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Prognostic value of histologic parameters in alcoholic hepatitis: a word of caution

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Abbreviations
ALD, alcoholic liver disease; AH, alcoholic hepatitis

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The authors declare they have no competing interests

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Pierre Deltenre: study concept and design; drafting of the manuscript; critical revision of the
To the Editor:

We read with great interest the article by Lackner et al on the development of the SALVE grading and staging system, a histologic prognostic score for alcohol-related liver disease (ALD) [1]. The authors suggested using this score to assess patient prognosis across the whole clinical spectrum of ALD. While we acknowledge that histologic features may have some prognostic value in ALD, we have some concerns about their robustness in alcoholic hepatitis (AH).

More than 40% of the study population in the Lackner study had histological AH. While the landmark study from Altamirano et al. [2] already identified several histologic prognostic factors in AH, we failed to confirm their results in two independent cohorts of patients [3]. Interestingly, several histologic features of the SALVE scoring system developed by Lackner et al were also assessed in our study. We agree that fibrosis is the most robust histologic prognostic factor in AH. When patients without cirrhosis and those with Laennec stage 4A cirrhosis were considered together and compared to patients with Laennec stages 4B and 4C, there was a trend toward better survival in the former group (91% vs 68% at 3 months, p=0.13; and 82% vs 64% at 6 months, p=0.2, respectively). This observation was expected as the extend of liver fibrosis is correlated to the degree of portal hypertension and related complications [4]. However, we failed to identify any prognostic value of bilirubinostasis. This finding may be due to several confounders that may explain the association observed between the risk of death and the presence of cholestasis in AH patients. Of note, infection is a common feature in this context that occurs in up to 50% of patients, either at admission or during hospitalization [5]. Interestingly, the presence of bilirubinostasis was associated with the development of infection in the Altamirano study [2], a finding that suggests that cholestasis may be an indirect marker of sepsis in AH. Indeed, bacterial products such as lipopolysaccharide down-regulate some bile transporters, a factor which may explain cholestasis, as correctly pointed out by Lackner et al.

Another point of concern is related to the treatment that AH patients received. While the authors
stated that patients received “standard of care”, no data were provided concerning the use of corticosteroids. Similarly, the Lille score was not included in the multivariate analysis, despite its well demonstrated prognostic value in this setting [6]. In the end, as non-response to steroids may explain the development of infection and, as there is no doubt that these two factors drive prognosis in AH patients, cholestasis may be an indirect marker of non-response to steroids and/or to sepsis rather than a factor that itself impacts the prognosis of AH patients. Another point of interest would be to assess if histologic parameters can predict response to steroids.

Lastly, the study from Lackner et al assessed the impact of abstinence, a factor which is recognized to have the greatest impact on long-term prognosis both in patients with compensated and decompensated ALD [7] and in AH patients, regardless of whether the Maddrey discriminant function is <32 [8] or >32 [9, 10]. If alcohol behavior was associated with the prognosis of patients with compensated ALD, it is surprising that abstinence was not associated with the risk of death in the subgroup analysis performed in decompensated patients with or without AH.

Thus, we believe that the Lackner study represents a valuable effort to improve the assessment of prognosis of patients with ALD. However, their results should be validated in other independent prospective cohorts of patients with AH that should take into account all prognostic factors including sepsis and response to corticosteroids.

References


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