Peer Review File
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Reviewer A

I have read and reviewed the submitted manuscript “Palliation of malignant esophageal stent-associated esophagorespiratory fistula with rigid bronchoscope and Y silicone trachea stent: experience with seven patients”. The authors conduct a single institution study that encompasses 5 years and identifies 7 patients with SERF (stent induced esophagorespiratory fistula). There are many areas to require some clarification. In addition, since placing Y silicone stents is an option for treatment of these rare patients, how does this differ from a paper by Herth et al (see Major Point 8 below). What more does this manuscript add to the literature?

Major Points:
Comment 1: The term “SERF” is used in the abstract but not defined until the body of the INTRODUCTION. This term needs to be defined in the abstract.
Reply 1: Thank the reviewer for the valuable comments. Based on your comment 2, we have changed the entire text from "Malignant Esophageal SERF" to "Malignant Esophageal Stent Esophageal Infiltration Fistula (ERF)” and added the definition of it in both Abstract section and Introduction section.
Changes in the text: We have modified our text as advised (see Page 2, line 42-44; Page 4, line 95-96)

Comment 2: In the METHODS section, “malignant esophageal SERF patients” is said, but ERF has been defined as esophagorespiratory fistula. This could be reworded for clarity otherwise the sentence reads: malignant esophageal stent esophagorespiratory fistula.
Reply 2: Thank the reviewer for the valuable comments. In the original manuscript, the full name for "malignant esophageal SERF" was "malignant esophageal stent associated esophagorespiratory fistula". We believe that the comments provided by the reviewer can make the statement more concise. We have changed "malignant esophageal stent associated esophagorespiratory fistula" to "malignant esophageal stent esophagorespiratory fistula (ERF)".
Changes in the text: We have changed the entire text from "Malignant Esophageal SERF" to "Malignant Esophageal Stent Esophageal Infiltration Fistula (ERF)”. Since this concept was mentioned too many times in the manuscript, we are not going to mention one by one where it appears.

Comment 3: In the RESULTS section of the abstract, it states that the cause of death was pneumonia in a patient, yet in the CONCLUSION section of the abstract it states that the procedure “prevent from recurrent aspiration pneumonia”. These two statements are at odds. Please review and consider clarifying.
Reply 3: Thanks for the reviewer's reminder. We apologize for the confusion caused by our unclear statement. We originally wrote in the results, "Cause of death in the patients included disease progression, pneumonia, massive hemoptysis, and respiratory insufficiency." In this

context, pneumonia refers to novel coronavirus pneumonia. One patient died of COVID-19 infection in December 2022, which was just the time when the epidemic situation in our country was lifted, and numerous people got infected. For the patients with advanced tumor stage and malignant ERF, who were already physically weak, were more likely to develop severe pneumonia. During the follow-up, the family specifically explained that the patient's symptoms had been well controlled after the procedure. Unfortunately, he died of COVID-19 infection.
Changes in the text: Changes in the text: We have modified our text as advised (see Page 3, line 65; Page 9, line 240)

Comment 4: The statement that Y-stents have the advantage of greater radial strength is likely untrue. I would direct the authors to: Medical Engineering and Physics 2015;37:408-15. The conclusion is that silicone stents produce the lowest levels of stress. Please review and consider revision or explanation to back the authors claims.
Reply 4: Thanks for the reviewer's correction. Indeed, as the reviewer pointed out, silicone stents produce the lowest levels of stress compared with balloon-dilated metal, self-expanding metal, and covered self-expanding metal. The weak contact between the silicone stent and the trachea makes them have higher propensity for migration. In this study, we chose to use Y-shaped silicone stents with the aim of fully leveraging the strengths and avoiding weaknesses of silicone stents. Choosing a silicone stent instead of a metal stent is to reduce pressure on the edge of the fistula and prevent further expansion. The selection of Y-shaped instead of straight tube silicone stent is to combine with the special anatomical structure of the airway and reduce migration rate. In addition, the radial force of the Y-shaped silicone stent is mainly concentrated in the carina area, which can reduce the dilation force at the edge of the fistula.
Changes in the text: We have modified our text as advised (see Page 11, line 301-316)

Comment 5: The METHODS becomes unclear. Was the Y-stent placed in the airway or the esophagus? If the airway, how was a rigid bronchoscope used in the airway with an intubated patient to place a Y-stent? In section 3.2, the authors state that the Y-stent was placed in the airway. This requires rewrite of a few areas to clarify.
Reply 6: We apologize for the confusion caused by our unclear expression. We have rewritten the surgical procedure section. After administering general anesthesia with mask oxygen inhalation, tracheal intubation with an endotracheal tube size less than 7.0 was performed using a video laryngoscope and a tracheal catheter. Once proper placement of the tracheal tube was confirmed, mechanical ventilation was initiated using an anesthesia machine for all patients. After that, we inserted the rigid bronchoscopy into the esophagus with necessary balloon expansion and thermal ablation to remove the esophageal metal stent. The incarcerated esophageal stent was folded and rotated by rigid forceps for removing. Once the esophageal stent was removed, we removed the trachea intubation and inserted the rigid bronchoscope in the trachea with Ventilation maintained via the side port of the rigid bronchoscope. Then, the Y

silicone stent was deployed and positioned in the airway to fully cover the fistula.

Changes in the text: We have modified our text as advised (see Page 6, line 142-147)

Comment 6: What was the time interval for the remeasurement of the KPS? Did the increase happen within 30 days or 180 days? Did the value stabilize?

Reply 6: Thank the reviewer for the valuable comments. Quality of life was assessed by Karnofsky Performance Score (KPS) before the procedure and 30days after the procedure. Among 7 patients, 5 patients achieved 80 score and 2 patients achieved 70 score. According to our follow-up, these patients have maintained a basic self-sufficient state for a long time, only occasionally coughing up phlegm.

Changes in the text: We have modified our text as advised (see Page 7, line 185-186)

Comment 7: The authors cite that SERF occurs in 9% of patients. How many patients over the time period of this study had esophageal stents placed? What was their rate of SERF?

Reply 7: Thank the reviewer for the valuable comments. During the process of major revision, we retrospectively collected the medical records of malignant esophageal stent ERF patients. Most of them place the original esophageal stent at other hospital. In addition, the placement of esophageal stent is mainly handled by the digestive endoscopy department in our hospital. And we have no authority obtain the original data of the patients who underwent esophageal stent placement in digestive endoscopy department during this period. Therefore, we are sorry that we are unable to provide you with the occurrence rate of SERF in our center.

Changes in the text: NA.

Comment 8: A paper by Herth et al (Eur Respir J 2010;36:1370-4) is missing from the discussion as it looked at 112 patients with malignant esophageal fistula and outcomes associated with were the stents were placed (airway alone, esophagus alone, and both). Consider reviewing this paper and putting your results in the context of this paper.

Reply 2: Thank the reviewer for recommendation of this high-quality article which is closely related to us. Herth et al included patients with ERF and compared the treatment effects of single tracheal stent, esophageal stent, and double stent. The results showed that the survival time of single tracheal stent was the shortest. However, the population we included is different from Herth et al. In Herth's study, esophageal stents were not the main cause of fistula and can be used to seal the fistula. However, in our study, fistula was caused by esophageal stents. If not removed, it is equivalent to a constant risk factor. Besides, placing another tracheal stent without removal can affect the position of the stent and the effectiveness of treatment. In addition, dual stenting in both esophagus and trachea may increase the forces on the tissue of the anterior esophagus and posterior trachea, potentially increasing the risk of necrosis, fistula healing, or even exacerbating the condition.

Changes in the text: We have modified our text as advised (see Page 10, line 267-270)

Comment 9: In addition to the paper by Bick et al (ref 2), consider reviewing Park et al in addition (Am J Roentgenol 2012;198:453-9). This may help in the DISCUSSION.

