The Comparisons of Three Stapler Placement Methods for Intrathoracic Mechanistic Circular Stapling in Ivor Lewis Minimally Invasive Esophagectomy

Bo Zhang[1,2], Zixiang Wu[1], Qi Wang[1], Saibo Pan[1], Lian Wang[1], Gang Shen[1], Huiping Chai[3*], Ming Wu[1*]

[1]Department of Thoracic Surgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China
[2]Department of Thoracic Surgery, Taizhou Hospital, School of Medicine, Zhejiang University, Taizhou, China
[3]Department of Thoracic Surgery, The First Affiliated Hospital of Anhui Medical University, Anhui, China

Correspondence to: Wu Ming, MD, PhD, Department of Thoracic Surgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, 88 JieFang Rd, Hangzhou 310009, China. Email: iwuming22@zju.edu.cn.
Huiping Chai, MD, PhD, Department of Thoracic Surgery, The First Affiliated Hospital of Anhui Medical University, 218 Jixi Rd, Hefei 230022, China. Email: ing520323@yahoo.cn

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Research Square

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Original Article:

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Abstract

Objectives: To analyze the impact of the reversal penetrating technique (RPT) for intrathoracic gastroesophageal mechanical anastomosis on the development of anastomotic complications in Ivor Lewis minimally invasive esophagectomy (ILMIE) and further identify the risk factors for the development of anastomotic leakage and stricture.

Methods: A retrospective observational study was conducted using clinical data of 316 patients with esophageal carcinoma (EC) who underwent ILMIE from January 2012 to December 2019. The participants were divided into three groups of RPT, transoral Orvil technique (TOT), or purse-string technique (PST) according to the different stapler placenent methods for intrathoracic mechanistic circular stapling.
Multivariable analysis was performed to investigate the association of risk factors with anastomotic leakage and stricture.

Results: There were 154 patients with RPT, 78 with TOT and 84 with PST intrathoracic gastroesophageal circular stapling in ILMIE. There was no differences in intraoperative anastomosis related conditions inclouding conversion of open operations, ways of esophageal reconstruction, lymph nodes harvested between the three groups. Whereas, The mean total operative time, and gastroesophageal anastomosis time in the RPT group were significantly shorter than those in other groups (both $p<0.05$). The rates of anastomotic leakage and stricture showed no statistical differences between three groups, respectively (Leakage: $p=0.941$; Stricture: p=0.942). Multivariate analysis revealed that the PRT method of the anvil placement does not increase the probability of anastomotic leakage (PRT: reference; TOT: odds ratio(OR) 2.845, $P=0.255$; PST: OR 2.234, $p=0.242$) and stricture (PRT: reference; TOT: OR 1.976, $P=0.556$; PST: OR 1.872, $p=0.284$).

Conclusions: The PRT method of the anvil placement for intrathoracic gastroesophageal circular stapling does not increase the risk of anastomotic complications in ILMIE, but had significantly shorter surgical time and anastomosis time.

Keywords: esophageal carcinoma, reversal penetrating technique, Ivor Lewis esophagectomy, minimally invasive esophagectomy

Introduction

Subtotal esophagectomy with radical lymph node dissection remains the mainstream choice for the treatment of esophageal cancer (EC) [1]. In recent years, Ivor Lewis minimally invasive esophagectomy (ILMIE) increasingly has been performed in the treatment of middle and lower esophageal cancer because it avoids complications related to cervical anastomosis and reduces the higher morbidity and mortality in conventional open esophagectomy [2][3].

Mechanistic circular stapled technique is the most frequently implemented approach for intrathoracic esophagogastric anastomosis in ILMIE [4]. It requires insertion of the anvil into the proximal esophagus stump and anastomosis of the anvil rod with the stapler shaft. However, the appropriate placement of the anvil into the esophageal stump is a challenging step in a thoracoscopic operation [5]. Depending on the manner of anvil introduction, the main methods of circular stapled intrathoracic anastomoses include a transoral technique with the Orvil device (TOT) and a hand-sewn purse-string technique (PST). In recent years, the reversal penetrating technique (RPT), a modified anastomotic technique for ILMIE has been reported to be a simple and effective approach, and its practice experience has been accumulating in some centers [5][6][7]. However no study has yet compared RPT and the former two methods in intrathoracic anastomoses for esophagogastrostomy.

