

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-24-201>

Reviewer A

The investigators of the study, “robot-assisted minimally invasive esophagectomy versus minimally invasive esophagectomy for thoracic lymph node dissection: a retrospective comparative cohort study” present an interesting review of a single-surgeon experience with the two methods of performing Mckeown esophagectomy for SCC. Comments/questions below:

Comment 1: The title of the article could be refined. These operations were 100% three-field/Mckeown esophagectomies done for esophageal SCC. Consider revision of the title.

Reply 1: (We have modified the text as suggested. See page 1, line 3-4.)

Comment 2: One significant weakness of this study is that it is a single-surgeon, single-center study. How long had the surgeon been performing MIE prior to the start of the study? How many of these cases had they done? How about non-MIE esophagectomies? How experienced was the surgeon in terms of robotic operations that were not esophagectomies? Understanding the details of the surgeon’s prior experience is critical for interpreting this study.

Reply 2: (Your suggestions is spot on. However, only one surgeon on our team is currently qualified to perform esophagectomy using the robotic platform. We have added additional instructions as advised. See page 4, line 96-98.)

Comment 3: Do any other surgeons at your institution perform robotic esophagectomy?

Reply 3: (Only one surgeon on our team is currently qualified to perform esophagectomy using the robotic platform. However, the number of qualified surgeons will increase in the near future.)

Comment 4: The limitations sections is perfunctory and much more thought/effort should be put into this.

Reply 4: (We have added additional instructions as advised. See page 12, line 313-324.)

Comment 5: When were the MIE cases done in relation to the RAMIE cases? How was the decision between operating with MIE and RAMIE made? Did the surgeon switch

from doing only MIE to only RAMIE? How much of an overlap was there in terms of use of the 2 methods? Could an era or experience effect account for the difference in lymph node yields? This should likely be discussed in the limitations section.

Reply 5: (We have added additional instructions as advised. See page 12, line 313-324.)

Comment 6: “Nine” should be “ninth” (line 109).

Reply 6: (Content has been removed as suggested.)

Comment 7: If the technical details of your method are discussed in other published articles, reference to these articles and reducing the amount of description in your manuscript is appropriate. If you are going to keep this much detail about port placement, though, adding figures would be helpful.

Reply 7: (Content has been removed as suggested.)

Comment 8: How was the abdominal phase of the operation handled? Minimally invasive? Robotic?

Reply 8: (Minimally invasive, this study did not involve the abdomen and was not listed.)

Comment 9: I am surprised that such a high pressure of insufflation was used in the chest. Is that a misprint?

Reply 9: (It may have been overwritten by a previous revision, sorry, my oversight, it was originally 6-8mmHg. We've revised it. See page 5, line 122.)

Comment 10: The percentage of patients receiving neoadjuvant therapy in each group should be included in the Results section.

Reply 10: (We have added additional instructions as advised. See page 7, line 186-188.)

Comment 11: Did any patients suffer from a chylothorax? If none, this should be stated also.

Reply 11: (When information on complications was collected retrospectively, information on chylothorax was missing, which was not included in the analysis.)

Comment 12: It is not surprising that the RAMIE group did not have a significant difference in short-term outcomes vs MIE. I am not sure that this has anything to do with the higher stage patients in the RAMIE group. Please state the specific type of complications that were lower in the RAMIE group in other studies, and address your findings in the context of this (line 233).

Reply 12: (We have added additional instructions as advised. See page 9, line 236-243.)

Comment 13: Is there a way to compare the rate of upstaging between RAMIE and MIE? Perhaps you could look at just patients who did not receive neo-adjuvant. This would be useful information.

Reply 13: (No stats on the rate of upstaging, but it's a good point. look at just patients who did not receive neo-adjuvant. It's a great idea, and we'd like to compare it that way, but there are fewer of these types of robotic-assisted esophageal cancer surgeries without neoadjuvant therapy.)

