Cirrhosis is a leading cause of morbidity and mortality throughout the world. Patients with cirrhosis may develop decompensated disease with portal hypertension and functional impairment of the liver, resulting in numerous complications including infection, variceal bleeding, hepatic encephalopathy (HE), and hepatorenal syndrome (HRS).

Along with decompensation of cirrhosis, the concept of acute-on-chronic liver failure (ACLF) has emerged. This involves an acute precipitating event, such as the development of infection in a patient with cirrhosis, which leads to acute deterioration of hepatic function and extrahepatic organ failure. Such complications, when severe, represent indications for management in an intensive care setting.

**Impaired immune system**

Patients with cirrhosis have a relative immunodeficiency that puts them at risk of developing infections. A lack of complement and protein C production by the liver impairs the adaptive immune response. Along with a weakened immune system, altered gut microflora and translocation of intestinal bacteria also contribute to the development of infection. The most common types of infection encountered by decompensated cirrhotic patients are spontaneous bacterial peritonitis, urinary tract infections, bacteraemia, pneumonia, and skin infections.

Bacterial infections may also cause ACLF and patients with ACLF not triggered by infection are at high risk of developing bacterial infections. The severity of ACLF, as measured by the prevalence of organ failures and the need for critical care and organ support, was greater when ACLF was caused by infection than if it developed from non-infectious aetiologies.

**ACLF grading system**

ACLF is an important syndrome since it is relatively common and often necessitates intensive care unit (ICU) admission for intensive organ support. ACLF is divided into 3 grades depending on the number of extrahepatic organ failures present, as defined by the chronic liver failure sequential organ failure assessment (CLIF-SOFA) score.
Grade 1 ACLF involves patients with only renal failure, patients with a single organ failure combined with renal dysfunction (creatinine between 1.5 mg/dl to 1.9 mg/dl) and/or mild to moderate HE (West Haven grade 1 or 2), or patients with HE and renal dysfunction. Grade 2 ACLF involves patients with 2 organ failures and grade 3 ACLF involves at least 3 organ failures.

The relevance of grading ACLF based on the number of organ failures is based on studies showing that mortality significantly increases as the number of organ failures increase in patients with ACLF, as shown in a study where 28-day mortality based on ACLF grade was 22%, 32%, and 77% for grade 1, grade 2, and grade 3 ACLF, respectively.

Prognostication in patients with ACLF

Prognosis in ACLF is dependent on candidacy for liver transplantation (LT) and the burden of multi-organ failure. However, consideration of ICU admission in cirrhotic patients can be a challenge. This is due to the often irreversible nature of the disease course without LT and the need to balance limited resources, cost, and benefit against futility.

Recently, scores like the Chronic Liver Failure Consortium ACLF (CLIF-C ACLF) score have been proposed and utilised to determine the prognosis of patients with ACLF and to determine when initiating and continuing intensive care treatment in patients with cirrhosis and ACLF is futile. Overall, the CLIF-C ACLF score is calculated based on bilirubin, creatinine, HE grade, international normalised ratio (INR), mean arterial pressure (MAP), and a partial pressure of arterial oxygen (PaO2), which gives an overview of the number of organ failures present, along with age and white cell count.

For patients who are not LT candidates, if clinical improvement is not seen within 48 to 72 hours post-ICU admission, serious consideration should be given to palliation as opposed to continued aggressive ICU management. For those patients who are LT candidates continued aggressive therapy may allow bridging to LT.

Source: JHEP Reports
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