

Peer Review File

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Reviewer A

Comment 1: There are other studies describing the technique reported by the authors. It is not clear what would be new to the proposed procedure.

Reply1: Thank you for your careful reading of our manuscript. We admit that the technique described in the present study has been reported in previous literatures. Zhang *et al* [1] reported a case of a patient, and Zhao *et al* [2] reported three cases of patients, who underwent simultaneous resection of synchronous esophageal and gastric cancers. Considering the small number of cases in previous studies, the safety of the proposed surgical procedure, in which part of the proximal stomach was preserved, has not been clearly verified. In addition, due to the rare incidence and diagnosis of these patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers, the proposed surgical procedure was rarely performed in clinical practice. Given above reasons, we tend to think that the proposed surgical procedure might be considered as a new surgical procedure.

1. Zhang, X.T., et al., *Treatment of esophageal-gastric double primary cancer by pedunculated remnant gastric interposition, esophageal-gastric anastomosis and gastrojejunal Billroth II anastomosis: A case report*. *Oncol Lett*, 2015. **10**(2): p. 891-894.
2. Zhao, Y. and B. Cong, *A new surgical procedure for synchronous esophageal squamous cell carcinoma and gastric adenocarcinoma: Case report: three cases reports*. *Medicine (Baltimore)*, 2019. **98**(9): p. e14725.

Comment 2: The authors reported a morbidity rate of 46%, similar to other studies with colon interposition or small bowel interposition for esophageal reconstruction. What should be better with this technique. How about the quality of life after this procedure?

Reply2: Thank you for the valuable comment. According to a previous study [3], among patients who underwent total gastrectomy, 63.4% in the colon group and 45.5% in the jejunum group experienced major complications. In another study with colon interposition for esophageal reconstruction [4], pneumonia occurred in four patients (19.0%) and anastomotic leakage was observed in five patients (23.8%). In the present study, postoperative complications occurred in eight patients and accounted for 44.4% of all patients. Pneumonia occurred in one patient (5.6%) and anastomotic leakage was observed in four patients (22.2%). Although the complications, including hydrothorax, gastric retention and pneumonia, were observed postoperatively in the present study, they were less severe and more treatable illnesses.

Colon interposition and jejunal interposition for esophageal reconstruction were also performed by our team. However, the number of cases is still relatively modest, and these patients are more likely to have poor postoperative quality of life because of suffering postoperative ileus and dyspepsia, which may be due to the changes of digestive tract especially the loss of stomach. Compared with traditional surgical procedure with colon or small bowel interposition for esophageal reconstruction, the proposed surgical procedure

preserves part of proximal stomach, which is conducive to the food digestion. Therefore, this surgical procedure seems to induce a lower depression of digestion physiology function compared with alimentary tract reconstruction using colon or jejunum. However, due to our inadequate consideration in the retrospective study, indicators reflecting the nutritional status of patients, such as body fat indexes, triceps skinfold thickness and serum albumin, were not completely recorded during follow-up period. We are sorry for the absence of those missing data in the present study. In the following studies, we will pay more attention to the postoperative quality of life of patients receiving esophagectomy. We are sorry for the imperfection in the current study, and the discussion of this short point was added in the section of “Discussion”. (see Page 7, line 271-277)

3. Park, B., et al., *Simultaneous Resection of Synchronous Esophageal and Gastric Cancers*. Thorac Cardiovasc Surg, 2016. **64**(7): p. 611-618.
4. Saeki, H., et al., *Esophageal replacement by colon interposition with microvascular surgery for patients with thoracic esophageal cancer: the utility of superdrainage*. Dis Esophagus, 2013. **26**(1): p. 50-6.

Comment 3: The main problem of the study is the comparison between the “new technique” proposed by the authors and different techniques performed by other groups. The patients are different as the diagnosis previously to the procedure. The authors make it seem that it is possible to make a case-control comparison between techniques, but the heterogeneity of the populations studied was not considered.

Reply3: Thank you for the valuable comment. We admit that it is inapposite to make a comparison between the surgical procedure in the present study and different techniques performed by other groups. Considering heterogeneity of the populations and surgeons from different medical centers, the results of comparison between techniques are not compelling. However, due to the rare incidence and diagnosis of patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers in last decades, it is hard to conduct a prospective clinical study. In addition, total gastrectomy was always performed in these patients, and the colon or jejunum has been frequently used as an esophageal substitute. Thus, the surgical procedure in the present study was rarely performed in clinical practice. Between July 2012 and December 2021, only 18 patients who underwent the proposed surgical procedure were enrolled in the retrospective study. With the increasing number of cases, we may make a comparison between the surgical procedure and surgery with colon or small bowel interposition for esophageal reconstruction in our following studies.

