

Different entities of liver failure need clear definitions

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The definition of acute liver failure (ALF) is universally accepted and usually implies acute damage to the liver with no previous liver injury, which is one of the most dangerous complications in hepatologic patients. ALF goes along with a coagulopathy due to hepatic dysfunction and an altered level of consciousness because of hepatic encephalopathy. Moreover, altered liver function due to ALF can completely regenerate and return to its original capacity.

However, at least two complementary entities need to be distinguished in liver failure. In contrast to ALF, acutely decompensated cirrhosis and acute-on-chronic liver failure (AOCLF) without signs of cirrhosis are clinical conditions that are associated with a much lower capacity of liver regeneration. The term acutely decompensated cirrhosis is widely accepted and refers to the development of ascites, encephalopathy, gastrointestinal hemorrhage, or any combination of these disorders in patients with prediagnosed cirrhosis (Fig. 1).^[1]

A lot of controversies exist in recent years concerning the term acute-on-chronic liver failure, a term originally suggested by Jalan and Williams. The European Association for the Study of Liver well as the Asian Pacific Association for the Study of Liver (APASL) proposed definitions for AOCLF, which unfortunately are not in full accordance. This unclear terminology complicates the clinical definition of this entity and discussions in research on this topic.^[2-4]

Therefore, this study proposed new and adapted definitions regarding acute damage of the liver. Like the APASL, we propose to define AOCLF as a clinical syndrome consisting of severely impaired liver function in patients with a known chronic hepatic injury where signs of cirrhosis are absent. Preexisting chronic liver damage, e.g., in the form of non-alcoholic fatty liver disease (NAFLD) explicit without signs of cirrhosis, predisposes to the development of AOCLF. Thus, we propose to define patients with liver failure, with preexisting liver damage (independent of the cause, e.g., fatty liver disease, chronic viral hepatitis, and so on), with no cirrhosis, and no prior history of compensation as AOCLF.

Patients with cirrhosis, independent of decompensation events, should be grouped as acute-on-cirrhosis liver failure (AOCi). Per definition,

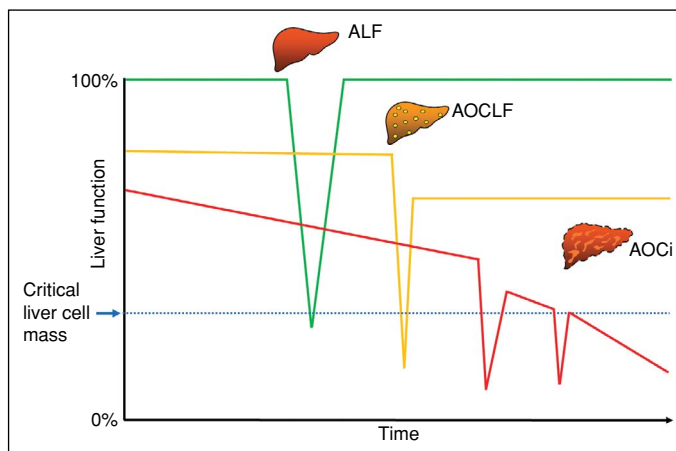


Figure 1. Three entities of liver failure with different clinical courses and different capacities of regeneration after acute injury. Green line, acute liver failure (ALF); yellow line, acute on chronic liver failure (AOCLF); red line, acute on cirrhosis liver failure (AOCi).

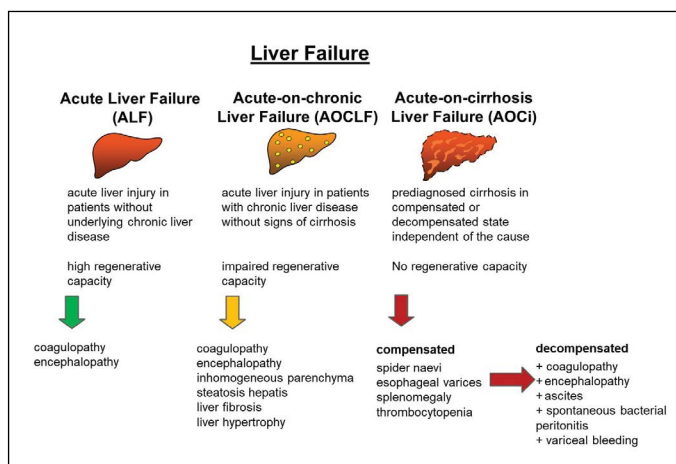


Figure 2. Differences and similarities of ALF, AOCLF, and AOCi.

patients with AOCi must present with certain clinical features such as typical skin signs (e.g., spider naevi) and splenomegaly with thrombocytopenia or esophageal varices. Conversely, these signs of advanced liver disease are lacking in patients with AOCLF (Fig. 2). Per definition, preexisting liver damage with or without signs of cirrhosis excludes an ALF.

Why do we see the necessity to distinguish AOCLF from AOCi? The prevalence of patients with metabolic liver damage such as NAFLD and non-alcoholic steatohepatitis is rising worldwide. Estimates assume a 25% prevalence of NAFLD, which would make NAFLD the

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leading cause of chronic liver disease worldwide.^[5] By introducing the new definitions of AOCLF and AOCi, the large group of patients with chronic liver disease but without cirrhosis is reflected as more differentiated. Thus, the large number of patients with chronic liver disease worldwide justifies the implementation of clear definitions. Additionally, it seems biologically plausible and reasonable that this large cohort of patients has to be looked at from a different perspective than the patients without any kind of liver damage. Prospective studies are needed to evaluate the outcomes and clinical courses of these different groups of patients in the context of acute liver injury.

To conclude, this article would like to refer to the letter to the Editor “ALF after bariatric surgery” by Onem et al.^[6] which was published in Volume 1, Issue 3, Year 2020 of *Hepatology Forum*. The authors report a case of presumed ALF in a young patient after bariatric surgery. This case would be grouped as AOCLF instead of ALF according to the proposed nomenclature of this study. It has to be assumed that the reported patient suffered from NAFLD in the context of metabolic syndrome, which, per definition, excludes ALF as a correct diagnosis.

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