PRIMEVIEW

ACUTE-ON-CHRONIC LIVER FAILURE IN CIRRHOSIS

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There are several competing definitions of acute-on-chronic liver failure (ACLF). The European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) Consortium defines ACLF as a condition that occurs on the background of cirrhosis and involves acute impairment in liver function (decompensation) that emerges concurrently with organ failure. Together, these events result in 28-day mortality rates of ~30%.

PATHOPHYSIOLOGY

CIRRHOSIS
Compensated or decompensated liver cirrhosis can lead to ACLF

PRECIPITATING EVENTS
Events that induce inflammation can trigger ACLF

40% of ACLF cases have no known trigger

CYTOKINE STORM
Excessive inflammation can cause tissue damage

Alcoholic hepatitis

Viral hepatitis

Sepsis

Drug-induced liver injury

Surgery

ACUTE LIVER DECOMPENSATION

ORGAN FAILURE

HIGH SHORT-TERM MORTALITY

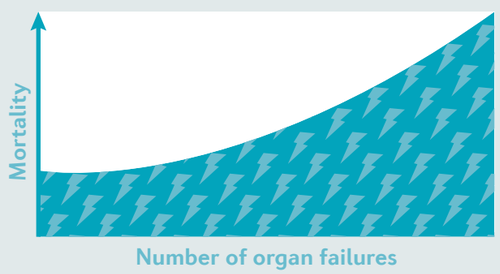
MANAGEMENT

Liver transplantation is the only definitive treatment for ACLF. Medical management involves treatment of the precipitating event and supportive care, and often takes place in an intensive care unit. Preventive strategies involve effective treatment of viral hepatitis and bacterial infections using antimicrobial agents before they can trigger ACLF.

Liver transplantation increases the 6-month survival of patients with ACLF grade 2 and grade 3 from ~10% to ~80%

DIAGNOSIS

A patient with cirrhosis must fulfil both decompensation and organ failure criteria to be diagnosed with ACLF. Acute liver decompensation involves the development of ascites (the accumulation of large amounts of fluid within the peritoneal cavity), encephalopathy, gastrointestinal haemorrhage and/or bacterial infection. Organ failure is assessed using the CLIF Consortium Organ Failure score. Patients with ACLF can either have kidney failure alone, another single organ failure if it is associated with kidney or brain dysfunction or a combination of two or more organ failures of any type. The most commonly failed organs and systems in ACLF include the kidneys (~56% of patients), the liver (~44% of patients) and coagulation (~28% of patients). ACLF is graded on the basis of the number of organ failures present, with a higher number of organ failures associated with a greater mortality risk.



Severe alcoholic hepatitis is implicated in 20% of ACLF cases. Affected livers show signs of inflammation and cell death.

Bacterial sepsis triggers 30% of ACLF cases. Patients with cirrhosis have excessive inflammatory responses to bacterial infection.

EPIDEMIOLOGY

Prevalence measures for ACLF differ according to the characteristics of the study population and the definition of ACLF used. Generally speaking, in at-risk populations — such as those with cirrhosis or patients hospitalized with decompensated cirrhosis — the rate of ACLF ranges from ~25% to ~35%. The relative importance of precipitating events varies geographically, with bacterial infection and alcoholism being common triggers in western populations and viral hepatitis more common in Asia. These differences are part of the reason why no single definition of ACLF has been agreed on.

OUTLOOK

The specific ways in which poorly controlled systemic inflammation leads to liver decompensation and extrahepatic organ failure in ACLF remain largely unknown. Moreover, in a considerable proportion of patients, the precipitating event that triggers inflammation to cause ACLF is also unknown. Dysbiosis of gut microbiota, the translocation of bacteria and/or bacterial products across the gut and the release of damage-associated molecular patterns from the diseased liver might play a part in these cases, but these hypotheses have not been validated experimentally.

A universal definition of ACLF should not be made on the basis of consensus agreements alone, but will need to involve more research into the mechanisms and outcomes of the condition across different populations

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