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Original Article

Influence of oblique anastomosis on esophagogastric anastomotic leak and its risk factors

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Abstract: Objective: To investigate the benefit of oblique anastomosis on esophagogastric anastomotic leak and the risk factors of this technique. Methods: According to surgical method, one hundred and five patients with esophageal cancer were retrospectively included and divided into the experimental group (n=45, side to side anastomosis) and the control group (n=60, end to side anastomosis). The patients in the experimental group underwent oblique anastomosis while those in the control group underwent end-to-side anastomosis. The area around the anastomotic stoma, total amount of drainage after operation, bed rest time and adverse outcomes were compared between the two groups. The patients were followed-up for 3 years to observe the survival rates in both groups. Results: The anastomotic area in the experimental group was significantly larger than that in the control group; the total amount of drainage after operation in the experimental group was significantly lower than that in the control group and the bed rest time was also significantly shorter. There were no significant differences in the complications in the two groups except higher anastomotic leak incidence in control group (P=0.347, P=0.546). The incidence of adverse reactions (anastomotic leakage, anastomotic stenosis and chest-stomach syndrome) in the control group was higher than that in the experimental group (P=0.010). Multivariate analysis showed that age (OR: 4.422, 95% CI: 1.284-15.225) and anastomotic mode (OR: 4.302, 95% CI: 1.109-16.688) were the independent risk factors for anastomotic leak and increasing incidence of anastomotic leakage was found with older age. Survival curves showed that sixty-eight patients (64.76%) survived over three years after operation and there was no significant difference in the 3-year survival rate between the two groups (P=0.245). Conclusion: Age and anastomotic mode are the independent risk factors for anastomotic leak. Oblique anastomosis can increase anastomotic area, reduce postoperative drainage and bed rest time and the total incidence of complications; however, it has no significant impact on patient survival.

Keywords: Oblique anastomosis, anastomotic leak, esophageal cancer

Introduction

With the continuous improvements of living standards, people's lifestyle and dietary structure have been gradually changing. The incidence of malignant gastrointestinal cancer has been rising and there is a recent trend of cancer development in younger patients [1]. According to the American cancer database in 2016 [2], more than 1.6 million cancer patients were newly diagnosed while nearly 600,000 people died. Esophageal cancer (EC) is the eighth most common malignant tumor in the world. However, most EC patients are found in developed countries [3]. Esophageal cancer patients in China alone accounted for 46.6% of global EC and the 5-year survival rate of such patients was less than 30% [4]. With such high morbidity and mortality, finding improved means of effective treatment and prevention is the key to reduce the incidence and the complications of EC.

At present, clinical treatments for EC include chemotherapy, biotherapy, targeted therapy and surgical treatment [5-7]. The most important mode of EC treatment is surgery. Although some patients are unable to receive surgical treatment due to their severe conditions after admission, it is undeniable that surgical treatment can significantly improve the prognosis and survival of early stage EC patients [8].

However, different complications may occur after surgical treatment, among which anastomotic leak is the most serious one [9]. With continuous improvements in the operative technique, the incidence of anastomotic leaks has decreased significantly, but around 8%-13% still have complications postoperatively [10]. Clinical study has shown [11] that once anastomotic leak occurs, food and digestive juices can spill out through the fistula. If the diagnosis is not made in time, local or systemic infection can occur and the mortality rate may exceed 40%. In clinic, the primary method for anastomosis after esophagectomy is the end-to-side anastomosis. Although it can resect the tumors to the greatest extent, recent studies have shown that more than 1/4 of the patients had serious complications such as esophagitis, anastomotic leak, anastomotic stenosis and chylothorax. At present, opinions on how to improve the anastomosis and reduce complications are not uniform.

It is of utmost importance to find an improved surgical method which has minimal complications and the greatest improvement in the quality of life in such patients. Oblique anastomosis is a new surgical concept that can be used to improve the outcome. On the basis of the end-to-side anastomosis, the esophagus can be anastomosed to the stomach at an angle of 45°-60°, so as to achieve optimal esophageal reconstruction. However, the benefit of the new technique over the traditional end-to-side method is still unclear. In this study, we improved the end-to-side anastomosis method and performed oblique anastomosis based on end-to-side anastomosis to compare the incidence of anastomotic fistula in patients with esophageal cancer, so as to provide a new plan for clinical treatment.