Anastomotic failure in the form of stricture or leak is common and critical [8] [9]. Anastomotic leakage is the main cause of postoperative morbidity, mortality and prolonged hospitalization [10]. Anastomotic stricture requires serial anastomotic dilatation and significantly impairs long-term quality of life. The anastomotic technique might be one major factor that influences anastomotic complications [11]. Therefore, in this study, we analyzed the impact of RPT on the incidence of anastomotic complications and we also further identified the risk factors for the development of anastomotic leakage and stricture following ILMIE.

Methods

Patients

The clinical data were collected of the patients receiving total laparoscopic or thoracoscopic Ivor Lewis esophagectomy with intrathoracic esophagogastric anastomosis from Jan 2012 to Dec 2019 in our institution. All patients were diagnosed with esophageal cancer by gastroscopy and had received overall pre-operative assessment including clinical symptoms, physical examination, and auxiliary laboratory and imaging examinations, etc. Cardiopulmonary function was evaluated by pulmonary function, electrocardiogram, color Doppler echocardiography and blood gas analysis. All patients underwent esophageal ultrasonography, supraclavicular lymph node ultrasonography, enhanced thoracoabdominal CT, cranial magnetic resonance imaging or PETCT for clinical staging. The anastomosis techniques employed during esophagectomy were PST, TOT or RPT. After surgery, all patients were staged according to the 8th edition staging system of the American Joint Committee on Cancer (AJCC) [12]. This study was approved by the ethic committee of the second affiliated hospital of Zhejiang University. Informed consent was obtained from all included patients. Clinical data were obtained and were retrospectively analyzed from the electronic medical record database, including demographic characteristics, pathological data, anastomosis related conditions anastomosis complications and so on

Surgery methods

Ivor Lewis MIE with intrathoracic mechanistic circular esophagogastric anastomosis, which was performed similarly to procedures described in previous literature[5,13], was conducted when the patient was under combined general-epidural anesthesia and double-lumen endotracheal intubation. A gastric conduit was created in most cases and fusiform stomach for the rest. The intrathoracic esophagogastric anastomosis was conducted by a circular stapling device (ECS 25mm; Ethicon Endo-Surgery). The methods of anvil placement included transoral technique (the Orvil device; TOT), hand-sewn purse-string technique (PST) and reversal penetrating technique (RPT).

(1) Transoral technique[14]: Esophageal dissection was done with a linear stapler. Then the Orvil anvil (DST Series EEA Orvil Device; Covidien) was attached to an orogastric tube, which was fully lubricated and inserted transorally by the anesthesiologist under laryngoscope. The tube passed out through an incision created at the tip of the esophageal stump and the anvil was sent to and fixed at the predetermined position. The circular stapler was placed into the gastric conduit through gastrotomy. The pneumoperitoneum was reconstructed with an airtight space made by incision with protective sheath and sterile gloves. Then the circular stapler was docked with the anvil to complete the intrathoracic esophagogastric anastomosis.

(2) The hand-sewn purse-string technique[15-16]: 3-0 suture was used to create a hand-sewn purse string through the muscular layer of the esophagus at least 5 cm proximal to the tumor. A transverse incision was made 2 cm distal to the purse-string suture of the esophagus and the anvil was inserted and fixed by tightening the purse string. Then the esophagus was transected. The gastric conduit was pulled out from the abdominal cavity into the thoracic cavity and the circular stapler was introduced into the gastric conduit to dork with the anvil to construct the intrathoracic anastomosis. The bottom opening of the gastric conduit was closed with linear stapler.

(3) Reverse penetrating technique[5,17]: The main operative steps in the ILMIE are shown in Figure 1. A 2-0 prolene suture stitch was linked to the tip of the ancillary rod with a knot. A longitudinal incision was made more than 3.0 cm above the tumor margin on the esophageal wall. The anvil with suture was inserted into the esophagus lumen through the incision. Then the suture penetrated the esophagus wall reversely at the predetermined anastomosis position, roughly 5.0 cm above the tumor margin. The suture was pulled to guide the penetration and positioning of the anvil on the esophagus wall. Then the linear stapler was used to transect the esophagus and obtain

the sample. The circular stapler was placed in the gastric conduit through gastrotomy and docked with the anvil to complete the intrathoracic anastomosis. The bottom opening of the gastric conduit was sutured with absorbable line or closed with linear stapler.

