

Dear editor Yuan Qi and reviewers,

Thank you for your letter and the reviewers' comments concerning our manuscript entitled "Procedure-related complications in gastric variceal obturation with tissue glue". Those comments are valuable and very helpful for revising and improving our paper. We have studied the comments carefully and made some revisions which are marked in red in the manuscript.

The responses to the three reviewers' comments are as following:

Reviewer #1 (00724362)

1. Please write full name for abbreviations like GOV, IGV.

Response: The full name for abbreviations like GOV, IGV were written in the manuscript.

2. Were there some differences between the complications according the Child Pugh grade and GOV1, GOV2, IGV1, IGV2?

Response: We evaluated the complication "Sticking of the needle to the varix" according the Child Pugh grade. There was no statistical difference of the complication among the patients with liver function of Child-Pugh A, B and C. The result was embedded in the manuscript. This study is a retrospective study, we mainly investigated the medical records and some endoscopists didn't describe the details of complications. Although we had tried to ask the endoscopists for details, sometimes they forgot which varix the needle stuck to because they usually obliterated several gastric varices in one procedure. So we could not obtain the exactly data and evaluate the complication among GOV1, GOV2, IGV1 and IGV2.

The complication "Blockage of the injection catheter" mainly correlated to the

equipment of injection, glue and the speed of injection (see discussion of the manuscript). So we didn't evaluate this complication according the Child Pugh grade and the types of varices. The incidence of complications "Glue adhesion to the endoscope resulting in difficulty withdrawing the endoscope" and "Sticking of the ligation device to the esophageal varices" were too low to be evaluated the differences according the Child Pugh grade and the types of varices.

Reviewer #2 (02999941)

Major Points 1. To give the reader a better sense of the patient population, the authors rightfully include Child-Pugh Class to clarify the stage of liver disease. However, because this population was selected without the reader being aware of the "selection" criteria, it would be beneficial to know the platelets and INR – and whether this goes into decision-making. Furthermore, noting that only 18% of the patients were Child-Pugh C, does this go into decision-making for the procedure. This would be relevant to the current paper since one might expect more complications in CP-C or patients with lower platelets/higher INR.

Response: This is a very good question. First, endoscopic gastric variceal obturation (EGVO) was performed in all patients admitted to our department who need secondary prophylaxis of variceal haemorrhage unless there were contraindications. Only a few special patients received EGVO as primary prophylaxis of variceal haemorrhage. Child-Pugh C nearly didn't go into decision-making for the procedure. Child-Pugh grades listed in the manuscript were the results of first admission of the patients but most of the patients were admitted to our hospital to receive sequence of endoscopic treatments for more than two times. Child-Pugh grades of the patients might change, as well as platelets and INR, which included huge amounts of data. EGVO were performed very carefully in the patients with very low platelets (lower than $20-30 \times 10^9/L$) and long prothrombin time (longer than 25-30

seconds), but those two factors were not contraindications for EGVO. Actually, a series of studies about sequence of endoscopic treatment for esophageal and gastric varices are going in our center and many data are being collected. The effect of platelets and INR on the outcome of sequence of endoscopic treatment would be discussed in the future. Based on the present data, we evaluated the complication “Sticking of the needle to the varix” according the Child Pugh classification (see Reviewer #1).

Major Points 2. Is it protocol that all these patients are placed on Octreotide or somatostatin? The manuscript only mentions a small group that recent somatostatin.

Response: In our department, there are two kinds of patients. In nearly two third of patients, variceal haemorrhage was already stopped in other hospitals and they were admitted to our hospital for endoscopic treatment of esophageal and gastric varices. In nearly one third of patients who were admitted for active variceal haemorrhage, octreotide or somatostatin was administered in all patients. Most of time, endoscopic treatment of esophageal and gastric varices would be performed after the bleeding ceased at least 24 hours. In patients whose bleeding could not be stopped by octreotide or somatostatin, an emergency endoscopic treatment would be performed.

Minor Points 1. Table 1 lists, under Etiology of gastric varices, “Others”. Can the authors clarify what this category included? Were these all patients with portal hypertension due to liver disease or were there cases of senestrial portal hypertension?

Response: We clarified the “Others” under etiology of gastric varices of Table 1, including portal hypertension due to non-liver disease. We didn’t list the exactly data as the numbers were small.

Minor Points 2. Can the authors clarify the protocol at the institution?

Specifically, for whom do you consider repeated sequential therapies? Is the sequence utilized for treatment based on evidence from the current body of literature?

Response: We clarified the protocol of sequential therapies at our institution in the MATERIALS AND METHODS of the manuscript. We performed the treatment mainly according to Baveno Consensus and UK guidelines on the management of variceal haemorrhage in cirrhotic patients. We just combined the treatment of esophageal varices and gastric varices and gave it the name “Sequence endoscopic treatment”.

Minor Points 3. How many providers perform this exam? Are there different levels of proficiency that would affect the complication rate?

Response: This study is a retrospective study which enrolled 519 patients underwent at least one EGVO from January 2011 to December 2016 in our department of endoscopy. EGVO was carried out formally in our center since 2008 but the technique was not so mature, so we didn't analyze the data before 2011. After 2011, we had a very tenured, senior, mature medical team including about 9-11 endoscopists. The protocol of EGVO and sequential therapies were also standard. There may be some different levels of proficiency among different endoscopists but not apparent.

Reviewer #3 (02441070)

We are grateful for the reviewer's positive comments to our study and it seems no question need to be responded to.

Best regards,

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