Zhu et al. BMC Surgery (2024) 24:260
https://doi.org/10.1186/s12893-024-02562-5

BMC Surgery

RESEARCH

Open Access

Predictive factors for intrathoracic anastomotic leakage and postoperative mortality after esophageal cancer resection

Jian Zhu[1], Tianxiao Tao[1], Gengxin Zhang[1] and Shenhui Dai[1*]

Abstract

Background Esophageal cancer is currently one of the high-risk malignant tumors worldwide, posing a serious threat to human health. This study aimed to analyse the causes of postoperative mortality and intrathoracic anastomotic leakage(IAL) after esophagectomy.

Methods A retrospective analysis was conducted on 172 patients with esophageal cancer resection and focused on the preoperative and postoperative indicators. Cox regression analysis was performed to identify factors affected IAL and evaluated the potential factors on postoperative mortality. The Kaplan-Meier curve was applied to evaluate the effect of leakage on postoperative mortality after propensity score matching.

Results Univariable and multivariable Cox regression analysis showed that infection and high BMI were significant risk factors for IAL, patients with BMI over 24 kg/m^2 in IAL group was two times higher than that of the group without IAL (95% CI = 1.01–6.38; P = 0.048). When patients were infected, the hazard ratios(HRs) of anastomotic leakage was twice that of patients without infection (95% CI = 1.22–4.70; P = 0.011). On the other hand, IAL was a significant cause of postoperative mortality, the 40-day postoperative mortality rate in the leakage group was significantly higher than the non leakage group (28.95% in leakage group vs. 7.46% in non leakage group, P<0.01). After propensity score matching, IAL still significantly affected postoperative mortality. The total length of hospital stay of the leakage group was inevitably longer than that of the non leakage group (22.19 ± 10.79 vs. 15.27 ± 8.59).

Conclusion IAL was a significant cause of death in patients underwent esophageal cancer resection. Patients with high BMI over 24 kg/m^2 and infection may be more prone to developing IAL after esophagectomy. IAL inevitably prolonged the length of hospital stay and increased postoperative mortality.

Keywords Esophagectmy, Mortality, Anastomotic leakage, Risk factors

*Correspondence:
Shenhui Dai
2427112534@qq.com
[1]Cardiothoracic Surgery Department, the first Affiliated Hospital of Anhui University of Science & Technology (Huainan First People's Hospital), Huainan 232001, Anhui Province, China

Introduction

Esophageal cancer is currently one of the high-risk malignant tumors worldwide, posing a serious threat to human health [1, 2]. Esophageal cancer is the sixth leading cause of cancer related mortality, and its morbidity continues to increase every year [3]. Currently, surgical resection of the diseased esophagus is still the mainly treatment of esophageal cancer [4, 5]. Although the surgical methods for esophageal cancer have improved in recent years, traditional esophageal cancer surgeries are still being used in some primary hospitals in China due to limited medical resources. However, the complications of anastomotic leakage after esophagectomy remain serious that need to be addressed by thoracic surgeons worldwide [6–8]. Anastomotic leakage inevitably causes serious complications and affects prognosis. For example, esophageal anastomotic leakage may cause food residues stray into trachea, leading to pneumonia or pulmonary abscess. In addition, long-term anastomotic leakage may lead to weakened immunity, anemia, and other problems, which seriously affect patient's health. Patient may suffer from high incidence and mortality rates when anastomotic leakage occurs. It is reported that up to 40% of esophagectomy deaths are related to anastomotic leakage [9, 10].

Thoracic anastomosis and neck anastomosis are the two main methods for upper gastrointestinal reconstruction. The prognosis and incidence of intrathoracic and cervical anastomotic leakage are significantly different due to medical conditions and surgical experience, our study mainly focus on the risk factors for the occurrence of intrathoracic anastomotic leakage(IAL) during esophageal cancer resection. In this study, we collected clinical datas on patients who diagnosed as malignant tumors of esophagus and underwent esophagectomy. Our aim was to explore the mortality after esophagectomy and risk factors for IAL.