Reply 9: Thank the reviewer for the valuable comment. We appreciated for the recommendation of this interesting literature. This study increases our knowledge of how radiation therapy makes an impact on airway complications after covered stent placement for malignant

esophageal stricture. We have added this paper in the discussion section.
Changes in the text: We have modified our text as advised (see Page 4, line 93-95; see Page 9, line 251-252)

Minor Points:
Comment 1: There are some issues with grammar and syntax that will need to be addressed prior to publication. An example is the final sentence of the abstract.
Reply 1: Thank the reviewer for the kind reminder. The grammar and syntax have been double-checked by the authors.

Comment 2: The Mellows-Pinkas scoring system for dysphagia was an adaption of what was proposed by Ogilivie in 1982 (Gut 1982;23:1060-7).
Reply 2: Thank the reviewer for the kind reminder. We have made corresponding changes to the citation of the Mellows-Pinkas scoring system for dysphagia.
Changes in the text: We have modified our text as advised (see Page 7, line 187-189)

Comment 3: The initial stents that were placed, where they all SEMS? If so, the median indwelling time is quite long at 95 days. Most recommendations are to remove/exchange stents every 10-12 weeks to prevent ingrowth or erosion.
Reply 3: Thank the reviewer for the valuable comments. As the reviewer pointed out, most recommendations are to remove/exchange the esophageal stents every 10-12 weeks to prevent ingrowth or erosion. However, the esophageal stents of these patients were placed in other hospital. These patients didn't come to our hospital for medical treatment until the occurrence of ERF, which could not be handled in their original hospital. Therefore, the only thing we can do is to tell them the necessity of follow up after a procedure.
Changes in the text: NA.

Comment 4: The point about stent complications is a bit misleading. Most complications are actually stent migration. Can the authors consider clarifying this point in the DISCUSSION?
Reply 4: Thank the reviewer for the valuable comments. In the last version of submission, we included pneumonia in stent-related complications in table 3. Besides, we wrote "Esophageal stents are commonly used to palliate malignant dysphagia, fistula, or ERF when cancer invaded esophagus or trachea. However, the reported complication rate associated with esophageal stent placement range from 20% to 53% (2, 12-14). Despite successful sealing of the fistula, there remains a risk of reopening in 0-39% of patients (15). Prior publications showed that malignant esophageal SERF occur in approximately 9% of patients, but little is known about the treatment of this severe complication (12, 14)." in the first paragraph of discussion section, which is quite confusing. As the reviewer pointed out, stent complications mainly consisted of stent migration, granulation, and sputum retention. Therefore, we have made relative revision in the manuscript.
Changes in the text: We have modified our text as advised (see Page 7, line 177-183; Table 3)

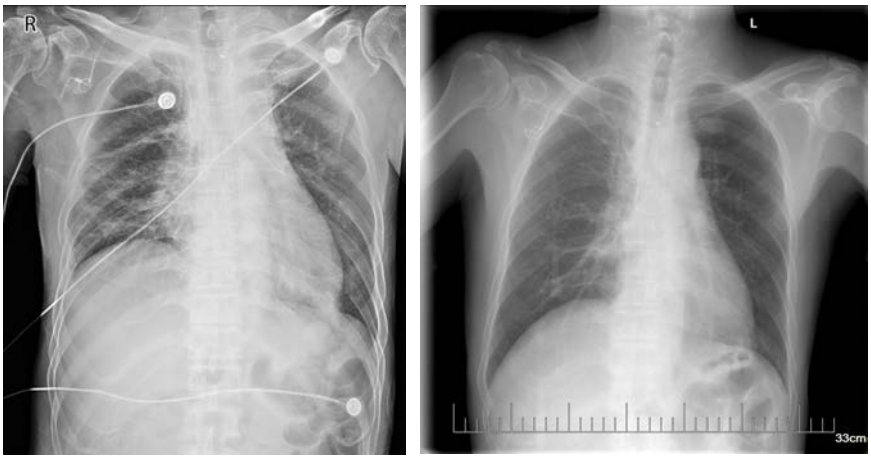
Comment 5: When citing an author, only the last name (surname) of the first author is required followed by "et al.". As an example, if I was to cite this manuscript I would write "Wang et al reported 7 patients with SERF…" Please correct throughout the manuscript.

Reply 5: Thank the reviewer for the valuable comments. We have corrected the form of author citing throughout the manuscript.
Changes in the text: We have modified our text as advised (see Page 10, line 270)

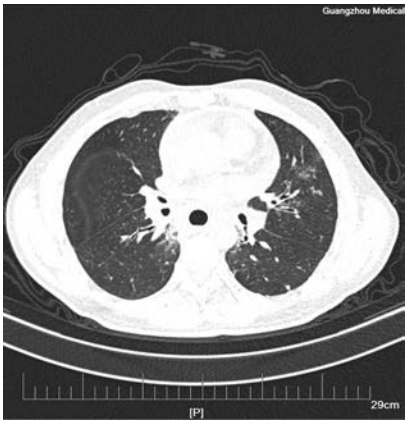
Reviewer B

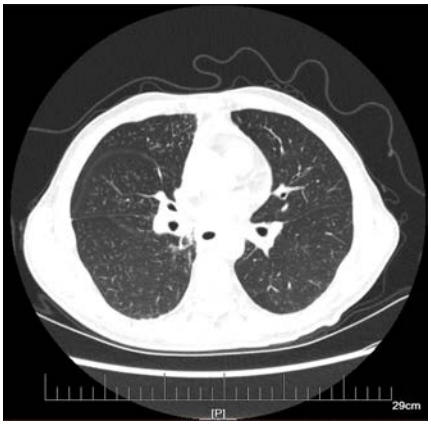
Authors are thanked to have submitted their original work to the journal.
The study is interesting, nevertheless it presents several limitations and major revisions are required.
Airway stenting for malignant esophago-respiratory fistula has largely been described. The present study dealing with the specific esophageal stent-associated esophago-respiratory fistula is original but because of several limitations, it does not allow to reach definitive conclusions.

Comment 1: The main limitation of the study consists of the absence of a control group and a randomization, that would enforce the results of statistical analysis.
Reply 1: Thank the reviewer for the valuable comments. As suggested by the reviewer, we have added a control group for double stent, although in the past three years, only three patients in our center have received this treatment. We compared our method with double stent and found that our method has more advantages in controlling pneumonia and survival. In the previous manuscript, we mentioned that 5 out of 7 patients had pneumonia, because during the follow-up process, even if the patients had only a small amount of inflammation on the chest X-ray or CT, we classified it as having pneumonia. In fact, they all showed significant improvement in the symptoms of pneumonia after the procedure. The following is the comparison of chest X-ray or CT images of 5 patients with pneumonia before and after surgery, as mentioned earlier.
Patient 1

