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23 February 2023

Dear Editor

Subject: World Journal of Gastrointestinal Pathophysiology review of Manuscript NO: 81904

Thank you for the helpful comments from the reviewer of our manuscript No 81904. We have answered all the comments/suggestions from the reviewer and have highlighted the changes/additions in the revised manuscript

Reviewer #1:

Reviewer comment No 1 Please specify how many patients submitted to sTIPS had concomitant HCC, and/or portal vein thrombosis

Author reply: Thank you for this comment. The following sentence has been included in the manuscript and highlighted **No patients had a concomitant HCC or portal vein thrombosis at the time of TIPS insertion.**

Reviewer comment No 2 Please define in material and methods a list of contraindications to sTIPS in your center.

Author reply: Thank you for this comment. The following sentence has been included in the manuscript and highlighted in the methods section **Contraindications to sTIPS in our unit were severe pulmonary hypertension, severe tricuspid regurgitation, congestive heart failure, fibropolycystic liver disease, uncontrolled systemic sepsis and unrelieved biliary**

obstruction. Relative contraindications were congenital hepatic fibrosis, portal vein thrombosis, obstruction of all hepatic veins and severe coagulopathy (INR > 5).

Reviewer comment No 3 Please specify uncontrollable variceal bleeding exactly.

Author reply: Thank you for this comment. The following sentence has been included in the manuscript and highlighted in the methods section **The study protocol followed the Baveno recommendations and defined uncontrolled or persistent variceal bleeding as the need for a transfusion of 4 units of blood or more within 6 h and the inability to achieve an increase in systolic blood pressure to 70 mmHg or more or a pulse reduction to less than 100/min.**

Reviewer comment No 4 "Bleeding persisted in two patients" what was the rescue therapy, if any, for those patients with uncontrolled variceal bleeding after sTIPS failure?

Author reply: Thank you for this comment. The following sentence has been included in the manuscript and highlighted in the methods section **The two patients with persistent bleeding after TIPS underwent repeat endoscopy and ultrasound-guided Histoacryl and coil injection of residual gastric varices with resolution. The patient with recurrent bleeding in hospital underwent a gastric devascularization for control of gastric varices.**

Reviewer comment No 5 "Nine of the 12 (75%) patients who required pre-sTIPS balloon tamponade died". Please specify which type of balloon, i.e. Sengstaken-Blakemore, Linton Nachlas, Minnesota?

Author reply: Thank you for this comment. The following word has been included and highlighted in the methods section **Minnesota**

Reviewer comment No 6 Specify if patients who died prior sTIPS were on glipressin or somatostatin infusion. -"while all nine (100%) patients who were hypotensive....".

Author reply: Thank you for this comment. The following two words have been included and highlighted in the methods section **somatostatin infusion**

Reviewer comment No 7 Please define "hypotension" in brackets

Author reply: Thank you for this comment. The following sentence has been included and highlighted in the methods section (systolic blood pressure <70mmHg)

Reviewer comment No 8 I would add a short comment about a possible bias in this study:

Author reply: Thank you for this comment. The following sentence has been included and highlighted in the limitations paragraph of the discussion There are inevitable and specific limitations to our study. Firstly, this investigation is limited by its small sample size, retrospective design, and lack of a control group. Secondly, the study has a clear selection bias which restricts universal applicability as these patients were treated in a single, well-resourced tertiary care referral center with round the clock skilled endoscopic and TIPS access.

Reviewer comment No 9 So what is your recommendation if uncontrolled variceal bleeding is present in patients with a CABIN C score (16-20)? I'd appreciate it if you could add and propose a simple algorithm for uncontrolled variceal bleeding based on CABIN categories.

Author reply: Thank you for this comment. The following sentence has been included and highlighted in the concluding paragraph of the discussion

Despite the fact that mortality was 75% for CABIN B, 87.5% for CABIN C, and 83% for CABIN scores >10 in this study, this high-risk category should not be denied consideration for an emergency TIPS and be assessed on a case by case basis especially in units where there is prompt access to liver transplantation after sTIPS.

Reviewer comment No 10 One typo: - "The median CABIN score in the 24 in-hospital TIPS survivors"... 24h

Author reply: This is not a typo and refers to 24 in-hospital TIPS survivors

Yours sincerely

A handwritten signature in dark ink, appearing to read 'J. Krige', with a long horizontal line underneath it.

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