Postoperative management

All patients were treated with regular fast, gastrointestinal decompression, analgesia, antibiotics and antacid therapy. Parenteral nutritional support started 24h after the operation. The drainage tube was removed on the 3rd postoperative day. Upper gastrointestinal radiography with iodized oil and oral administration of methylene blue dilution were given on the 7th postoperative day to evaluate the integrity of the anastomosis. Fluid diet was resumed on the 6th postoperative day, semifluid diet on the 8^{th} day. Patients with no manifestation of discomfort were discharged from the hospital on the 9-10^{th} postoperative day.

Perioperative variables and surgical complications

Clinical data were obtained and were retrospectively analyzed from the electronic medical record database, including patient demographic characteristics, tumor features , anastomosis related conditions, anastomosis complications and so on. The following anastomosis-related conditions were recorded: conversion rate, anastomosis position, surgical time, ways of esophageal reconstruction, and number of lymph nodes harvested. The postoperative anastomosis complications included the following: anastomosis leakage, stricture, esophagotracheal leakage, and reflux esophagitis. Anastomosis leakage was defined as blue fluid outflowing from the drainage tube, or contrast leakage from the site of intrathoracic anastomosis or clinical suspected leakage requiring alteration of therapy. In our study, we further differentiated minor leakage and major leakage on the basis of the classification system of the Esophagectomy Complications Consensus Group (ECCG) [18]. Minor leakage corresponds to type I leakage in the ECCG classification, which referred to leakage associated with no or minor clinical presentation and necessitating no additional intervention [19]. The major leakage corresponds to Type II and III leakage in the ECCG classification, which referred to leakage presenting signs of inflammation and necessitating related intervention [19]. Anastomosis stricture was defined as development of a feeding obstruction or anastomosis narrowing less than 1cm under endoscopy or gastrointestinal radiograph and dysphagia requiring at least one endoscopic dilatation to relieve [20].

Statistical analysis

All statistical analyses were performed with SPSS 22.0 (SPSS Inc., Chicago, IL). All tests were two-sided with a significance level of 0.05. The continuous variables were shown as means ± standard deviation (SD) and compared by ANOVA or Kruskal-Wallis test between more than two groups. The categorical variables were focused on frequencies and proportions,and compared by Chi-square or Fisher exact tests between groups. The non-parametric test was used if the one-way ordered R×C list (grade data) does not meet the chi-square test premise. Logistic regression model were used to analyze the influence of clinical and pathological factors on anastomotic leakage and stricture. Univariate analysis was used to determine the correlation between factors and anastomotic leakage or stricture. Candidate variables that showed a univariate relationship with outcome or that were considered clinically relevant were included in the multivariate logistic regression analysis to generate the multivariate logistic regression model. 95 % confidence intervals (CI) and odds ratio (OR) were calculated.

Results

A total of 316 patients with EC receiving ILMIE were included in the present analysis. There were 154 patients in RPT group, 78 in TOT group, and 84 in PST group. The clinical characteristics of the patients in each study group are listed in Table 1. Except for the method of anvil placement, the perioperative treatment strategy was the same for all the included patients. The patients of the three groups were not statistically different with respect to demographics, comorbidities, preoperative therapy, tumor location, or 30-days mortality (all p>0.05).

The anastomosis-related conditions in esophagectomy are summarized in Table 2. The total conversion rate, the rate of conversion due to anastomosis, the gastroesophageal anastomosis position, ways of esophageal reconstruction, number of total lymph nodes harvested, number of mediastinal lymph nodes harvested were not significantly different between groups (all p>0.05). However, the total surgical time and anastomosis time among three groups was statistically significant (both p<0.05). Further, the multiple comparisons with the Dunnett's test (TOT vs RPT and PST vs RPT) showed that the total surgical time and anastomosis time in the RPT group was significantly shorter than that in both the PST group and TOT group (all p<0.05).