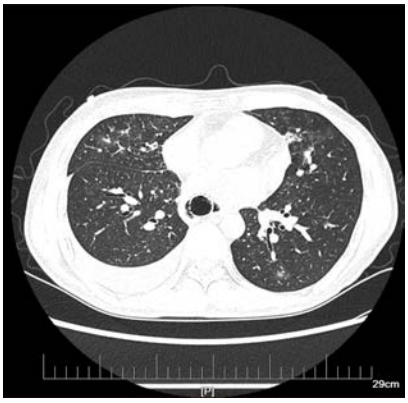


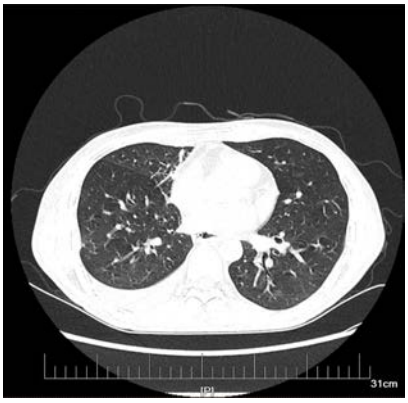
Patient 4



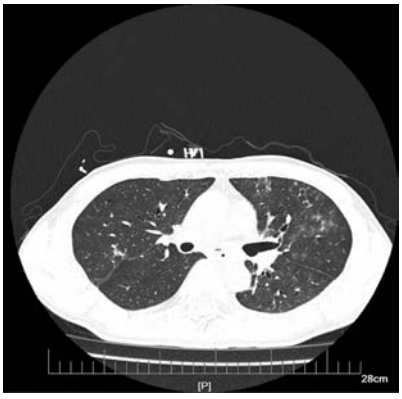


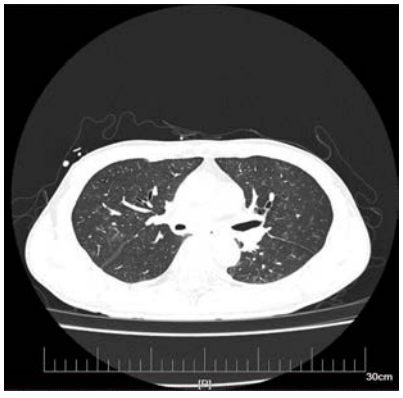
Patient 5



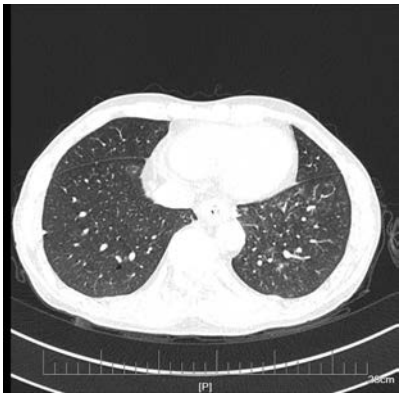


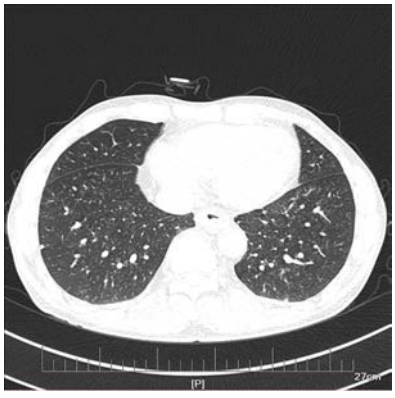
Patient 6





Patient 7





The images of patients 2 and 3 are lacking because they completed the examination in other hospital and cannot be retrieved from our hospital's records. But both stated during the follow-up process that there was no pneumonia, no obvious cough or sputum, and their survival time was relatively long, one was 575 days and the other was 389 days. The 575 days patients died of severe pneumonia at the COVID-19 epidemic. In summary, we believe that our treatment can effectively improve and control the patient's aspiration pneumonia.
Changes in the text: We have modified our text as advised (see Page 2-3, Line 47-67; Page 5, line 116-121; Page 7-9, Line 196-242; Table 1, 2, 3; Figure 3, 4)

Comment 2: Authors report a long period of observation, but information lacks about the average follow-up time of the patients, after the procedure.
Reply 2: Thank the reviewer for the valuable comments. In this study, the survival time was calculated from the day of the procedure to the day of the patient's death. Since all patients died during the process of the study, the follow-up time of each patient was his/her survival time.
Changes in the text: We have modified our text as advised (see Page 7, Line 173-174; Figure 4)

Comment 3: Clinical outcomes are promising but no precise information is given on re-alimentation. Considering that Authors define that airway stenting in these patients has improved dramatically their quality of life, with most patients able to resume liquid or semi-liquid diets, the question is how re-alimentation has been re-introduced in the group of study? Did patients receive enteral/parenteral feeding even to increase the nutritional intake, to support mucosal trophism?
Reply 3: Thank the reviewer for the valuable comments. At our center, patients can try eating 6 hours after anesthesia of the procedure. We suggest that patients drink water first to check for coughing. If not, they can eat according to their own condition and comfort level, gradually transitioning to a semi liquid and normal diet. However, even if patients no longer have coughing during swallowing, we recommend them to undergo percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ) to set up the way of enteral nutrition, to reduce the stimulation of food on the esophageal fistula during repeated swallowing and reduce the risk of further enlargement of the fistula.

Patients often need to keep fasting for 6-8 hours before the procedure. Adding waiting time often requires more time. Patients cannot eat immediately after the procedure. During this process, to prevent the patient from becoming too weak, we will supplement parenteral feeding to ensure adequate nutrition. However, this is not the main method of nutrition supply for daily life afterwards.
Changes in the text: We have modified our text as advised (see Page 6-7, Line 159-171; Page 12, Line 323-331)

Comment 4: Have patients been kept fasting for a few days after stent's replacement?
Reply 4: Thank the reviewer for the valuable comments. At our center, patients can try eating after 6 hours after anesthesia of the procedure. We suggest that patients drink water first to check for coughing. If not, they can eat according to their own condition and comfort level, gradually transitioning to a semi liquid and normal diet. However, even if patients no longer have coughing during swallowing, we recommend them to undergo percutaneous endoscopic

gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ) to set up the way of enteral nutrition, to reduce the stimulation of food on the esophageal fistula during repeated swallowing and reduce the risk of further enlargement of the fistula.

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Changes in the text: We have modified our text as advised (see Page 6-7, Line 159-171; Page 12, Line 323-331)

Comment 5: What is Authors' experience of double stenting? Did any of the presented patient need double stenting during the follow-up? Has enlargement of fistula or ischemic injury from pressure exerted by airway stent been observed after bronchoscopic stent substitution?

Reply 5: Thank the reviewer for the valuable comments. According to our understanding, for patients occurring ERF with indwelling esophageal stents, double stenting refers to placing a stent directly in the airway to seal the fistula without removing the esophageal stent. After carefully considering the opinions of several reviewers, we included patients with double stent in the control group in this study. The results showed that double stent was not as effective as our treatment scheme in pneumonia control and survival. The 7 patients, who experienced esophageal stents removal and Y silicone stents placement through rigid bronchoscope, did not need double stenting during the follow-up process. Because their pneumonia was well controlled, the ERF was not enlarged, and the stents were in good position. We did not make too much interventional treatment among them, with only a few patients underwent simple granulation resection and sputum suction.

Changes in the text: We have modified our text as advised (see Page 2-3, Line 47-67; Page 5, line 116-121; Page 7-9, Line 196-242; Page 10-11, Line 275-292; Table 1, 2, 3; Figure 3, 4; Supplementary Figure 2; video 6)

Comment 6: Have granulation tissue been described because of Y stenting, during the follow-up? If yes, how was it treated? Does the choice of Y stent in the study is standardized of it relies on the position of the fistula? When fistula is on the cervical esophagous of far from the carina, what methods of exclusion do Authors suggest?

Reply 6: Thank the reviewer for the valuable comments. During the follow-up process, 2 out of 7 patients had granulation hyperplasia, with one patient occurring at the edge of the trachea limb of the Y silicone stent and the other occurring at the edge of the left main bronchus limb of the Y silicone stent. If the granulation hyperplasia causes less than 50% lumen narrowing, we do not make special intervention, but continue to observe. If the granulation continues to grow and causes lumen narrowing beyond 50%, we will perform interventional treatment on the granulation.

