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EDITORIAL

Acute-on-chronic liver failure: a time to step forward

Acute-on-chronic liver failure (ACLF) is defined as a syndrome characterized by acute deterioration of liver function on a chronic liver disease, associated with extrahepatic organ failure and high short-term mortality (≥ 15%) (1). This concept represents a disruption in the traditional spectrum of liver diseases, particularly in liver cirrhosis (2). ACLF may appear during liver disease ranging from compensated to long-standing cirrhosis (3). Despite the heterogeneity of definitions, it is clear that ACLF results from different types of precipitants in patients with underlying chronic liver disease, mimicking the prognosis of acute liver failure (4). In this scenario, some new prognostic scores have been proposed instead of MELD or Child-Pugh scores. In the current issue, a retrospective Portuguese study (N = 177) carried out by Barosa et al. explored the usefulness of CLIF scores identifying high mortality rates among cirrhotic patients suffering from ACLF (5).

The CLIF Consortium Organ Failure (CLIF-C OF) score, derived from the SOFA score (6), has been developed to diagnose ACLF. Interestingly, the number of organ failures increases both the 28-day and 90-day mortality rates. Consequently, ACLF is categorized into grade 1, grade 2, and grade 3 (according to the number of organ failures), which are associated with increased mortality respectively (1). In addition to confirming the increasing risk of death depending on the organs affected, about 20% of overall admissions in the Gastroenterology ward had ACLF in the study performed by Barosa et al. (5). This amount of patients represents a relevant burden in hospitalization for liver diseases. Also, the ACLF syndrome has a dynamic course, which requires regular prognostic evaluations. In fact, up to 10% of patients developed ACLF during admission in the attached paper. In this setting, the CANONIC population showed that assessing ACLF grade on days 3-7 after diagnosis provides a better prediction of 28-day and 90-day mortality as compared to ACLF grade at diagnosis (7). Therefore, in view of all this, regularly assessing whether ACLF is present is definitely recommended (8).

Child-Pugh and MELD scores (together with their modifications, such as the MELD-Na) have been the traditional scoring systems to assess prognosis in liver disease. Consequently, their use has been extended to patients with ACLF. Nevertheless, ACLF involves various extrahepatic organ failures that are not considered by the MELD and Child-Pugh scores, so the accuracy of the latter to predict prognosis is often limited (9). The CANONIC study has also served to develop and validate a new specific scoring system. After an exhaustive analysis, CLIF-C ACLF was developed including CLIF-OFs, age, and white cell count (representing the inflammatory component). In this population, MELD, MELD-Na, and Child-Pugh scores were compared to CLIF-C ACLF in the prediction of prognosis for patients with ACLF at different times during follow-up. The final result was that CLIF-C ACLF was able to predict 28-day, 90-day, 180-day, and 365-day mortality better than the other systems (10). Since the publication of these results, many studies have confirmed the superiority of CLIF-C ACLF over MELD or Child-Pugh scores (11,12), including the paper by Barosa et al.

Anticipating an ACLF episode is key. However, there is no identifiable trigger in up to 50% of cases, whereas infection and active alcoholism are the most commonly reported triggers (13). Barosa et al. identified a similar proportion of triggers, finding 40% of infection and 32% of active alcoholism (5). Probably, serum or urinary biomarkers could play a relevant role to anticipate the development of this syndrome, such as neutrophil gelatinase-lipocalin (14), but further studies are needed to achieve robust conclusions. Anyhow, to date, the presence or absence of a precipitating event has borne no relationship ACLF severity or 28-day mortality rate.

The admission of cirrhotic patients to an intensive care unit (ICU) is challenging due to high mortality rates, high costs per admission, and shortage of ICU beds (15). On the other hand, the benefit of ICU admission for ACLF patients is poorly defined. However, ACLF is accompanied by organ failures (unlike acute decompensation) that may be reversible after intensive support. Theoretically, given that ACLF is a reversible condition in half of cases, its presence might justify easier acceptance by ICUs versus acutely decompensated cirrhotic patients (16). The usefulness of artificial liver support systems in ACLF patients must be defined (17). In addition, due to the potential indication of liver transplantation, ACLF patients should be managed in, and transferred to, a transplant center (18).

CLIF scores should be systematically used in Gastroenterology departments for several reasons. Firstly, clinicians need to use the same definition of ACLF to render management and treatment homogeneous, which ultimately will improve prognosis. Secondly, we need to be able to anticipate and predict the prognosis of patients with ACLF accurately. Regarding prediction, CLIF-OF and CLIF-ACLF appear to be reasonably good for this purpose. However, ACLF prevention will likely require biomarkers. Thirdly, to identify an appropriate site for the hospitalization of patients suffering from ACLF, distinguishing between those who

will benefit from an ICU and those with poor prognosis who will require futility rules. This latter aim, a consequence of the above, will permit a better allocation of patients, thus saving money and resources. Moreover, selection criteria for liver transplantation and instructions for prioritization on the waiting lists must be defined. Taking everything into account, and given the dynamic course of this syndrome, ACLF patients should be intensively cared (at an ICU or enhanced care unit), and decisions about later management (i.e., liver transplantation or discontinuation owing to futility) should be made on day 7 (19).

