Reply to the Reviewers:

Thank you for your kind comments and suggestions. We have revised the manuscript in accordance with your recommendations. All corrections are in blue letters, but the text corrections corresponding to the reviewer's comments are further highlighted in yellow. We would appreciate it if you could review it again. Our response to each comment is provided below.
First, we apologize for changing the title from "Treatment of the gastric varices based on balloon-occluded retrograde transvenous obliteration" to "Balloon-occluded retrograde transvenous obliteration for treatment of gastric varices" at the suggestion of the English proofreader considering the content of the review.

Reviewer #1:
I have read with great interest the review entitled "Treatment of gastric varices based on ballon-occluded retrograde transvenous obliteration" and the correspondent bibliography. It is a review focused on BRTO. The paper is well-written. The explanations of the techniques are supported with the excellent drawings of one of the authors. However, the paper needs structural changes to contribute with new information.

Answer
Thank you for reading carefully and for your kind comments. We have corrected our slightly biased opinion in line with your comments below. However, as a review from Asia, especially Japan, we intend to widely introduce the usefulness of BRTO to the world.

My comments: - Authors should update the references: papers from the last years are missing. - Statements as "BRTO has been established as the primary treatment of GV" sustained in the Abstract, Core-tip, in page 7 (Advantages of BRTO over other treatments) and in page 12 (Conclusions) should be rewritten. According to current bibliography, conclusions about which technique is superior are not clear. Although promising data about BRTO have been published in the last years, comparison with TIPS is difficult. It has to be considered the previous use of bare TIPS. Also, geographical-related differences play an important role. Regarding TIPS efficacy and

risks (Advantages of BRTO, page 7), specific data should be provided. If the studies mentioned where done with bare or cover TIPS should be considered and detailed. Data and references should be updated.

Answer
The description as if BRTO is superior to TIPS has been revised. Regarding TIPS, we also added a description of the difference between bare stents and covered stents in the results, and added recent literature. Furthermore, BRTO is performed mainly in Asia and the United States, but rarely in Europe, and we also describe such geographical situations.

- Also, the indication of BRTO as prophylactic treatment of GV should be sustained with caution. Current recommendation in guidelines worldwide, as from Baveno VI consortium and AASLD, are using beta-blockers as first step. BRTO has not been evaluated in high quality clinical trials in prophylaxis.

Answer
Beta blockers are widely used to prevent bleeding in esophagogastric varices based on a great deal of evidence, so we have added a description about it. However, this review omits a further description of them because its focus is interventional procedures. We also added that preemptive TIPS is also recommended.

- Disadvantages of BRTO, as the increase risk of developing esophageal and ectopic varices, with potential to bleed, or the inability to control bleeding from esophageal varices, should be highlighted (and supported with data).

Answer
As you pointed out, I also added the disadvantages of BRTO.

- Tables summarizing the results of the different papers are mandatory in a review to help with the interpretation of the data. As a suggestion, they could provide the favorable results using BRTO, and the different management proposed (CARTO, PARTO); the percentage of complications could also be included. Also, data comparing

BRTO vs TIPS could be provided as a table. - Authors could also highlight the importance of BRTO in a group of patients with GV and HE and provide data.

Answer
We have created four tables summarizing comparative studies on TIPS and BRTO. Since there are figures for various BRTO modification methods such as PARTO, CARTO, and so on, we have only described them in the text and did not use the table. The usefulness for hepatic encephalopathy is a characteristic of BRTO, so we added it.

- The last statement about that the best technique suggested is BRTO plus partial splenic embolization should be mentioned with caution. It is an interesting management, but randomized clinical trials are lacking, and splenic embolization can result in serious complications (that should be mentioned), moreover in cirrhotic patients. - Abbreviations should be mentioned together.

Answer
Thank you for your advice. Although PSE can be safely performed, it is undoubtedly an invasive procedure, and its complications are also cited in the literature in the text.

Reviewer #2:
The authors summarized the recent advances in the application of BRTO for GVs, mainly include the following aspects: indications and contraindications for BRTO, advantages of BRTO over other treatments, conventional BRTO procedure, BRTO modifications and combined treatment. This review article has an overall reasonable logic, which would be helpful for clinicians to have a full picture of BRTO. However, there are still some questions that remain to be solved.

Answer
Thank you for reading carefully and for your kind comments. We have accepted your suggestions and revised the manuscript.

In the “Advantages of BRTO over other treatments” section, The authors seemed to

underestimate the value of TIPS. Although BRTO may be more effective in the prevention of variceal rebleeding, the selection of BRTO or TIPS for patients with GVs should also depend on the comorbidities such as ascites. Study conducted by Yu Q et al. [1] indicated that BRTO treated patients are more likely to develop ascites aggravation. By contrast, TIPS counteracts the mechanism behind ascites by reducing the filtration pressure within the splanchnic capillaries, so excessive fluid can be drained via the lymphatic system. For patients with severe ascites or when SBP is a concern, TIPS might be a more appropriate option than BRTO.

Answer

We haven't underestimated TIPS, but we overemphasized BRTO's advantage over TIPS in the first manuscript. We properly mentioned the advantages and disadvantages of both, accurately presented data from comparative studies, and concluded that rather than eliminating one or the other, appropriate treatment choices should be made according to the pathology of the individual case.

In the “BRTO modifications” section, some modified BRTO techniques included CARTO, PARTO, M-CARTO and CARTO-II have been cited in the manuscript. All the above methods could avoid the retention of the balloon, but have the disadvantage of high cost. A recent study [2] has proposed a new modified method – balloon-assisted antegrade transvenous obliteration (BAATO). In BAATO procedure, the retrograde occlusion balloon catheter is used to occlude the GRS, followed by antegrade trans-TIPS catheter injecting cyanoacrylate rather than sclerosant. The distribution of cyanoacrylate in GVs could be controlled by adjusting the balloon size for the blood flow velocity varies as the balloon size changes. Thus, BAATO might be valuable alternative option as well. References [1]. Yu Q, Liu C, Raissi D. Balloon-occluded Retrograde Transvenous Obliteration Versus Transjugular Intrahepatic Portosystemic Shunt for Gastric Varices: A Meta-Analysis. J Clin Gastroenterol. 2021 Feb 1;55(2):147-158. [2]. Liu J, Yang C, Huang S, et al. The combination of balloon-assisted antegrade transvenous obliteration and transjugular intrahepatic portosystemic shunt for the management of cardiofundal varices hemorrhage. Eur J Gastroenterol Hepatol. 2020 May;32(5):656-662.

Answer

Thank you for your advice. We added a description about cost. Thank you for providing

information on the article about BAATO. We recognized that BAATO was also a very reasonable treatment, so we added BAATO as well.

Reviewer #3:

Thank you very much to let me have the opportunity to read a comprehensive review about the balloon-occluded retrograde transvenous obliteration treating bleeding gastric varices. This manuscript is well written and much detail to descript the hemodynamic of the complicated gastrorenal shunt in cases with left side portal hypertension.

Answer

We are honored to have you understand our review article well and appreciate it.