Regarding to the issue of stent selection, after several attempts, Y silicone stent was found to be the most suitable stent for the population who develop ERF with an indwelling esophageal stent, regardless of where the fistula occurs. We have tried other stents before, including metal stents and straight tube silicone stents, but the results were not good. We do not use metal stent

because of the greatest radial force among stents. The radial force of straight tube silicone stents is the smallest. But due to this reason, the straight tube silicone stents have higher risk of migration. Therefore, we do not choose straight tube silicone stents and choose Y-shaped silicone stents instead. The Y-shaped silicone stents can simultaneously solve the problems of high radial force and high migration rate. The radial force of Y-shaped silicone stent on the tracheal wall is mainly concentrated at the carina and the edge of the stent, which can reduce further expansion of the fistula. In addition, the Y-shaped silicone stent is stuck in the left and right main bronchi, which is hard to migrate.

From the questioning, we found that the reviewer also noticed the issue when the fistula occurred far away from the carina, such as in the upper part of the trachea or near the glottis. This problem has also troubled us for a long time. The structure of the area from the glottis to the upper part of the trachea is quite unique, with a narrow upper section and a wide lower section. We have tried placing a stent with wide lumen diameter that suits with the wide lower section in this area. The result is that the stent severely compresses the area near the glottis, leading to severe inflammatory edema and narrowing of the airway, putting patients at risk of suffocation. We have also tried placing stents with narrow lumen diameter that suits with the narrow upper section, but due to insufficient radial force, the stents are prone to migration. We have also tried internal and external fixation on the stents, but the results were not satisfactory, and severe inflammation may occur at the anastomotic site. We have also tried a straight tube stent from the glottis to the end of trachea, but the stent is still prone to displacement. Besides, the too long length of the stent leads to a sharp decrease in the patient's sputum excretion ability and increases their discomfort. We have also attempted to place a narrower stent at the narrow upper section and a wider stent at the wide lower section, resulting in a huge radial force at the overlap of the two stents, leading to inflammatory edema and necrosis. When the ERF occurs near the glottis, we only need to customize a Y silicone stent with a longer trachea limb. Therefore, we conclude that for patients who had ERF with indwelling esophageal stents, the best option is to place a Y-shaped silicone stent after removing the esophageal stent.

Changes in the text: We have modified our text as advised (see Page 7, Line 179-181; Page 9, Line 231-233; Table 3)

Reviewer C

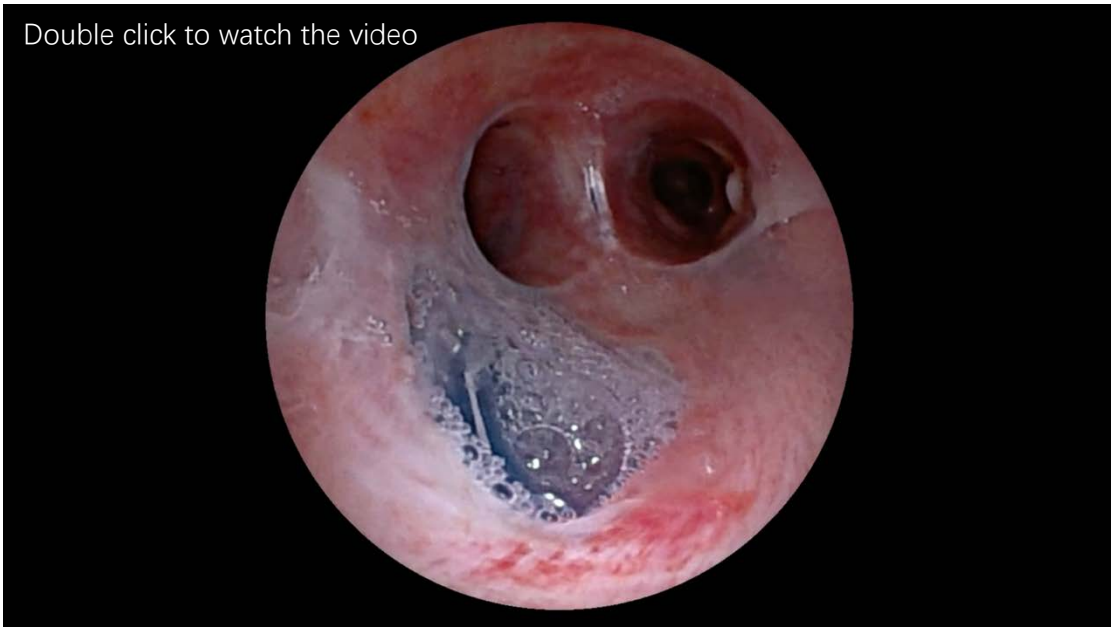
In the present paper Wang Q et al; described a new procedure for the treatment of the stent-associated oesophagus-respiratory fistula, which consists of removing the oesophageal stent through rigid bronchoscope, and subsequently implanting an Y stent in the airway to seal the fistula. Despite the number of patients analysed is limited, the approach described in the paper is interesting, considering the lack of shared treatments in the management of this rare and life-threatening condition. However, the paper is burdened by some limitations that need to be clarified and requires major revision.

Comment 1: In the “clinical outcome” paragraph it is written:” The result of bronchoscopy and CT after the procedure showed that the fistulas were completely sealed”. Although the imaging criterion is useful, often is not sufficient to guarantee successful closure of the fistula. Have the patients undergone oesophageal transit with contrast to check the absence of aspiration after

the placement of the stent in the airways? This test is very important, because in our experience oesophageal material can leak to the sides of the tracheal stent even when endoscopic examination and CT scan shows a good outcome of the operation.

Reply 1: Thank the reviewer for the valuable comment. In our center, esophagography is not generally used as a routine examination before and after the procedure. If the patient gradually recovers their diet after the procedure, starting with trying to drink water and gradually transitioning to semiliquid, and there is no obvious coughing, we can assume that the fistula has been well sealed and proceed without the next step of esophagography. If we have little confidence in well sealing the fistula after the procedure or if the patient has obvious coughing after the procedure, we will inject methylene blue into the patient's esophagus, observe whether there is blue secretion overflowing at the fistula opening through bronchoscope, and then observe whether there is blue secretion overflowing inside the stent and at the edges of the stent. The 7 patients we included did not experience coughing after drinking water and eating semi liquid food. And the fact also proves that the pneumonia situation of these patients has improved after surgery, so we believe that their fistulas have been well sealed. (see video 5)

Changes in the text: We have modified our text as advised (see Page 6-7, Line 159-166, video 5)



Comment 2: “shorter operation time was associated with longer survival time”. I think, that this analysis can be eliminate, because I don’t believe that in a population with an average survival of 381 days, the duration of the operation can have any prognostic implications.

Reply 2: Thank the reviewer for the valuable suggestion. As suggested by the reviewer, we have deleted the analysis on the association between the operation time and survival.

Changes in the text: We have deleted the relative content in the manuscript.

