



End-to-End Versus End-to-Side Hand-Sewn Anastomosis for Minimally Invasive McKeown Esophagectomy

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ABSTRACT

Background. Standard anastomotic configuration for esophagogastric anastomosis is not conclusive. This study aimed to compare the short-term outcomes of end-to-end (ETE) cervical double-layer hand-sewn anastomoses with those of end-to-side (ETS) anastomoses for minimally invasive McKeown esophagectomy.

Methods. Between January 2016 and December 2017, the clinical data of 252 consecutive patients who underwent minimally invasive esophagectomy were reviewed retrospectively. The 252 patients comprised 130 patients in the ETS group and 122 patients in the ETE group. The same surgical procedures were applied in both groups, except for esophagogastric reconstruction. Short-term outcomes including leakage, stricture, reflux, operative features, and other surgical complications were analyzed for a comparison of the two configurations.

Results. The ETS and ETE groups did not differ significantly in terms of leakage rate ($P = 0.34$), anastomotic stricture rate ($P = 0.70$), or postoperative reflux ($P = 0.66$). However, the ETS group had a longer operation time ($P = 0.011$), a longer anastomosis time ($P < 0.001$), and a longer postoperative hospital stay ($P = 0.009$) than the ETE group, and the postoperative gastric dilation rates were lower in ETE group than in the ETS group

($P = 0.025$). The two groups did not differ significantly in terms of other postoperative complications.

Conclusions. The major postoperative complications were comparable for the two anastomotic configurations. However, the patients with ETE anastomosis showed a favorable outcome in terms of a decreasing postoperative thoracic gastric dilation rate. End-to-end anastomosis also seemed to have slight advantages in terms of shorter operation and anastomosis times as well as a shorter postoperative hospital stay.

Esophagectomy followed by esophagogastrectomy involving resection of tumor and relevant lymph nodes has been established as the most important treatment for esophageal cancer when surgical resection is indicated.^{1,2} However, postoperative complications such as anastomotic leakage, benign stricture, and pneumonia still occur frequently and contribute to significant mortality, morbidity, and reduced quality of life.³

Independently of what substitution is used for reconstruction, a wide range of anastomotic techniques has been applied for esophageal anastomosis including hand-sewn suture, semi-mechanical suturing, and circular or linear stapling, with different types of anastomotic configurations (end-to-end, side-to-side, or end-to-side). The various types of anastomotic techniques have their own merits and drawbacks, and the best procedure has not been established.^{4,5} Furthermore, performing an anastomosis is a technical matter, and anastomotic complications are related to the personal experience and skills of the surgeon,⁶ which should be refined and optimized to reduce the risk of postoperative complications.

At our institution, we usually construct a modified end-to-side (ETS) double-layer hand-sewn anastomosis, and it has proved to be very safe for both intrathoracic and cervical

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anastomosis.⁷ We had conducted a retrospective study comparing one-layer anastomosis with double-layer anastomosis using ETS configuration. Our findings showed that the anastomotic leakage rates were 5.8% and 0%, respectively. The anastomosis stricture rate also was significantly decreased in the double-layer anastomosis group.⁶

However, ETS anastomosis has its disadvantages, such as a longer operation time and a longer gastric tube needed for reconstruction compared with end-to-end (ETE) anastomosis. The longer gastric tube leaves a longer ischemic proximal end with an additional risk for dehiscence of the distal gastric stump (Fig. 1).⁸ This leads us to consider using ETE anastomosis for cervical esophagogastronomy, which might overcome these shortcomings. Nevertheless, the standard and optimal anastomotic configuration for esophagogastric reconstruction is not conclusive, and studies are very limited.^{6,8,9}

No study has compared ETE with ETS anastomosis using the hand-sewn double-layer technique for esophagectomy. This study aimed to analyze the short-term outcomes of double-layer hand-sewn ETE versus ETS cervical anastomoses for patients undergoing minimally invasive McKeown esophagectomy (MIE) for esophageal cancer.

METHODS

Patients

This study reviewed 252 consecutive patients who underwent MIE with cervical double-layer hand-sewn

anastomosis, including 130 patients who underwent ETS anastomosis from January 2016 to December 2016 and 122 patients who underwent ETE anastomosis from January 2017 to December 2017. This study was approved by the Institutional Review Board of West China Hospital, and informed consent was obtained from all the patients.