Patients and methods

Patients

A retrospective analysis was conducted on 172 patients with esophageal malignant tumors in the department of Cardiothoracic Surgery of the first Affiliated Hospital of Anhui University of Science & Technology (Huainan First People's Hospital) from January 1, 2019 to December 31, 2023. All patients underwent gastroscopy and obtained the final pathological results. Among them, 38 patients developed anastomotic leakages, while 134 patients were discharged smoothly. 102 are males and 70 are females, aged between 62 and 83 years old, with an average age of 68.34±9.33 years old. We collected and analyzed potential risk factors for postoperative mortality and IAL in patients by reviewing relevant literature and clinical experience.

Diagnostic criteria for thoracic anastomotic leakage

The definition of esophageal anastomotic leakage: The leakage that occured due to incomplete or poorly healed anastomosis between the esophagus and stomach. Some cases involved perforation of the stomach or esophagus caused by too deep or too tight sutures when embedding the anastomotic opening, also defined as a fistula [11].

The symptoms of thoracic anastomotic leakage: The clinical manifestations were mainly toxic symptoms: persistent high fever, coughed a large amount of pus and phlegm, severe chest pain, dyspnea, hydrothorax. Some patients may experienced toxic shock if not diagnosed and treated timely [12, 13].

Auxiliary examination: Chest X-ray and esophagography were used to confirm anastomotic leakage. If non-invasive examination failed to detect a small fistula or a localized fistula, thoracentesis with cloudy liquid or food residue could also diagnose thoracic anastomotic leakage. Gastroscopy was not a routine examination item, but it could clearly diagnose the location and types of the fistula and distinguished it from thoracogastric necrosis perforation.

Esophagectomy procedure: Open surgery: Patient was placed in a right lateral position, and a left posterior external incision was made through the 5th or 6th intercostal space to enter the thorax, separated the tissues surrounding the esophagus in thoracic esophagus. After opened the diaphragm, performed gastric dissection in the abdominal cavity, completed the dissection and cut off the esophagus, and then cut off the tubular stomach or only performed local resection of the proximal stomach; Some patients underwent intrathoracic lymph node dissection, after elevated the stomach through the thorax, esophago-gastric anastomosis was performed by using the circular stapler in thorax, we strictly followed the manufacturer's instructions (CDH25A, Johnson & Johnson MedTech, the USA). **Minimally invasive surgery**: Chest surgery: Patient was placed in a left lateral position, the 7th intercostal space on the right midaxillary line was regarded as the observation hole, the 5th and 8th intercostal spaces were the main operating holes. After removed mediastinal lymph nodes, the esophagus was separated up to the entrance of the chest and down to the level of the diaphragm. Abdominal surgery: Established artificial pneumoperitoneum through a 1.0 cm incision at the lower edge of the navel, with an pneumoperitoneum pressure of 12mmHg (1mmHg=0.133 kPa), made 1.0 cm incisions at the intersection of the navel and the clavicle midlines, and then made 0.5 cm incision under the rib arches at the left and right axillary lines. Cut off the abdominal lymph nodes, separated the hiatus of the esophagus and diaphragm, enlarged the hiatus to 5 cm, made a 3 cm small incision under the xiphoid process, and used a sling to take the stomach out of the abdominal cavity to create a tubular stomach. Finally, anastomosed the esophagus and stomach in the chest cavity by using the circular stapler (CDH25A, Johnson & Johnson MedTech, the USA).

Definition of infection: (1) Patients had clinical symptoms like fever, inflammatory indicators such as leukocyte and procalcitonin increased or positive blood bacterial culture. (2) Postoperative examination of chest and abdominal computerized tomography (CT) scan revealed abnormal lesions including ascites, pleural effusion, signs of pulmonary inflammation etc. Finally, the above points must exist simultaneously and diagnosed as infection after consultation with relevant department doctors. We particularly emphasized that infection was the precipitating factor for anastomotic leakage, as we observed in our study, patients firstly experience symptoms of infection before developed IAL.

Clinical observation indicators

We collected the potential risk factors for postoperative death and anastomotic fistula in esophageal cancer patients including sex, age, body mass index (BMI, Normal:18.5–23.9 kg/m^2; Overweight:≥24 kg/m^2; Underweight: <18.5 kg/m^2. Classify according to World Health Organization's standards [14]), pathological type. Some geriatric diseases like cardiovascular and diabetes, tumor location, tumor size, infection and pathological tumor node metastasis (TNM) stage.

