**Authors' reply-**

# From prognostic factors to personalized medicine

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Dear Editor,

We thank Kumar and colleagues for their interest in our new algorithm for risk-stratification in candidates to secondary prophylaxis of variceal bleeding.

In this algorithm, patients that bleed without other manifestations of hepatic decompensation are classified as low-risk without measuring the hepatic venous pressure gradient (HVPG). Using our new algorithm, a large number of invasive and costly HVPG measurements can be saved. More importantly, the number of high-risk patients who did not rebleed during follow-up (the "grey zone") decreased from 43% to 23%, demonstrating great accuracy in selecting high-risk patients.

Kumar criticise that restricting measurements of HVPG-response can leave some high-risk patients unrecognized. This is true but is of little practical relevance as current guidelines do not suggest changing therapy based on a poor HVPG-response, but after rebleeding. Although HVPG-guided therapy may improve outcomes, this is not the standard of care. Following our algorithm HVPG-guided therapy could be restricted to high-risk patients, thus facilitating studies comparing standard of care vs HVPG-guided therapy and its clinical implementation if beneficial.

Kumar suggests that omitting HVPG measurements in patients bleeding without ascites/hepatic-encephalopathy would ignore some cases with HVPG>20mmHg that might benefit from TIPS. A HVPG≥20mmHg at admission is a sign of poor prognosis in acute bleeding (1) that one study used to select patients for pre-emptive TIPS. However, it is unknown if this poor prognosis is true if measuring HVPG after the bleeding episode. Importantly, the benefit quoted by Kumar was not associated with improved survival. Our findings suggest that increased survival is more likely if restricting TIPS to patients in our high-risk category (bleeders with ascites/hepatic-encephalopathy, baseline HVPG>16 mmHg, non-responders to NSBBs). Admittedly, this strategy needs confirmation in RCTs.

Finally, Kumar correctly suggest that the algorithm could be modified using the acute HVPG-response to IV propranolol instead of the chronic HVPG-response, this would save additional HVPG measurements (2,3). Again, it is unknown if non-responders submitted to TIPS would have a better survival.

In conclusion, although the prognostic significance of HVPG-response in undeniable, it is also true that its clinical applicability is limited by the cost and expertise required. The challenge is developing tools that such as our algorithm help predicting treatment response in a given patient while minimizing the need of non-generally available examinations. This will open the possibility of a personalized medicine approach to the treatment of portal hypertension.

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