All the surgical procedures were performed by surgeons from the same group in the department of thoracic surgery. The esophageal cancer staging was determined according to the Union for International Cancer Control (UICC) classification, 7th edition.

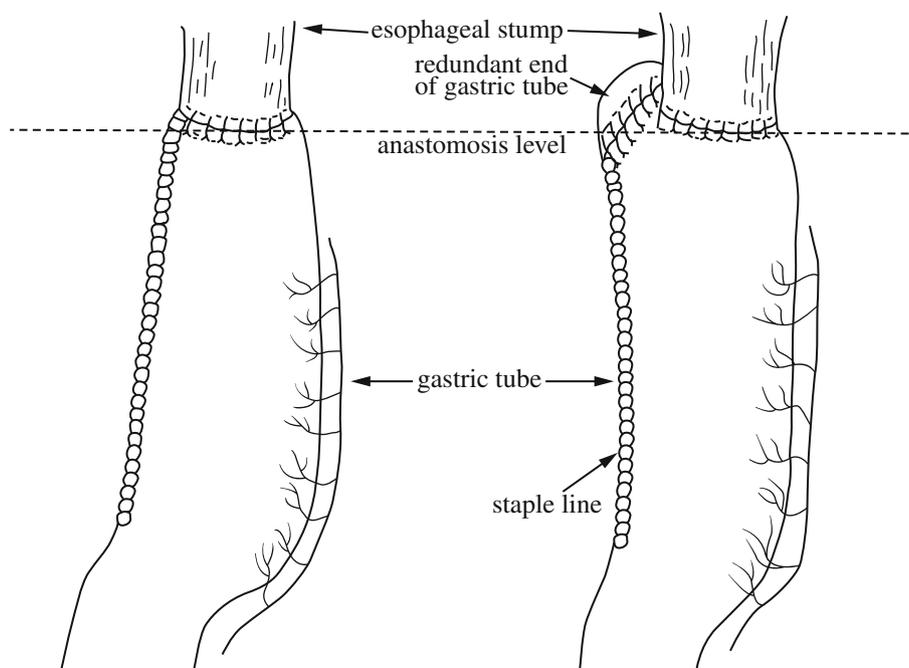
The inclusion criteria for this study required a pathologic diagnosis of esophageal carcinoma, performance of the minimally invasive McKeown esophagectomy procedure, completion of left cervical esophagogastric reconstruction by hand-sewn double-layer anastomosis, and use of the posterior mediastinal route for reconstruction. The exclusion criteria ruled out unresectable lesions or residual tumor at the esophageal stump after surgery, prior gastric surgery, and concurrent gastric cancer.

Surgical Procedures

All the patients in the study underwent the same procedures for right thoracoscopic esophagectomy and laparoscopic mobilization of the stomach except for the esophagogastric anastomosis. The esophagogastric anastomosis was performed via the hand-sewn double-layer technique with ETE or ETS configuration.

To perform ETE anastomosis, the tip of the gastric tube was tailored into a “cone shape” to fit the esophageal

FIG. 1 Demonstration of end-to-end (left) and end-to-side (right) configurations



lumen (Fig. 2a). The tip of the gastric tube and the esophageal stump were clamped together to facilitate reconstruction by using a three-leaf clamp. The gastric tube wall then was divided into a seromuscular layer and a mucosal layer, and the esophageal wall was scissored into a muscular layer and a mucosal layer to complete a double-layer anastomosis (Fig. 2a). As the posterior side of the outer layer, the seromuscular layer of gastric tube and the muscular layer of esophagus were sutured with interrupted 5-0 silk threads (Fig. 2b). Next, the mucosal layers of the gastric tube and the esophagus were incised, appearing as the mucosal lumen of the anastomosis. As the inner layer of the anastomosis, the mucosal layers of esophagus and stomach were sutured with a continuous suture using 4-0 antibacterial Vicryl from the posterior to anterior side at 4-mm intervals (Fig. 2c). Finally, the anterior muscular layer of the esophagus and the seromuscular layer of the stomach, as the anterior outer layer of the anastomosis, were closed by interrupted 5-0 silk threads, and the three-leaf clamp was removed for completion of the hand-sewn double-layer anastomosis (Fig. 2d).⁷