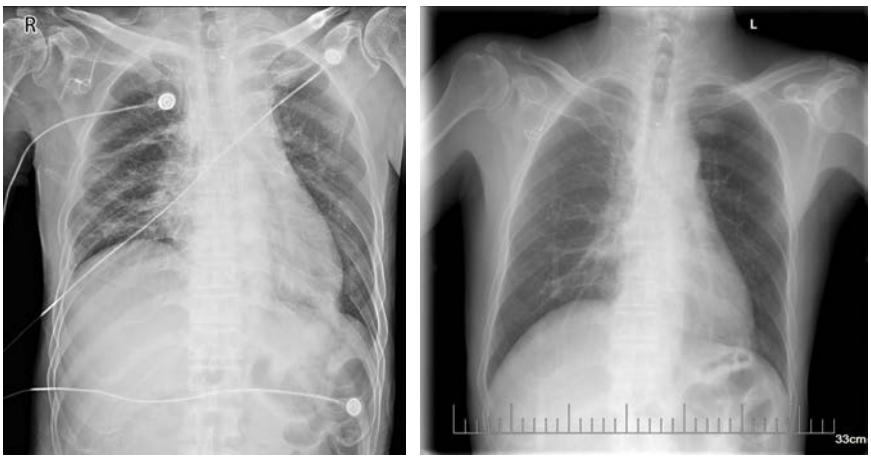
Comment 3: In the discussion section I suggest mentioning the possibility of endoscopic intervention which involve the use of autologous tissue between the two stents to seal the fistula and avoid necrosis of the tracheal wall (Front. Surg., 27 April 2023 Volume 10 - 2023 |

https://doi.org/10.3389/fsurg.2023.1107461).
Reply 3: Thank the reviewer for the valuable comment. We appreciated for the recommendation of this interesting literature. The population happens to be the one we are discussing—malignant esophageal stent ERF. We have added the use of autologous tissue in the treatment of malignant esophageal stent ERF to the discussion section.
Changes in the text: We have modified our text as advised (see Page 10, Line 263-265)

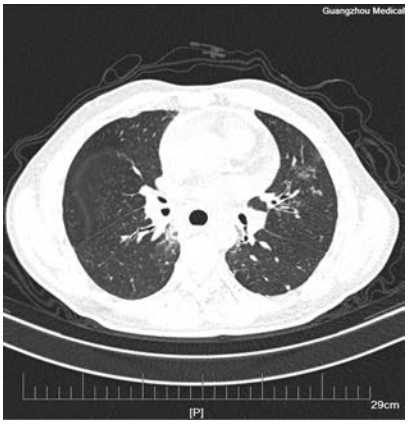
Reviewer D

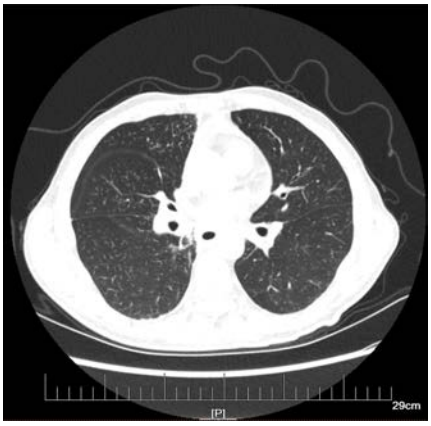
Comment 1: Why were the patients performed fiberoptic bronchoscopy for follow-up (e.g., pneumonia, granulation)? The authors mentioned about sputum retention, is it the reason?
Reply 1: Thank the reviewer for the valuable comment. At our center, we recommend patients to undergo a bronchoscopy examination every month after undergoing the procedure, even if they have no symptoms. The purpose of doing this is as follows. Firstly, if the stent fails to effectively seal the fistula, we can promptly detect and reduce the incidence of aspiration pneumonia. Secondly, the implantation of stents will reduce the patient's sputum excretion ability. In addition, many of the patients included in this study have received radiotherapy and chemotherapy, and their sputum excretion ability will also be worse than that of normal individuals. Therefore, regular bronchoscopy reexamination can help to extract secretions, improve patient comfort, and reduce the risk of breathing difficulties. Thirdly, placing a stent may lead to proliferation of granulation tissue or narrowing of the airway due to inflammatory stimulation. Regular bronchoscopy follow-up can reduce the risk of respiratory distress caused by airway stenosis in patients.
Changes in the text: We have modified our text as advised (see Page 7, Line 173-189)

Comment 2: How often is pneumonia complicated by resumption of meals?
Reply 2: Thank the reviewer for the valuable comment. The 7 patients we included did not experience worsening pneumonia after resuming their meals, but all showed improvement. The following is the comparison of chest X-ray or CT images of 5 patients with pneumonia before and after surgery, as mentioned earlier.
Patient 1