Materials and methods

Patients

One hundred and five patients with esophageal cancer treated in Tengzhou Central People's Hospital Affiliated to Ji'ning Medical University from February 2014 to February 2016 were retrospectively analyzed. All patients had squamous cell carcinoma of the stomach. According to the patient's general health condition, examination results and surgeon preference, 45 patients who underwent oblique anastomosis were classified as the experimental group while 60 patients who underwent end-to-side anastomosis were classified as the control group in this study. This study was approved by the Medical Ethics Committee of Tengzhou Central People's Hospital Affiliated to Ji'ning Medical University.

Inclusion and exclusion criteria

Inclusion criteria: Patients who had complete clinical data; patients whose age >18 years old; patients who were confirmed by clinical pathological examination to have esophageal cancer with pathological staging in line with the 8th edition of the AJCC TNM stage [12]; patients who were expected to survive for more than 3 months; patients who had no abnormal bleeding or coagulation dysfunction preoperatively.

Exclusion criteria: Patients with other tumors; patients could not be operated upon because of their clinical conditions; patients with congenital heart, liver, lung, brain or kidney function defects; pregnant or lactating women.

Surgical interventions

The experimental group received oblique anastomosis, while the control group received end-to-side anastomosis. Patients in both groups had right-sided thoracotomy. The lower lung ligaments along with the lymph nodes were cleaned after the tumor was dissected strictly according to the principles of tumor resection. After resection, the patient was put in the supine position. The stomach was then freed through a supine mid-abdominal incision. The esophagus was cut off at least 5 cm away from the upper margin of the tumor. The experimental group used forceps or hand to suture the purse. The purse plane and the long axis of the esophagus were at 45°-60° angle and inclined to the stomach which was pre-anastomosed. In the control group, the purse plane was kept perpendicular to the long axis of the esophagus. The nail holder was placed, the purse was tightened and knotted and the esophagus was cut off 2 mm below the knot. In the experimental group, the long axis of the nail pedestal was kept perpendicular to the purse plane to ensure that the esophagus is obliquely anastomosed to the stomach at an angle of 45°-60°. In the control group, the long axis of the nail pedestal was also kept perpendicular to the purse plane to complete the end-to-side anastomosis of esophagus and stomach (**Figure 1**).

