Editorial

Portuguese Journal of Gastroenterology

GE Port J Gastroenterol 2018;25:4–5
DOI: 10.1159/000484095

Received: October 10, 2017
Accepted after revision: October 11, 2017
Published online: December 21, 2017

# Acute (Not Decompensation)-on-Chronic Liver Failure

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**Keywords**
Acute-on-chronic liver failure

**Agudização (Não a Descompensação) da Doença Hepática Crónica**

**Palavras Chave**
Lesão renal aguda · Falência de orgão

Ideally, a certain disease has a defined etiopathogenesis, a set of signs and symptoms, a treatment, and a prognosis with homogeneous categories.

Decompensated liver cirrhosis is characterized by great heterogeneity of clinical manifestations, complications, and prognosis. Some patients rapidly develop typical decompensations such as hepatic encephalopathy, gastrointestinal bleeding, ascites, or infection. However, at admission about 30% have new hepatic and/or extrahepatic organ failure(s), which is associated with high short-term mortality rates, 15 times higher than that of decompensated cirrhosis [1]. The designation and concept of acute-on-chronic liver failure (ACLF) has been subject of some skepticism. Often the definition was based on expert opinions, and several scientific societies (American, Asian, and European) defined different criteria [2]. The concept that differentiates organ failure and dysfunction was also defined a priori, with a group of experts modifying the SOFA score for CLIF-SOFA [1]. A recent meta-analysis demonstrated that the latter score has greater accuracy for ACLF mortality prediction [3]. ACLF is a dynamic entity, potentially reversible, if the precipitating factor is identified and controlled, but this happens in only 50% of cases. Thus, defining diagnostic criteria and identifying patients at risk of progression to multi-organ failure will assist in the early implementation of supportive measures and prioritization in the liver transplant list. The presentation in 2013 of the results of a prospective observational European study (CANONIC) that included 1,343 patients hospitalized for liver cirrhosis allowed to clarify some of these concepts and was remarkable in this area.

The authors of the article published in this issue of *GE – Portuguese Journal of Gastroenterology* retrospectively analyzed their experience over the last 3 years [4]. This analysis was carried out in a very particular context of an intensive care unit of a liver transplant center which would have had an impact on patient selection and characteristics. The primary objectives of the study were to evaluate the evolution and mortality and to compare the evolution of ACLF patients with and without bacterial infection as precipitant. Additionally, they evaluated the presence of acute kidney injury and its impact on prognosis.

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The authors report that of the 29 included patients only 9 survived (69% mortality) at 28 and 90 days. Surprisingly, the mortality rate was the same 28 and 90 days after admission, which differs from other data such as the CANONIC study, where it was 33% at 28 days and 51% at 90 days. Possible explanations for this may be the retrospective analysis as well as the selection criteria for hospitalization in that specific unit.

Bacterial infection was detected in 14 of 29 patients (48.7%). The prevalence of infection was similar to that described by others (37% of bacterial infections at the time of diagnosis and 46% during the first 4 weeks) [5]. Mortality was independent of the presence or absence of bacterial infection in this sample. On the contrary, others have shown that patients with ACLF and bacterial infections (at the time of diagnosis or during evolution) have higher levels of systemic inflammation markers at the time of diagnosis and a significantly worse evolution (ACLF grade 2–3 at the end: 47 vs. 26%, $p < 0.001$) and a lower probability of survival at 90 days (49 vs. 72.5%, $p < 0.001$) than noninfected ACLF patients. Bacterial infections were independently associated with mortality in patients with grade 1 or grade 2 ACLF. Fungal infections are uncommon (2% of ACLFs), and the majority occur after the diagnosis of ACLF but have a high mortality rate (71%) at 90 days [5]. However, accurate great differentiation of SIRS from infection is a recognized unmet need. A lower accuracy in the isolation of bacterial and fungal agents and the small sample size may contribute to the explanation of the data obtained in this analysis.

83% of patients developed acute kidney injury, and their mortality at 28 and 90 days was 65.5%, significantly higher than that of patients without acute renal injury. The implementation of renal replacement techniques allowed a significant mortality reduction at 28 and 90 days. In the CANONIC study, the prevalence of isolated organ failure was 65% (mortality 14.6%), but the presence of isolated renal failure was associated with mortality higher than the 15% threshold (18.6%). 13.2% of patients had lower degrees of renal dysfunction and 55.8% had renal failure. In other words, mortality increased progressively in the ACLF categories in ascending order: no failure/isolated nonrenal failure, without renal or cerebral dysfunction/isolated renal failure/isolated nonrenal failure, with renal and/or cerebral dysfunction/2 organ failures/more than 3 organ failures.

Of the 29 patients included, 3 were transplanted and overall 9 patients survived after 28 days [4]. The authors correlate the value of model for end-stage liver disease (MELD) with the qualitative parameter of ACLF (number/type of organ failure). It would have been interesting to better characterize these cases of positive prognosis, with and without hepatic transplantation, such as grade and/or CLIF/SOFA score at entry and its evolution (day 3 and day 7). Often our daily decisions may lead to therapeutic futility, namely which patients with grade 3 ACLF would have been considered or not too sick to benefit from a liver transplant [6].

Let us hope that the data of all works are correctly interpreted, their limitations acknowledged, and that no biased assimilation occurs, for as Francis Bacon argued in the 17th century, "the human understanding when it adopts an opinion draws all else to support and agree with it."

## Disclosure Statement

The author has no conflicts of interest to declare.

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