For ETS anastomosis, the tip of the gastric tube was transected by a linear stapler, and the stapling line was enhanced by interrupted sutures (Fig. 3a). The anterior wall of the gastric tube was chosen for ETS anastomosis. Two stitches were placed on the anterior wall of the gastric tube, located about 3 cm away from the transected line of the gastric tube and serving as the center point for the

anastomotic orifice of the stomach (Fig. 3a). Next, the anterior wall of the gastric tube and the esophagus stump were fixed by a three-leaf clamp and divided into two layers successively as the ETE anastomosis (Fig. 3b). The procedures of ETS anastomosis were the same as those of the ETE method (Fig. 3b-d).⁷ The pyloroplasty was not applied after anastomosis, and the nasoduodenal nutrition tube or jejunostomy tube was not implanted during the operation.

Postoperative Management and Follow-Up Evaluation

The postoperative nutrition was supported by total parenteral nutrition. A nasogastric tube was placed as gastric drainage only when severe thoracic gastric dilation was evident by chest x-ray on postoperative day 1 (POD 1). The patient initiated oral feeding with water on POD 5 and a liquid diet on POD 6 if no signs of anastomotic leakage were observed. Oral feeding then was continued gradually with a semi-liquid diet, and a soft diet was initiated on POD 9. If no signs of leakage or other complications were observed, the patients were discharged to home without any tube on POD 9-10. After discharge from the hospital, they received oral feeding totally, and a regular diet was resumed on POD 21.

Postoperative follow-up visits were scheduled at 1, 4 months, and then every 6 months thereafter, and the diameter of anastomosis was measured at the anterior

FIG. 2 End-to-end double-layer hand-sewn anastomosis. **a** The “cone-shape” tip of the gastric tube was pulled out to the left neck. **b** The gastric tube and the esophagus stump were fixed by a three-leaf clamp. The posterior side of the outside layer (muscular layer of the esophageal stump and seromuscular layer of the gastric tube) for the anastomosis was sutured with interrupted sutures. **c** The inner layer (mucosal layers of the esophagus and stomach) for the anastomosis was sutured with continuous sutures. **d** The anterior side of the outside layer of the outside layer was sutured with interrupted sutures

