Author’s response to reviews

Title: Endoscopic Injection of Human Fibrin Sealant in Treatment of Intrathoracic Anastomotic Leakage After Esophageal Cancer Surgery

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Author’s response to reviews:

Dear Vipin Zamvar,

We are very glad to receive your reply to our original article entitled “Endoscopic Injection of Human Fibrin Sealant in Treatment of Intrathoracic Anastomotic Leakage After Esophageal Cancer Surgery” (JCTS-D-20-00057).

Meanwhile, we are truly grateful to yours and other reviewers’ critical comments and thoughtful suggestions. Based on these comments and suggestions, we have made careful modifications on the original manuscript. All changes are made to the text in the revised version of word file. In addition, we have consulted native English speakers for paper revision before the submission this time. We hope the new manuscript will meet your magazine’s standard.

Below you will find our point-by-point responses to the reviewers’ comments/questions:

Response to Reviewer #1:

1. Background part. At present, the incidence rate of esophageal malignant tumor is about 13/100,000 in China, ranking first in the world. In the first sentence of the background, please list the references.
Response: Thanks for your valuable suggestion and kindness. The first sentence of the background was supported by the specific references.

2. General Information part. Oval silicone vacuum suction tube Length or diameter is 5mm? In my experience, the tube still needs a lot of side holes, please describe it in detail and add a picture description.
Response: Thanks for your kindness and please forgive my carelessness. The detailed information of oval silicone vacuum suction tube was clearly described in the revised manuscript accordingly.
3. Clinical Symptoms and Diagnosis part. Do all patients develop symptoms one week after operation? Please describe the time range in detail and described as x± s.
Response: Thanks for your constructive suggestion and kindness. The details of the time range in the clinical symptoms and diagnosis were clearly described in the section of materials and methods.

4. Treatment part. Are all patients examined by gastroscope 28 days after operation to observe the anastomotic leakage? Whether there is a situation in which some cases have healed at an early stage. Is there no case of failure in this method? Have you deliberately removed any failed cases from this set of data?
Response: Thanks for your suggestion and kindness. In this study, all patients are examined by gastroscope 28 days after operation to observe the anastomotic leakage, and no case has healed at an early stage, and there was no failure in this method. Meanwhile, we have not deliberately removed any failed cases from this set of data.

5. Table 1 Please use three-line table format.
Response: Thanks for your valuable suggestion and please forgive my carelessness. The tables were revised to three-line table format.

6. This method is mainly suitable for anastomotic leakage with smaller diameter. If you have any other suggestions for anastomotic leakage whose diameter is larger than 1cm, the discussion section focuses on the indications and precautions of your method. When will surgical treatment be taken?
Response: Thanks for your reconstructive suggestion and kindness. I am sorry to tell you that we have no idea about the treatment for anastomotic leakage whose diameter is larger than 1cm. And the surgical treatment would be taken after the enrollment.

7. In my experience, I also use fasting, gastrointestinal decompression, nutritional support, adequate drainage and conservative treatment of intrathoracic anastomotic leakage. Another important factor when choosing conservative treatment is that when the lungs are dilated completely, the lungs can act as a barrier to block the fistula and promote the healing of the fistula.
Response: Thank for your kindness for providing your valuable experience, and maybe in the foreseeable future, we would try our best to apply this method in the further investigation.

8. At present, there are only 7 related studies, the number is small, the study has some limitations, I hope you will continue to sum up in the future work and continue to carry out this work.
Response: Thanks for your kindness and help. And in the further investigation, we would endeavor ourselves to resolve these limitations in the foreseeable future.

9. Conclusion part: this method is mainly suitable for small diameter anastomotic leakage and is an alternative method for the treatment of small diameter anastomotic leakage.
Response: Of course, this method mainly focused on the small diameter anastomotic leakage and is an alternative method for the treatment of small diameter anastomotic leakage.

10. Please quote the SCI literatures as much as possible, the data should be supported by the literatures, and the latest literatures should be selected at the same time. About 20 references are needed, and the references of this magazine can be cited appropriately.
Response: Thanks for your constructive suggestion and help. The references in this manuscript were revised to meet the standards of this journal.

Response to Reviewer #2:

In this study, Zhu and colleagues report on 7 patients with anastomotic leak after esophagectomy who were treated with fibrin sealant injection. The authors report decreased drainage volume, CRP and WBC.

My comments are meant to be used to improve the manuscript.

1. Please characterize the leaks, were they contained or free.
Response: Thanks for your kindness and help. The definition and characteristics of leaks were carefully provided in the revised version.

2. Please comment on why was the fibrin sealant applied 3 weeks after detection of the leak.
Response: Thanks for your wonderful question. In general, fibrin sealant became the first modern era material approved as a hemostat in the United States in 1998. It is the only agent presently approved as a hemostat, sealant, and adhesive by the Food and Drug Administration (FDA). The product is now supplied as patches in addition to the original liquid formulations. Both laboratory and clinical uses of fibrin sealant continue to grow [1]. In this study, the fibrin sealant was applied three weeks after detection of the leak just due to the haematemesis before three weeks.

3. Please clarify when the lab values were obtained, and how they fluctuated.
Response: Thanks for your valuable suggestion and kindness. The lab values were obtained just after the finish of the assays and sometimes they fluctuated as the experimental conditions changed or just due the individual difference.

4. Please comment on when the leak sealed and pleural tubes were removed.
Response: Thanks for your reconstructive suggestion and kindness. Patients with leaks can be safely discharged with their pleural tubes. These tubes can be safely removed even if the patients have a pneumothorax, if the following criteria are met: the patients have been asymptomatic, have no subcutaneous emphysema after 14 days, and the pleural space deficit has not increased in size. However, it is difficult to determine when the leak sealed because the environment in vitro is complicated and there is a great difference between individuals.

5. Please provide numbers and p-values in the text of manuscript and abstract.
Response: Thanks for your valuable suggestion and kindness. The numbers and p values were carefully provided in the revised version.

6. The abstract conclusion comments on symptom improvement. How were symptoms assessed?
Response: Thanks for your helpful suggestion. And the symptoms were comprehensively added in the section of abstract.
Response to Minor comments:

1. Please clarify the 5mm length of the silicone tube.
   Response: Thanks for your help. The 5mm length of the silicone tube was clearly clarified in the revised version.

2. Please consider re-wording "white fur" or the leak site
   Response: Thanks for your valuable suggestion and kindness. The statements of “white fur” or “leak site” were replaced by other words.

Sincerely yours,

Dr Zhu

References