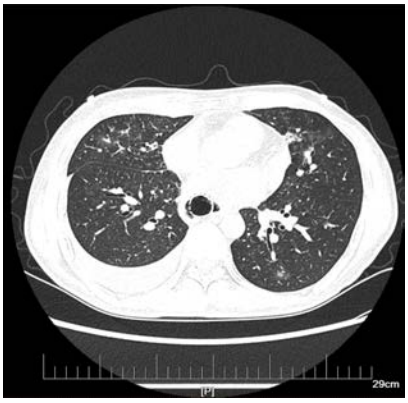


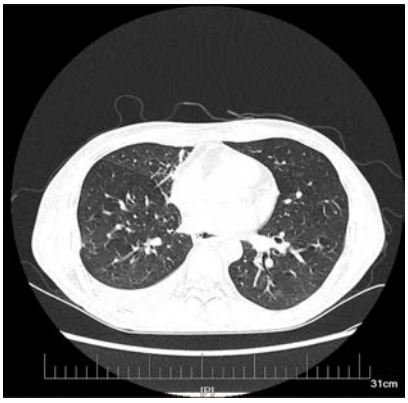
Patient 4



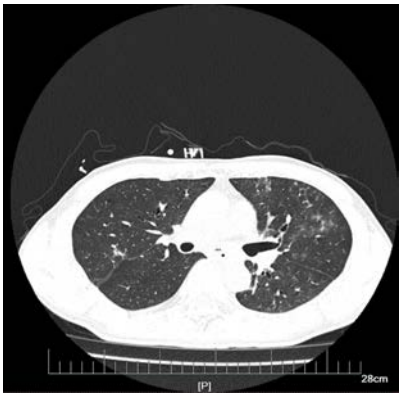


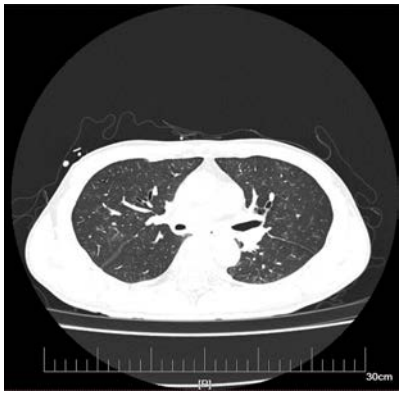
Patient 5



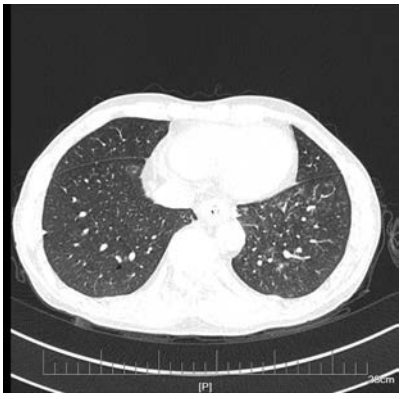


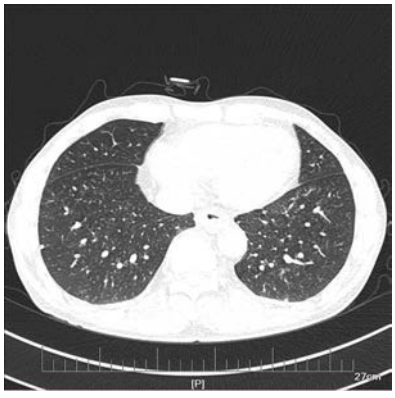
Patient 6





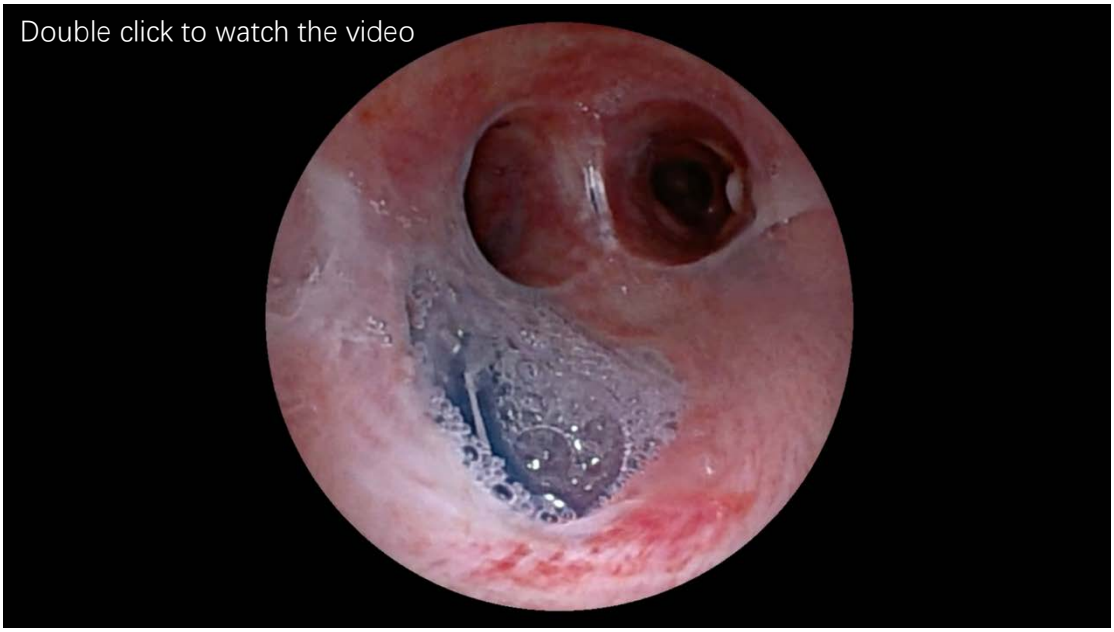
Patient 7





The images of patients 2 and 3 are lacking because they completed the examination in other hospital and cannot be retrieved from our hospital's records. But both stated during the follow-up process that there was no pneumonia, no obvious cough or sputum, and their survival time was relatively long, one was 575 days and the other was 389 days. The 575 days patients died of severe pneumonia at the COVID-19 epidemic. In summary, we believe that our treatment can effectively improve and control the patient's aspiration pneumonia.
Changes in the text: We have modified our text as advised (see Page 9, Line 234-236)

Comment 3: Have the patients been performed esophagography?
Reply 3: Thank the reviewer for the valuable comment. In our center, esophagography is not generally used as a routine examination before and after the procedure. If the patient gradually recovers their diet after the procedure, starting with trying to drink water and gradually transitioning to semiliquid, and there is no obvious coughing, we can assume that the fistula has been well sealed and proceed without the next step of esophagography. If we have little confidence in well sealing the fistula after the procedure or if the patient has obvious coughing after the procedure, we will inject methylene blue into the patient's esophagus, observe whether there is blue secretion overflowing at the fistula opening through bronchoscope, and then observe whether there is blue secretion overflowing inside the stent and at the edges of the stent. The 7 patients we included did not experience coughing after drinking water and eating semi liquid food. And the fact also proves that the pneumonia situation of these patients has improved after surgery, so we believe that their fistulas have been well sealed. (see video 5)
Changes in the text: We have modified our text as advised (see Page 6, Line 160-166)



Comment 4: Who are the four patients underwent gastrostomy and jejunostomy? And who are the patients improved the degree of dysphagia score?
Reply 4: Thank the reviewer for the valuable comment. Patient 3 underwent jejunostomy before the procedure. Patient 1 underwent gastrostomy after the procedure. Patients 4 and 5 underwent jejunostomy after the procedure. The degree of dysphagia among these four patients are 4

before and after the surgery. These patients did not have difficulty in swallowing or coughing during their diet after the procedure. But we suggest patients use drainage as the main way of Enteral nutrition, to reduce the stimulation of food on the esophageal fistula during repeated swallowing and reduce the risk of further enlargement of the fistula.
Changes in the text: We have modified our text as advised (see Page 12, Line 329-331; Table 1,3)

Comment 5: In this study, silicone Y stent placement is a prerequisite, but depending on the location of the fistula and considering the fitness, there may be an option to place only metal stents. Why the authors choose silicon Y stent at first?
Reply 5: Thank the reviewer for the valuable comment. In fact, we have tried other stents before, including metal stents and straight tube silicone stents, but the results were not good. We do not use metal stent because of the greatest radial force among stents. The radial force of straight tube silicone stents is smaller than that of metal stents. But due to this reason, the straight tube silicone stents have higher risk of migration. Therefore, we do not choose straight tube silicone stents and choose Y-shaped silicone stents instead. The Y-shaped silicone stents can simultaneously solve the problems of high radial force and high migration rate. The radial force of Y-shaped silicone stent on the tracheal wall is mainly concentrated at the carina and the edge of the stent, which can reduce further expansion of the fistula. In addition, the Y-shaped silicone stent is stuck in the left and right main bronchi, which is hard to migrate.
Changes in the text: We have modified our text as advised (see Page 11, Line 301-316)

Comment 6: How did the authors measure the size of fistula? And in table 1, how many fistulas are there in each patient?
Reply 6: Thank the reviewer for the valuable comment. We use flexible bronchoscope to measure the size of the fistula. We inserted the flexible bronchoscope in the airway. Once the fistula is located, we will place the front end of the bronchoscope at the lower edge of the fistula, and then measure the size of the fistula according to the markings on the bronchoscope or by comparing it to another known anatomical landmark.
Changes in the text: We have modified our text as advised (see Page 8, Line 203-204; Table 1)

Reviewer E

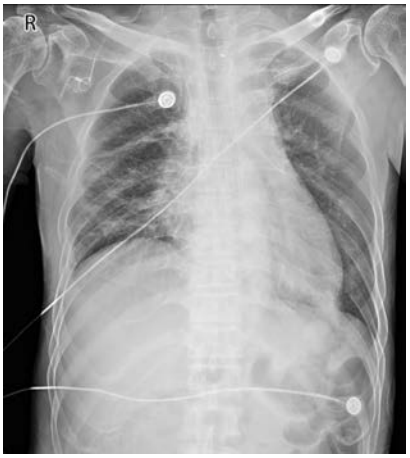
Your conclusions are that removing the esophageal stent and implanting the Y silicone stent through a rigid bronchoscopy is a safe and feasible treatment for malignant stent-associated esophagorespiratory fistula, as well as successful procedure in terms of sealing the fistula and prevention of recurrent pneumonia.
There are several problems that should be addressed by you before thinking about the publication of the paper.

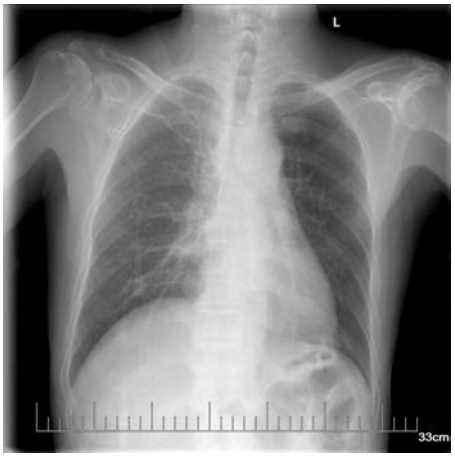
Comment 1: Only 7 patients have been treated in this way and the results have not been compared to a control group of patients treated according to ESGE guidelines which suggest the use of double stenting (combined airway and esophageal stenting), considered more effective in sealing the fistula, reducing aspiration during oral feeding. In this study 5 out of 7

patients developed pneumonia. So, I am not sure that this procedure is effective in preventing a recurrent aspiration pneumonia.