Table 3 shows postoperative anastomotic complications in all patients, as well as the differences in anastomotic complications among the PRT, TOT and PST groups. Anastomotic leak occurred in 39 patients (12.34%), of which 22 cases were minor anastomotic leakage and 17 cases were major ones. However, none of the anastomotic leakage rates, regardless whether total rate, minor anastomotic leakage rate or major anastomotic leakage rate, were significantly different between the three experimental groups (all p>0.05). All included patients received postoperative endoscopic evaluation. In total, 49 patients (15.51%) presented anastomotic stricture in all groups (Table 3). However, the stricture rates among the RPT, TOT and PST groups were not significantly different (p>0.05). Furthermore, no significant difference among three groups was noted in esophagotracheal leak, reflux esophagitis (anastomositis), and frequent dependence on anti-reflux medication (all p>0.05).

The results of univariable and multivariable analyses for prediction of anastomotic leakage and stricture are listed in Table 4 and Table 5, respectively. The multivariable logistic regression analyses using a enter model revealed that BMI, smoking history, pathological stage, and neoadjuvant therapy predict anastomotic leakage, rather than the methods of anvil placement. Moreover, anastomotic stricture was significantly influenced by the presence of BMI, smoking history,conversion, and neoadjuvant therapy rather than by the methods of anvil placement.

Discussion

The reversal penetrating technique (RPT), a modified method of stapler placement applied in Ivor-Lewis MIE has been reported to be a simple and effective approach, and its practice experience has been accumulating in some centers in the past few years[4,21]. We performed this retrospective study to investigate the influence of RPT compared with PST and TOT on anastomotic leakage and stricture. We also performed multivariate analysis to analyze the influence of risk factors on the anastomotic leakage and stricture in patients undergoing Ivor Lewis MIE.

Our analysis results revealed that the surgery time and anastomosis time of the RPT group was significantly shorter than that in the TOT and PST group. However, the other anastomosis-related conditions including conversion rate and number of lymph nodes dissected, and anastomosis complications including anastomosis leakage and stricture of RPT group were not significantly different from those in the TOT and PST groups.

The shorter surgery time and anastomosis time clearly indicated that the reverse penetrating technique was simpler and easier to perform than TOT or PST. During the anastomosis procedure of RPT, a small incision was made to allow introduction of the anvil into the esophageal lumen. The operation is easier than in TOT. In the latter operation, the anvil was transorally introduced by guidance of an orogastric tube, and was performed by an anesthesiologist in cooperation with the surgeon. The penetration of stitch and suture and anvil rod in RPT made the positions of esophagus and anvil more fixed, thus avoiding excessive surgery and unnecessary esophageal injury. The demanding operation of purse-string hand sewing under endoscopy was avoided in RPT and achieved instead by cutting and closure of a linear stapler. This modification made the operation easier and the cutting edge more regular. Moreover, we can speculate that the less demanding operations in RPT may greatly shorten the learning curve of surgeons.

Anastomosis leakage is the most serious complication post esophagectomy. The rate of anastomosis leakage in this study was 12.34%, which is slightly higher than the pooled anastomosis leakage rate of 7.1% among 1791 cases receiving stapler anastomosis for minimally invasive esophagectomy [22] or 6% among 700 cases received circular stapler anastomosis for MIE reported by Yang et al [23]. The inconsistency may be attributed to the diverse definitions used for anastomotic leak after esophagectomy and different surgeons performing the surgery in different studies. However, the standardized definitions for anastomosis leakage proposed by the Esophagectomy Complications Consensus Group (ECCG) [18] have been adopted in our study and hopefully may standardize the anastomosis leakage definition in future studies. However, the major leakage rate in this study was 5.38%, well comparable to the leakage rate of 5.7% requiring treatment after intrathoracic mechanical esophagogastric anastomosis in the study by Harustiak et al [19].

