

Peer Review File

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Reviewer Comments

Reviewer A

This is an excellent review of surgical anastomosis techniques in robotic assisted esophagectomy, by one of the leading experts in the field. I have a few questions and comments.

Comment 1: Can the author confirm that the tables describing the different techniques are exclusive to RAMIE and not any other minimally invasive approach?

Reply 1: Yes, I confirm that tables 1-3 exclusively describe published series of RAMIE.

Comment 2: It will be very insightful if the author shares his own experience and what is his own preference in terms of anastomosis technique, size of stapler, number, type, location and duration of drains that he does use to minimize the clinically significant leakage rate; and whether or not he does use tissue reinforcement (i.e. pericardial fat pad)

Reply 2: A summary of my preferences has been added to the discussion section. Lines 167-174.

Comment 3: Regarding the linear stapling technique, I did not see mention of the size of stapler (45 or 60 mm) in the reported studies. I think that can influence the stricture rate.

Reply 3: Size has been added to Table 2, which details descriptive studies of linear linear-stapled anastomotic technique with 10 or more patients.

Comment 4: The legend in some of the figures may have to be more extensive and comment / describe the different steps of the procedure (Fig 2 A, B, C...etc.). Figure 3 has to be edited (the original legend is featured).

Reply 4: The figure legends have been expanded to explain the panel in figures 1-4. The previously published figure legend has been cropped out of Figure 3.

Reviewer B

Comment 1: The authors have given an interesting overview of different anastomotic techniques in RAMIE.

With increased adoption of RAMIE techniques and article like this could be of interest to physicians working in these clinics, or looking to start a RAMIE program.

Reply 1: Thank you.

Comment 2: However, the current manuscript is not sufficient to answer these questions.

Major comments

1) The aim of the article is not clear.

If the aim is to describe the different techniques: describe them in more detail.

Reply 2: Thank you for pointing out this shortcoming. The aim of the article is to familiarize surgeons interested in robotic esophageal surgery with common anastomotic techniques. This aim has been added to the abstract. Pursuant to this aim, an overview that includes basic operative steps and review of relevant literature to guide interested surgeons in obtaining more information is given for each technique.

Comment 3: For instance: In circular stapling: a mini-thoracotomy is necessary to introduce the stapling device: however, this is not described in the manuscript. Or information on whether assistance is required.

Reply 3: Thank you for bringing this omission to my attention. This information has been added to the manuscript. Lines 85-86.

Comment 4: Consider making an overview table for a concise overview

Reply 4: An overview can be found in Table 4 of the revised manuscript.

Comment 5: If the aim is to compare techniques: a systematic review should be performed.

Adding a systematic review of available literature would really strengthen the article.

Reply 5: Plat and colleagues published a systematic review on this topic in early 2020, which we discuss and cite in the revised manuscript (PMID: 31796219). Although a handful of studies have been published since their analysis, I do not believe that another systematic review is needed at this time.

Comment 6: In the discussion please also address how to adopt of these new techniques. (visit a specialist center, be observed by a proctor etc etc). In order to minimize anastomotic leaks caused by surgeons in their proficiency gain curve.

Reply 6: Thank you for this suggestion. I have added my recommendations on how to adopt these techniques to the discussion section, Lines 207-214.

Comment 7: For readability I'd strongly recommend to not abbreviate CS, HS and LS in the manuscript.

Reply 7: These abbreviations have been removed from the manuscript.

Reviewer C

Comment 1: First, the authors should present the majority of anastomotic site. Which is major, intrathoracic or cervical incision? Please mention concisely before anastomotic technique section.

Reply 1: In this review, I have focused on techniques for intrathoracic anastomosis. This is concisely stated in line 64 of the revised manuscript prior to discussing the techniques as the reviewer has requested.

Comment 2: Regards to the CS anastomosis, double stapling and semi-double stapling should be described.

Reply 2: Thank you for your comment. I am not clear on what technique the reviewer is referring to. The use of the OR-Vil, (described) may utilize “double stapling” but it is not a requirement. The outcomes of double-stapling have also been referred to in the discussion.

Comment 3: Please compare these three technique using a data of previous reports. The authors have made tables of case series of these techniques.

Reply 3: Table 4 compares the 3 techniques and complements the data presented in Tables 1-3. It is difficult to directly compare the case series due to heterogeneity in patient selection and the criteria used to define the reported outcomes.

