Response to Reviewers' Comments:

Reviewer #1

Comment 1: The disadvantage is that the quantity is small. The results of multi-center and multi-sample studies are more clinically significant.

Reply: Thank you for your comment. We acknowledge that we do have a small number of patients, which had been mentioned in the limitations, as follows, which is also highlighted in yellow in the last paragraph of the Discussion section. In the future, we will conduct a large prospective study to test our conclusion.

Our study has some limitations. First, the total number of the patients included was relatively small in this study.

Comment 2: In addition, subgroup analysis of PPI dose is recommended to explore the impact of postoperative PPIs on post-EVT GIB and other post-EVT complications during hospitalizations.

Reply: Thank you for your comment. Unfortunately, it may not be reasonable to do subgroup analyses of PPIs dose in this study. There are two major explanations.

First, PPIs data was extracted until post-EVT GIB episodes developed, so the duration of PPIs was generally shorter in patients who developed post-EVT GIB than those who did not. Similarly, the total dose of PPIs was also lower in patients who developed post-EVT GIB than those who did not.

Second, in our real-world clinical practice, the daily dose of the PPIs would be decreased, if the patient's condition was improved. By contrast, the daily dose of the PPIs would not be decreased, if post-EVT GIB occurred. Therefore, the grouping according to the daily dose of PPIs will be biased. Certainly, your suggestion should be considered in our future prospective studies and RCTs.

Reviewer #2

Comment 1: why did you include just the patients hospitalized?

Reply: Thank you for your comments. There are two major explanations. First, EVT procedure is invasive, which has a risk of postoperative complications, especially postoperative bleeding. Therefore, nearly all of our patients undergo EVT procedures during hospitalization, so that the patient's postoperative conditions can be observed timely and sufficiently, and active treatment can be employed, if necessary.

Second, the data on PPIs use during hospitalization can be obtained more accurately than those at clinics.

Therefore, this study mainly selected the patients hospitalized.

Comment 2: you didn't include the patients admitted to intensive care?

Reply: Thank you for your comment. In our hospital, the Intensive Care Unit is different from the Department of Gastroenterology. In our study, only the patients admitted to the Department of Gastroenterology were included.

Comment 3: how many days did you hospitalize the patients?

Reply: Thank you for your comment. According to your suggestion, we have added the information on the median hospital stay after EVT, as follows, which is also highlighted in yellow in the "Patient characteristics" of the Results section.

After EVT, the median hospital stay was 6 (2-16) days.

Comment 4: what about the follow-up?

Reply: Thank you for your comment. We focused on the in-hospital outcome without the follow-up data in this study, which has been mentioned in the limitations, as follows, which is also highlighted in yellow in the last paragraph of the Discussion section.

Fifth, follow-up data were lacking to assess 6-week and long-term mortality.

Comment 5: you have to rewrite the subgroup analyses because it is the same sentences with different numbers!!!

Reply: Thank you for your comment. We have adjusted the structure of the subgroup analyses, as follows, which is also highlighted in the "Subgroup analyses" of the Results section.

In all subgroup analyses according to the enrollment period, type and route of PPIs after the index EVT, use of PPIs before the index EVT, use of vasoactive drugs after the index EVT, indications of EVT, PVST, ascites, and HCC, logistic regression analyses showed that postoperative use of PPIs was not significantly associated with the risk of post-EVT GIB (**Figure 3**) or other post-EVT complications (**Figure 4**).

Comment 6: Why did you combine pantoprazole with esomeprazole for one patient?

Reply: Thank you for your comment.

First, intravenous pantoprazole was firstly given in this patient, and then oral esomeprazole was substituted. Due to a change in the route of PPIs, the type of PPIs has changed.

Second, due to accidental drug supply problem in the hospital, we have to change the type of PPIs used.

Regardless, to avoid the influence of the type and route of PPIs, we also performed the subgroup analyses. It doesn't make a difference.

Comment 7: Can you precise information about the use of PPI: dose?

Reply: Thank you for your comment. The dose of postoperative PPIs given to patients is usually 80mg twice daily, 40mg twice daily, or 40mg once daily. These are decided by the attending physician according to the specific patients' conditions and adjusted according to the change in the patient's

conditions. We have added the information on PPIs dosage, as follows, which is also highlighted in yellow in the "PPIs after the index EVT" of the Methods section.

Enrollment period, type (i.e., esomeprazole and pantoprazole), route (i.e., intravenous and oral), **dosage (i.e., 40mg once daily, 40mg twice daily, and 80mg twice daily)**, date of starting and discontinuation, and duration of PPIs after the index EVT were reviewed.

Comment 8: why did you use PPI both orally and intravenously in 47%!!??

Reply: Since the patients are not allowed to take food and water for the first 1-3 days after EVT, PPIs are firstly given intravenously. After that, oral administration is selectively substituted according to the patients' conditions.

Comment 9: you conclude that postoperative use of PPI could not be supported for reducing the development of complications but your study didn't show any correlation between PPI and complication? especially with retrospective study with a few complications!!

Reply: Postoperative complications of EVT usually include postoperative bleeding, retrosternal discomfort, nausea, vomiting, and so on. In this study, post-EVT complications were divided into post-EVT GIB and other post-EVT complications for analysis. P values for the impact of PPIs on both post-EVT GIB and other post-EVT complications were greater than 0.05, indicating no statistical significance. Therefore, we concluded that postoperative use of PPIs could not be supported for reducing the development of complications.

You are right that the number of post-EVT GIB was small. It has been acknowledged in the limitation, as follows, which is also highlighted in yellow in the last paragraph of the Discussion section. However, 67 patients developed other post-EVT complications in this study, about 47 percent of all patients, which is considered high enough.

Second, the number of post-EVT GIB was small, which made our statistical

analyses underpowered and increased the possibility of type II errors (i.e., false-negative findings).

Comment 10: can you precise why 23 patients of the non-PPI group took PPI before the index EVT? why did you stop it? Cordially

Reply: Thank you for your comment. We re-reviewed the data and modified the sentence as "24 patients of the non-PPIs group took PPIs before the index EVT", which is highlighted in yellow in Table 2. Of the 24 patients, 23 were admitted with acute gastrointestinal bleeding, in whom their causes of the gastrointestinal bleeding had not been identified at admission yet. As known, PPIs have been shown to be beneficial for non-variceal bleeding, so PPIs should be considered in such patients. However, they discontinued PPIs after EVT, because there are no clear indications for PPIs by endoscopic examinations. The remaining patient was routinely taking PPIs for a recent diagnosis of a peptic ulcer. However, endoscopy indicated that the ulcer had healed, and then PPIs were stopped.