Both minor and major leakage rates in the RPT, TOT and PST groups were not significantly different. The multivariate analysis in our study revealed that factors of BMI, smoking history, pathological stage, and neoadjuvant therapy rather than the methods of anvil placement may predict anastomotic leak. This result was consistent with most previous studies, which suggested that anastomotic leak may not be affected by the methods of anvil placement[22][23]. The minor leak was speculated to be affected mainly by sewing skills of surgeons during manual anastomosis [19]. In this study, the anastomosis was generated by a mechanical circular stapler, so the concerning about sewing skills can be ignored in the comparison among circular stapler anastomosis techniques. One factor that may increase anastomosis leakage after using RPT is that the end-to-end anastomosis may cross the linear stapler line, thus potentially increasing the risk of anastomosis leak. However, according to the analysis result, the anastomosis leakage rate in the RPT group was not increased but slightly lessened compared with other groups, so this concern also is unnecessary. On the other hand, major leakage might be associated with tissue ischemia that occurs after altered blood perfusion. Therefore, major leakage may not be affected by the methods of anvil placement but by surgical skills and some systemic or intrinsic factors that may influence blood perfusion, such as esophageal separation location, stomach stretching, or diabetes[24][25]. Our findings by multivariate analysis confirmed this presumption that the method of anvil placement is not a risk factor of anastomotic leakage.

Anastomosis stricture is one common long term complication and seriously reduces life quality of patients. The rate of anastomotic stricture was 15.51% in our study, comparable with 13.6% reported by Tanaka K et al[26]. The results of our study found no difference with respect to anastomotic stricture between the experimental groups. Furthermore, the multivariate analysis revealed that the factors which may influence the development of anastomotic stricture included BMI, smoking history and conversion rather than placement of the anvil. According to a previous study, the surgical factors associated with anastomotic stricture after esophagectomy may include small size of anastomotic stapler, end-to-end anastomosis, excessive tension at anastomosis，local tissue pressing, etc[27]. These results and our study suggest that these three ways of anvil placement might not be an influence factor for stricture.

The other anastomotic complication rates did not significantly differ between RPT, TOT and PST groups. In conclusion, these results indicated that using RTP would not increase the risk of anastomosis-related complications; thus, it is as safe and feasible as TOT or PST.

Besides simplicity, easier operation, safety and feasibility, RPT may also have the following advantages in clinical application: 1. In RPT, the technique can be applied after a small modification of the anvil. In the Orvil technique, a specific Orvil circular stapler and transoral anvil introduction tube were needed; thus, RPT is more economical than the Orvil method. 2. During the anastomosis procedure, involvement of excessive or inadequate esophageal tissues is bad for anastomosis and may cause leakage. The cases of esophageal dilation may be difficult for the purse-string technique, as the involvement of the whole circle of the esophageal stump will create redundant esophageal tissue enrolled in anastomotic doughnuts, which makes the anastomosis less secure. In the RPT technique, only part of the stump is involved in anastomosis, so the anastomosis formation will be less influenced by the excessive esophageal tissues. Therefore, in this situation, the RPT technique has obvious superiority [5]. Previously, one limitation of RPT was that the RPT requires adequate length of normal esophageal tissue. In the RPT technique, the esophageal wall penetration site is 2 cm or more above the esophageal incision and the esophageal incision is 3 cm or more above the tumor margin, thus the anastomosis site is 5 cm or more from the tumor. However, using a flexible curved intraluminal stapler makes the RTP technique still applicable in cases of tumor in much upper locations.

This is the first study comparing RPT with other two methods of anvil placement in ILMIE. However, the inherent limitation of the retrospective study design suggests the patient demographics and baseline clinical parameters were not well balanced. In the future, well-designed randomized trials are warranted for further comparison.

Conclusion

Compared with TOT and PST methods of the anvil placement for intrathoracic gastroesophageal circular stapling in ILMIE, the RPT method performed does not increase the risk of the anastomotic leakage and stricture, but involves significantly shorter surgical time and anastomosis time. Therefore RPT method is a safe, effective and easier-to-perform anastomotic technique, worth further application and popularization in the ILMIE.

Abbreviations

RPT: the reversal penetrating technique; ILMIE: Ivor Lewis minimally invasive esophagectomy; EC: esophageal carcinoma; TOT: the transoral Orvil technique; PST: the purse-string technique; OR: odds ratio; AJCC: the American Joint Committee on Cancer; ECCG: the Esophagectomy Complications Consensus Group; SD: standard deviation; CI: confidence intervals

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None.

