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Causes of variability in listing and access to liver transplantation for critically ill cirrhotic patients: acknowledging the elephant in the room.

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Acknowledging the elephant in the room: causes of variability in listing and access to liver transplantation for critically ill cirrhotic patients

We appreciate the interest of Yehuda et al. in our study (reference). They raise two important points.

First, they note that a "fast-track pre-transplant assessment is impractical in many ICU-admitted unlisted ACLF-3 patients since essential pre-transplant cardiac workup is frequently unobtainable in critically ill candidates". We beg to differ. First, transthoracic echocardiogram is easily available in ICUs. Second, though patients cannot undergo cardiac stress tests, coronary angiography can be performed, even if it sometimes requires transferring the patients to another hospital temporarily. Finally, further explorations of right heart function and pressure can be directly performed in the ICU when required with pulmonary artery catheterization. While cardiac evaluation raises technical issues that can be overcome, the authors underline another obstacle to fast-track assessment: social and psychiatric assessment of alcohol addiction. True, the ICU is not an appropriate setting to undergo such evaluation. But there is no way around this predicament and evaluating critically ill patients with alcohol related liver disease for transplant candidacy will always remain an ethical puzzle and rely on some degree of subjectivity on the part of individual clinicians and transplant teams. Listing patients while they are in the ICU is therefore both a technical and an ethical challenge and we hope that our article constitutes a springboard to debate the role of liver transplantation for critically ill cirrhotic patients and the importance of collaborations between intensivists and transplant teams.

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The second point that Yehuda et al. raise concerns the underlying causes of variability in listing and transplanting practices. While we agree in theory that epidemiological factors and illness severity may conceivably drive some of the variability, our study shows variation in access to transplantation to a degree (from 0% to 29% of patients transplanted with decompensated cirrhosis across centers) that cannot be explained solely by these factors.

Concerning epidemiological factors, useful clinical granular data concerning critically ill cirrhotic patients in Europe simply do not exist to assess the epidemiology of ACLF-3 across Europe meaningfully. Besides, dramatic variations in transplant practices are also observed across French transplant centers, despite this country's single organ allocation algorithm and presumably smaller epidemiological variations than those potentially at play at the level of Europe (1).

Concerning illness severity, the study period was 18 months long, which left enough time for patients with various degrees of illness severity to be admitted in each center. Besides, we believe that there is no straightforward way of assessing illness severity for a critically ill cirrhotic transplant candidate throughout their stay in the ICU. The MELD, SOFA and CLIF scores predict transplant-free mortality (2) but not post-transplant outcomes for patients in the ICU (3). An additional pitfall of clinical scores is that they fail to capture the dynamic dimension of illness severity during the ICU stay, which can change dramatically within hours. At the bedside, subjective clinical judgement, which apprehends organ failures dynamically and with greater detail (taking into account the dose of norepinephrine and its variation through time, for example), which takes into account specific ICU biomarkers (such as arterial lactate level) and which captures the subtleties of sepsis (the virulence of the germ involved, the response to treatment), supersede attempts to categorize complex critically ill transplant candidates along a single, simplistic scale. Capturing the objective reason for which a critically ill patient in the ICU was deemed too sick to be transplanted is therefore extremely complex both retrospectively and prospectively.

To conclude, one of the aims of our study is not so much to provide an airtight scientific causal account of the variability observed across transplant centers but rather to acknowledge and illustrate the practical lack of consensus which the transplant community faces on this topic in Europe, leading to disparities of access to a life-saving treatment.

1. Artzner T, Legeai C, Antoine C, Jasseron C, Michard B, Faitot F, et al. Liver transplantation for critically ill cirrhotic patients: results from the French transplant registry. Clinics and Research in Hepatology and Gastroenterology. 2021
2. Jalan R, Saliba F, Pavesi M, Amoros A, Moreau R, Ginès P, et al. Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. J. Hepatol. 2014
3. Artzner T, Michard B, Weiss E, Barbier L, Noorah Z, Merle J-C, et al. Liver transplantation for critically ill cirrhotic patients: stratifying utility based on pre-transplantation factors. Am. J. Transplant. 2020