

Peer Review File

Article Information: <https://dx.doi.org/10.21037/jgo-23-923>

Reviewer A

The authors investigate the outcome of minimal invasive esophagectomy in a retrospective single center series.

MIE has become the gold standard in esophageal surgery and since the implementation of total minimal invasive esophagectomy is technically challenging, this experience could be of great interest to the readers.

Unfortunately, some of the relevant informations are missing and the discussion part does not focus on the suspected reasons of your findings and there are no conclusions drawn that could be adapted by someone willing to implement these new techniques.

1) Line 67-70. You could cite this work regarding the benefit of a transthoracic approach: Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, van Dekken H, Ten Kate FJ, Obertop H, Tilanus HW, van Lanschot JJ (2007) Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg* 246(6):992–1000 discussion 1000-1

Reply 1. Will add the reference and appreciate the recommendation (Reference 5). Added the line (67-68): “However, the transthoracic and trans hiatal approaches have reported similar long-term oncologic outcomes”

2) Line 180: the camera is then moved to the subscapular...

Reply 2: It was corrected to add the word then line 180. Thank you for finding the error.

3) Line 201: ...through the jejunal feeding tube... Did you place this tube in all patients? Since it is not mentioned in the description of the abdominal part. Please state if this was part of your standart procedure.

Reply 3. Yes, we did place J tubes in all but 1 patient. We added the following text to the abdominal portion: (lines 215-216)

“We routinely place a jejunostomy feeding tube size 14, 15cm distal to the ligament of Treitz..”

4) Line 225: Please state the reasons for conversion and on wich part of the operation it I (abdominal/thoracic phase?)

Reply 4. Thank you for the questions we added a line in the manuscript- only adnominal conversions one for bleeding and the others for adhesions in lines 307-308.

5) Line 233 ff: Leak rates: A leak rate of 23.8% seems to be quite high compared to the reported data in the literature. You describe a drastic drop in leak rate to 3.4% after a learning curve. This should be addressed in more detail in the discussion section. What is your explanation for this dramatic improvement? Was there a change in technique? Also, additional information regarding the management of these insufficiencies could be helpful in understanding the severity, e.g. how many revisional surgeries? Endoscopic vacuum treatment?

Reply 5. A couple of differences, the first one is a transition from one stapler company to another and challenges adjusting to the correct staple load. Additionally, there was an adoption of a minimal touch technique of the gastric conduit, finally we had better identification of ischemia by visual inspection as well as by usage of ICG green when questions arose. Lastly, in the later part of the experience the evidence of radiation changes in the margin indicated a need to resect and additional margin of the esophagus. We added highlight box 2. With technical lessons learned

6) 238 ff: Smoking: Since your paper is focusing on the effects of the surgical approach, the effect of smoking seems interesting but none the less irrelevant to me.

Reply 6. We appreciate the reviewers' comments, and we removed line 246-247, we are interested in smoking as we have anecdotally seen more complications especially anastomotic leaks and pulmonary complications in patients that continued to smoke within a month of surgery.

7) I have read your paper with great interest and you describe your operative technique very well. Nevertheless, some questions raised which were not addressed in your work:

- Was the anastomotic technique altered during the course of the study period?

Reply 7a: Besides the adjustment of the staple loads from different stapler companies, the anastomosis was not changed over time. There were a few cases where the anastomosis was performed hand sewn, and a few with larger anvil size/ purse string. But most anastomoses were performed with the Orvil, especially over the last 130 cases

- did you always use a 25 mm circular stapler? Since it is known that larger stapler size is associated with lesser strictures. I assume that you were using a 25 stapler since this is the only size the orvil system comes but this should be discussed. Did you consider different approaches for anastomosis e.g. side to side anastomosis or since you used a robot a hand sewn anastomosis? What is your explanation for the drop in strictures rates after the first 50 cases?

Reply 7b We use the Orvil routinely, please see the above response (Reply 7a). We believe that the increased leak rate seen initially was associated with the increased stricture rate in the first 100 cases.

- how was anastomotic stricture diagnosed? Was there routine endoscopic follow up? How many patients needed endoscopic treatment of the stenosis?

Reply 7c We routinely perform an endoscopy within 1 year of surgery or at any point if patient has dysphagia. Most patients presented with dysphagia leading to the stricture diagnosis. Rarely the strictures were found when asymptomatic.

- did you use a grading of the anastomotic leaks? Would there be an endoscopy in abnormal findings during CT scan or contrast swallow?

Reply 7d. Most of the leaks were diagnosed on imaging alone, we transitioned from an UGI alone in the first 50 cases to UGI plus CT scan for the next 150 cases. Most were managed with endoscopic therapy. Only one patient required double diversion.

- since pneumonia is the most common complication after esophagectomy. you should address the perioperative regime regarding peridural pain catheter and physical therapy. In the discussion, you state that the pneumonia rate improved after improvements in technical measures. What were those measures exactly?

