



Failure to control variceal bleeding: Definition matters

To the Editor:

Acute variceal bleeding (AVB) is recognized as a leading cause of mortality in patients with cirrhosis.¹ Importantly, an episode of AVB comprises not only the risk of bleeding and re-bleeding but also the risk of triggering other complications, among which acute-on-chronic liver failure (ACLF) stands out.^{2–5} The term ACLF defines an abrupt worsening of hepatic and extrahepatic organ failure in patients with underlying liver disease. On the other side, transjugular intrahepatic portosystemic shunt (TIPS) is a highly effective tool to treat patients with portal hypertension and variceal bleeding, thus markedly reducing the risk of rebleeding, further liver decompensation and death. One of the main concerns regarding TIPS is its potential deleterious impact on patients with a markedly deteriorated liver function and ACLF, given that TIPS insertion could reduce hepatic perfusion and worsen liver function.

In this setting, we read with great interest the study by Kumar *et al.* “Determinants of mortality in patients with cirrhosis and uncontrolled variceal bleeding”⁶ that addresses the important issue of whether the insertion of a rescue TIPS in patients with failure to control AVB (with or without ACLF) improves survival. Kumar *et al.* evaluated data from 174 consecutive patients with failure to control AVB admitted to their intensive care unit; however, only 78 patients received TIPS and 104 were managed differently. The study published herein evaluated survival according to the presence or not of ACLF at the moment of TIPS placement, demonstrating that TIPS improved survival in patients with failure to control AVB and ACLF but not in those without ACLF.

Despite the great implications of this study, its results should be interpreted carefully before extrapolating them to general practice. The study sends a confusing message as it seems to challenge the need for TIPS in patients with refractory bleeding. It is striking that, according to the authors’ results, TIPS insertion does not affect survival in patients without ACLF, thus calling into question the need to provide a definitive treatment with TIPS in patients with failure to control AVB. Most probably, the problem lies in the definition of “failure to control bleeding”. Refractory bleeding is usually defined as a variceal bleeding that does not respond to the combination of vasoactive drugs and endoscopic treatment. Nevertheless, the authors have expanded the notion to patients that still had endoscopic options, thus confusing the reader when stating that patients that did not undergo TIPS had a similar survival than those that did. Also, the authors do not detail the treatment applied in patients that did not undergo TIPS, which would undeniably have influenced survival. How was failure to control bleeding controlled without using TIPS?

On another note, this study sets the perfect scenario to establish the cut-off point and futility criteria for TIPS placement

in patients with failure to control AVB. Although the authors show that the presence of grade 2–3 ACLF prior to the acute episode of variceal bleeding is an independent prognostic factor of mortality, unfortunately, they do not show whether there is a subgroup of patients with new-onset ACLF in whom TIPS may be futile. Also, it would have been interesting to see whether the different events triggering ACLF (infection, alcoholic hepatitis), or the presence of ACLF prior to bleeding, influence outcomes.

Finally, it is worth mentioning that the authors do not detail the proportion of patients that would have fulfilled criteria for preemptive TIPS (pTIPS) before exhibiting failure to control AVB. Admittedly, and in spite of the overwhelming amount of data supporting the use of pTIPS, it is a fact that in the real-life setting the implementation of pTIPS is not as high as it should be.^{7,8} Accordingly, the present study also shows the lack of implementation of pTIPS, which could justify the large number of patients reaching the point of requiring a rescue TIPS. Nevertheless, it would have been interesting to present these data (proportion of patients that would have fulfilled criteria for pTIPS) as a means of reinforcing the concept that, at least to some extent, the setting evaluated by the present study could have been avoided.

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Conflict of interest

The authors declare no conflict of interest.

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Authors’ contributions

A. Baiges, C. Bureau and JC. García-Pagán contributed to the letter concept and design as well as draft of the manuscript.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2021.01.012>.

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Reply to: “Failure to control variceal bleeding: Definition matters”

To the Editor:

We thank Baiges *et al.*¹ for their keen interest and observations regarding our study.² We completely agree that the definition of ‘failure to control bleeding’ is difficult to apply in individual clinical cases and in general its interpretation is dependent upon many factors including how sick the patients is, whether they have ongoing bleeding during an endoscopy session and the severity of bleeding. In our study,² we defined ‘failure to control bleeding’ strictly as failure to achieve haemostasis despite 2 endoscopies or need for adjuncts such as Sengstaken-Blakemore tube (SBT) or a stent within 5 days of the first bleed in combination with vasoactive drugs.

Baiges *et al.* raise several important questions.

1. What is the role of transjugular intrahepatic portosystemic shunt (TIPS) in patients without acute-on-chronic liver failure (ACLF) with ‘failure to control bleeding’?

We believe that our paper is underpowered to make any new conclusions about the role of rescue TIPS in patients with failure to control bleeding but without ACLF. As is the current clinical practice, these patients should be offered TIPS.

2. How was ‘failure to control of bleeding’ controlled without TIPS?

As a large proportion of our patients were referred from other centres, we found that many still had endoscopic options. Out of 174 patients in our study, further therapeutic endoscopy was successful in achieving satisfactory haemostasis in 82 (47.1%).

3. Whether there is a sub-group in whom TIPS is futile?

As reported in the paper² and correctly observed by the Baiges¹ *et al.*, none of the patients who had grade 2–3 ACLF “prior to the acute episode of variceal bleeding” survived, irrespective of their TIPS status. Of the patients who developed ACLF following an

episode of variceal bleeding, all the survivors had a CLIF-C ACLF score of 62 or below. This confirms the previous futility cut-off in patients with ACLF for whom liver transplantation is not an option. Patients with a CLIF-C ACLF score of >64 after 48 hours of intensive care unit care are at high risk of death and those with a score of >70 almost invariably die irrespective of the aetiology or precipitant.³ Although these criteria provide a strong guide, futility of ongoing care needs to be decided on a case-by-case basis.

4. Would preemptive TIPS (pTIPS) have prevented the need for rescue TIPS?

The population studied was a highly selected patient group, most of whom were referred from other centres. It is extremely difficult to analyse this complex patient population in a retrospective study and come to any meaningful conclusion about whether pTIPS would have prevented the need for rescue TIPS. Despite high quality published data,^{4,5} the role of pTIPS is still a matter of debate in the UK, which has been further fuelled by the recent negative trial from the Hayes group.⁶ A large UK trial of pTIPS is in the process of being set up to definitively address this issue.

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Conflict of interest

Rajiv Jalan has research collaborations with Yaqrit and Takeda. Rajiv Jalan is the inventor of OPA, which has been patented by UCL and licensed to Mallinckrodt Pharma. He is also the founder of Yaqrit Ltd, a spin out company from University College London. He is also a Founder of Thoeris Ltd.

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