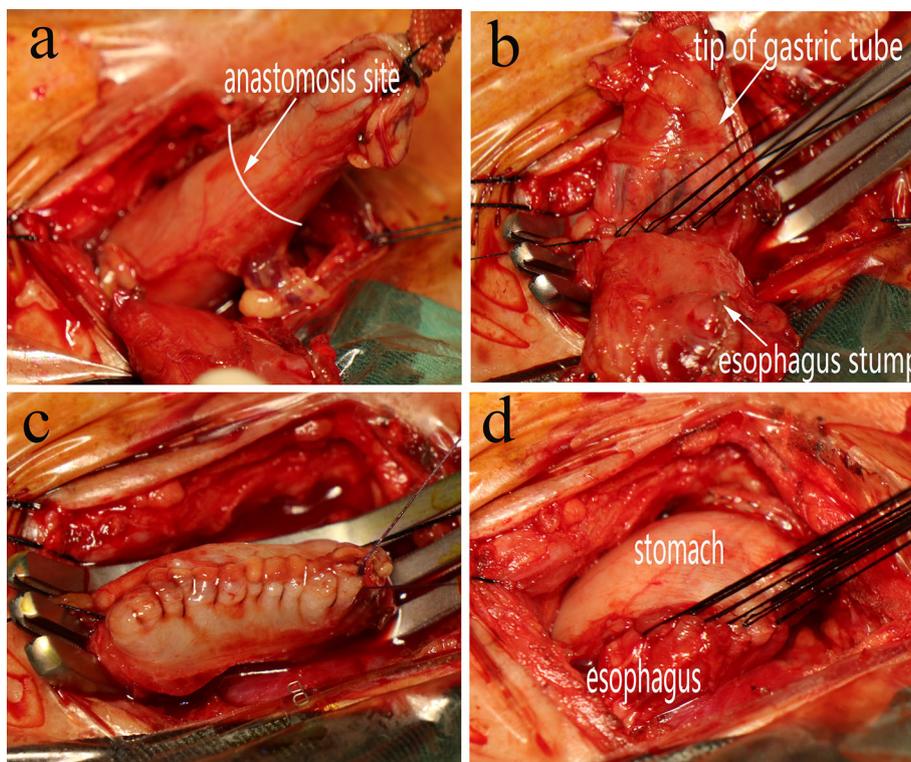
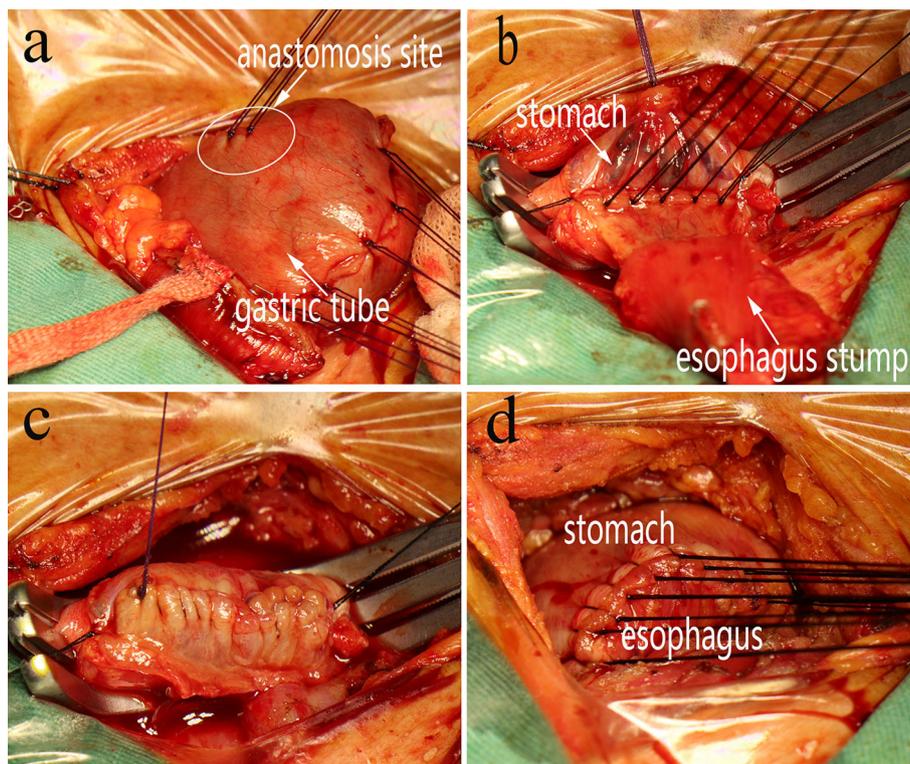


FIG. 3 End-to-side double-layer hand-sewn anastomosis. **a** The tip of the gastric tube was transected, and the stapling line was enhanced by interrupted sutures. Two stitches were placed on the anterior wall of the gastric tube as the center point for the anastomotic orifice of the stomach. **b** The anterior wall of the gastric tube and the esophagus stump were fixed by a three-leaf clamp. The posterior side of the outside layer (muscular layer of the esophageal stump and seromuscular layer of the gastric tube) for the anastomosis was sutured with interrupted sutures. **c** The inner layer (mucosal layers of the esophagus and stomach) for the anastomosis was sutured with continuous sutures. **d** The anterior side of the outside layer was sutured with interrupted sutures



position on a barium esophagram image at the 1-month follow-up visit.

Outcome Measures

Patient clinical characteristics and short-term outcomes were reviewed. The primary outcomes of this study were surgery-related complications such as leakage, benign stricture, vocal cord paralysis, chylothorax, gastric dilation, gastroesophageal reflux, pneumonia, and cardiac complications. The complications were described according to the Clavien-Dindo (CD)¹⁰ and Esophagectomy Complications Consensus Group (ECCG) classifications.^{11,12}

The secondary outcomes were operation parameters such as operative time, blood loss, lymph nodes retrieved, and postoperative hospital stay. “Anastomotic stricture” was defined as reported dysphagia with endoscopic and/or barium esophagram evidence of stricture (the anastomosis diameter was < 0.8 cm) but no tumor recurrence at anastomosis. Intrathoracic gastric dilation was evaluated by chest X-ray examination on POD 1. Diagnosis of severe dilation could be determined when the widest part of the gastric tube was larger than 6 cm.

