

Response to Reviewers

Dear Reviewers,

We deeply appreciate your positive comments on our manuscript (Manuscript number: 76406, Retrospective Study). We have benefited enormously from these opinions, and we have carefully revised our paper. All amendments are highlighted in red in our revised paper ([as Supplementary Material](#)). Point-by-point responses to the comments are listed below this letter.

Looking forward to hearing from you,

With kind regards

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the changes that have been made in response to each reviewer comment

Reviewer 1

1. Why was there no stenosis of EGJ after endoscopic treatment? Please comment and discuss about this issue. The authors should indicate whether tumor circumference affected or did not affect stenosis.

Response: Thanks for raising this important issue. There was no stenosis of EGJ after endoscopic treatment. It may be related to the absence of circumferential lesions. There was a circular lesion in the middle esophagus in our center. No stenosis occurred after STER resection, but muscularis defect was the reason of

diverticular appearance. Stenosis depends on the area of mucosal defect after ESD and EFTR resection([Lines54-55, 266, 292-296](#)).

Reviewer 2

2. Did the authors perform EUS-FNA on SMT in this study? If the tumor is a leiomyoma, the need for resection is basically low, and if it is a GIST, if the possibility of en bloc resection is low, we think it is better to consider other treatment methods.

Response: Thanks for raising this important issue. We did not perform EUS-FNA on our resectable SMT to confirm the pathological diagnosis. Because it was an invasive examination that would increase patient's pain and cost, as well as a waste of medical resources. In the present study, all GISTs were en bloc resected, and all lesions that received piecemeal resection were leiomyomas ([Lines 226-227,318-327](#)).

3. Please mention the size of GIST alone and the rate of en bloc resection.

Response: Thank you for your advice. We have added the size of GIST alone and the rate of en bloc resection ([Lines207, 226-227](#)).

4. Would the authors consider resection in the future at any size? Please explain.

Response: Thank you for your question. The evaluation of how large tumor can be resected by a Endoscopy Center was based on the comprehensive treatment capacity of the hospital, including the technical level of operators, as well as the comprehensive capacity of the Endoscopy Center and other related departments such as Department of Thoracic Surgery. The maximum diameter of the tumor in the present study was 100mm, which was the long diameter rather than transverse diameter of the tumor.

5. SMT resection involves an incision in the muscle layer or in all layers, closure of the wound after resection is sometimes difficult. Please explain in detail whether you were able to close the incision completely in each case and technique, and the method of closure

Response: Thank you for your suggestion. All defects could be closed completely using metal clip or Purse-string suture with Nylon loops and metal clip if needed. We had responded your query in detail and put forward the method of closure

among the article([Lines165-175, 232-233](#)).

6. Please describe the SMT in EGJ for which surgical operation rather than endoscopic resection is recommended.

Response: Thank you for your question. There were no specific guidelines for how large a tumor should be surgically or endoscopically removed. Compared with surgical operation, Endoscopic resection had the advantage of being more minimally invasive with a shorter procedure time and hospital stay. According to a retrospective study, Submucosal tunneling endoscopic resection for tumors with a transverse diameter ≥ 3.5 cm and an irregular shape was associated with relatively high risk for piecemeal resection, adverse events, and technical difficulties.

Reviewer 3

7. In the regression analysis, the number of explanatory variables is large compared to the number of cases, making interpretation of the results difficult. If possible, any opinions of statistical experts should be consulted.

Response: Thanks for raising this important issue. Statistical experts had been consulted. They considered that the statistical methods and techniques mentioned in the current study were appropriate for the research.

8. Please indicate whether closure of defect were performed in all cases and the success rate.

Response: Thank you for your question. In ESD group, when there were deeply dissected areas or muscularis defect on the wound, it was necessary to close the wound, otherwise not. In STER group, the tunnel entry site should be closed with clips. In EFTR group, closure of defect should be performed([Lines165-175](#)).

9. Please indicate in the table any cases that required postoperative emergency surgery.

Response: Thank you for your suggestion. There was no case that required postoperative emergency surgery.

10. It is important to show how well the actual shape matched the preoperative EUS findings (regular or irregular).

Response: Thank you for your question. EUS can determine whether the tumor shape is regular or irregular, however, it is difficult to determine what the irregular

shape is.

11. Please indicate the surgeon's experience with each of the three techniques.

Response: Thank you for your suggestion. We have indicated the surgeon's experience with each of the three techniques. For tumors located in esophagocardiac or cardiac region, STER was mainly selected. ESD was chosen for gastroduodenal SMTs. EFTR was chosen for the tumors with a predominant extraluminal growth pattern located in gastroduodenal region ([Lines 160-164, 282-290](#)).

12. Since these cases include some of the larger sized cases, please indicate how they will be collected. Also, please discuss how to deal with cases that cannot be collected in one piece.

Response: Thank you for your question. Although some large lesions were resected intactly, it was difficult to remove them integrally from the submucosal tunnel due to the high risk of laceration of mucosa in the entrance of the tunnel. Importantly, all lesions that received piecemeal resection in the present study were leiomyomas. We usually close the defect first and then obtain the resection specimen through the mouth by snare. If the tumor is large, a snare will be applied to cut the tumor into pieces and then obtain through the submucosal tunnel and mouth.

13. Please provide a definition of "complete resection".

Response: Thanks for raising this important issue. We neglected to explain before, and this time we added the definition. ([Lines 134-136](#)).

14. Table(s) and figure(s): There are 5 tables and 3 figures, and most should be improved except figure 1 and 2. Table 3-5 could be merged into 1 table. The figure 3B is not easy to be read.

Response: Thanks for your suggestion. Table 3-5 were merged into 1 table. The figure 3B shows the size of the tumor in STER group, EFTR group and ESD group. The circle dots above the horizontal line represent tumors larger than 4 cm.

15. A total of 27 references are cited, including 11 published in the last 5 years. There are 7 self-cited references of the authors. Although the self-cited references are overall reasonable, it is unusual to be over 25% of self-citation. The reviewer didn't request the authors to cite

improper references published by him/herself.

Response: Thanks for your question. The seven self-cited references are all reasonable. We developed the technique of submucosal tunneling endoscopic resection (STER) for the treatment of SMTs originating from the MP layer. There are many studies in this area in our team, which are also representative studies. So we cited those references.