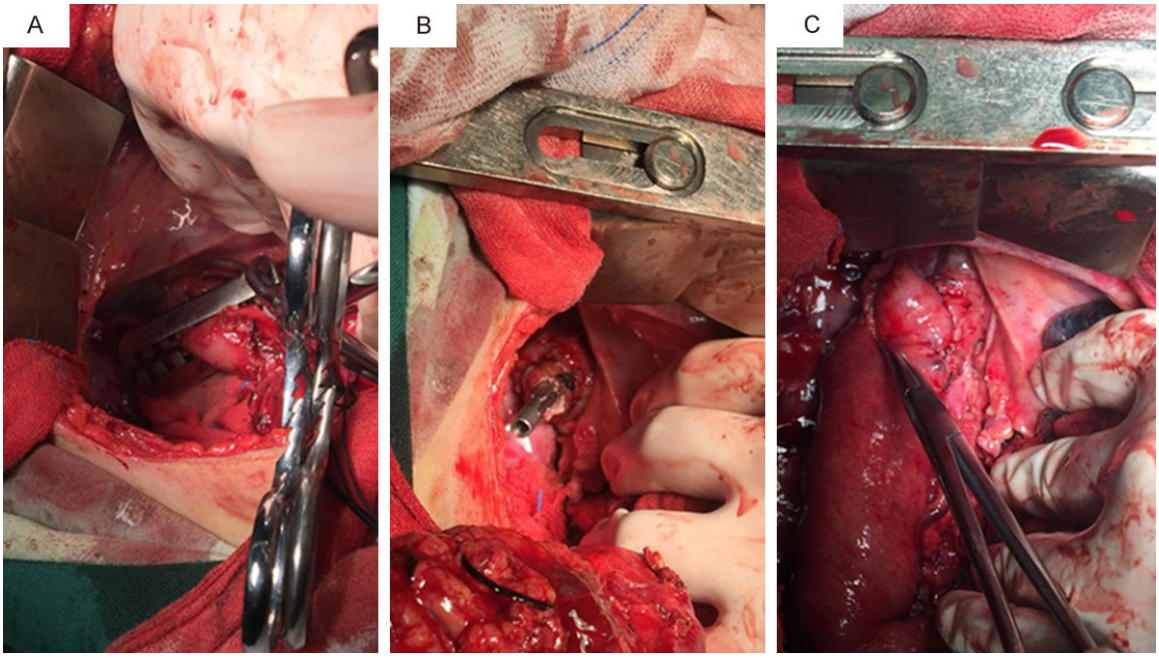

Figure 1. Oblique anastomosis. A: Grab the esophagus with forceps at 45° angle to cut off the esophagus; B: Place stapler anvil heads; C: The anastomotic plane formed a 45° angle with the long axis of esophagus after gastroesophageal anastomosis.

Follow-up

The patients were followed-up mainly by telephone and outpatient review every 3 months after discharge for a total of 3 years.

Observation indicators

Primary observation indicators which included the area around the anastomotic stoma, total drainage after operation, bed rest time and adverse reactions (incidence of anastomotic leak, anastomotic stenosis and thoracic gastric syndrome) were compared between the two groups. Patients were further grouped according to the occurrence of anastomotic leak and its independent risk factors were analyzed. All the factors were analyzed by multivariate analysis.

Secondary observation indicators included the clinical data, 3 years follow-up and 3-year survival rate of the two groups.

Statistical methods

SPSS 20.0 software (IBM Corporation, Chicago, USA) was used to analyze the data. GraphPad Prism 7 (Software Company, San Diego, USA) was used to derive relevant images. K-S was used to analyze the data distribution. The enumeration data were expressed by rate (%) and tested by chi-square test (χ^2). The ranked data were tested by non-parametric test. Measurement data were expressed by mean ± standard deviation (SD ± mean). Student's t-test was used to analyze the data which were normally distributed and independent sample t-test was used for inter-group comparison. Data that do not conform to normal distribution were tested by rank sum test, denoted by Z. Multivariate logistic regression was used to analyze the risk factors of anastomotic leak. K-M survival curve was used to plot the 3-year survival of patients, and Log-rank test was used to analyze them. Differences were considered significant when $P<0.05$.

Results

No significant difference of population characteristics between two groups

Clinical data including age, gender, body mass index (BMI), past medical history, smoking history, alcohol abuse history, residence, tumor location, lymph node metastasis and TNM stage were compared between the experimental group and the control group and no significant differences were found (all $P>0.05$; **Table 1**).

Table 1. No significant difference of population characteristics between the two groups

	Experimental group (n=45)	Control group (n=60)	$t/\chi^2/Z$	P
Age (year)	60.3±7.2	61.2±6.9	0.649	0.518
Gender			0.223	0.637
Male	28 (62.22)	40 (66.67)		
Female	17 (37.78)	20 (33.33)		
BMI (kg/m^2)	20.84±1.88	21.01±1.92	0.453	0.652
Past medical history				
Hypertension	21 (46.67)	31 (51.67)	0.257	0.612
Diabetes	18 (40.00)	26 (43.33)	0.117	0.712
Smoking history			0.133	0.716
Yes	30 (66.67)	42 (70.00)		
No	15 (33.33)	18 (30.00)		
Alcohol abuse history			0.309	0.578
Yes	13 (28.89)	19 (31.67)		
No	32 (71.11)	41 (68.33)		
Residence			0.875	0.350
City	30 (66.67)	45 (75.00)		
Country	15 (33.33)	15 (25.00)		
Tumor location			-0.505	0.614
Upside	15 (33.33)	21 (35.00)		
Midpiece	18 (40.00)	17 (28.33)		
Hypomere	12 (26.67)	22 (36.67)		
Lymph node metastasis			0.205	0.650
Transferred	19 (42.22)	28 (46.67)		
Not transfer	26 (57.78)	32 (53.33)		
TNM stage			-0.540	0.589
I	15 (33.33)	17 (28.33)		
II	20 (44.44)	28 (46.67)		
III	10 (22.22)	15 (25.00)		

Note: BMI, body mass index.