Statistical Analysis

Comparative statistical analysis was performed using SPSS statistics software (IBM SPSS Statistics for

Windows, version 19.0; IBM Corp., Armonk, NY). Continuous variables were expressed as mean \pm standard deviation or median with 25th and 75th percentiles (P_{25} – P_{75}), and the differences between the groups were analyzed with Welch’s unequal variances two-sample *t* test or the Wilcoxon rank-sum test. Categorical variables were expressed as counts and percentages, and comparisons between groups were performed using the Chi square test or Fisher’s exact probability test. The correlation between categorical variables, including leakage and stricture, leakage and gastric dilation, was analyzed with Spearman’s correlation analysis. All tests were two-sided, and *P* values lower than 0.05 were considered statistically significant.

RESULTS

The most common histologic type was squamous cell carcinoma (98%, 247/252). The patients’ clinical and pathologic characteristics are presented in Table 1. No statistically significant differences were found between the two groups.

The operative features and short-term surgical complications of the patients are presented in Table 2. The operative time was slightly longer in the ETS group than in the ETE group (243 ± 43 vs. 229 ± 49 min; $P = 0.011$), as were the anastomosis time (33 ± 1 vs. 27 ± 1 min; $P < 0.001$) and the postoperative hospital stay (median,

TABLE 1 Demographic and clinical characteristics of the patients

General statistics	ETS group (<i>n</i> = 130), <i>n</i> (%)	ETE group (<i>n</i> = 122), <i>n</i> (%)	<i>P</i> value
Gender			0.240
Male	99 (76.2)	89 (73.0)	
Female	31 (23.8)	33 (27.0)	
Mean age (years)	62.8 ± 8.0	61.4 ± 8.2	0.161
Mean BMI (kg/m ²)	22.2 ± 3.0	22.6 ± 2.9	0.252
Smoking history	85 (65.4)	75 (61.5)	0.519
Drinking history	75 (57.7)	78 (63.9)	0.311
Diabetes	5 (3.8)	11 (9.0)	0.093
Hypertension	14 (10.8)	22 (18.0)	0.100
Pulmonary disease history	19 (14.6)	11 (9.0)	0.170
Heart disease	12 (9.2)	9 (7.4)	0.595
Pathology			0.623
Squamous cell carcinoma	127 (97.7)	120 (98.4)	
Adenocarcinoma	2 (1.5)	2 (1.6)	
Small cell carcinoma	1 (0.8)	0 (0)	
Pathologic staging (TNM)(TNM)			0.967
0	2 (1.5)	1 (0.8)	
1	27 (20.8)	25 (20.5)	
2	41 (31.5)	40 (32.8)	
3	55 (42.3)	53 (43.4)	
4	5 (3.8)	3 (2.5)	
Tumor location			0.385
Upper	21 (16.2)	15 (12.3)	
Middle	89 (68.5)	81 (66.4)	
Lower	20 (15.4)	26 (21.3)	
Neoadjuvant therapy	19 (14.6)	17 (13.9)	0.877

ETS end-to-side anastomoses, ETE end-to-end anastomoses, BMI body mass index, TNM tumor-node-metastasis classification of malignant tumors

10 days [P₂₅–P₇₅, 9–14 days] vs 10 days [P₂₅–P₇₅, 9–11 days]; *P* = 0.009). Other surgical features did not differ significantly.

Anastomosis leakage (ECCG type 2) occurred for five patients (3.85%) in the ETS group (*n* = 130) and three patients (2.46%) in the ETE group (*n* = 122), with the difference not reaching statistical difference (*P* = 0.72). Two patients in the ETS group had gastric stump necrosis (ECCG type 1). No gastric tube necrosis was identified in the ETE group.

Seven patients in the ETS group and three patients in the ETE group experienced gastrointestinal leakage, either anastomotic leakage or gastric tube necrosis. All the patients with leakage were managed by nonsurgical therapy including drainage from the cervical incision and/or chest, enteral nutrition through a naso-duodenal tube implanted by endoscopy, and anti-infection by antibiotics. The mean time for leakage healing was 17 days (range

10–45 days). Three of the eight patients with anastomosis leakage experienced late stricture (CD grade 3A), including one case in the ETE group and two cases in the ETS group.

After a mean follow-up period of 22 months and a minimum follow-up period of 10 months, benign anastomotic strictures (CD grade 2–3A) developed in seven ETE patients (5.7%, 7/122), whereas stricture was found in nine ETS patients (6.9%, 9/130). The difference between the groups did not reach statistical significance (*P* = 0.70). Dysphagia was observed in two ETE patients and four ETS patients about 1 month after surgery. The remaining patients reported dysphagia approximately 3 months postoperatively.

