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Outcomes after early liver transplantation for patients with severe alcoholic hepatitis: Additional evidence from a meta-analysis

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Dear Editors,

We read with interest the article from Dr. Lee and colleagues about early liver transplantation for severe alcoholic hepatitis [1]. We compliment them for their exhaustive collection of data on patients transplanted for alcoholic hepatitis across the US in the retrospective ACCELARATE-AH study. We would like to add some comments that may contribute to the debate on this hot topic.

First, in this study, a liver biopsy was not systematically performed, as it should preferably have been [2]. The fact that alcoholic hepatitis was observed on the liver explant in only 59% of the cases (vs. 100% in the landmark study of Mathurin and colleagues [3]) strongly suggests that a significant proportion of patients were transplanted for decompensated cirrhosis without alcoholic hepatitis, which made the study population heterogeneous. Whether this heterogeneity in the study population explains the surprisingly high rates of survival is a matter of debate.

Second, as the authors acknowledged, the rate of any alcohol relapse was higher in their study than in Mathurin and colleagues study [3] as well as in other studies using stringent criteria for patient selection. This observation was also made in a recent meta-analysis of trials evaluating alcohol relapse after liver transplantation among patients with alcoholic hepatitis [4]. This meta-analysis (which also included some patients from the Lee and colleagues study) observed a substantial decrease in rates of alcohol relapse when only studies that used a stringent selection process for deciding which patients should be transplanted were selected. In the subgroup analysis that included only patients transplanted for clinically severe alcoholic hepatitis and that did not include studies that did not use stringent criteria for selecting candidates for liver transplantation (patients motivated to stay abstinent from alcohol following liver transplantation, good psychosocial

support, and/or a favorable patient psychological profile), only 14% of patients had alcohol relapse after liver transplantation (95% CI=0.08-0.23). No heterogeneity was identified in this analysis (p=0.6, I^2=0%) which is a strong indicator of confidence in these results. Thus, these stringent criteria should be used to select patients with a low risk of alcohol relapse after liver transplantation. Avoiding alcohol relapse after liver transplantation is a major issue since patients who relapse after liver transplantation usually return to harmful drinking patterns (pooled estimate rate in the recent meta-analysis: 0.15, 95% CI=0.07-0.27, I^2=3% [4]) and, as Dr. Lee and others [5] have highlighted, patients with significant alcohol relapse have decreased survival rates. Furthermore, as the use of liver transplantation for patients with severe alcoholic hepatitis is gaining interest, the application of a strict selection process will help to avoid any problems of equity in liver graft allocation [6]. This conservative strategy for patient selection will contribute to the continued adoption of severe alcoholic hepatitis non-responsive to medical therapy as a new indication for liver transplantation by public opinion and healthcare providers [7].

Overall, Lee and colleagues study provides additional evidence that prospective studies aimed at identifying factors predicting alcohol relapse after liver transplantation are urgently needed. The first results of an ongoing prospective trial with the primary goal of assessing alcohol relapse after liver transplantation (NCT01756794) are expected at the end of 2018 and will be of interest.

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