Comment 4: Finally, the authors proved that the technique is feasible. However, it is not clear what are the advantages. A paragraph with study limitations is needed. The conclusion should be softened.

Reply4: Thank you for the valuable comment. With advances and developments in sophisticated detection methods, especially endoscopic techniques for upper gastrointestinal tumors, an increasing number of patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers have been diagnosed in recent years. Total gastrectomy was always performed in these patients, and the colon or jejunum has been frequently used as

an esophageal substitute. We do not deny the applicability of these surgical procedures. In the present study, the in-hospital morbidity rate was 44.4% (n=8) and the mortality rate was 5.6% (n=1). The surgical procedure yielded a lower morbidity rate and, at the same time, not a higher mortality rate, compared with alimentary tract reconstruction using the colon or jejunum reported in other studies. Our study aims to provide another treatment option for selected patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers. And the surgical procedure might be a new treatment option for these selected patients, especially those with previous history of intestinal surgery. We have modified our manuscript as advised and a paragraph with study limitations was added in the section of "Discussion". (see Page 6-7, line 263-277) And the conclusion was softened, which is shown in the section of "Conclusion". (see Page 7, line 282-284)

Reviewer B

Comment: This is a unique and interesting technique. Given the technical challenges of preserving the right gastroepiploic and making a tubular stomach and a gastrojejunostomy, more pictures or cartoon diagrams would be helpful. Does the gastroj go to the posterior gastric conduit? How do you ensure the right gastroepiploic is not injured with the distal gastrectomy? Do you confirm with ICG or another modality or just visualize?

Reply: We are grateful for your effort reviewing our manuscript and your positive feedback. The technique described in the present study has been reported in previous literatures. Zhang *et al* [1] reported a case of a patient, and Zhao *et al* [2] reported three cases of patients, who underwent simultaneous esophagectomy and distal gastrectomy. The cartoon diagram has been shown in figure 3 in previous study [2]. Considering the small number of cases in previous studies, the safety of the surgical procedure, in which part of the proximal stomach was preserved, has not been clearly verified. This study aims to evaluate the technical feasibility of the surgical procedure and provide another treatment option for selected patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers.

Sorry for that we are not clear about the mean of "Does the gastroj go to the posterior gastric conduit?" A gastrojejunostomy anastomosis was performed in the distal residual stomach. A part of small bowel, along with the tubular stomach and right gastroepiploic artery were in the right direction when sent to the esophageal mediastinal bed.

After the distal gastrectomy, a tubular stomach was formed when the lesser curvature of the stomach tissue was removed. The pulse wave was observed and palpated to ensure that right gastroepiploic artery is not injured. In addition, the color of the tubular stomach was observed to ensure its blood supply.

1. Zhang, X.T., et al., *Treatment of esophageal-gastric double primary cancer by pedunculated remnant gastric interposition, esophageal-gastric anastomosis and gastrojejunal Billroth II anastomosis: A case report*. *Oncol Lett*, 2015. **10**(2): p. 891-894.
2. Zhao, Y. and B. Cong, *A new surgical procedure for synchronous esophageal squamous cell carcinoma and gastric adenocarcinoma: Case report: three cases reports*. *Medicine (Baltimore)*, 2019. **98**(9): p. e14725.

Additional comments:

Comment 1: You state “each patient had at least 1 complication,” that is a postop morbidity rate of 100%? How did you calculate 44.4%

Reply1: We are sorry for this typographical error. Ten of eighteen patients recovered well without any complications. Each of other eight patients experienced at least 1 complication, corresponding to an overall postoperative morbidity rate of 44.4%. We have corrected it in the manuscript. (see Page 5, line 179-180)

Comment 2: Do you have more data on gastric margins? It seems to make a gastric conduit; you would have minimal margins?

Reply2: In the present study, gastric cancer was located in the antrum in all patients. Distal gastrectomy was performed with a resection margin > 5 cm from the gastric cancer tissue. No gastric cancer cells were observed in intraoperative rapid frozen sections of the gastric margins. And no positive margins were found in paraffin-embedded tissue. The tubular stomach was formed by greater curvature of proximal stomach.

Comment 3: Only 1 patient received neoadjuvant therapy which is not standard of care for the stages listed. Why was no preop therapy given for either the gastric or esophageal cancer? And what was the final pathology?