Reply 7e. we routinely recommend and use epidural catheters; experience help us decrease operative time, blood loss and fluid requirements. This combination plus more aggressive ambulation helped us decrease some of the postoperative complications.

We added a line in the post operative care to reflect this interventions line 213.

- since your main focus lies on the operative outcome, did you do an overall grading of complications using for example the Clavien Dindo classification or even more the CCI?

Reply 7f . Our database does not include the CCI or the C-D classification. This is part of our institutional database that includes esophagectomies since 1999. But appreciate your idea to add this gradation to our database.

- Table 1 and 2. Cohort Demographics. There seems to be a shift in columns

Reply 8: this has been fixed, thank you. (tables1-2)

Reviewer B

I would like to congratulate the authors; the information was presented clearly and in a very concise way. A valuable experience that supports the concept of the learning curve in mastering minimally invasive esophagectomy.

The authors should share the modifications made that helped them improve outcomes. Any changes, or refinements in the technique and in the postoperative care that the authors consider made an impact in improving the surgical results. This would be of great utility for other groups to adapt and learn from your experience.

Reply reviewer B: We very much appreciate the reviewer' comments as there are no one factor that makes outcomes better. Is the combination of poignant surgical improvements such as no-touch of the gastric conduit, better recognition of perfusion adequacy of the conduit, improvement in surgical time and decrease in blood loss and need for IVF plus more aggressive early ambulation and early recognition of complication help us improve the outcomes.

Reviewer C

ongratulations for both your excellent clinical work and the quality of your paper.

Reply Reviewer C: We appreciate your comments and review.

Reviewer D

The authors described 200 cases of esophagectomies (Ivor Lewis Esophagectomy) performed by a single surgeon in which the abdominal phase is performed laparoscopically and the thoracic phase is performed robotically. The main issue of this paper is the learning curve, but this paper has many points to be revised for publication.

#1 In the Introduction section, the author describes the history of esophagectomy, but the rest of the section is unnecessary except for the description of MIE.

The introduction section should clearly state what is known, what is not known, and the purpose of the study.

Reply #1. We appreciate the comments. The introduction has been edited to be more concise. Lines 58-135

#2 In the introduction paragraph, the author states the purpose of this study, but from the content of the manuscript, it appears that the purpose of this study is to examine the learning curve of LRMIE. The purpose of the study should be stated clearly and precisely.

Reply#2. We appreciate the comment, our purpose for the manuscript was double, first to explain the technical factors that correspond to the most current technique as the result of experience, and how the experience/learning curve has impacted our outcomes. We believe that there is value in discussing the technical aspects to point at salient portions of the operation.

#3 The authors have approximated the change in surgical outcome over time with a curve. However, they should clearly indicate the function of this curve and the correlation coefficient to make the inflection point easier to understand. Alternatively, the change in outcome over time can be obtained using the Cumulative Sum Method or other methods. It is recommended to consult a statistical expert for this purpose.

Reply #3. Thank you for this comment. Figure 5 is intended to demonstrate the exploratory analyses performed for visual inspection to first clarify if any actual improvement in outcomes was observed. If no trend was observed, then we would not have proceeded with statistical testing for inflection points shown in Table 2. No hypothesis testing was performed, so there are no statistical values to report. The figure legend has been edited to clarify that these are exploratory analyses only. If preferred, these figures could instead be included as supplemental material. However, we feel that clarifying the Figure Legend should address your concerns. Thank you for drawing this to our attention. (lines 683-695)

#4 The classification used to determine the lymph node numbers should be described in the text.

Reply#4 we used the lymph node stations based on the AJCC8. We have added to the manuscript thank you. Citation 16.

#5 The Surgical Technique paragraph is too long. Also, although the authors mention an salient technical point, their technique is the commonly used laparoscopic and robotic Ivor Lewis esophagectomy technique, which does not seem novel.

Reply#5 The details of the surgical technique were one of the objectives of this manuscript as some of these details have been learned through trial and error and have contributed to better outcomes and to a more expedient surgery.

#6 Table 1 numbers are out of alignment with the items and very difficult to read. It should be corrected.

Reply #6 We appreciate the reviewers' comments and have corrected.

#7 What is the purpose of the Cases 101-200 entry in Table 2? This element should be deleted. Also, each outcome should have a value before and after the inflection point and a P value. In addition, the scatter plots and curvilinear functions that determined the inflection point for each outcome should be shown graphically.

The purpose of the Cases 101-200 column was to describe the outcomes after we felt the learning curve had been surpassed. However, you are correct that since the inflection learning curve for the varying outcomes was different, this may not make sense. This column has been deleted. We instead added a column to Table 2 that describes, as you have recommended, the measure of each outcome before and after each inflection point, with a P value.

We chose not to include the exploratory scatter plots used to select inflection points for the other outcomes, because these are binary outcomes (except for the ones shown in Figure 5) with values of either 1 or 0. As a result, the scatter plots do not appear "scattered," in essence a visual representation of a logistic regression curve, which is not methodologically incorrect, but we feel is more confusing to most readers and obscures the manuscript somewhat. We hope the reviewers and editors understand our concern. We feel Table 2 is significantly improved as a result of the changes made. Thank you

#8 Discussion paragraph is only a presentation of results and needs more comparison with other papers.

