

Peer Review File

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Reviewer A

Zheng et al. conducted a meta-analysis on the studies investigating the efficacy and safety of endoscopic resection and esophagectomy for early esophageal cancer. They concluded that endoscopic resection is minimally invasive and safe, whereas esophagectomy was associated with better long-term survival.

This study has several significant problems and may mislead the readers. At first, the optimal subjects for endoscopic resection and esophagectomy are not the same. Endoscopic resection is a choice for patients with less invasive tumors and less possibility of lymph node metastasis. If physicians satisfy such criteria, endoscopic resection will provide a better prognosis. Esophagectomy should be indicated for patients with tumors that possibly metastasize to lymph nodes and is often performed for patients after non-curative endoscopic resection. Therefore, it isn't very meaningful to compare the long-term survival between the modalities.

Response to Reviewer A

We are appreciative of the reviewer's suggestion. Indeed, many factors affect the long-term survival of patients, including patients selection, R0 resection, lymph nodes metastases, and so on. We admit that our conclusion about long-term survival is not the strongest evidence, and we have already discussed this in the article. However, for now, the long-term survival rate is still an important indicator to compare the outcome of two treatment modalities.

In our article, endoscopic resection was associated with lower R0 resection rate and higher tumor recurrence rate, which will decrease overall survival. Marino et al. used the NCDB after propensity matching and found that esophagectomy was associated with better survival after 90 days (HR, 1.34; P=0.02). Similarly, Zeng et al. used the

SEER registry and also found poorer OS (HR, 1.690; P<0.001) in the ER group than in the esophagectomy group.

After carefully studies your comments, we agree that it does not have important clinical guidance significance to compare the long-term survival between the modalities. However, this still has certain significance for future clinical research. Therefore, we finally decided to keep the content about long-term survival in the article.

Thank you again for your positive comments on our manuscript. We seek for your tolerance and understanding and would be glad to respond to any further questions and comments that you may have.

Response to Reviewer B

Thank you very much for your letter and advice on our manuscript. We very much appreciate the careful reading of our manuscript and valuable suggestions. We have carefully considered the comments and have revised the manuscript accordingly.

Comment 1: Page 2 line 17-19: This is a confusing sentence and might benefit from being split into two

Reply 1: As for the referee's concern, we have revised the sentence.

Changes in the text: See Page 3, line 5-10

Comment 2: Page 2 line 10: should this read "There may be some advantage..."

Reply 2: As for the referee's concern, we have revised the sentence.

Changes in the text: See Page 2, line 18

Comment 3: Page 2 line 19: T1a perhaps should be defined. Furthermore, EEC is referring to T1a and T1b and this should be clarified.

Reply 3: As for the referee's concern, we have revised the sentence.

Changes in the text: See Page 3, line 5-7

Comment 4: Page 4 line 2 – 4: needs to be re-worded

Reply 4: As for the referee's concern, we have revised the sentence.

Changes in the text: See Page 5, line 6-8

Comment 5: Page 6 line 25-27: You have focused on the findings of Jin et al finding no significant difference in major complication between surgery and endoscopic resection though this contradicts the finding of your meta-analysis which is quite confusing (page 6 line 16). Is there a reason this study has been specifically referred to. It has little comparative weight in the meta-analysis (page 14 figure 2A) and is not significant (p=1.0)

Reply 5: We are very sorry for our illogical writing. After carefully studying your comments and advice, we have re-worded the sentence.

Changes in the text: See Page 9, line 5

Comment 6: Page 6 line 19: To say the oncologic outcomes of ER therapy is 'favourable' is not entirely true given the meta-analysis demonstrated a high tumour recurrence rate. This should be clarified

Reply 6: According to your suggestions, we have corrected the sentence.

Changes in the text: See Page 8, line 18

Comment 7: Page 10 line 20 reference 12 – this paper is on GEJ adenocarcinoma Siewert II. Can this be generalised to an esophageal cancer population?

Reply 7: Indeed, the classification of GEJ adenocarcinoma is still under debate. According to the 8th edition AJCC/UICC staging of cancers of the esophagus and esophagogastric junction, GEJ adenocarcinoma Siewert II should be generalized to esophageal cancer. Besides, as thoracic surgeons, we are also more inclined to classify GEJ adenocarcinoma Siewert II as the staging of esophageal cancer.

Changes in the text: NA

Comment 8: Page 16 reference Gong 2016: This paper is from 2017 as listed in the bibliography page 10 reference 12

Reply 8: The article was accepted on December 1, 2016, and published on December 19, 2016. Therefore, we classify it as a 2016 article.

Changes in the text: See Page 14, line 19

Comment 9: Page 5 page 25 discusses the R0 resection rate. This is then repeated on page 7 line 6-12. These paragraphs should be consolidated.

Reply 9: According to your suggestions, we have corrected the sentence.

Changes in the text: See Page 7, line 16-17

Comment 10: General Comments

Reply 10: Thank you again for the time and effort you have put into your comments. We have carefully considered the comments and have revised the manuscript accordingly. We acknowledge your comments very much, which are valuable in improving the quality of our manuscript. I would be glad to respond to any further questions and comments that you may have.

Changes in the text: See Page 9, line 14-20; Page 10, line 1-8