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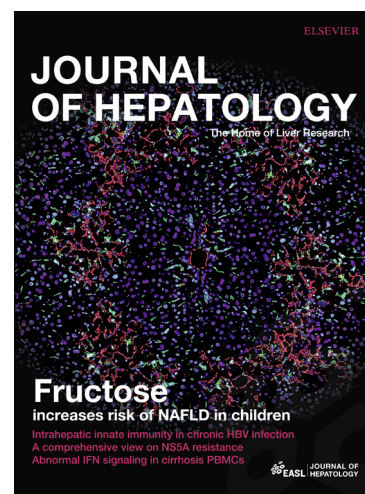
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Assessment of the risk of alcohol relapse following liver transplantation for alcoholic hepatitis using a meta-analysis approach

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Dear Editors,

We read with interest the editorial from Dr. Kubiliun and colleagues about early liver transplantation for alcoholic hepatitis (AH) [1]. We would like to add some recent data to complete their excellent overview on this highly debated topic.

One of the main concerns when liver transplantation is discussed for a patient suffering from severe alcoholic hepatitis is related to the risk of alcohol relapse. We fully agree with Dr. Kubiliun that the 6-month rule poorly identifies patients with alcoholic liver disease who will have recurrent alcohol use after liver transplantation [2, 3] and that this rule is not applicable to patients with AH who have no other therapeutic options and who have a high risk of death within 6 months after the onset of the disease. As early liver transplantation is gaining attention as a therapeutic option for non-responders to corticosteroids, a precise estimate of the risk of alcohol relapse after liver transplantation is mandatory in this particular setting in which the 6-month sobriety period is not respected. To assess the rate of recurrent alcohol consumption after liver transplantation for AH as precisely as possible, we recently performed a meta-analysis of trials evaluating liver transplantation among patients with AH [4]. This statistical approach is currently one of the best for assessing the magnitude of impact of a particular factor as it enables pooling data from trials to decrease random errors.

This meta-analysis included transplanted patients with recent jaundice and severe AH, as well as transplanted patients in whom the diagnosis of AH was made on the explant. The

pooled estimate rate for alcohol relapse after liver transplantation was 0.22 (95% CI=0.12-0.36) with high heterogeneity between studies ($p<0.001$, $I^2=76\%$). In the subgroup analysis that included only patients transplanted for clinically severe AH, only 14% of patients had alcohol relapse after liver transplantation when a discrepant study that did not use stringent criteria for selecting candidates for liver transplantation (patients' motivation to stay abstinent from alcohol following liver transplantation, good psychosocial support, and/or a favorable patient psychological profile) was excluded (pooled estimate rate: 0.14, 95% CI=0.08-0.23). Importantly, no heterogeneity was identified in this analysis ($p=0.6$, $I^2=0\%$), a strong indicator of confidence in these results. In addition, once again when studies that did not use stringent criteria for selecting candidates for liver transplantation were excluded, AH transplanted patients had a similar risk of alcohol relapse compared to patients with alcoholic cirrhosis who underwent elective liver transplantation following a standard sobriety period (OR=1.68, 95% CI=0.79-3.58, $p=0.2$), with low heterogeneity between studies ($p=0.3$, $I^2=16\%$). However, in cases of recurrence, most patients had harmful drinking patterns (pooled estimate rate: 0.15, 95% CI=0.07-0.27), with negligible heterogeneity between studies ($p=0.4$, $I^2=3\%$), as has already been shown for patients transplanted for alcoholic cirrhosis after a 6-month sobriety period [5].

Overall, these results provide additional support for the conclusions from Dr. Kubiliun and colleagues. They indicate that alcohol relapse is not a frequent event among AH patients who undergo liver transplantation, assuming that stringent selection criteria are applied. Currently, these criteria are the best way to select patients with a low risk of alcohol relapse after liver transplantation. In line with this, the first results of an ongoing prospective trial with the primary aim to assess alcohol relapse after liver transplantation (NCT01756794) are expected in 2018 and will be of interest. This study may contribute to the identification of factors predicting alcohol relapse after liver transplantation in daily practice.

References

1. Kubiliun M, Patel SJ, Hur C, Dienstag JL, and Luther J. Early liver transplantation for alcoholic hepatitis: Ready for primetime? *J Hepatol* 2017.
2. DiMartini A, Day N, Dew MA, Javed L, Fitzgerald MG, Jain A, et al. Alcohol consumption patterns and predictors of use following liver transplantation for alcoholic liver disease. *Liver Transpl* 2006;12:813-20.
3. Foster PF, Fabrega F, Karademir S, Sankary HN, Mital D, and Williams JW. Prediction of abstinence from ethanol in alcoholic recipients following liver transplantation. *Hepatology* 1997;25:1469-77.
4. Marot A, Dubois M, Trepo E, Moreno C, and Deltenre P. Liver transplantation for alcoholic hepatitis: A systematic review with meta-analysis. *PLoS One* 2018;13:e0190823.
5. Pageaux GP, Bismuth M, Perney P, Costes V, Jaber S, Possoz P, et al. Alcohol relapse after liver transplantation for alcoholic liver disease: does it matter? *J Hepatol* 2003;38:629-34.