Authors' contributions

Bo Zhang and Ming Wu conceived the study design. Zixiang Wu, Qi Wang, and Saibo Pan acquired the data for the study. Bo Zhang, Zixiang Wu, and Lian Wang analyzed and interpreted the data. Bo Zhang drafted the manuscript. Gang Shen, Huiping Chai and Ming Wu revised the manuscript critically. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki. This research project was approved by Ethics Committee of the 2nd Affiliated Hospital, School of Medicine, Zhejiang University as approval number 2020-122. Due to the retrospective design of the study, the local ethic committee confirmed that informed consent was not necessary from participants.

Consent for publication

Not applicable.

Competing interests

All authors have no potential competing interests.

Author details

[1]Department of Thoracic Surgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, 88 JieFang Rd, Hangzhou 310009, China. [2]Department of Thoracic Surgery, Taizhou Hospital, School of Medicine, Zhejiang University, 150 Ximen Rd Taizhou 317000, China. [3]Department of Thoracic Surgery, The First Affiliated Hospital of Anhui Medical University, 218 Jixi Rd, Hefei 230022, China.

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Table 1: Characteristics of Patient and Tumor

Characteristics	RPT group N=154	TOT group N=78	PST group N=84	F/X^2	*P*
Age (mean, years)	62.87±8.65	62.85±9.73	62.10±11.62	F=0.192	0.826
Female: Male, n	20:134	18:60	12:72	4.160	0.125
BMI (mean, kg/m2)	21.55±2.70	20.88±2.31	21.49±3.11	1.685	0.187
Co-morbidity, n (%)					
Hypertension	42(27.27)	23(29.49)	29(34.52)	1.371	0.504
Diabetes	19(12.34)	8(10.26)	10(11.90)	0.221	0.895
COPD	11(7.14)	5(6.41)	6(7.14)	0.049	0.976
Previous chest or abdominal surgery	7(4.55)	1(1.28)	2(2.38)	1.628	0.456 *
Smoking history, n (%)	88(57.14)	42(53.85)	46(54.76)	0.269	0.874
Alcohol history, n (%)	70(45.45)	36(46.15)	35(41.67)	0.414	0.813
Tumor location, n (%)				1.387	0.500
Middle third	66(42.86)	30(38.46)	40(47.62)		
Lower third	88(57.14)	48(61.54)	44(52.38)		
pT, stage, n (%)				8.969	0.011#
T1	34(22.08)	10(12.82)	18(21.43)		
T2	24(15.58)	6(7.69)	18(21.43)		
T3	94(61.04)	60(76.92)	47(55.95)		
T4	2(1.30)	2(2.56)	1(1.19)		
pN, stage, n (%)				10.102	0.006#
N0	84(54.55)	40(51.28)	56(66.67)		
N1	28(18.18)	5(6.41)	16(19.05)		
N2	25(16.23)	15(19.23)	10(11.90)		

N3	17(11.04)	18(23.08)	2(2.38)		
Pathological stage, n (%)				8.244	0.016#
I	34(22.08)	10(12.82)	20(23.81)		
II	52(33.77)	30(38.46)	36(42.86)		
III	49(31.82)	20(25.64)	25(29.76)		
Ⅳ	19(12.34)	18(23.08)	3(3.57)		
Neoadjuvant therapy, n (%)	12(7.79)	9(11.54)	8(9.52)	0.888	0.641
In-hospital/30-days mortality, n (%)	3(1.95)	1(1.28)	1(1.19)	0.325	1.000*

Note: RPT=Reversal Penetrating Technique; PST=Purse string stapled anastomotic technique; TOT=Transoral Orvil stapled anastomotic technique; BMI=body mass index; COPD=chronic obstructive pulmonary disease; * represents calculation by Fisher exact test; # represents calculation by Kruskal-Wallis test.