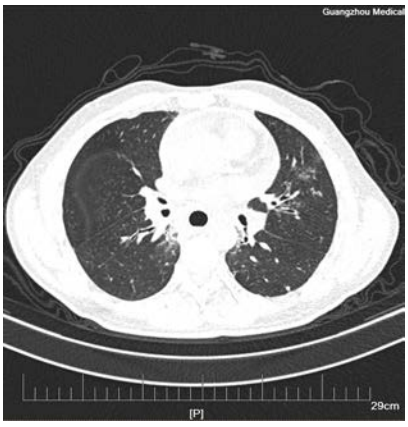
Reply 1: Thank the reviewer for the valuable comment. As suggested by the reviewer, we have added a control group for double stent, although in the past three years, only three patients in our center have received this treatment. We compared our method with double stent and found that our method has more advantages in controlling pneumonia and survival. In the previous manuscript, we mentioned that 5 out of 7 patients had pneumonia, because during the follow-up process, even if the patients had only a small amount of inflammation on the chest X-ray or CT, we classified it as having pneumonia. In fact, they all showed significant improvement in the symptoms of pneumonia after the procedure. The following is the comparison of chest X-ray or CT images of 5 patients with pneumonia before and after surgery, as mentioned earlier.

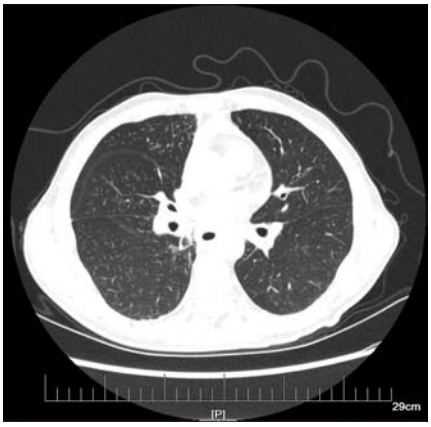
Patient 1



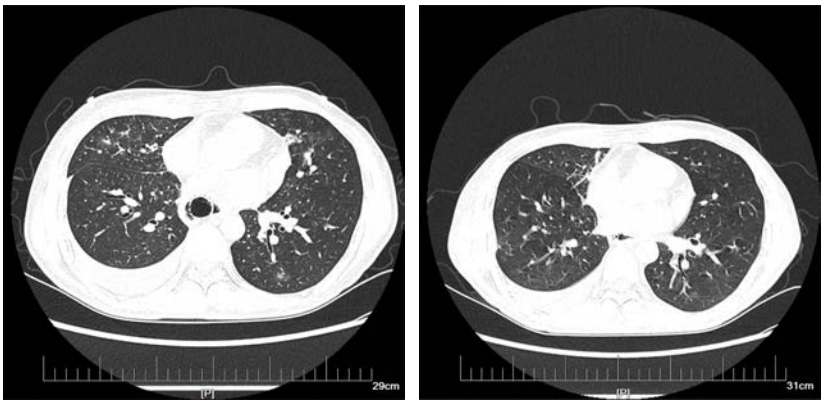


Patient 4

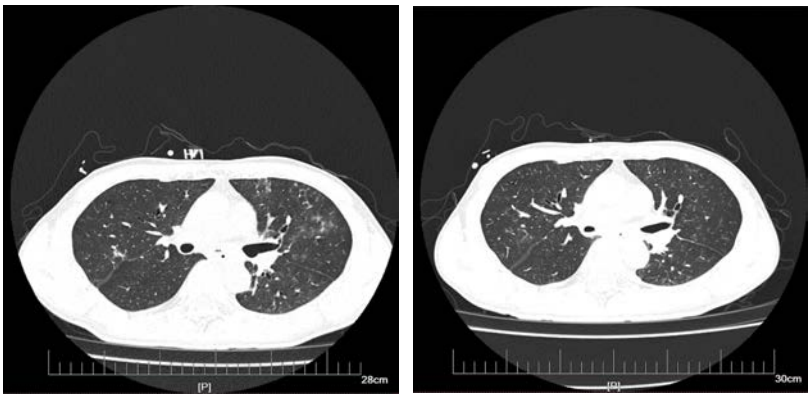




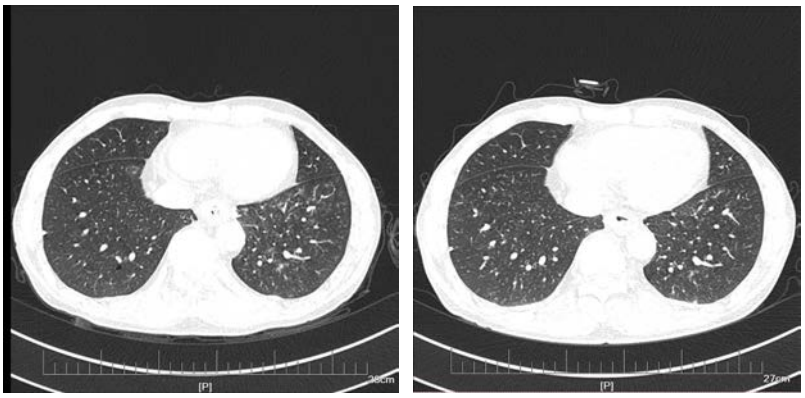
Patient 5



Patient 6



Patient 7



The images of patients 2 and 3 are lacking because they completed the examination in other hospital and cannot be retrieved from our hospital's records. But both stated during the follow-up process that there was no pneumonia, no obvious cough or sputum, and their survival time was relatively long, one was 575 days and the other was 389 days. The 575 days patients died of severe pneumonia at the COVID-19 epidemic. In summary, we believe that our treatment can effectively improve and control the patient's aspiration pneumonia.

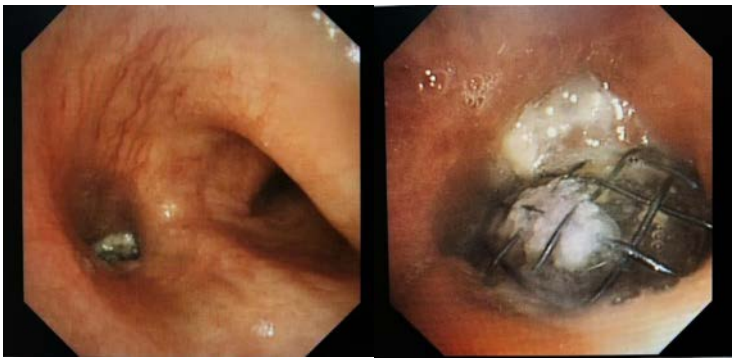
Changes in the text: We have modified our text as advised (see Page 2-3, Line 47-67; Page 5, line 116-121; Page 7-9, Line 196-242; Table 1, 2, 3; Figure 3, 4)

Comment 2: In two cases you were forced to combine the Ysilicone stent with a covered self-expanding metal stent (SEMS) because the silicone Y stent was not enough to seal the fistula. I wonder whether leaving the esophageal stent in place would have been useful in avoiding the

placement of another stent. Please, add a comment on this aspect.

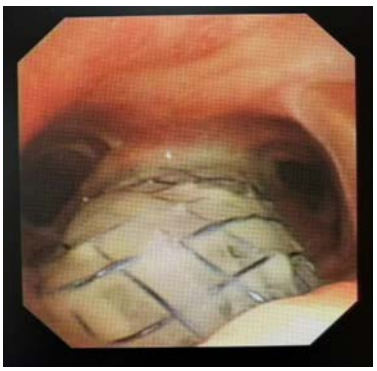
Reply 2: Thank the reviewer for the valuable comment. In our study, two patients needed additional SEMS to seal the fistula. The following images are bronchoscopy images of patient 3, 5, and 10. We can see that the left main bronchus of patient 3 has been penetrated by the esophageal metal stent, causing obstruction of the lumen. If the esophageal stent is not removed, it is difficult to place airway stent. And if the airway stent is not placed, the fistula cannot be sealed, because the fistula itself is caused by the esophageal stent. If the esophageal stent is continued to be retained, it may lead to further enlargement of the fistula just like the following picture of patient 10.

