

Dear Editor,

Thank you for allowing us to revise our manuscript (Manuscript ID: 74054) entitled "Modified endoscopic ultrasound-guided selective N-butyl-2-cyanoacrylate injections for gastric variceal hemorrhage in left-sided portal hypertension: A case report". We greatly appreciate editors and reviewers for their comments and suggestions. These comments and suggestions are valuable for improving our manuscript. All authors approve the revised manuscript for publication.

Response to the reviewer's comments was as follows:

Reviewer #1:

1. Response to comment: (Such innovative technique to solve a serious condition, we need to know the elongate follow up period and check any complications that occurred during this period)

Response: Thank you for your affirmation and encouragement. "No recurrent GI hemorrhage and other complications were reported during his three-month follow-up." has been added in the "Outcome and follow-up" section. This patient is still in the process of close follow-up, the initial follow-up period would be at least one year, and we will be more than happy to share his complications during the follow-up period with you.

Reviewer #2:

1. Response to comment: (It is necessary to clarify what type of IGV (IGV1 or IGV2) the patient had.)

Response: Thank you for your suggestion. "IGV1 by Sarin classification" has been added in the "Imaging examinations" section.

2. Response to comment: (It is necessary to clearly explain the choice of the injection site (the confluences of GVs, but not the feeding and perforating vessels, which are more dangerous) and a lower than usual dose of the N-butyl-2-cyanoacrylate.)

Response: Thank you for your suggestion. The choice of injection site was based on considerations to switch the intervention focus from the feeding and perforating vessels to confluences of GVs, which were in the source directions of these bleeding vessels and also at the junction between feeding and perforating vessels, and with the aim of reducing the NBC injection dose (4 to 6 ml of NBC may be used in conventional injection procedures; however, only 2 ml of NBC was used with the method in this case, which was explained in the "Treatment" section), and lower the risk of post-operational GI

bleeding and ectopic embolism. These were explained in the "Treatment" and "Discussion" sections.

3. Response to comment: (Why do the authors consider this approach to be more effective and safe? Of course, theoretically this is excellent, but it is necessary to give an explanation from the standpoint of evidence-based medicine.)

Response: Thank you for your question. At present, the preliminary application of this method has revealed a satisfactory hemostatic effect, and no recurrent GI hemorrhage or other complications were reported during this current postoperative follow-up period. Therefore, we have seen the potential efficacy and safety, and hope to share this method with more physicians and endoscopists. As you suggested, regarding the efficacy and safety, we need and expect further research from the standpoint of evidence-based medicine through more cases in the future.

4. Response to comment: (The authors should emphasize that the described technique can be used only in hemodynamically stable patients.)

Response: Thank you for your suggestion. "Currently, this described technique is recommended to be used only in hemodynamically stable patients." has been added in the last paragraph of the "Discussion" section.

5. Response to comment: (Given that the problem remained (splenic vein obstruction), how to explain the improvement of left-sided portal hypertension three months after the injection?)

Response: Thank you for your question. Regarding the reasons for the improvement of left-sided portal hypertension, we consider it related to the gradual reduction of peripancreatic inflammatory response after effective treatment and the subsequent partial relief of the inflammatory splenic vein stenosis caused by severe pancreatitis.

6. Response to comment: (The authors write: "When pancreatic disease obstructs the splenic vein flow, the pressure of the left portal vein system increases, and the collateral circulations between the splenic vein and the portal vein gradually open up, which would lead to gastric variceals". It should be clarified that in segmental portal hypertension, blood flows retrogradely through the short and posterior gastric veins and the gastroepiploic veins resulting in the formation of GVs.)

Response: Thank you for your suggestion. "When pancreatic disease obstructs the splenic vein flow, the pressure of the left portal vein system increases, and the collateral circulations between the splenic vein and the portal vein gradually open up, which would lead to GVs" has been modified to "When pancreatic disease obstructs the splenic vein flow, the pressure of the left portal vein system increases, and blood flows

retrogradely through the short and posterior gastric veins and the gastroepiploic veins, which would lead to GVs".

Reviewer #3:

1. Response to comment: (-Imaging examinations: The endoscopic description should be more detailed. "Gastroscopy confirmed GV hemorrhage" --> GV with signs of recent bleeding in the absence of active bleeding?.)

Response: Thank you for your suggestion. "Gastroscopy confirmed GV hemorrhage" has been modified to "Gastroscopy revealed GV with signs of recent bleeding in the absence of active bleeding" as requested.

2. Response to comment: (Furthermore the location of the treated GV should be reported (fundus?). Sarin's classification should be provided as well (IGV1?))

Response: Thank you for your suggestion. "IGV1 by Sarin classification" has been added in the "Imaging examinations" section.

Response to the editorial comments was as follows:

Science editor:

Response to comment: (Please describe the endoscopic findings in more detail, please indicate whether the IGV is IGV1 or IGV2, supplementary follow-up period content and whether there are any complications.)

Response: Thank you for your suggestion.

(1) "IGV1 by Sarin classification" has been added in the "Imaging examinations" section.

(2) "No recurrent GI hemorrhage and other complications were reported during his three-month follow-up." has been added in the "Outcome and follow-up" section.

Company editor-in-chief

Response to comment: (The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words). Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint.)

Response: (1) The title has been modified to "Modified endoscopic ultrasound-guided selective N-butyl-2-cyanoacrylate injections for gastric variceal hemorrhage in left-sided portal hypertension: A case report" (17 words), and "patients with" was deleted.
(2) Original figure documents were submitted in PowerPoint as requested.

Once again, we would like to express our great appreciation to editors and reviewers for their comments and suggestions and hope that the revised manuscript will meet with approval. We sincerely appreciate your kind consideration of our manuscript, and we look forward to hearing from you at your convenience.

Best regards,
Jun-Wen Zhang