Data collection and management

At the beginning of this study, a total of 245 patients were included, we excluded the following data: (1) The patient was diagnosed with esophageal malignant tumor but did not receive surgical treatment. (2) Failed to obtain informed consent from the patients. (3) Other types of anastomosis. (4) Incomplete clinical data.

The main purpose of this study was to analyze the predictive factors for intrathoracic anastomotic leakage and postoperative mortality. secondary measurements was the total length of hospital stay. For survival analysis, we integrated in-hospital mortality and 40-day mortality as postoperative mortality (POM). More than 95% of patients stayed in hospital within 40 days after surgery. Except for one who died at 42 days after surgery, the remaining patients died within 40 days after surgery. Therefore, 40-day postoperative mortality (POM40) was considered as the suitable primary measurements for survival analysis.

Statistical analysis

Continuous variables with normal distribution are represented as mean ± standard deviation, while categorical variables are represented as frequency or percentage. The chi-square test or Fisher's exact test was used to evaluate categorical variables. Cox regression analysis was used to evaluate the univariate and multivariate risks of potential risk factors for progression. The Kaplan Meier curve was used to plot the relationship between survival distribution and progression, and the logarithmic rank test was used to evaluate the differences in postoperative survival rates between subgroups. SPSS software (version 26.0; IBM Corp) was used for data processing. $P<0.05$ (bilateral) was considered statistically significant. To evaluate the prognostic value of leakage on IAL, propensity score matching(PSM) analysis was performed to reduce the potential bias between the leakage and non-leakage groups. Propensity scores were calculated through

Table 1 Clinical and pathological characteristics of the recruited cohort

Variables	Total ($n=172$)
Age(year), M (Q_1, Q_3)	71.00 (62.00, 75.25)
Tumor size(cm), M (Q_1, Q_3)	40.00 (30.00, 55.89)
Surgery time(min), M (Q_1, Q_3)	262.02 (234.50, 290.00)
Sex, n(%)	
Female	70 (40.70)
Male	102 (59.30)
BMI(kg/m^2), n(%)	
<18.5	31 (18.02)
18.5–23.9	88 (51.16)
≥ 24	53 (30.81)
Pathology, n(%)	
Squamous cell carcinoma	126 (73.26)
Adenocarcinoma	32 (18.60)
Other types	14 (8.14)
Diabetes, n(%)	
No	156 (90.70)
Yes	16 (9.30)
Cardiovascular disease, n(%)	
No	149 (86.63)
Yes	23 (13.37)
Tumor location, n(%)	
Upper thoracic esophagus	21 (12.21)
Middle thoracic esophagus	76 (44.19)
Lower thoracic esophagus	75 (43.60)
Infection, n(%)	
No	134 (77.91)
Yes	38 (22.09)
TNM stage, n(%)	
I/II	65 (37.79)
III	39 (22.67)
IV	68 (39.53)
Surgical Method, n(%)	
Minimally Invasive surgery	57 (33.14)
Open surgery	115 (66.86)
Anastomotic leakage, n(%)	
No	134 (77.91)
Yes	38 (22.09)

M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile. TNM: tumor-node-metastasis