Reply #8. We appreciate this comment and have added discussion and comparison with literature, references 19,21-22-23 to be able to benchmark and be able to support our conclusion.

#9 Conclusion paragraph states that Totally Minimally Invasive Esophagectomy is a safe and good short and long term outcome, but this conclusion cannot be drawn from the analysis of this paper. The only conclusion that can be drawn from this paper is the learning curve.

Reply 9. We understand your comment, please see Reply 8 and the addition of lessons learned.

Reviewer E

Congratulations to the authors on their impressive results for totally minimally Ivor Lewis esophagectomy for esophagogastric adenocarcinoma. The description of the technique used for this procedure by the authors is particularly robust, and the postoperative outcomes after the initial learning curve are commendable. The figures are clear and pertinent to the message. I

have comments meant to help improve the quality of the manuscript.

Introduction: The historical aspect of first paragraph of the manuscript is unnecessary. The first paragraph should simply introduce the topic and need for the study, not describe the history of the procedure. This takes away from the message of the manuscript.

Reply: Thank you for the comments. The introduction has been edited to be more concise. Lines 58-135

Introduction: It is probably unwise to suggest that most of the data surrounding technique utilization come from single institutional data, as there are several multicenter trials published evaluating differences in outcomes using various techniques.

Reply: Thank you for the comments. The introduction has been edited. Lines 58-73

Introduction: The objective statement is not clear. The title and abstract make it seem like the manuscript should be discussing the learning curve of the LRAMIE, and this should be more clearly stated if this is the case.

Reply: We appreciate the comment, our purpose for the manuscript was double first to explain the technical factors that correspond to the most current technique as the result of experience and how the experience/learning curve has impacted outcomes. We believe that there is value in discussing the technical aspects to point at salient portions of the operation.

Methods: The implication is that a certain cohort of patients, i.e., an early cohort of patients, is being compared to a later group of patients to determine a learning curve. This should be described in the methods.

Reply We commented on this in the text, thank you very much. Lines 291-292

Methods: Outcomes should be more explicitly described. Surgical outcomes and complications are vague and should be expanded.

Reply We have described specific outcomes evaluated. Thank you for the suggestion. Line 148-150

Methods: The statistical analysis should be the last paragraph of the methods, after description of the surgical technique and postoperative care.

Reply. This is a great suggestion. The change has been made.

Results: There should be a description of how the 200 patients were obtained in the study. I.e., there were 350 esophagectomies by this surgeon, were the 200 all consecutive minimally invasive esophagectomies, or were there patients excluded for other reasons?

Reply, 225 esophagectomies were performed by the surgeon, supplemental Figure 1 specifically addresses this question.

Results: The improvement of clinical leak rate after the first 80 cases is impressive. What do the authors attribute to this improvement? Is it decreased time under anesthesia and thus less

time under altered perfusion, is it improved technique when creating the anastomosis, when mobilizing the conduit? This should be the main topic of discussion in my opinion.

The radiographic apparent leaks were...

Reply We appreciate these comments, we added a highlight box for technical lessons learned. Specially as it relates to minimal conduit manipulation, better perfusion assessment and finally decrease operative time and blood loss leading to less needs for fluids and pressors during surgery.

Discussion: Based on your results, it appears the actual learning curve was 80 cases, rather than 50. While some outcomes improved after 50 and 60 cases, in my opinion the most important outcome of leak improves after 80 cases. I would at least suggest a range of 50-80 as a learning curve rather than suggesting it is at 50 cases where outcomes improve.

Reply. We appreciate this comment and agree that the biggest change in outcomes was seen after 50-80 cases we have adjusted the manuscript and abstract.

Discussion: Overall, this section could be expanded upon. There is mention of some other studies and prior studies by the authors related to this study, but what do the results of this study mean? How can surgeons improve the learning curve? Can training on the robotic platform affect timing to competency or improved outcomes? Can coaching by surgeons who have surpassed the learning curve to surgeons still learning this challenging technique improve both patient outcomes and speed to full competency? What other future studies would be needed to evaluate these questions?

Reply: The learning experience, led to us developing standardized procedure guidelines and progressive step wise technical entrustment that we have utilized also to coach new faculty. We are tracking the results of new faculty to see effectiveness of new process. (Highlight box #2.)

Bias: This was one surgeon performing the operations for this study. Would this study be repeatable with other surgeons? Was there a difference in this surgeon's practice regarding the involvement of trainees in performing the operation, which parts of the operation they performed, etc.?

Reply. There was a surgical trainee in all these procedures, usually at the fellow level, the level of entrustment in the procedure was dependent on their prior experience, comfort level with robotic platform and number of procedures performed in fellowship. As these were not thoracic surgery fellows, the experience with the thoracic lymphadenectomy was in general minimal. But most of them completed the abdominal portion with some assistance.