Comment 14: What was the rate of positive lymph nodes found in each group?

Reply 14: (We envision reflecting the lymph node positivity rate in another article comparing neoadjuvant effects.)

Comment 15: The duration of the operation, and specifically the duration of the thoracic phase of the operation, should be included.

Reply 15: (Great advice, it's a shame that the timing of the surgery wasn't incorporated due to the design at the beginning.)

Comment 16: The conversion rate of the two groups should be included.

Reply 16: (Great advice. There is no conversion rate if you go between the two groups. So, the context doesn't mention this.)

Comment 17: Additional, subjective information is welcome in the discussion section. Having some insight into when/where they felt RAMIE was “better” than MIE from a technical point of view would be helpful.

Reply 17: (We have modified the text as suggested. See page 10, line 246-254, line 264-265.)

Comment 18: How are lymph nodes assessed during the operation? It seems like they are sent separately during the dissection. But do the investigators dissect lymph nodes off of the esophagogastrostomy specimen after it is removed from the body? Please elaborate in your methods section.

Reply 18: (We have added additional instructions as advised. See page 5, line 125-130.)

Comment 19: Table 1 does not need to include tumor pathology type, surgical method, or surgical procedure.

Reply 19: (Table 1 has been modified as suggested, but the staging information has been retained. See Table 1.)

Comment 20: There appears to be mistake with labelling of the groups under “neoadjuvant therapy” in Table 1.

Reply 20: (Table 1 has been modified as suggested.)

Comment 21: There appeared to be more lymph nodes at station 107 removed with MIE than RAMIE. Please discuss.

Reply 21: (We have added additional instructions as advised. See page 11, line 274-280.)

Comment 22: 30-day and 90-day mortality rates are more useful data points than in-hospital mortality for esophagectomy.

Reply 22: (Great advice. It's a shame it wasn't added in the design session.)

Reviewer B

A well written paper on a very important subject.

Reviewer C

A well written, thorough manuscript; congratulations

The question posed is a very relevant one, and the outcomes published add to the field.

Comment 1: I wonder whether it is worth including about the presence of lymphatic metastases in the stations examined. This would be useful/interesting information in keeping with what the Tiger study is looking to investigate (probably worth citing in the paper)

Reply: (We envision reflecting the lymph node positivity rate in another article comparing neoadjuvant effects. Your proposal is very useful.)

Comment 2: The authors acknowledge the retrospective/single centre nature of the study, but the numbers included, inclusion/exclusion criteria are all appropriate.

Reply: (Thank you very much for your recognition.)

Reviewer D

In the era of robotic surgery articles like this are of great interest for the journal's readership. Furthermore, it is a well structured paper.

Reviewer E

Hereby I would like to give my comments to the “Robot-assisted minimally invasive esophagectomy versus minimally invasive esophagectomy for thoracic lymph node dissection: a retrospective comparative cohort study”. In this article the authors describe differences in lymph node count and number of lymph node station resected between RAMIE and MIE. Although this information is not new, it is interesting to read that some stations are better resected with RAMIE. However, I have some major concerns.

Comment 1: There is still debate on the added value of upper mediastinal lymph node dissection, therefore it would be of added value to show the pathology of the lymph node stations that were resected in both groups.

Reply: (Upper mediastinal lymph node dissection is important in upper-middle esophageal cancer, and it is a shame that the design of this study did not include pathologic lymph node positivity.)

Comment 2: The authors show in table 1 a difference in the extent of lymph node dissection. Does this resemble intention? Otherwise, this would explain the results and is not per se related to the robotic approach.

Reply: (The differences in the extent of lymph node dissection mentioned above, e.g., two-field, two-and-a-half-field, and three-field, the main point of difference is in the extent of cervical lymph node dissection, which does not affect the lymph node dissection operation in the thoracic cavity.)