Table 2. Larger size of anastomotic area, lower volume of drainage and shorter bed rest time in the experimental group

Group	Area of anastomotic stoma (cm^2)	Total amount of drainage after operation (mL)	Bed rest time (d)
Experimental group (n=45)	2.52±1.22	444.55±25.81	2.82±0.98
Control group (n=60)	1.40±0.52	506.50±48.58	4.52±1.32
t	6.350	7.767	7.228
P	<0.001	<0.001	<0.001

Larger size of anastomotic area, lower volume of drainage and shorter bed rest time in the experimental group

When the area of anastomotic stoma, the total amount of drainage after operation and the bed rest time were compared between the two groups, it was found that the anastomotic area of the experimental group was significantly larger than that of the control group, the total amount of drainage after operation was significantly lower than that in the control group and the bed rest time was significantly shorter than that in the control group (all P<0.05; **Table 2**).

Lower incidence of adverse reactions in the experimental group

Statistical analysis of adverse reactions in the two groups showed that 13 cases of anasto-

Table 3. Lower incidence of adverse reactions in the experimental group (n, %)

Group	Anastomotic leak	Anastomotic stenosis	Horacic-stomach syndrome	Total incidence
Experimental group (n=45)	3 (6.67)	4 (8.89)	3 (6.67)	10 (22.22)
Control group (n=60)	13 (21.67)	9 (15.00)	6 (10.00)	28 (46.67)
χ^2	4.479	0.885	0.365	6.654
P	0.034	0.347	0.546	0.010

motic leak, 9 cases of anastomotic stenosis and 6 cases of thoracic-stomach syndrome were found in the control group while 3 cases of anastomotic leak, 4 cases of anastomotic stenosis and 3 cases of thoracic-stomach syndrome were found in the experimental group. In addition, there was no statistical difference in any complication except for anastomotic leak (all P>0.05), and the incidence in the control group was higher than that in the experimental group (P<0.05; **Table 3**).

Analysis of risk factors related to anastomotic leak

Patients were divided into the anastomotic leak group and the non-anastomotic leak group according to the postoperative anastomotic leakage. Clinical and pathological data of the two groups were collected for univariate analysis. The analysis showed that there were no differences in gender, BMI, past medical history, smoking history, alcoholism, residence, location of tumor, lymph node metastasis, TNM stage, anastomotic area, the total amount of drainage and bed-ridden time between the two groups (all P>0.05). However, there were significant differences in age and anastomosis mode between the two groups (both P<0.05). The indices with single factor differences were assigned values and analyzed using binary logistic regression in LR. The analysis showed that age (OR: 4.422, 95% CI: 1.284-15.225) and anastomotic mode (OR: 4.302, 95% CI: 1.109-16.688) were independent risk factors for anastomotic leak (**Tables 4**-**6**).

No significant difference of three-year survival rates in the two groups

All patients were followed-up for 3 years. Sixty-eight patients (64.76%) survived for 3 years after the operation. A comparison of the 3-year survival rate of the patients between the control group and the experimental group showed that there was no significant difference (P=0.245; **Figure 2**).

Discussion

Esophageal anastomotic leak is the most serious complication after esophagectomy and esophageal reconstruction. Study has shown [13] that the occurrence of anastomotic leak after surgery directly affects the survival of patients with esophageal cancer. Therefore, reducing the occurrence of anastomotic leak is one of the most urgent problems for clinicians.

