MAP. The need for renal replacement therapy (RRT) is associated with a mortality > 80% [4]. Goals of extracorporeal support [i.e., bridging to renal recovery or liver transplantation (LT)] should be defined prior to its initiation. Regional citrate anticoagulation is an alternative to systemic heparin for RRT.

5. What about bleeding and anticoagulation?

Clotting factors and endogenous anticoagulants are typically equally reduced leading to rebalanced hemostasis. Routine blood tests such as INR do not accurately reflect

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Fig. 1 Organ failure and therapeutic option in acute-on-chronic liver failure (ACLF). Early management of extrahepatic and hepatic organ failure using monitoring of vital signs (ACLF grade 1) and organ support therapies at the ICU (ACLF grade \geq 2) seems to be of central importance. Furthermore, goals of support should be defined prior to its initiation. Repeated risk stratification, reevaluation of the accomplishment of therapeutic goals, assessment of future therapeutic options, communication with the patient, family and clinical team, and incorporation of evaluation of therapeutic limitations and end-of-life decisions in the clinical decision-making process are cornerstones of the management of patients with ACLF at the ICU. *ACLF* acute-on-chronic liver failure, *AKI* acute kidney injury, *CVC* central venous catheter, *GCS* Glasgow Coma Scale, *GIB* gastrointestinal bleeding, *HRS* hepatorenal syndrome, *INR* international normalized ratio, *LT* liver transplantation, *MELD* model of end-stage liver disease, *ROTEM* rotational thomboelastometry, *SBP* spontaneous bacterial peritonitis, *TEG* thromboelastography, *TIPS* transhepatic portosystemic stent shunt

coagulation performance but are established to monitor synthetic function. The best predictors of new onset of bleeding in ICU cirrhosis are platelet count and fibrinogen [10]. Point-of-care testing (ROTEM, TEG) may reduce blood product administration. Venous thrombosis and thromboembolism are substantial risks. Thromboprophylaxis reduces the rate of AD and portal vein thrombosis and increases survival [11].

6. How should I treat HE?

Hepatic encephalopathy is brain dysfunction caused by liver insufficiency and/or portosystemic shunt with a wide range of clinical presentations [12]. Pathophysiologic hallmarks of HE are elevated circulating ammonia levels and systemic inflammation. Therapy includes treatment of precipitating events, lowering ammonia with oral lactulose and reduction of inflammation with rifaximin as add on [13]. Short-acting drugs such as propofol should be used for sedation; analgesia with non-accumulating opioids such as alfentanil should be considered; benzodiazepines should be avoided. Patients with HE grade 3/4 who are for active management should be considered for intubation for airway protection. The role of ventilation for CO_2 control and management of intracranial pressure has not been established in ACLF. Extracorporeal therapies may help to improve refractory HE; the best data are available for albumin dialysis [7, 8].

7. What do I have to consider in respiratory insufficiency in ACLF?

Respiratory insufficiency in cirrhosis can be caused by alterations of the lung parenchyma (such as pneumonia, COPD), alterations of the pulmonary vascular bed (hepatopulmonary syndrome, portopulmonary hypertension) and extrapulmonary causes (ascites, hepatic hydrothorax). The goals of respiratory support should be defined before its initiation. Assessment for endotracheal intubation for airway protection in the presence of upper GIB should be individualized. Ventilation strategies in ACLF are identical to those for patients without cirrhosis. In case of prolonged weaning, percutaneous tracheostomy can be performed safely.

8. How should I feed the critically ill patient with cirrhosis?

Adequate nutrition is critical. Nutritional support is necessary if patients are not able to maintain adequate intake by themselves and should primarily be provided enterally. Nasogastric tubes may be used safely in patients with esophageal varices; in those with banded varices, placement should be discussed with gastroenterology because of the risk of band dislodgement. Glucose hemostasis should be monitored closely to maintain normoglycemia. Thiamine deficiency is frequent and should be treated empirically [14].

9. Where should I treat patients with ACLF and who should be evaluated for LT?

Although there are no prospective studies to help answer these questions, patients with ACLF grade ≥ 2 need some form of organ support at the ICU. Patients with ACLF grade 1 require monitoring of vital signs [8]. LT leads to significantly decreased mortality rates in patients with ACLF, but this is not established practice and further stretches the shortage of transplantable organs [6]. Patients with ACLF, however, deserve discussion of candidacy for LT with transplant centers. Perceived contraindications for LT should not preclude this consultation as patients may also benefit from the expertise and supportive measures in dedicated centers [8, 14].

10. What should I consider in end-of-life decisions?

Acute-on-chronic liver failure is a dynamic disease that may improve or worsen during treatment. Decision on futility, withholding or discontinuation of ICU should be based on the patients' wishes, etiology and severity of underlying chronic disease, organ failure reversibility, repeated risk stratification, therapeutic options and clinical judgment. Repeated evaluation of the clinical condition and prognosis should be communicated to the patient and family [14, 15].

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Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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References

- O'Brien A, Welch C, Singer M et al (2012) Prevalence and outcome of cirrhosis patients admitted to UK intensive care: a comparison against dialysis-dependent chronic renal failure patients. Intensive Care Med 38:991–1000
- Fuhrmann V, Kneidinger N, Herkner H et al (2011) Impact of hypoxic hepatitis on mortality in the intensive care unit. Intensive Care Med 37:1302–1310
- Moreau R, Jalan R, Gines P et al (2013) Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology 144:1426–1437
- Staufer K, Roedl K, Kivaranovic D et al (2017) Renal replacement therapy in critically ill liver cirrhotic patients—outcome and clinical implications. Liver Int 37:843–850

- McPhail MJ, Shawcross D, Abeles RD et al (2015) Increased survival for patients with cirrhosis and organ failure in liver intensive care and validation of the chronic liver failure-sequential organ failure scoring system. Clin Gastroenterol Hepatol 13:1353–1360
- Artru F, Louvet A, Ruir I et al (2017) Liver transplantation in the most severely ill cirrhotic patients: a multicenter study in acute-on-chronic liver failure grade 3. J Hepatol 67:708–715
- Hernaez R, Sola E, Moreau R et al (2017) Acute on chronic liver failure an update. Gut 66:541–553
- Nadim M, Durand F, Kellum J et al (2016) Management of the critically ill patients with cirrhosis: a multidisciplinary perspective. J Hepatol 64:717–735
- 9. European Association for the Study of the Liver (2010) EASL clinical practice guideline on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome. J Hepatol 53:397–417
- Drolz A, Horvatits T, Roedl K et al (2016) Coagulation parameters and major bleeding in critically ill patients with cirrhosis. Hepatology 64:556–568
- 11. Tripodi A, Primignani M, Mannucci P et al (2017) Changing concepts of cirrhotic coagulopathy. Am J Gastroenterol 112:274–281
- Weiss N, Jalan R, Thabut D (2017) Understanding hepatic encephalopathy. Intensive Care Med. https://doi.org/10.1007/s00134-017-4845-6
- EASL clinical practical guideline (2014) Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the European association for the study of the liver and the American association for the study of the liver. J Hepatol 61:642–659
- 14. Olson J, Wendon J, Kramer D et al (2011) Intensive care of the patient with cirrhosis. Hepatology 54:1864–1872
- 15. McPhail M, Auzinger G, Bernal W, Wendon J (2016) Decisions on futility in patients with cirrhosis and organ failure. Hepatology 64:986