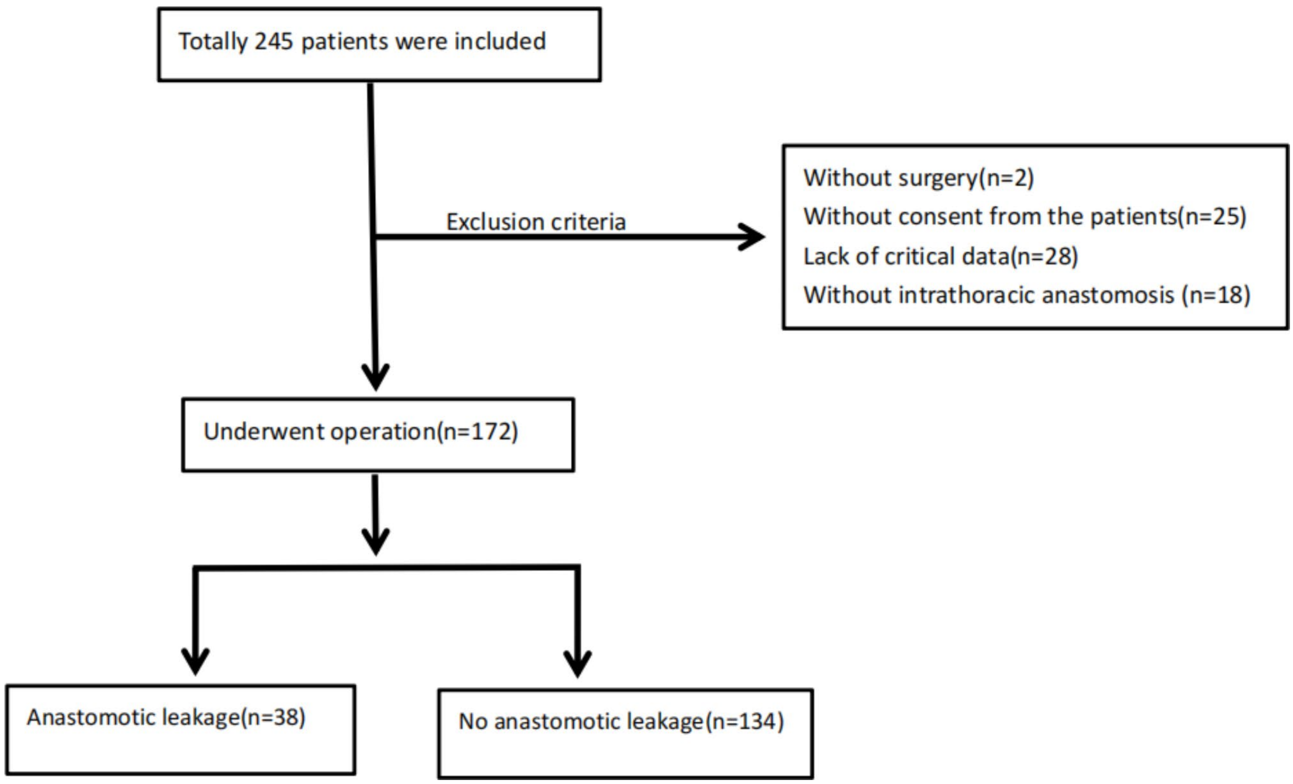

Fig. 1 Inclusion and exclusion process for esophageal cancer patients

logistic regression for each patient in the leakage and non leakage groups. Covariate balance was examined by the chi-square test. Survival comparisons were then performed for the matched patients using the same methods as those in the unmatched patients.

Results

The basic information of patients

Our study collected data on patients who underwent esophagectomy at the Cardiothoracic Surgery Department of first Affiliated Hospital of Anhui University of Science & Technology (Huainan First People's Hospital) from January 1, 2019 to December 31, 2023. They were strictly screened according to inclusion and exclusion criteria, some statistical information included was summarized in Table 1. As shown in Figs. 1 and 172 cases met the requirements, among the 172 cases included, 38 cases experienced postoperative IAL, with an incidence rate of 15.5%. The earliest occurrence of anastomotic leakage was on the 6nd day after surgery, and the latest was on the 15st day after surgery, with an average time of 10±3.6 days. Among patients with IAL, the majority of them were considered to diagnosis as IAL due to high fever or purulent drainage from the incision. Esophagography or gastroscopy was performed to confirm the presence of anastomotic leakage. 30 cases (78.95%) of IAL patients improved after conservative treatment and were discharged.

Clinical and pathological risk factors for postoperative mortality

In order to identify potential factors affected postoperative mortality in esophageal cancer patients, we conducted univariate and multivariate Cox regression analyses. 40-day postoperative mortality(POM40) was the primary outcome measurement. The results were summarized in Table 2. During the follow-up period of 40 days after surgery, a total of 21 people died, accounting for 8.57% of the total number. Univariable and multivariable Cox regression analysis showed that IAL was a significant cause of death after esophagectomy. The HRs (95% CIs) of leakage for POM40 in univariable and multivariable analyses were 4.52 (2.46–8.31; $P<0.01$) and 3.66 (1.89–7.10; $P<0.01$), respectively. Other potential variables, such as sex, age, BMI, pathological type, tumor size, surgical time did not show significant effects on POM40.