In regular practice, end-to-side anastomosis is the primary method for esophageal anastomosis. Recent studies have shown that the incidence of anastomotic leak in end-to-side anastomosis is still high. Although the incidence is related to the surgical method and the experience of clinician to a certain extent, whether different anastomotic methods could also lead to the occurrence of anastomotic leak remains controversial [14, 15]. Oblique anastomosis is a new surgical technique developed by us. It refers to the anastomosis of the esophagus with the stomach at an angle of 45°-60° on the basis of end-to-side anastomosis so as to achieve esophageal reconstruction. However, its clinical benefit in practice is unclear. Hence we have explored this technique clinically in our study. Haverkamp et al. [16] showed that end-to-side anastomosis could reduce anastomotic stenosis and shorten hospitalization time compared to end-to-end anastomosis. In this study, we have compared the area around the anastomotic stoma, the total amount of drainage after operation and the time of bed rest between the experimental group and the control group. The results showed that the anastomotic area increased, the total drainage volume decreased and the time of bed rest decreased in the experimental group. This shows that oblique anastomosis can reduce the drainage volume and bed-ridden time after operation and increase the anastomotic area of patients, which is better than end-to-side anastomosis. We speculate that oblique anastomosis increases the anastomotic area of patients,

Table 4. Univariate analysis of risk factors about anastomotic leak (n, %)

	Anastomotic leak group (n=16)	Non-anastomotic leak group (n=89)	$t/\chi^2/Z$	P
Age (year)			6.088	0.014
≥60	12 (75.00)	37 (41.57)		
<60	4 (25.00)	52 (58.43)		
Gender			0.599	0.439
Male	9 (56.25)	59 (66.29)		
Female	7 (43.75)	30 (33.71)		
BMI (kg/m^2)				0.598
≥21	7 (43.75)	46 (51.69)		
<21	9 (56.25)	43 (48.31)		
Past medical history				
Hypertension	8 (50.00)	44 (49.44)	0.252	0.616
Diabetes	7 (43.75)	37 (41.57)	0.026	0.871
Smoking history			1.330	0.249
Yes	9 (56.25)	63 (70.79)		
No	7 (43.75)	26 (29.21)		
Alcohol abuse history			0.267	0.605
Yes	4 (25.00)	28 (31.46)		
No	12 (75.00)	61 (68.54)		
Residence			2.131	0.144
City	9 (56.25)	66 (74.16)		
Country	7 (43.75)	23 (25.84)		
Tumor location			-0.430	0.667
Upside	5 (31.25)	31 (34.83)		
Midpiece	5 (31.25)	30 (33.71)		
Hypomere	6 (37.5)	28 (31.46)		
Lymph node metastasis			0.210	0.647
Transferred	8 (50.00)	39 (43.82)		
Non-transferred	8 (50.00)	50 (56.18)		
TNM stage			-0.403	0.687
I	4 (25.00)	28 (31.46)		
II	8 (50.00)	40 (44.94)		
III	4 (25.00)	21 (23.60)		
Anastomotic methods			4.479	0.034
End-to-side anastomosis	13 (81.25)	47 (52.81)		
Oblique anastomosis	3 (18.75)	42 (47.19)		
Area of anastomotic stoma (cm^2)			0.256	0.613
≥2	7 (43.75)	33 (37.08)		
<2	9 (56.25)	56 (62.92)		
Total amount of drainage after operation (mL)			0.148	0.701
≥500	6 (37.50)	29 (32.58)		
<500	10 (62.5)	60 (67.42)		
Bed rest time (d)			0.403	0.526
≥4	10 (62.50)	48 (53.93)		
<4	6 (37.50)	41 (46.07)		

Note: BMI, body mass index.

Table 5. Assign a value table

Factor	Valuation
Age	≥60=1, <60=0
Anastomotic methods	End-to-side anastomosis =1, Oblique anastomosis =0
Anastomotic leak	Appeared =1, non-appeared =0

Table 6. Multivariate logistic analysis of risk factors related to anastomotic leak

Factor	B	S. E	Wals	Sig.	Exp (β)	95% CI
Age	1.487	0.631	5.554	0.018	4.422	1.284-15.225
Anastomotic methods	1.459	0.692	4.451	0.035	4.302	1.109-16.688

