

## **Response to reviewers**

First of all, thank you very much for your positive comments, and we totally agree with your constructive suggestions which might be of great help to improve the quality of our manuscript.

1. How did the authors measured the exact diameter of the mucosal penetration?

**Answer:** In POEM procedure, an additional cap attached at the top of the gastroscopy was required. With the outside cap diameter (12.0 mm) as reference, the penetration size was estimated.. Moreover, we have added this point in MATERIALS AND METHODS (POEM procedure, Paragraph 2, Line 1).

2. Please give data regarding type of myotomy related to mucosal penetration. Because if selective myotomy was performed then the outer longitudinal muscle layer could be a barrier and so for such small mucosal penetrations, only prolonged fasting could be enough to close, as this was the case in other studies. So it is not clear if the mucosal closure was due to fibrin sealant or it could have been closed spontaneously zvz.

**Answer:** Data regarding type of myotomy has been presented in Table 1, inner circular muscle myotomy was performed in 10 procedures, full-thickness myotomy in 1, glasses-style anti-reflux myotomy in 1, and progressive full-thickness myotomy in 9. Moreover, we have made a statement “In previous studies evaluating intraoperative mucosal penetration during POEM, the injured mucosa could be closed only by prolonged fasting in those who received inner circular muscle myotomy. In the present study, 10 patients had an inner circular muscle myotomy, 1 had a full-thickness myotomy, 1 had a glasses-style anti-reflux myotomy, and 9 had a progressive full-thickness myotomy. Further research is needed to determine if the injured mucosa was more likely to close spontaneously in those who received inner circular muscle myotomy than in those who received a full-thickness myotomy” in (Discussion, Paragraph 5, Line 5).

3. Fibrin sealant was not effective in closure e.g. post bariatric surgery fistulas? Why the authors found it easy and effective in closure of mucosal penetrations during POEM? A discussion a comparison could be of interest. May be these small penetrations could have been closed spontaneously without fibrin sealant? 4. Nobody knows, if these small gastric cardia penetrations during POEM, could had been spontaneously closed only by prolonged fasting?? 5. It would be of interest the

parameters related to mucosal penetration, such as operator experience, type of achalasia (e.g. spastic type III or vigorous achalasia type II), type of myotomy (selective v.s full thickness?)

**Answer:** The data of Chicago classification and myotomy type have been presented in Table 1, 2 cases were classified as type I, 18 as type II, and 1 as type III. We have added a discussion “Given that the sizes of the mucosal penetrations in this study were all relatively small, it is not clear whether the defects could have been observed and would have closed spontaneously. Therefore, a prospective randomized controlled trial comparing observation without special treatment to treatment with fibrin sealant is warranted.” In (Discussion, Paragraph 5, Line 1).

6. Another issue of this study is that the authors used combined clipping and fibrin sealant to close small cardia mucosal penetration. This is confusing and made this study questionable. How many patients received only fibrin sealant and how many combined clipping and fibrin sealant to close the mucosal penetration?

**Answer:** Only one case received clipping combining with fibrin, and the remaining 20 cases received only fibrin. Moreover, the detailed data has been presented in Table 4.

7. What is glasses style antireflux myotomy?

**Answer:** Glasses-style anti-reflux myotomy retains about 1 cm of longitudinal muscle at the level of the dentate line after incision of the inner circular muscle, and makes selective incision of the longitudinal muscle right above and below the dentate line. The retained 1 cm of longitudinal muscle is expected to achieve the best result to prevent reflux after POEM. Moreover, this point has been added in MATERIALS AND METHODS (POEM procedure, Paragraph 4, Line 1).

8. Although mucosal penetration is considered as dangerous side effect during POEM this has not been proved in the practice as the majority cases with mucosal penetrations did not sequenced to life threatening complications<sup>1</sup> (Eleftheriadis N, Inoue H, Ikeda H, et al. Submucosal tunnel endoscopy: Peroral endoscopic myotomy and peroral endoscopic tumor resection. World J Gastrointest Endosc 2016;8:86-103.) So a comment on the mucosal entry penetration and its consequences should be made.)

**Answer:** We have added a discussion “The biggest risk of mucosal penetration is that the fluids from the stomach or the esophagus could

flow into the submucosal tunnel or the mediastinum and cause tunnel-infection, ulceration, esophagitis, mediastinal leak, or peritoneal leak” in (Discussion, Paragraph 2, Line 5). Moreover, Eleftheriadis N et al’s study, mentioned above, has been cited in the manuscript.

9. English language mistakes.

**Answer:** This manuscript has been thoroughly edited by a native English speaker from an editing company. And Editing Certificate has been provided.

10. The authors should also discuss the other methods of closure of mucosal penetrations such as clipping, Overstitch (Apolo system) etc.

**Answer:** We have added a discussion “Treatment for this complication has varied, with some patients undergoing observation without special treatment, being sealed by multiple clips or an endoscopic suture device (OverStitch™ Endoscopic Suturing System; Apollo Endosurgery Austin, Texas), or being treated with the defect being closed using fibrin sealant. Closure using hemostatic clips is not an ideal method. Once target mucosa is clipped, adjacent mucosa has the tendency to spontaneously split, making it hard to completely seal the penetration. Using

endoscopic suture with the OverStitch system is usually considered when the mucosal penetration is large and difficult to close using conventional clips” in (Discussion, Paragraph 1, Line 13).