Patient 3



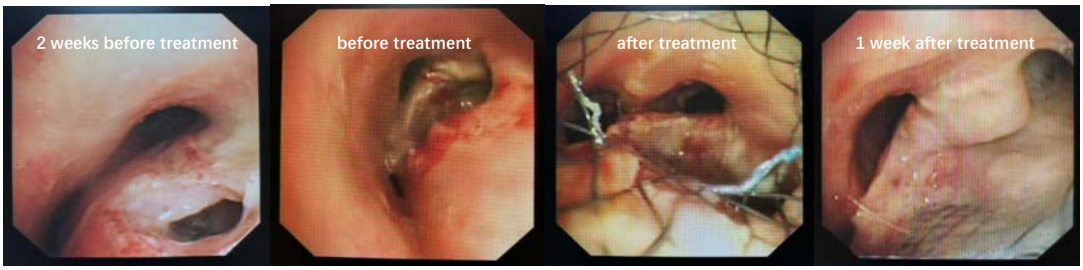
The following is the case with patient 5, where the esophageal stent has broken through the carina, spanning the left and right main bronchus. The carina and the right main bronchus are missing. If we directly place a Y silicone stent without removing the esophageal stent, the esophageal stent will affect the placement of the airway stent and affect the effectiveness of the procedure. The result will be that both airway stent and the esophageal stent cannot effectively seal the fistula. Therefore, the esophageal stent must be removed. Since the stress of the silicone stent is concentrated at the carina and the edge of the stent. We combine the Y silicone stent with a SEMS to extend the edge of the stent, reduce the stress on the fistula edge, and reduce the stimulation of the stent edge on the fistula, transferring stress to a distant location. Because

Patient 5



The counterexample is Patient 10, where a SEMS was placed in the trachea without removal the indwelling esophageal stent. Both SEMS and the esophageal stent cannot seal the fistula effectively. The pneumonia was not under control. He passed away soon after the procedure.

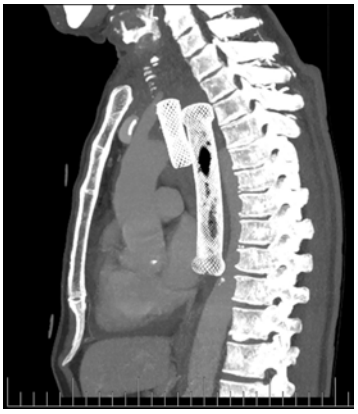
Patient 10

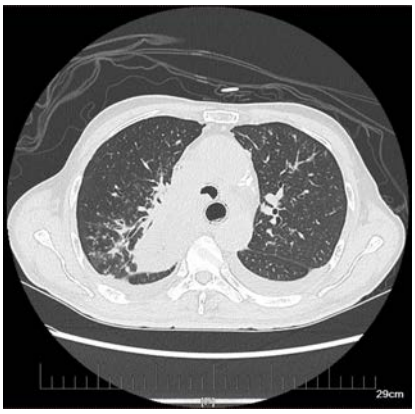


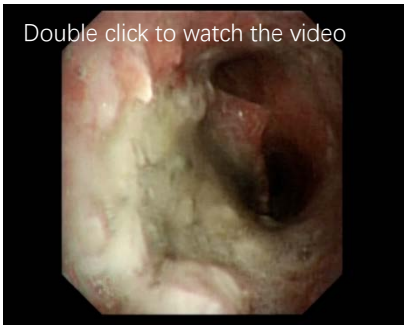
Changes in the text: We have modified our text as advised (Page 6, Line 153-155; Page 10-11, Line 275-292; Page 11, Line 310-316)

Comment 3: The advantages reported by you in using this procedure are rather subjective (e.g: quality of life assessed only by the Karnofsky Performance Score) and in any case not comparable to those obtained with double stenting, as there is no control group. Have you treated any patients with an esophagorespiratory fistula with double stenting? If yes, you could use that group of patients as control group.

Reply 3: Thank the reviewer for the valuable comment. As the reviewer pointed out, it is important to compare the findings of this study with double stent treatment to enhance the persuasiveness. During the study period, a total of 3 patients in our center underwent double stent treatment. We found that patients underwent double stent treatment had poorer control over pneumonia compared to those in the esophageal stent removal group. In addition, the survival time in the esophageal stent removal group was much longer than that in the double stent group. Previous studies suggested that for patients with ERF, the longest survival time is achieved by double stents treatment. But the population included in our study is different from the pure ERF population. For patients who develop ERF with indwelling esophageal stents, the esophageal stent is already a key triggering factor for ERF. If not removed, it will continue to worsen the occurrence of fistulas. Patient 9 is a typical example. When we place double stents, we hope that the two stents can precisely seal the position of the fistula while minimizing the antagonistic pressure on the tissue outside the fistula. In this way, the two stents need to be as parallel as possible to reduce angularity. However, this is an idealized idea that is difficult to achieve. Both the esophagus and trachea are active, after long-term swallowing and coughing, the two stents are easily angled, increasing pressure on the tissue, and leading to the occurrence of new fistulas. In addition, under the premise that there is already a stent in the esophagus, the placement of the tracheal stent will be limited, and the position of the tracheal stent will be difficult to achieve the expected state, which will affect the sealing effect of the fistula and thus affect the treatment effect. (see video 6)







Changes in the text: We have modified our text as advised (see Page 2-3, Line 47-67; Page 5, line 116-121; Page 7-9, Line 196-242; Table 1, 2, 3; Figure 3, 4)

Comment 4: As inclusion criteria you reported “esophageal stent incarceration cannot be removed by digestive endoscopy or surgery”. How then can you claim that it is safe to remove the stent with the rigid bronchoscope? Please add a comment.

Reply 4: Thank the reviewer for the valuable suggestions. Indeed, the writing “esophageal stent incarceration cannot be removed by digestive endoscopy or surgery” can cause unnecessary ambiguity and give people an illusion that we can solve any situation that cannot be solved by digestive endoscopy or surgery. We have deleted this sentence from the manuscript. The main message we want to convey is that removing stents through rigid endoscope is a safe and mature technology that has been used for many years. But according to our observation, rigid endoscope is rarely used in digestive endoscopy nowadays, at least in our center and our domestic digestive endoscopy centers. Those stents without too much tissue embedding are relatively easy to remove by a soft endoscope. However, those esophageal stents that are embedded with a large amount of tissue were hard to be removed by soft endoscope. The average indwelling time of the esophageal stents in our study is 95 days, which is longer than most recommendations of 10-12 weeks. The stents were embedded with a large amount of tissue, which were hard to be removed by soft endoscope. The force of the soft endoscope is not enough to twist and pull the stents out. And the space for manipulation is limited. Soft endoscope can only perform simple rotation and traction on the edge of the stents. It is difficult to finely separate the contact between the stent and the esophageal wall for soft endoscope, which can easily cause unexpected tearing of the esophageal wall. Compare with the soft endoscope, rigid bronchoscope can implement greater traction force. The stent can be gradually folded from proximal to distal, and then the sheath of the rigid endoscope can be inserted to separate the esophageal stent from the esophageal wall, making the separation between the stent and the esophageal wall more controllable and reducing the risk of tearing the esophagus.

Changes in the text: We have modified our text as advised (see Page 5, Line 135-137)