The clinical risk factors for 40-day IAL rate

The above studies indicated that IAL could lead to a higher postoperative mortality rates, however the etiology of IAL was very complex. We collected possible factors related to the occurrence of 40-day IAL rate by

Table 2 Clinical risk factors for 40-day postoperative mortality

Variables	Univariable Cox analysis		Multivariable Cox analysis	
	HR (95%CI)	*P*	HR (95%CI)	*P*
Age(year)	1.01 (0.98–1.05)	0.487		
Tumor size(cm)	1.00 (0.99–1.01)	0.764		
Surgery time(min)	1.00 (0.99–1.00)	0.436		
Sex				
Female	1.00 (Reference)			
Male	0.94 (0.51–1.74)	0.841		
BMI(kg/m^2)				
<18.5	1.00 (Reference)			
18.5–23.9	0.47 (0.20–1.09)	0.079		
≥ 24	1.39 (0.63–3.07)	0.409		
Pathology type				
Squamous cell carcinoma	1.00 (Reference)		1.00 (Reference)	
Adenocarcinoma	0.28 (0.09–0.93)	0.037	0.42 (0.13–1.40)	0.159
Other types	0.92 (0.33–2.59)	0.873	0.61 (0.21–1.77)	0.367
Diabetes				
No	1.00 (Reference)			
Yes	0.46 (0.11–1.89)	0.280		
Cardiovascular disease				
No	1.00 (Reference)			
Yes	0.44 (0.14–1.44)	0.175		
Tumor location				
Upper thoracic esophagus	1.00 (Reference)			
Middle thoracic esophagus	1.53 (0.59–3.99)	0.382		
Lower thoracic esophagus	0.55 (0.19–1.58)	0.266		
Infection				
No	1.00 (Reference)		1.00 (Reference)	
Yes	2.63 (1.41–4.92)	0.002	1.88 (0.98–3.61)	0.058
TNM stages				
I/II	1.00 (Reference)			
III	0.34 (0.12–1.00)	0.051		
IV	0.96 (0.51–1.82)	0.905		
Surgical Method				
Minimally Invasive surgery	1.00 (Reference)			
Open surgery	0.81 (0.43–1.53)	0.517		
Anastomotic leakage				
No	1.00 (Reference)		1.00 (Reference)	
Yes	4.52 (2.46–8.31)	< 0.001	3.66 (1.89–7.10)	< 0.001

M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile, TNM: tumor-node-metastasis, HR: hazard ratio, CI: confidence interval

reviewing relevant literature and clinical experience. Univariate and multivariate Cox regression analysis were conducted and the results indicated that infection and high BMI were significant risk factors for IAL. Patients with BMI in the normal range had lower possibility of IAL compared to patients with BMI outside of the normal range especially when BMI higher than 24 kg/m^2. In addition, from the Cox regression analysis result, we found that the BMI over 24 kg/m^2 in IAL group was two times higher than that of the group without IAL(95% CI = 1.01–6.38; P = 0.048). On the other hand, infection was also a risk factor for anastomotic leakage. When patients developed infection, the higher the probability of IAL could occured. From the Cox analysis result summarized in Table 3. When patients were infected, the hazard ratios(HRs) of anastomotic leakage was twice that of patients without infection(95% CI = 1.22–4.70; P = 0.011). From the perspective of tumor location, the likelihood of postoperative anastomotic leakage in middle thoracic esophagus also increased, but it did not reached statistical differences. In addition, there was no statistically significant difference in gender, age, pathological type and surgical method.