Comment 3: Throughout the methods, it is mentioned that patients underwent McKeown esophagectomy via right thoracotomy with lymphadenectomy were included. I assume this is a typo that needs to be corrected.

Reply: (We have modified the text as suggested. See page 4, line 98-99.)

Comment 4: In the methods it is stated that thoracoscopic pressure was 68 mmHg, I assume the authors mean 6-8 mmHg? This needs to be corrected.

Reply: (It may have been overwritten by a previous revision, sorry, my oversight, it was originally 6-8mmHg. We've revised it. See page 5, line 122.)

Reviewer F

Authors reported their work named "Robot-assisted minimally invasive esophagectomy versus minimally invasive esophagectomy for thoracic lymph node dissection: a retrospective comparative cohort study" and concluded "Our study shows that RAMIE is more effective than MIE in terms of the number thoracic lymph nodes dissected and the extent of dissection. Moreover, RAMIE is not associated with additional surgical complications.". I have the following comments:

Comment 1: Please try to do propensity score matching between both groups and assess the outcomes. Please try to report the standard mean difference between matched groups (SMD).

Reply: (That's great advice and was considered in the design, but sample size is an issue. The sample size decreases after propensity matching, and data from a single center may have the difficulty of having an insufficient sample size.)

Comment 2: Please try to add a table with some of the published meta-analyses on same topic and their included patients numbers, studies numbers, and outcomes.Link: https://scholar.google.com/scholar?hl=en&as_sdt=0,33&q=robotic+esophagectomy+meta-analysis.

Reply: (I'm sure that's a great way to do it, and I'm ashamed we didn't design it that way.)

Comment 3: Statistical analysis should be revised and edited by statistician eg ANOVA is used to compare means across > 2 groups. For non-normally distributed variables, Mann-Whitney test should be used instead of t-test.

Reply: (Changes have been made as suggested. Continuous variables were tested for normality and a U-test was used for continuous variables that were not normally distributed.)

Comment 4: Please try to specify the outcomes and try to report a multivariable analysis for your primary outcome.

Reply: (This is a great proposal, and I'm ashamed that I didn't design a multivariate analysis.)

Comment 5: Please delete categories that have 100% from table 1 and write a footnote for that eg SCC, surgical method, surgical procedure (McKewn). Please revise Neoadjuvant therapy as something is missing. I believe you mean radiotherapy and chemotherapy.

Reply: (Changes have been made as suggested.)

Comment 6: Table 2 is distracting in the current format with those abbreviations. Please revise and edit it. Please report Lymph node ratio (pathological positive nodes/ total nodes *100).

Reply: (It's a shame we didn't include lymph node-positive rates in our study.)

Comment 7: Please spell out abbreviations in their first time eg CD in table 3.

Reply: (Changes have been made as suggested.)

Reviewer G

A large series comparing LN dissection with Robotic assistance vs RVATS for ESCC in patients undergoing mckeown esophagectomy improved LN yield without increased complications with RAMIE.
a few critiques

Comment 1: bundling of patients with and without neo adjuvant therapy may potentially bias the LN yield- would it be better to compare the cohorts separately -- ie MIE vs RAMIE with and without neo adjuvant CRT separately also.

Reply: (Very excellent advice, more therapeutic differentiation is indeed more helpful. There was a preponderance of no neoadjuvant therapy in the MIE group, and there may have been an impact on the regional lymph node dissection comparisons.)

Comment 2: also no comparison of preoperative staging provided- the difference in staging post op could be due to upstaging due to inc LN yield or due to higher pre op stage.-- so would be beneficial to give routine staging protocol for w/u and pre operative clinical stage determined prior to surgery.

Reply: (The lack of upper staging is very humbling, mainly due to the lack of clinically experienced attending physicians to help with this part of the process. The good news is that the pathologic staging is intact.)

Comment 3: some points redundant in table can be removed- (lines) such as type, MIE vs RAMIE, HTN, DM.

Reply: (Changes have been made as suggested.)