

Clinical Classification of Liver Failure

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Annotation: Liver failure (LF) is a clinical syndrome with complex clinical manifestations. The clinical diagnosis and classification of LF are still considerably different internationally. Based on the pace of the disease progression and its possible reversibility, LF can be divided into two categories: acute and chronic LF.

Keywords: Clinical manifestations; Chronic LF; Acutenecrosis; Jaundice; Liver transplantation

Introduction

Liver failure (LF) is a clinical syndrome characterized by jaundice, coagulopathy, ascites, and hepatic encephalopathy. It is a devastating illness, with extremely high morbidity and mortality rates. Traditionally, LF is classified clinically as acute liver failure (ALF) or chronic liver failure (CLF). More recently, the entity of acute-on-chronic liver failure (ACLF) has been delineated. Pathological changes leading to LF consist of two types: 1) severe acute necrosis of liver tissues and 2) chronic progressive damage to liver cells [1].

Materials And Methods

Failure of the liver, the center of the body's metabolism, is not limited to the liver itself, but also has a wide effect on the brain, kidneys, lungs, and other organs. Thus, LF may be considered multi-organ failure. First, we must recognize that LF is a functional diagnosis rather than a disease diagnosis. Second, we should focus on the difference between liver dysfunction and LF. Because the liver has a large reserve capacity and the ability to regenerate, mild or moderate liver damage usually does not result in overt dysfunction.

Results And Discussion

The CLF guidelines are non-uniform, only appropriate guidelines or consensus for the complications of cirrhosis, such as ascites, hepatic encephalopathy, and hepatorenal syndrome, have been published [2].

Chronic Liver Failure, Mechanisms and Management, edited by Gines et al., were published in 2011 [2]. Williams [1] proposed that LF be divided into three categories: ALF, ACLF, and CLF. According to the Liver Failure Guidelines in China, issued in 2006 and revised in 2012, LF is divided into four categories: ALF, sub-acute LF (SALF), ACLF and CLF (**Table 1**).

The establishment of CLF as a distinct entity is necessary in order to maintain the continuity and integrity of LF classification. However, there is lack of uniformity of CLF guidelines. The cause of this lack might be thought of as the decompensated stage of liver cirrhosis, and appropriate guidelines or consensus for complications of cirrhosis are those mentioned above.

Table 1: The current main categories of liver failure and definitions.

Three categories (United Kingdom) [2]: ALF, ACLF and CLF		Four categories (China)[3]: ALF, SALF, ACLF and CLF
Definitions	ALF defined as HE within 8 weeks	ALF defined as more than Grade II HE within 2 weeks.
		SALF defined as clinical manifestations of liver failure within a period of 15 days-25 weeks.

	ACLF defined as acute deterioration of preexisting chronic liver disease, usually related to sepsis, alcohol, or bleeding.	ACLF defined as acute deterioration on a base of chronic liver disease.
	CLF defined as progression of end-stage liver disease.	CLF defined as chronic deterioration of preexisting liver cirrhosis.
ALF: Acute Liver Failure; SALF: Sub-acute Liver Failure; ACLF: Acute-On- Chronic Liver Failure; CLF: Chronic Liver Failure; HE: Hepatic Encephalopathy; TBIL: Total Bilirubin; PTA: Prothrombin Activity.		

Given the lack of generally accepted, evidence-based diagnostic criteria, the diagnosis of LF varies within China and between China and other countries. These differences might be due to the variety of causes of LF, the complexity of its clinical manifestations, and differences in expert opinions from various centers. For example, alcoholic cirrhosis constitutes 50% to 70% of all underlying liver diseases of ACLF in western countries, whereas hepatitis B- or C-related cirrhosis constitutes about 10% to 30%. In most Asian countries, however, hepatitis B constitutes about 70% of ACLF, and alcohol abuse only approximately 15% [2]. These factors notwithstanding, the more important barrier to achieving consensus in LF classification lies in the variations in LF diagnostic standards. For example, the current definition of ACLF differs greatly in various countries. The APASL definition stresses the occurrence of ascites and/or encephalopathy occurring within a period of four weeks in patients with underlying chronic liver disease, whereas the AASLD/EASL definition underlines the occurrence of multi-organ failure in patients with chronic liver disease, resulting in three-month mortality (Table 2). This difference has led to a misconception between ACLF and acute decompensation of liver cirrhosis [4]. Moreau et al. reported that ACLF is a different syndrome from that of acute decompensation of cirrhosis. Since the majority of ACLF patients in the Moreau study had alcohol-induced cirrhosis, this conclusion cannot be extended to virus-related ACLF.

Table 2: Definitions of ALF and ACLF by major societies.

LF	Proposed by	Definitions
ALF	AASLD (2006)	No previous history of cirrhosis; deterioration of liver function occurred in 26 weeks; coagulopathy (INR \geq 1.5); any degree of altered consciousness (encephalopathy).
ACLF	APASL (2009)	Acute hepatic insult manifested as jaundice and coagulopathy, complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.
	AASLD/EASL (2011)	Acute deterioration of preexisting chronic liver disease usually related to a precipitating event and associated with increased mortality at 3 months due to multisystem organ failure.

Conclusion

In summary, considering the numerous causes of LF and clinical manifestations caused by liver damage, differences in the classification of LF are to be expected. Some definitions of LF as ACLF might be conducive to evaluation of short-term prognosis and be harmful to early intervention of disease, versus other definitions. This classification of LF proposed by the author might be more suitable for determining therapy and estimating prognosis. This classification, if adopted worldwide, could help achieve uniformity in the classification and therapeutic guidelines for liver failure. However, the validity of this classification should be further tested in clinical practice.

References

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