Table 3 Clinical risk factors for 40-day postoperative IAL

Variables	Univariable Cox analysis		Multivariable Cox analysis	
	HR (95%CI)	*P*	HR (95%CI)	*P*
Age(year)	0.98 (0.95–1.02)	0.399		
Tumor size(cm)	1.00 (0.98–1.01)	0.725		
Surgery time(min)	1.00 (1.00–1.00)	0.777		
Sex				
Female	1.00 (Reference)			
Male	0.77 (0.40–1.46)	0.417		
BMI(kg/m^2)				
<18.5	1.00 (Reference)		1.00 (Reference)	
18.5–23.9	0.60 (0.22–1.62)	0.313	0.62 (0.22–1.69)	0.347
≥ 24	2.69 (1.10–6.60)	0.030	2.54 (1.01–6.38)	0.048
Pathology type				
Squamous cell carcinoma	1.00 (Reference)		1.00 (Reference)	
Adenocarcinoma	0.12 (0.02–0.90)	0.039	0.20 (0.09–1.02)	0.054
Other types	1.78 (0.78–4.09)	0.174	1.19 (0.50–2.85)	0.695
Diabetes				
No	1.00 (Reference)			
Yes	0.48 (0.12–1.99)	0.312		
Cardiovascular disease				
No	1.00 (Reference)			
Yes	0.28 (0.07–1.17)	0.081		
Tumor location				
Upper thoracic esophagus	1.00 (Reference)			
Middle thoracic esophagus	1.22 (0.46–3.23)	0.686		
Lower thoracic esophagus	0.44 (0.15–1.31)	0.140		
Infection				
No	1.00 (Reference)		1.00 (Reference)	
Yes	3.02 (1.57–5.82)	< 0.001	2.39 (1.22–4.70)	0.011
TNM stage				
I/II	1.00 (Reference)			
III	0.79 (0.33–1.87)	0.587		
IV	1.15 (0.56–2.37)	0.707		
Surgical method				
Minimally invasive surgery	1.00 (Reference)			
Open surgery	1.05 (0.52–2.11)	0.902		

M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile, TNM: tumor-node-metastasis, HR: hazard ratio, CI: confidence interval

Effect of IAL on postoperative mortality

Through the above study, we found that the main cause of postoperative death in esophagectomy was postoperative anastomotic leakage. Also, IAL would inevitably lead to an extension of hospital stay. We compared the hospital stay and postoperative 40 day mortality rates of patients with and without IAL (supplemental Table 1), the results showed that the total length of hospital stay of the leakage group was longer than that of the non leakage group(23.42±4.56 vs. 14.89±5.32), and the 40-day postoperative survival rate in leakage group was significantly lower than non leakage group (83.33% in leakage group vs. 94.41% in non leakage group, P<0.05). These findings suggested that IAL led to increased postoperative mortality rates and prolonged postoperative hospital stay.

Although Cox regression analysis showed that IAL was an important risk factor for postoperative mortality, some clinical features of the two groups are not balanced. More patients in the non leakage group had pathological TNM stage and histological type. This imbalanced distribution may lead to potential biases in statistical evaluation. Therefore, in order to reduce this potential bias between two groups, we conducted propensity score match (PSM) analysis. As a result, the distribution of patients among subgroups was balanced (Table 4). The Kaplan Meier curve and log rank test indicated that IAL significantly affected survival within 40 days after surgery in both the original dataset and PSM dataset(Fig. 2).

Disscussion

Esophageal cancer is one of the most common cancers and its the sixth leading cause of cancer-related deaths. The overall five-year survival rate ranges from 15–25% [15]. Surgical resection is currently the main treatment for esophageal cancer, esophagectomy and esophagogastrostomy procedures performed via the esophageal bed are conventional surgical procedures, but there exists some complications [16–18]. Anastomotic leakage is a common and serious complication after radical resection of esophageal cancer, especially intrathoracic anastomotic leakage(IAL), which is more likely to cause severe thoracic infection, sepsis, and even multiple organ failure [19–21]. It is also an important factor leading to postoperative death and affecting the quality of patients' life. However, in our study, the in-hospital mortality rate of patients with IAL is 3.27%, and the 40 days mortality rate was 4.49%, which was lower than previous studies, this may be related to the experience of doctors [22, 23]. On the other hand, our study suggested that IAL was the main cause of postoperative death while high BMI and infection were the main causes for IAL. Patients with BMI in the normal or low range had lower postoperative anastomotic leakage compared to patients with BMI over than 24 kg/m^2. Besides, we found that the postoperative IAL of patients with BMI≥24 kg/m^2 was more than twice that of patients with BMI under normal range. As is known to as all, BMI is a commonly used to measure the degree of obesity and health of the human body, a

Table 4 Clinical characteristics of the recruited cohort stratified by IAL and the PS-matched cohort