Reviewer D

Comment 1: The authors provide an excellent review of a technique in rapid evolution. In particular, gastroesophageal anastomotic complications remain the most dreaded complication regardless of operative approach. Delineating the optimal technique is of critical importance. The authors review CS, LS and HS techniques and delineate their associate rates of anastomotic leak and stricture. In addition, a description of learning curve is made.

Overall the manuscript is well written and complete. It suffers from minor grammatical errors on occasion.

I believe it warrants publication

Reply 1: Thank you. Several grammatical errors have been corrected in the revised manuscript.

Reviewer E

Comment 1: I would like to compliment the author on the manuscript called “Intrathoracic Anastomotic Techniques in Robotic Assisted Minimally Invasive Esophagectomy (RAMIE)”. The manuscript provides a non-systematic review of several anastomotic techniques for intra-thoracic anastomosis during robot-assisted esophagectomy (e.g. circular stapled, linear stapled and handsewn). The introduction is clear and several figures are used to clarify the different techniques used.

Reply 1: Thank you.

Comment 2: The methods and results sections seem to be combined in three sections, one for each anastomotic technique.

I have several comments on the manuscript:

- What was is the definition of either anastomotic stenosis or stricture? This makes paragraph line 80-87 hard to read.

- I have the same question for anastomotic leakage. The aforementioned paragraph is also hard to read because 3 different percentages of anastomotic leakage rates are

mentioned.

- Consider giving a clear definition of such complications in the beginning of the manuscript. Or if the articles included each use a different or unclear definition please mention this, for example in the discussion section.

Reply 2: The definitions used when examining rates of either stenosis/stricture or anastomotic leak vary from study to study. Some investigators note if either has occurred; others only examine stenoses or leaks requiring intervention.

Comment 3: The discussion section lacks progression and I am somehow confused of what the author is trying to say in each paragraph.

Reply 3: The discussion section has been reorganized.

Comment 4: Some arguments in Table 4 are important, but are not specifically mentioned in the discussion section.

Reply 4: The revised discussion touches on all the points summarized in table 4.

Comment 5: Conclusion: I think the conclusion is a bit general. The choice for a specific technique depends on surgeons experience and preference. The handsewn and linear stapled seems to be better suited for robot-surgeons or novel surgeons. Whereas the circular stapled requires a lot of laparoscopic experience. Is this what the author is trying to mention?

Reply 5: Yes, the surgeon's experience and preferences are key to determining which anastomotic technique they will likely be most comfortable with during RAMIE, particularly while adopting the robotic approach. A surgical team with a lot of laparoscopic and thoracoscopic experience may face fewer hurdles adopting the circular-stapled technique.

Comment 6: Some minor language issues that should be addressed:

Line 54: "the lie of the esophagus". I think "lie" is an odd word choice here. Consider replacing it.

Reply 6: The phrase in question has been replaced (lines 61-62 in the revised manuscript).

Comment 7: Line 72: Not sure what is meant by description.

Reply 7: The phrase in question has been clarified and can be found in lines 91-93 of the revised manuscript.

Comment 8: Line 160 "overall rates of leak and anastomotic failure between the techniques are suggested but not clearly delineated" not sure what is meant here.

Reply 8: The phrase in question has been clarified and can be found in lines 221-222 of the revised manuscript.

Reviewer F

Comment 1: The terms EEA and Orvil are trademarked names and should be listed as

such with the manufacturer being Medtronic.

Reply 1: Thank you for pointing out this omission. The manufacturer is now noted.

Comment 2: The authors stated in a few places the importance of experience of the surgeon. It was also included in their conclusions on page 5. I happen nto agree with them With that in mind, it would be important to provide and elaborate on one or two references that substantiate that notion.

Reply 2: The effects of surgeon experience, particularly a surgeon's experience with conventional minimally invasive esophageal surgery, on their learning curve during RAMIE adoption and patient outcomes after RAMIE require further investigation. In the revised manuscript, the experience of the surgeon is only mentioned in the concluding paragraph, where it is expressed as an opinion. Studies of the learning curve for RAMIE are now cited in a new paragraph suggesting next steps in adopting any of the techniques for robotic intrathoracic anastomosis discussed in the review.

Reviewer G

Comment 1: I wonder if the authors have got permission to use the figures.

Reply 1 : We have obtained permission to use the 5 figures in the manuscript.

Comment 2: The authors should reorder the references in the tables according to the published years.

Reply 2: The table entries have been reordered chronologically.

Comment 3: Please describe how to introduce the circular stapling device into the thoracic cavity during robotic-assisted MIE.

Reply 3: Thank you for bringing this omission to our attention. This information has been added to the manuscript. Lines 85-86.