The patients with stricture classified as CD grade 3A were managed by repeated endoscopic dilations. Of four ETS patients who underwent endoscopic dilation, three had complete remission after two to four cycles of endoscopic

TABLE 2 Surgical features and short-term surgical outcomes of the patients

General statistics	ETS group (<i>n</i> = 130) <i>n</i> (%)	ETE group (<i>n</i> = 122) <i>n</i> (%)	<i>P</i> value
Mean operation time (min)	243 ± 43	229 ± 49	0.011
Median blood loss: ml (P ₂₅ –P ₇₅)	50 (40–60)	50 (40–60)	0.054
Mean anastomoses time (min)	33 ± 1	27 ± 1	< 0.001
Median no. of lymph nodes (P ₂₅ –P ₇₅)	18 (14–24)	19 (15–25)	0.128
Gastrointestinal leakage	7 (5.38)	3 (2.46)	0.336 ^a
Anastomotic leak (ECCG type 2)	5 (3.85)	3 (2.46)	0.723 ^a
Conduit necrosis (ECCG type 1)	2 (1.5)	0 (0)	1.000 ^a
Mean anastomoses diameter (cm)	1.2 ± 0.3	1.2 ± 0.4	0.998
Anastomotic stricture	9 (6.92)	7 (5.74)	0.700
CD grade 2	5 (55.6, <i>n</i> = 9)	4 (57.1, <i>n</i> = 7)	0.949
CD grade 3A	4 (44.4, <i>n</i> = 9)	3 (42.9, <i>n</i> = 7)	
Severe gastric tube dilation	17 (13.1)	6 (4.9)	0.025
Reflux	98(75.4)	89(73.0)	0.659
CD grade 1	80 (61.6)	77 (63.2)	0.796
CD grade 2	18 (13.8)	12 (9.8)	0.326
Vocal cord injury (ECCG type 1A)	14 (10.8)	8 (6.6)	0.237
Arrhythmia (CD grades 1–2)	9 (6.9)	5 (4.1)	0.328
Pneumonia (CD grades 1–2)	14 (10.7)	9 (7.4)	0.350
Chylothorax (ECCG type 2A)	1 (0.8)	0 (0)	1.000 ^a
90-Day and in-hospital mortality	0	0	
Median postoperative hospital stay: days (P ₂₅ –P ₇₅)	10 (9–14)	10 (9–11)	0.009

ETS end-to-side anastomoses, ETE end-to-end anastomoses; P₂₅–P₇₅ 25th–75th percentiles, CD Clavien-Dindo classification, ECCG Esophagectomy Complications Consensus Group

^aFisher's exact test

dilation, and one had recurrence stricture after three endoscopic dilation procedures in 3 months and received three additional cycles of endoscopic dilation. Of three ETE patients who underwent endoscopic dilation, two had complete remission after three or four cycles of endoscopic dilation, and one had recurrent stricture after three endoscopic dilation procedures in 4 months and finally underwent two additional cycles endoscopic dilation.

During the follow-up period, no patient had delayed leakage, anastomotic tumor recurrence, or reflux aggravation. No statistically significant differences with regard to other postoperative complications were observed including reflux, vocal cord injury, arrhythmia, chylothorax, and pneumonia. No 90-day or in-hospital mortality was found in either group. However, the ETS group had a higher incidence of intrathoracic gastric dilation than the ETE group on POD 1 (13.1% vs. 4.9%; *P* = 0.025), which was treated by immediate nasogastric placement. The patients had a chest X-ray on POD 1 and were followed up further with barium esophagram. We did not find any actual delayed gastric emptying case in either group.

No significant correlation was observed between gastric dilation and leakage (correlation coefficient, 0.077; *P* = 0.23). Nevertheless, leakage was found to be positively correlated with late stricture formation (correlation coefficient, 0.188; *P* = 0.003).