Reply3: Thank you for your careful reading of our manuscript. Among 18 patients in the present study, one received preoperative chemoimmunotherapy with four cycles of pembrolizumab in combination with paclitaxel and cisplatin in a local hospital. (The data was added in the manuscript, see page 4, line 159-160) The patient was diagnosed with synchronous thoracic lower segment esophageal squamous cell carcinoma and gastric antrum adenocarcinoma during the first endoscopy. The postoperative pathology showed that fibrous tissue proliferated in esophageal with inflammatory cell infiltration, and small foci moderate dysplasia in gastric mucosa, and no cancer cells were found in resected specimens. China has a vast territory and a large population, with medical resources being limited in many parts of the country. There are still many patients who cannot receive standard of care, especially in impoverished areas. We believe that this situation will improve significantly with the development of our country.

The other 17 patients were also diagnosed with synchronous thoracic middle-lower segment esophageal and distal gastric cancers during the first endoscopy in local hospitals. They came to our hospital for further treatment. Neoadjuvant concurrent chemoradiotherapy has been recommended as the standard of care for resectable locally advanced esophageal cancer by NCCN, CSCO and other guidelines. While, considering the nutritional status of these patients who were intolerance of concurrent chemoradiotherapy, the operative risk increased by neoadjuvant therapy, and the lacking of clinical guidelines for the management of patients with synchronous esophageal and gastric cancers, there were no preoperative therapies given. Surgery followed by adjuvant therapy was the main treatment strategy in the People’s Republic of China several years ago, and adjuvant chemotherapy was recommended to patients with positive lymph nodes after surgery. In addition, our previous study showed that the cumulative OS rates at 5 years was 63% in patients with thoracic middle-lower segment esophageal squamous cell carcinoma who underwent upfront surgery followed by

adjuvant therapy [3]. The result is consistent in that of the Japan Clinical Oncology Group 9204 study [4], and it seems to be better than that in those of the Japan Clinical Oncology Group 9907 study, which proved better survival of preoperative chemotherapy over postoperative chemotherapy (55% versus 43%, respectively) [5]. Given above reasons, there were no preoperative therapies given in the other 17 patients.

3. Li, B., et al., *Esophagectomy With Three-Field Versus Two-Field Lymphadenectomy for Middle and Lower Thoracic Esophageal Cancer: Long-Term Outcomes of a Randomized Clinical Trial*. J Thorac Oncol, 2021. **16**(2): p. 310-317.
4. Ando, N., et al., *Surgery plus chemotherapy compared with surgery alone for localized squamous cell carcinoma of the thoracic esophagus: a Japan Clinical Oncology Group Study--JCOG9204*. J Clin Oncol, 2003. **21**(24): p. 4592-6.
5. Ando, N., et al., *A randomized trial comparing postoperative adjuvant chemotherapy with cisplatin and 5-fluorouracil versus preoperative chemotherapy for localized advanced squamous cell carcinoma of the thoracic esophagus (JCOG9907)*. Ann Surg Oncol, 2012. **19**(1): p. 68-74.

Comment 4: You quote this as being safer than a colon or jejunal interposition. However, the results suggest similar morbidity and mortality with worse margins. What is the reason for doing this procedure?

Reply4: Thank you for the valuable comment. The colon or jejunum is commonly used as an esophageal substitute for total gastrectomy. The morbidity and mortality rates of the proposed surgical procedure (44.4% and 5.6%) in the present study are similar to other studies with colon interposition (63.4% and 2.4%) or jejunal interposition (45.5% and 9.1%) for esophageal reconstruction. Although the complications, including hydrothorax, gastric retention and pneumonia, were observed postoperatively in the present study, they were less severe and more treatable illnesses. Among 18 patients, only one had a microscopic remnant tumor at the upper esophageal resection margin, which was confirmed by postoperative pathology. Considering the high operative risk and bad nutritional status, the patient was recommended postoperative local radiotherapy. Colon and jejunal interposition for esophageal reconstruction were also performed by our team. However, the number of cases is still relatively modest, and these patients are more likely to have poor postoperative quality of life because of suffering postoperative ileus and dyspepsia, which may be due to the changes of digestive tract especially the loss of stomach. Compared with traditional surgical procedure with colon or jejunal interposition for esophageal reconstruction, the proposed surgical procedure preserves part of proximal stomach, which is conducive to the food digestion. Therefore, this surgical procedure seems to induce a lower depression of digestion physiology function compared with alimentary tract reconstruction using colon or jejunum. Our study aims to provide another treatment option for selected patients with synchronous thoracic middle-lower segment esophageal and distal gastric cancers. And this surgical procedure might be a new treatment option for these selected patients, especially those with previous history of intestinal surgery. We have modified the section of “Conclusions” in the manuscript and a paragraph with study limitations was added in the section of “Discussion”. (see Page 6-7, line 263-284)