The following days after an ACLF episode are key to distinguish which patients will recover with intensive medical support, and which will exhibit a poor prognosis and will likely require liver transplant or futility rules. In this setting, scoring systems are needed with the ability to reflect the dynamic course and prognosis of this syndrome, providing outcome-driven treatment. All of these aspects are confirmed in the current issue of the Journal, since the study carried out by Barosa et al. demonstrated the relevant role of CLIF scores (5). Thus, efforts should be made to encourage clinicians to anticipate and identify ACLF using the specific CLIF prognostic scores to improve outcomes for this syndrome.

Javier Ampuero
Inter-Centre Unit of Digestive Diseases and CIBERehd. Hospital Universitario Virgen del Rocío. Sevilla, Spain

REFERENCES

1. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology 2013;144:1426-37.e9. DOI: 10.1053/j.gastro.2013.02.042
2. Solís-Muñoz P. Acute on chronic liver failure and prognostic factors: time for reevaluation. Rev Esp Enferm Dig 2011;103:169-76.
3. Arroyo V, Moreau R, Jalan R, et al. Acute-on-chronic liver failure: A new syndrome that will re-classify cirrhosis. J Hepatol 2015;62:S131-S143. DOI: 10.1016/j.jhep.2014.11.045
4. Clària J, Stauber RE, Coenraad MJ, et al. Systemic inflammation in decompensated cirrhosis: Characterization and role in acute-on-chronic liver failure. Hepatology 2016;64:1249-64. DOI: 10.1002/hep.28740
5. Barosa R, Roque Ramos L, Patita M, et al. CLIF-C ACLF score is a better mortality predictor than MELD, MELD-Na and CTP in patients with Acute on Chronic Liver Failure admitted to the ward. Rev Esp Enferm Dig 2017;109(6):399-405. DOI: 10.17235/reed.2017.4701/2016
6. Freire P, Romãozinho JM, Amaro P, et al. Prognostic scores in cirrhotic patients admitted to a gastroenterology intensive care unit. Rev Esp Enferm Dig 2011;103:177-83. DOI: 10.4321/S1130-01082011000400002
7. Gustot T, Fernandez J, Garcia E, et al. Clinical Course of acute-on-chronic liver failure syndrome and effects on prognosis. Hepatology 2015;62:243-52. DOI: 10.1002/hep.27849
8. Hernaez R, Solà E, Moreau R, et al. Acute-on-chronic liver failure: an update. Gut 2017;66:541-53. DOI: 10.1136/gutjnl-2016-312670
9. Peng Y, Qi X, Tang S, et al. Child-Pugh, MELD, and ALBI scores for predicting the in-hospital mortality in cirrhotic patients with acute-on-chronic liver failure. Expert Rev Gastroenterol Hepatol 2016;10:1-10. DOI: 10.1080/17474124.2016.1177788
10. Jalan R, Saliba F, Pavesi M, et al. Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. J Hepatol 2014;61:1038-47. DOI: 10.1016/j.jhep.2014.06.012
11. Kim HY, Chang Y, Park JY, et al. Characterization of acute-on-chronic liver failure and prediction of mortality in Asian patients with active alcoholism. J Gastroenterol Hepatol 2016;31:427-33. DOI: 10.1111/jgh.13084
12. Shi Y, Shu Z, Sun W, et al. Risk stratification of decompensated cirrhosis patients by Chronic Liver Failure Consortium scores: Classification and regression tree analysis. Hepatol Res 2017;47:328-37. DOI: 10.1111/hepr.12751
13. Sendra C, Ampuero J, Gallego Á, et al. Case Report: acute-on-chronic liver failure: making the diagnosis between infection and acute alcoholic hepatitis. Semin Liver Dis 2016;36:181-6. DOI: 10.1055/s-0036-1583203
14. Ariza X, Graupera I, Coll M, et al. Neutrophil gelatinase-associated lipocalin is a biomarker of acute-on-chronic liver failure and prognosis in cirrhosis. J Hepatol 2016;65:57-65. DOI: 10.1016/j.jhep.2016.03.002
15. Olson JC, Wendon JA, Kramer DJ, et al. Intensive care of the patient with cirrhosis. Hepatology 2011;54:1864-72. DOI: 10.1002/hep.24622
16. Saliba F, Ichaï P, Levesque E, et al. Cirrhotic patients in the ICU. Curr Opin Crit Care 2013;19:154-60. DOI: 10.1097/MCC.0b013e32835f0c17
17. Zhou P-Q, Zheng S-P, Yu M, et al. Prognosis of acute-on-chronic liver failure patients treated with artificial liver support system. World J Gastroenterol 2015;21:9614. DOI: 10.3748/wjg.v21.i32.9614
18. Li H, Chen H, Nyberg S. Extracorporeal Liver Support and Liver Transplant for Patients with Acute-on-Chronic Liver Failure. Semin Liver Dis 2016;36:153-60. DOI: 10.1055/s-0036-1583197
19. Putignano A, Gustot T. New concepts in acute-on-chronic liver failure: Implications for liver transplantation. Liver Transplant 2017;23:234-43. DOI: 10.1002/lt.24654