Dear Editor and Reviewers,

We are very grateful to you for giving us an opportunity to revise our manuscript. We appreciate you very much for your positive and constructive comments and suggestions on our manuscript entitled "Repeat peroral endoscopic myotomy with simultaneous submucosal and muscle dissection as a salvage option for recurrent achalasia" (ID: 82904).

We have studied reviewers' comments carefully and tried our best to revise our manuscript according to the comments. The following are the responses and revisions we have made in response to the reviewers' questions and suggestions on an item-by-item basis. Thanks again to the hard work of the editor and reviewers!

Best regards,

Ningli Chai

Response to the comments of Reviewer #1

Comments No.1: The case is interested and well described.

Response: Thank you very much for your positive comments.

Comments No.2: The aim is given under the heading of AIM, but repeated at the end of introduction, it is better to delete the repeated point.

Response: Thank you very much for your reminder. We have deleted the repeated point.

Comments No.3: Discussion needs paragraph rearrangement, since discussion-related literature review is mentioned first, and then your findings are compared and described.

Response: Thank you very much for your constructive suggestion. We have

supplemented new contents and carefully rearranged the discussion parts accordingly.

Comments No.4: The manuscript needs minor linguistic and grammatical polishing.

Response: Thank you very much for this constructive suggestion. According to your advice, we have examined the full text again and corrected any grammatical problems. At the same time, this manuscript has been thoroughly edited by a native English speaker from an editing company and the new editing certificate has been provided in the attached files.

Response to the comments of Reviewer #2

Comments No.1: Consent to perform a procedure is NOT the same as a consent to undergo a procedure with scientific purposes. I cannot read Chinese to interpretate the IRB docs. I would like the authors to clarify if informed consent was obtained from the 16 patients for scientific purposes or it was waived due to the retrospective nature of the protocol.

Response: Thank you very much for your kind reminder. Informed consent to participate in the study was obtained from the 16 patients, which was shown in the "(7) 82904-Signed Informed Consent Form" file. Besides, we have corrected the description in the manuscript to avoid confusing readers.

Comments No.2: I believe the manuscript lacks further discussion of the indications and of the results. E.g.,

2.1 why a redo-POEM just after the inituial procedure? (0 months was the minimun time). Why not a dilatation or a Heller + fundoplication?

Response: Thank you very much for this constructive suggestion, which is valuable and very helpful for us to improve our manuscript. We have reviewed literature again and made further discussion.

In our study, the minimum interval between initial POEM and redo-POEM was four months (0 months was the minimun time symptoms recurred after initial POEM).

In Ichkhanian *et al* study[1], Re-POEM had a higher clinical success rate in the management of patients with failed initial POEM when compared with LHM and pneumatic dilation. Re-POEM is much less invasive than Heller myotomy and requires fewer attempts than balloon dilation. In the current study, we found Re-POEM had a clinical success rate of 88.9%% for recurrent achalasia after initial POEM failure, which is similar with previous studies.

(1 Ichkhanian Y, *et al*. Management of patients after failed peroral endoscopic myotomy: a multicenter study. *Endoscopy* 2021; **53**(10): 1003-1010 [PMID: 33197943 DOI: 10.1055/a-1312-0496])

2.2 What is the meaning of a shorter "Submucosal tunnel length"? Is it good or bad?

In the Re-POEM-SSMD group, due to the presence of post-POEM adhesions and fibrosis, the submucosa and muscle layer are cut simultaneously from the adhesion site with aborted intended termination point of the submucosal tunnel, leading to a shorter submucosal tunnel than that created in conventional RE-POEM procedures. Based on our data, safety profile of Re-POEM-SSMD was comparable to that of patients with Re-POEM, and further prospective studies are required to compare the different length of tunnel.

2.3 Why the author´s technique has much less reflux than the conventional technique? The drawback of POEM is GERD. If this technique promoves less GERD should be standard.

Our study showed that fewer cases of symptomatic reflux occurred in the Re-POEM-SSMD group than in the Re-POEM group. Re-POEM-SSMD was more likely to be performed in the earlier myotomy site, while Re-POEM was usually performed in the opposite direction with a new myotomy site. Therefore, in Re-POEM-SSMD, less damage to the muscular layer may be

responsible for less symptomatic reflux. Nevertheless, follow-up EGD showed no significant difference in postretreatment LES pressure or incidence of esophagitis between the two groups. Therefore, the results should be interpreted with caution and effectiveness of Re-POEM-SSMD in reducing reflux must be verified in prospective studies with large samples.

2.4 Are there different indications for the 2 techniques? How patients were selected? etc, etc....

The orientation selection of Re-POEM and whether to use SSMD operation depends on the preference of the endoscopists and their own technical levels. Before retreatment, mucosal inflammation and submucosal fibrosis of the esophagus are classified to determine the degree of adhesion. If the previous operative region has obvious adhesions and the rest of esophagus has no or mild adhesions, another tunnel can be created at the contralateral esophagus to improve the success rate of Re-POEM. If the esophagus has severe and extensive adhesions and performing SSMD is necessary, the endoscopist can choose to create a tunnel at the original procedure site, which usually means a relatively comfortable operative orientation and may help to improve the technical success rate.

Response to the comments of Reviewer #3

Comment: It is a very interesting paper, and the medical occurrence is of importance. Treatment and diagnostic workup are convincing. I would only strongly suggest to avoid the acronym POEM; much more when added another 'S' behind (POEM-S.....). This is because there is a well known syndrome called POEMS (peripheral neuropathy, organomegaly, endocrinopathy, monoclonal plasmaproliferative disorder, skin changes). Such a double usage of the acronym POEM(S) will confuse readers. Consider using another one, or explain thoroughly in words all over the manuscript what you mean with POEM as a

myotomy procedure.

Response:

Thank you very much for your kind suggestion. We would like to choose the later for the following reasons:

Firstly, POEM has been commonly used to represent "poral endoscopic myotomy" in clinical practice of gastroenterology and hepatology, and the readers of *World J Gastroenterol* are much more likely to be from the field of gastroenterology and hepatology.

Secondly and more importantly, POEM has been widely used to represent "poral endoscopic myotomy" in various journals such as *World J Gastroenterol, N Engl J Med, Nat Rev Gastroenterol Hepatol, Lancet Gastroenterol, Gastroenterology* and *Gut* since 2010, and POEM-SSMD has been reported and used in journals such as *Gastrointest Endosc, Endoscopy* and *Chin Med J (Engl)* since 2016, which can be found in the references of our manuscript. Therefore, we believe it is proper to keep consistent with previous literature.

To avoid confusion, the abbreviation of POEM, RE-POEM and RE-POEM-SSMD are defined or explained in abstract, introduction, tables and figures in our manuscript and the sequential steps of RE-POEM and RE-POEM-SSMD procedure were described thoroughly in the manuscript according to your kind suggestion.