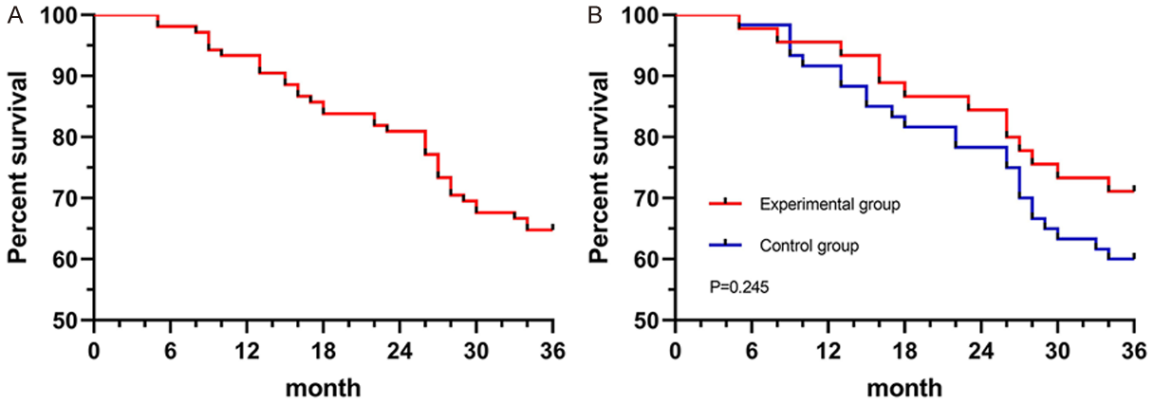

Figure 2. Three years survival. A: Three years overall survival; B: Comparison of 3-year survival rate between the control group and the experimental group (P=0.245).

promotes the healing of the surgical site and reduces the drainage flow after surgery, thus reducing the hospitalization of patients. We further analyzed the incidence of postoperative complications and found that the incidence of anastomotic leak in the control group was significantly higher than that in the experimental group and the total incidence of postoperative complications was also higher. This suggests that oblique anastomosis can effectively promote the postoperative recovery and reduce the occurrence of complications. In routine surgeries, end-to-side anastomosis [17], end-to-end anastomosis [18] and side-to-side anastomosis are performed [19]. For the first time, oblique anastomosis has been proposed for EC surgery in this study. Compared with end-to-side anastomosis, oblique anastomosis can significantly improve the prognosis of patients, but the impact of various anastomotic methods on the prognosis of patients was not explored.

In this study, we found that age and anastomotic mode are the independent factors affecting the occurrence of anastomotic leak in patients. ROC curve showed that the two indicators have certain value in patients with anastomotic leak. Due to the improvement in the quality of life and the gradual increase in the elderly population, studies have found that China has initially entered an aging society. Because of the low autoimmunity of the elderly who are accompanied by a variety of diseases, the patient's tolerance to surgery declines, thus resulting in complications [20, 21]. Anastomotic methods were not found to be independent risk factor in previous studies. In our study, we found that anastomotic mode is an independent risk factor for anastomotic leak. However, due to small sample size, only two types of anastomotic modes were included in this study. Whether they are representative or not is unclear. At the end of the study, we also evaluated the 3-year overall survival of the patients. The follow-up observations showed that the 3-year overall survival rate in the 105 patients was 64.76%, which was consistent with previous studies [22, 23]. Further analysis using survival curve showed that there was no significant difference in the

3-year survival rate between the two groups, suggesting that the new method did not have any improvement in patient survival over the traditional method.

In this study, we have analyzed the risk factors of anastomotic leak in patients with esophageal cancer and found that age and anastomotic method were independent risk factors for anastomotic leak, but they had no significant impact on the 3-year survival rate of patients. However, this study has some limitations. First, the study only considered end-to-side and oblique anastomosis while the other two anastomosis methods were not included, which makes the benefit of the new method over the other two methods questionable. Second, in this study we have carried out a 3-year survival follow-up for patients, however, a long-term survival follow-up would have been more informative. Therefore, more studies with a large sample size and including all the anastomotic methods along with long term follow-up are required.

In conclusion, age and anastomotic mode were found to be independently associated with anastomotic leak. Oblique anastomosis can increase anastomotic area while reduce postoperative drainage, bed rest time and the total incidence of complications. However, it has no significant impact on the survival of patients.

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Disclosure of conflict of interest

None.

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