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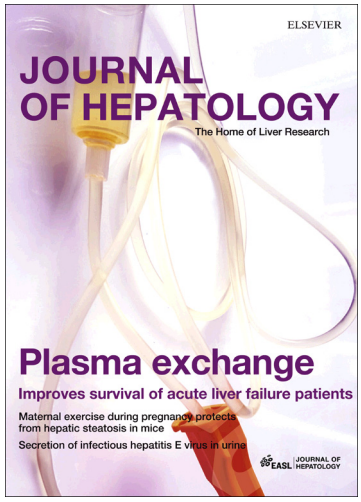

Reply to letter by Angelo Zamban De Mattos

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Reply to letter by Angelo Zamban De Mattos

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We would like to thank Angelo Zamban De Mattos et al for their interest and letter regarding our recently published manuscript.

We agree that using a fibroscan reading of >10 Kpa as an inclusion criteria may result in some patients without cirrhosis (and who had undergone an endoscopy for an alternative indication) being included and thus resulting in a prevalence of varices (23% in our study) lower than one would expect from screening a cohort with proven cirrhosis. An increasing number of patients are presumed to have cirrhosis based on non-invasive fibrosis assessment without a confirmatory liver biopsy. This can result in an incremental increase in the number of screening endoscopies and surveillance ultrasounds for HCCs. It is therefore of crucial importance to rationalize such decisions, as the positive predictive value of any non-invasive test for the diagnosis of cirrhosis is not more than 50%. (1) The purpose therefore of the study was not to assess the prevalence of varices in a cohort of cirrhotics but to ask if a LSM <20Kpa and platelets >150x10^3cells/L safely excluded patients who could avoid endoscopy. Moreover current cut-off values for F4 disease vary between aetiology and can be as low as 10kPa. (2) The issue addressed by BAVENO VI is that many clinicians do not differentiate between stages of cirrhosis and risk of decompensation, and our data highlights the recommendations for identifying low risk patients performs robustly.

Regarding the definition of high risk varices, we re-reviewed the endoscopy data, and 2 cases had red signs: one on large varices assigned as ‘clinically significant’ in the paper, and the other was in a 'short, small varix.' Given the equivocal description and tiny size of the latter it was described as low risk. This highlights an inherent limitation in assessing portal hypertension by the subjective assessment of varices, but also reflects real-world clinical decision making. If this varix was reassigned, there is no significant change to the performance of BAVENO VI: sensitivity 88%, specificity 34%, PPV 7%, NPV 98%, LR+ 1.33, LR- 0.37.

We fully agree that any screening test needs to be accessible, cheap and acceptable to patients especially in low- resource countries. There has been recent research validating the use of simple biochemical parameters for predicting significant fibrosis in viral hepatitis B in sub- Saharan Africa. (3) However, as the authors rightly identify, there are currently no

suitably simple, cheap and sensitive markers for identifying clinically significant port hypertension. This is an important area of future research. Further consideration must also be given to the cost saving by potential avoidance of endoscopy in a cohort of patients and this will require a cost-effectiveness analysis.

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