Table 2. Anastomosis related conditions

Characteristics	RPT group N=154	TOT group N=78	PST group N=84	F/X^2	*p*
Total conversion, n (%)	15(9.74)	6(7.69)	8(9.52)	0.371	0.944*
Conversion due to anastomosis, n (%)	3(1.95)	2(2.56)	3(3.57)	0.825	0.813*
Total surgical time (min)	262.86±28.29	301.31±33.13	284.14±35.64	40.514	0.000
Time of anastomosis, min	7.39±1.35	16.22±2.70	13.02±2.89	456.453	0.000
Gastroesophageal anastomosis position					
Above arch	104(67.53)	56(71.79)	64(76.19)	2.016	0.365
Below arch	50(32.47)	22(28.21)	20(23.81)		
Ways of esophageal reconstruction, n(%)					
Gastric conduit	113(73.38)	57(73.08)	65(77.38)	0.548	0.760
Fusiform stomach	41(26.62)	21(26.92)	19(22.62)		
No. of total lymph nodes harvested (range)	30.82±13.15	29.51±15.67	28.36±11.98	0.930	0.396
No. of mediastinal lymph nodes harvested (range)	16.01±9.07	14.33±6.04	15.10±8.16	1.150	0.318

Note: RPT= Reversal Penetrating Technique; PST=Purse string stapled anastomotic technique; TOT= Transoral Orvil stapled anastomotic technique; * represents calculation by Fisher exact test.

Table 3. Anastomosis complications

Anastomotic complications	RPT group N=154	TOT group N=78	PST group N=84	Total N=316	F/X^2	*p*
Anastomotic leak						
Minor(Type I), n (%)	10(6.49)	6(7.69)	6(7.14)	22(6.96)	0.146	0.929
Major(Type II, Type III), n (%)	8(5.19)	4(5.13)	5(5.95)	17(5.38)	0.176	0.949*
Total leak, n (%)	18(11.69)	10(12.82)	11(13.10)	39(12.34)	0.121	0.941
Esophagotracheal leak, n (%)	2(1.30)	1(1.28)	1(1.19)	4(1.27)	0.348	1.000*
anastomotic stricture, n (%)	23(14.94)	13(16.67)	13(15.48)	49(15.51)	0.119	0.942
reflux esophagitis(anastomositis), n (%)	68(44.16)	34(43.59)	34(40.48)	136(43.04)	0.313	0.855
Frequent Dependence on anti-reflux medication, n (%)	45(29.22)	22(32.05)	26(30.95)	93(29.43)	0.153	0.926

Notes: RPT=Reversal Penetrating Technique; PST=Purse string stapled anastomotic technique; TOT=Transoral Orvil stapled anastomotic technique; * represents calculation by Fisher exact test.

Table 4. Univariable and multivariable analyses for anastomotic leak

Variables		Total No.	No. of AL (%)	Univariable analysis			Multivariable analysis		
				OR	95% CI	*P*-value	OR	95% CI	*p*
Age (year)				1.056	0.534-2.089	0.875	1.574	0.656-3.780	0.310
	<60	126	16(12.70)						
	≥60	190	23(12.11)						
Gender				1.742	0.591-5.140	0.314	4.257	1.020-17.765	0.047
	Male	266	35(13.16)						
	Female	50	4(8.00)						
BMI (kg/m^2)				1.347	1.165-1.558	0.000	1.472	1.223-1.772	0.000
Smoking history				1.263	0.644-2.477	0.497	6.169	1.991-19.110	0.002
	Yes	130	18(13.85)						
	No	186	21(11.29)						
Alcohol history				0.665	0.339-1.303	0.234	0.378	0.135-1.059	0.064
	Yes	174	18(10.34)						
	No	142	21(14.79)						
Tumor location				1.299	0.664-2.543	0.445	2.268	0.962-5.347	0.061
	Middle third	136	19(13.97)						
	Lower third	180	20(11.11)						
Pathological stage									
	I	64	12(18.75)						
	II	118	14(11.86)	1.714	0.740-3.970	0.208*	3.415	1.186-9.831	0.023*
	III	94	9(9.57)	2.179	0.859-5.527	0.101*	5.568	1.584-19.570	0.007*
	Ⅳ	40	4(10.00)	2.077	0.620-6.956	0.236*	9.120	1.765-47.130	0.008*
Neoadjuvant				0.147	0.064-0.340	0.000	0.055	0.017-0.177	0.000

therapy									
	Yes	29	12(41.38)						
	No	287	27(9.41)						
Conversion				0.394	0.156-0.996	0.049	0.388	0.110-1.372	0.142
	Yes	29	7(24.14)						
	No	287	32(11.15)						
Time of anastomosis				0.967	0.898-1.042	0.380	0.906	0.763-1.075	0.259
Methods of anvil placement				0.935	0.629-1.389	0.738			
	PRT	154	18(11.69)						
	TOT	78	10(12.82)	0.900	0.394-2.056	0.803 #	2.845	0.470-17.214	0.255 #
	PST	84	11(13.10)	0.878	0.394-1.959	0.751 #	2.234	0.580-8.598	0.242 #

