Dear Editors,

I trust this email finds you well. We appreciate the meticulous review conducted by Reviewer #1 and Reviewer #2 on our manuscript titled "Direct Cost Variance Analysis of Per-Oral Endoscopic Myotomy versus Heller Myotomy for Management of Achalasia: A Tertiary Referral Center Experience,". We are grateful for their thoughtful insights and suggestions to enhance the quality of our work.

We have carefully addressed their comments and have made substantial revisions accordingly. Below, we provide a point-by-point response to the reviewers' feedback:

Response to Reviewer #1:

We extend our sincere gratitude to Reviewer #1 for their invaluable feedback and constructive comments regarding our comparative study on the costs of LHM and POEM for achalasia treatment. We concur that comprehending the cost discrepancies between these two treatments holds paramount significance for informed decision-making. In response to Reviewer #1's comments, we are committed to addressing the following key points in the revised version of our manuscript:

1. Patient Selection and Matching: We acknowledge the limitation of not providing detailed patient selection and matching information between the POEM and LHM groups. In our revised manuscript, we intend to rectify this by incorporating the primary determinant of treatment selection, which was based on provider type (Surgeon vs. gastroenterologist). Notably, we highlight that the clinical stage was comparable in both groups, including factors such as Eckhardt scores and previous treatments like dilations. While we acknowledge the potential benefits of employing randomized controlled trials (RCTs) or propensity score matching, we acknowledge the retrospective nature of our data and intend to emphasize the requisite caution in interpreting the outcomes.

2. Learning Curve: We greatly appreciate the feedback regarding the learning curve and have accordingly updated the manuscript to reflect that both the performing endoscopist and surgeon had completed a minimum of 20 procedures prior to the study period, thereby mitigating the impact of the learning curve.

3. Radiological Stage of Disease: We duly recognize the insightful observation of Reviewer #1 pertaining to the significance of the radiological disease stage, particularly concerning aspects like esophageal dilation and its potential influence on postoperative expenses. Regrettably, the data pertaining to this aspect is unavailable for incorporation into the manuscript.

4. Follow-Up Duration: We acknowledge the limitation stemming from the one-year follow-up duration and concur that an extended follow-up period is imperative to ascertain the sustainability of treatment outcomes and associated costs. Regrettably, owing to the conclusion of patient recruitment in 2020, an extension of the follow-up period was unfeasible. However, we intend to underscore the importance of prolonged follow-up in the discussion section and contemplate the ramifications of potential recurrences in future cost analyses.

5. Post-operative Costs: We deeply appreciate the feedback regarding post-operative costs. To address this concern, we have included PPI usage costs within the pharmacy cost category. Furthermore, post-operative tests conducted to evaluate symptoms have been accounted for in the one-year post-procedure cost category, attributing the encounter diagnosis (as outlined in the methods section) to the index procedure when these tests were performed. Additionally, expenses associated with treating refractory symptoms have been encompassed within the one-year post-operative costs.

Response to Reviewer #2:

We extend our sincere appreciation to Reviewer #2 for their valuable insights and feedback on our investigation comparing the cost-effectiveness of POEM and LHM in the treatment of achalasia. We fully acknowledge the limitation posed by our study's modest sample size and recognize that its representativeness may be compromised. In response, we are committed to enhancing the manuscript by incorporating a clear statement outlining this sample size constraint. Furthermore, we are actively exploring the feasibility of conducting a more comprehensive study to effectively address this limitation and establish a stronger foundation for our findings.

Regarding the concern raised by Reviewer #2 regarding the incidence of gastroesophageal reflux following POEM and its potential repercussions on associated costs, we share their perspective on its significance. However, it is important to note that evaluating the long-term effects of reflux disease would necessitate an extended follow-up spanning several years, for which the required data unfortunately remains beyond our reach. It is crucial to emphasize that our study's primary focus revolved around short-term costs and outcomes within a one-year timeframe. To ensure absolute clarity, we are steadfast in elucidating this aspect within our discussion section, elucidating the rationale behind our study's temporal scope and objectives.

We remain deeply appreciative of the critical evaluation undertaken by Reviewer #1 and Reviewer #2, which has undoubtedly enhanced the rigor and depth of our manuscript. Their insights have enabled us to fortify our study's contributions to the field, and we are optimistic that the revisions implemented will better serve the scholarly community.

Thank you for considering our revised manuscript, and we look forward to the opportunity to contribute to the scientific discourse in the pages of World Journal of Gastrointestinal Endoscopy.

Yours sincerely,

Syedreza Haider MD

Revision Reviewer

Specific comments to authors

The authors somewhat improved the paper. However: 1. The number of patients (15) in the 2 groups is too small 2. The allottement to one or the other treatment was equivocal and not fully explained in the revised manuscript. Since X-ray evaluation is non available, one can suppose that Stage IV disease (> 6 cm and sigmoid) were referred to surgeons more than to gastroenterologist, 3. The follow-up of 1 year is too short

Response 1: We sincerely appreciate your observation regarding the sample size. It is true that our study, conducted at a single tertiary academic center, faced limitations in terms of patient availability that met the specified inclusion criteria within the designated time period. Although a larger sample size could have provided enhanced statistical power, we firmly believe that our study, despite its limitations, contributes meaningful insights into the comparative analysis of POEM and LHM for achalasia treatment.

Response 2: We extend our gratitude for bringing up this important point. We recognize that the allocation process for patients undergoing either POEM or LHM was not extensively elucidated in the manuscript. Given the retrospective nature of our study, we encountered challenges in providing an exhaustive description of the allocation process. It is important to emphasize that our study lacked a randomization process, and allocation was influenced by multiple factors, including insurance coverage, medical comorbidities affecting surgical candidacy, and patient preferences following comprehensive risk-benefit discussions with their healthcare providers. Given the complex and individualized nature of these determinants, coupled with the retrospective study design, we encountered difficulty in precisely outlining the decision-making flow for each patient. To rectify this, we intend to incorporate a more explicit acknowledgment of these limitations in the manuscript to ensure a clearer understanding.

Response 3: We deeply appreciate your consideration of the follow-up duration. Your point is well-taken, and we understand that a one-year follow-up may not fully capture the long-term outcomes and cost differentials between the two procedures. Regrettably, due to the retrospective nature of our study, we were constrained by the available follow-up data within the defined time frame. We acknowledge this constraint in our discussion and underscore the importance of future research endeavors that extend the follow-up period to provide a more comprehensive evaluation of the sustained impact of both interventions.

Once again, we extend our heartfelt appreciation for your time, diligence, and invaluable feedback. Your constructive comments have significantly contributed to the refinement of our manuscript, and we look forward to further improving its quality.

Best regards,

Syedreza Haider MD MBA