Variables	**Before PSM**			**After PSM**		
	Non-leakage ($n=134$)	**Leakage ($n=38$)**	***P***	**Non-leakage ($n=46$)**	**Leakage ($n=27$)**	***P***
Age(years), M (Q_1, Q_3)	71.00 (63.00, 76.00)	69.73 (61.00, 74.00)	0.568	71.00 (64.50, 75.00)	70.00 (64.50, 74.00)	0.762
Tumor size(cm), M (Q_1, Q_3)	40.00 (30.00, 58.18)	39.65 (31.00, 55.30)	0.635	40.00 (34.02, 50.00)	39.29 (36.02, 59.65)	0.660
Surgery time(min), M (Q_1, Q_3)	263.17 (230.00, 295.00)	260.70 (246.36, 277.16)	0.890	267.33 (245.24, 284.64)	266.93 (249.00, 277.38)	0.797
Sex, n (%)			0.566			0.699
Female	53 (39.55)	17 (44.74)		20 (43.48)	13 (48.15)	
Male	81 (60.45)	21 (55.26)		26 (56.52)	14 (51.85)	
BMI(kg/m^2), n (%)			< 0.001			0.715
<18.5	24 (17.91)	7 (18.42)		10 (21.74)	5 (18.52)	
18.5–23.9	78 (58.21)	10 (26.32)		20 (43.48)	10 (37.04)	
≥ 24	32 (23.88)	21 (55.26)		16 (34.78)	12 (44.44)	
Pathology, n (%)			0.001			1.000
Squamous cell carcinoma	96 (71.64)	30 (78.95)		38 (82.61)	23 (85.19)	
Adenocarcinoma	31 (23.13)	1 (2.63)		3 (6.52)	1 (3.70)	
Other types	7 (5.22)	7 (18.42)		5 (10.87)	3 (11.11)	
Diabetes, n (%)			0.513			1.000
No	120 (89.55)	36 (94.74)		44 (95.65)	26 (96.30)	
Yes	14 (10.45)	2 (5.26)		2 (4.35)	1 (3.70)	
Cardiovascular disease, n (%)			0.096			0.983
No	113 (84.33)	36 (94.74)		44 (95.65)	25 (92.59)	
Yes	21 (15.67)	2 (5.26)		2 (4.35)	2 (7.41)	
Tumor location, n (%)			0.042			0.945
Upper thoracic esophagus	16 (11.94)	5 (13.16)		9 (19.57)	5 (18.52)	
Middle thoracic esophagus	53 (39.55)	23 (60.53)		22 (47.83)	14 (51.85)	
Lower thoracic esophagus	65 (48.51)	10 (26.32)		15 (32.61)	8 (29.63)	
Infection, n (%)			0.003			0.700
No	111 (82.84)	23 (60.53)		31 (67.39)	17 (62.96)	
Yes	23 (17.16)	15 (39.47)		15 (32.61)	10 (37.04)	
TNM stages, n (%)			0.954			0.753
I/II	50 (37.31)	15 (39.47)		21 (45.65)	10 (37.04)	
III	31 (23.13)	8 (21.05)		8 (17.39)	6 (22.22)	
IV	53 (39.55)	15 (39.47)		17 (36.96)	11 (40.74)	
Surgical Method, n (%)			0.534			0.949
Minimally Invasive surgery	46 (34.33)	11 (28.95)		15 (32.61)	9 (33.33)	
Open surgery	88 (65.67)	27 (71.05)		31 (67.39)	18 (66.67)	

M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile, TNM: tumor-node-metastasis, HR: hazard ratio, CI: confidence interval

high BMI means obesity [24–26]. In our study, patients with higher BMI were more likely to develop postoperative IAL, which was consistent with the study by Patrick J, McBee et al. [27]. We preliminarily infered that this may be due to the excessive fat in patients reduced the surgical field, made it difficult and risky for surgeons to see blood vessels visually during laparoscopic surgery, and even led to the destruction of the right gastric omentum vascular arch, thereby affected the blood supply to the tubular stomach [28]. In addition, patients with high BMI have more tissue fat content, which increased the likelihood of surgical incision fat liquefaction. Incision fat liquefaction may lead to infection, thereby eroding the anastomotic site and causing anastomotic leakage [29].