Notes: AL=anastomotic leak; BMI=body mass index; RPT= Reversal Penetrating Technique; PST=Purse string stapled anastomotic technique; TOT= Transoral Orvil stapled anastomotic technique; OR=odds ratio; CI=confidence interval; *Compared with I stage group; #Compared with PRT group.

Table 5. Univariable and multivariable analyses for anastomotic stricture

Variables		Patient No.	No. of AS (%)	Univariable analysis			Multivariable analysis		
				OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age (year)				1.277	0.691-2.361	0.435	1.759	0.851-3.635	0.127
	<60	126	22(17.46)						
	≥60	190	27(14.21)						
Gender				1.414	0.567-3.525	0.457	2.520	0.827-7.679	0.104
	Male	266	43(16.17)						
	Female	50	6(12.00)						
BMI (kg/m^2)				1.215	1.077-1.371	0.002	1.262	1.101-1.446	0.001
Smoking history				1.458	0.791-2.687	0.227	3.982	1.649-9.613	0.002
	Yes	130	24(18.46)						
	No	186	25(13.44)						
Alcohol history				0.680	0.369-1.252	0.215	0.558	0.246-1.263	0.161
	Yes	174	26(14.94)						
	No	142	23(16.20)						
Tumor location				1.094	0.592-2.019	0.775	1.548	0.765-3.134	0.225
	Middle third	136	22(16.18)						
	Lower third	180	24(13.33)						
Pathological stage									
	I	64	12(18.75)						
	II	118	21(17.80)	0.765	0.262-2.232	0.624*	1.553	0.633-3.805	0.336*
	III	94	6(6.38)	0.815	0.304-2.189	0.685*	3.080	1.070-8.861	0.037*
	Ⅳ	40	10(25.00)	1.482	0.500-4.399	0.478*	2.731	0.778-9.586	0.117*
Neoadjuvant therapy				0.299	0.129-0.690	0.005	0.191	0.069-0.525	0.001
	Yes	29	10(34.48)						

	No	287	39(13.59)						
Conversion				0.360	0.153-0.846	0.019	0.305	0.107-0.867	0.026
	Yes	29	9(31.03)						
	No	287	40(13.94)						
Time of anastomosis				0.977	0.912-1.046	0.505	0.941	0.815-1.086	0.405
Methods of anvil placement									
	PRT	154	23(14.94)						
	TOT	78	13(16.67)	0.878	0.418-1.844	0.734#	1.976	0.442-8.836	0.556#
	PST	84	13(15.48)	0.959	0.458-2.008	0.911#	1.872	0.595-5.887	0.284#

Notes: AS=Anastomosis stricture; BMI=body mass index; RPT=Reversal Penetrating Technique; PST=Purse string stapled anastomotic technique; TOT=Transoral Orvil stapled anastomotic technique; OR=odds ratio; CI=confidence interval; *Compared with I stage group; #Compared with PRT group.

Figure 1 The main operative steps of the reverse penetrating technique in Ivor Lewis minimally invasive esophagectomy. 1. Establishment of an anvil set (A). 2. Placement of the anvil in the esophagus: making a longitudinal incision on the esophageal anterior wall (B); inserting the anvil set into the esophageal lumen (C); penetrating reversely the esophageal wall with a stitch (D) and pulling out the anvil rod (E); transecting the proximal esophagus with linear stapler (F); detaching the ancillary trocar from the anvil rod and obtaining the anvil placement (G,H). 3. Completion of intrathoracic anastomosis: sending the shaft of the circular stapler into the gastric conduit through gastrotomy (I) and docked with the anvil to achieve anastomosis (J);