DISCUSSION

Anastomotic leakage has a multifactorial etiology, among which ischemia is considered one of the most important technical factors.¹³ Compared with ETE anastomosis, the ETS method requires a longer gastric tube for cervical anastomosis. Whereas the right gastroepiploic artery serves as the only blood supply for the gastric tube, a longer gastric tube in ETS represents a larger ischemic region in the stomach, which is the definite disadvantage of ETS compared with ETE. Besides, oversewing the staple line of the gastric stump might cause additional ischemia. The most ischemic redundant end of the gastric tube is left in situ for ETS anastomosis, adding to the risk of fistula on the gastric stump (Fig. 1).⁸

A randomized controlled study involving 128 patients with single-layer hand-sewn anastomosis showed that the overall leakage rate was significantly lower in the ETE group than in the ETS group (22% vs. 41%).⁸ In our study, leakage in two ETS patients was found to be gastric stump necrosis rather than an anastomotic leak, which also explains why stricture did not occur in these two patients. Furthermore, ETS anastomosis needs more length of stomach (Fig. 1), which is not a good choice when the patient's stomach is extremely small and short. Both tension and perfusion of the anastomotic site could be compromised when the gastric tube is too short for performance of cervical ETS anastomosis.

In our study, we did not observe a statistically significant difference in anastomotic leakage between the two anastomotic techniques. This can possibly be explained by one reason: the double-layer hand-sewn technique was used for both anastomotic configurations, and this method has proved to be highly effective in preventing anastomotic leakage and stricture.¹⁴ Furthermore, the low incidence of anastomotic complications and the relatively small number of patients in the study might have made the comparison underpowered.

Some studies have reported that ETE anastomoses had a significantly higher anastomotic stricture rate.^{8,9} Moreover, compared with the ETS method, a greater number of patients received dilation treatment with the ETE method.^{8,9} It was hypothesized that the diameter of ETS anastomosis was wider than that of the ETE anastomosis.⁹ However, in our study, we did not see the difference in anastomosis stricture formation between the two configurations, and the diameters of the anastomotic lumen 1 month after the operation were found to be equal between two groups (1.2 ± 0.3 vs. 1.2 ± 0.4 cm; $P = 0.998$).

Many studies have reported that anastomotic leakage was an independent risk factor for anastomotic stricture,^{15,16} consistent with our study. Besides, an inlay technique usually is needed to overcome the difference in luminal size during ETE anastomosis, which was thought to be the possible reason for the development of stricture in single-layer ETE anastomosis.⁹ Nevertheless, this was not the case with our double-layer ETE technique. The two layers for the esophageal stump and the gastric tube were incised and anastomosed separately. After completion of the reconstruction, the anastomotic lines for the two layers were at different levels, which might have contributed to the low incidence of postoperative stricture formation.

Notably, we found a higher incidence of thoracic gastric dilation with ETS anastomosis than with ETE anastomosis. Esophagectomy with vagotomy and gastric tube formation might provoke a degeneration of the myenteric plexuses,¹⁷ and gastric tube size was the most significant factor

affecting the incidence of delayed gastric emptying.¹⁸ Because the size of the gastric tube around the anastomosis was much wider in ETS than in ETE, it was not surprising that the wider gastric tube around the anastomotic site in the upper thoracic cavity was more prone to gastric dilation than the narrow gastric tube.

In our study, both groups showed relatively low rates of postoperative complications, which might be attributed to the implementation of a minimally invasive technique.¹⁹ However, compared with the ETE method, the operation time, anastomosis time, and postoperative hospitalization were longer for ETS anastomosis. Compared with ETE anastomosis, ETS anastomosis has two additional steps, namely, excision of the tip of the gastric tube and reinforcement of the staple line with interrupted sutures, which might have contributed to the longer anastomosis times observed in the ETS group.

In all our study cases, we found that the patients with leakage had a significantly longer hospital stay than those without leakage (median, 28 days [P₂₅–P₇₅, 23–53 days] vs. 10 days [P₂₅–P₇₅, 9–11 days]; $P < 0.001$), whereas other complications did not differ significantly. In addition, we found that leakage in the ETS group was positively correlated with hospital stay ($P = 0.001$), but there was no correlation in the ETE group ($P = 0.991$). It could be explained that the leakage in the ETE group was less than in the ETS group, and too few of cases might have made the analysis underpowered to detect any significant difference. Therefore, the available statistical results suggested that leakage complication was a major factor in prolonging the hospital stay, consistent with other reports.^{20,21}

CONCLUSION

In conclusion, major postoperative complications were comparable between the two anastomotic configurations. However, the patients with ETE anastomosis showed a favorable outcome in terms of a decreased postoperative thoracic gastric dilation rate. Slight advantages might also be seen for ETE anastomosis in terms of shortened operation and anastomosis times, as well as a shorter postoperative hospital stay.

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