Letters to the Editor


Reply to: “Mid-regional pro-adrenomedullin (MR-proADM): An even better prognostic biomarker than C reactive protein to predict short-term survival in patients with decompensated cirrhosis at risk of infection?”

To the Editor:

We thank Reuken et al. for their interest in our study. The prognostic evaluation of cirrhotic patients has improved in the last decade or so, with the consideration of extrahepatic complications common in cirrhosis, and with the dynamic assessment of prognostic scores. The first extrahepatic complication taken into account was hepatorenal syndrome, justifying the incorporation of serum creatinine in the MELD score. More recently, Arvaniti et al. proposed a prognostic classification in which bacterial infection defined the more severe stage of cirrhosis [1]. However, bacteriological tests that are mandatory for the diagnosis of infection may lack sensitivity in cirrhosis. Moreover, systemic inflammation associated with bacterial infection may persist, even after appropriate antibiotic treatment, thus having an impact on prognosis. Recently, the analysis of a large European cohort has confirmed that the occurrence of an acute-on-chronic liver failure is associated with systemic inflammation even in non-infected patients [2]. This is why our study (1) focused on a marker of systemic inflammation (rather than a marker of infection) and (2) considered as relevant only the case of persistent elevation of CRP for 15 days [3].

New prognostic markers are currently under evaluation in cirrhosis. Most of them are influenced by systemic inflammation. For example, our group demonstrated that elevated serum free cortisol is associated with high CRP levels and increased mortality in hemodynamically stable cirrhotic patients [4]. Copeptin, a surrogate of AVP secretion, also increases in the event of systemic inflammation [5] and recently appeared as a promising prognostic marker in cirrhotic patients [6]. For all these new markers, it seems important to determine their correlation with CRP levels. In addition, essential information for the clinician is their specific weight for prognosis, independent of MELD and CRP. Indeed, although these new markers appear attractive through their pathophysiological background, they are not routinely available, conversely to CRP.

The results presented by Reuken et al. are very interesting but deserve some comments. In their population including a majority of infected patients (52%), the mid regional fragment of pro-adrenomedullin (MR-proADM) appeared to be a reliable marker of spontaneous bacterial peritonitis (SBP). The authors emphasize the relationship between MR-proADM and SBP rather than systemic inflammation. We acknowledge that MR-proADM was a better diagnostic marker of SBP than CRP. However, given the high prevalence of infected patients and the more marked increase of MR-proADM in the event of bacterial infection in the study of Reuken et al. the prognostic value of MR-proADM remains to be demonstrated in non-infected cirrhotic patients. The authors should have provided specific data on this subgroup of patients. Another comment concerns the statistical method used by the authors. Their multivariate model seems questionable since MR-proADM, bacterial infection, SIRS, and MELD were implemented as independent variables, whereas univariate analyses showed that MR-proADM was significantly correlated with INR and creatinine, and was a “poor” but significant predictor of bacterial infection. Hence, the question of the true independent prognostic value of MR-proADM remains unresolved. In our study, CRP and MELD were not collinear, thus allowing us to state that persistently high CRP levels provided greater accuracy than the simple measurement of MELD for evaluating prognosis in cirrhotic patients.

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Conflict of interest

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