Besides, our study also indicated that when patients developed infection, the higher the probability of IAL could occured, our result indicated that the HRs of IAL were twice that of patients without infection. The relevant literature reports were consistent with our study, suggested that postoperative infection was an independent risk factor for anastomotic leakage after esophageal cancer resection [30, 31]. A multicenter study showed that patients with preoperative respiratory diseases had an increased risk of anastomotic leakage (OR=1.64) and postoperative pneumonia (OR=1.39), these may due to infection caused fever, high metabolic status, and even sepsis, the body's nutritional supply was further consumed, which may lead to the occurrence of postoperative anastomotic leakage [32, 33]. Due to pulmonary infection, increased secretions, sputum production, coughing stimulation or increased tension at the anastomotic site may also lead to anastomotic tearing and

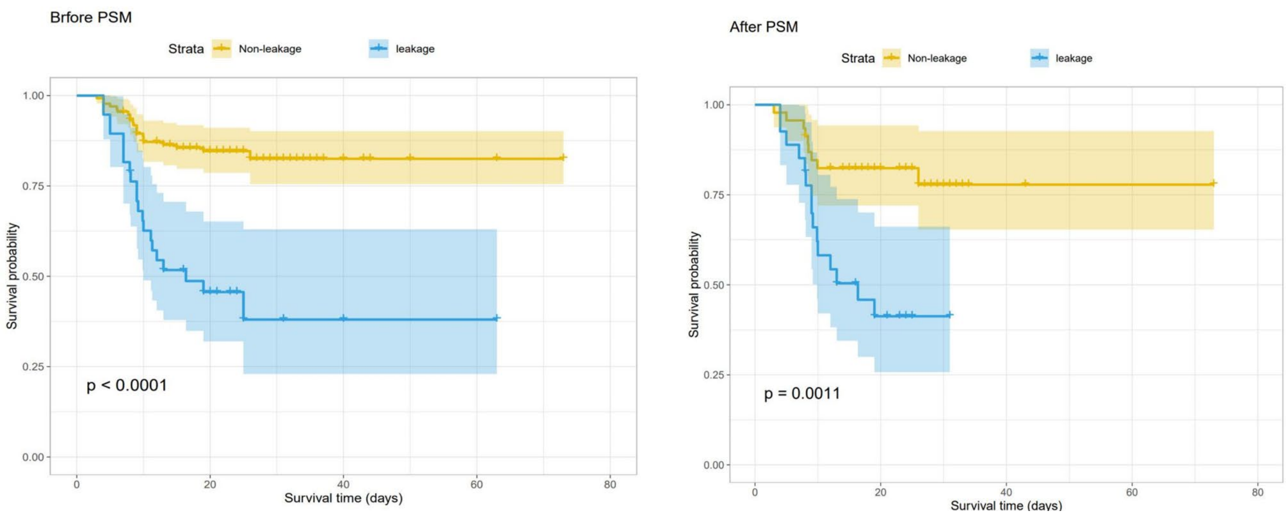

Fig. 2 Kaplan–Meier curves for postoperative mortality in the raw dataset and the propensity score matched dataset

the formation of anastomotic leakage [34]. Based on the above results, we consider that perioperative preparation should be made to reduce the occurrence of esophageal anastomotic leakage, such as enhancing physical fitness, improving overall condition, prophylactic use of antibiotics before surgery to reduce the risk of postoperative infection, and ensuring accurate alignment of the esophagus and stomach during anastomosis to avoid mucosal eversion and reducing anastomotic tension.

Our study has limitations. Firstly, there was inevitably selection bias in the selection of data, we should include a larger number of cases to prove the reliability of our results. Secondly, our study did not collect longer follow-up datas to verify the postoperative quality of life and complications of patients. Also, we did not include other types of anastomotic fistulas, such as neck anastomotic leakage, this was due to the surgical methods and experience of our surgeons. Many more factors should be involved in the occurrence of IAL, for example, neoadjuvant therapy, preoperative nutritional status, anastomotic technique, ASA score, and respiratory function etc. However the above issues did not affect the results, as our study involves multiple steps.

In summary, our study indicated that IAL led to serious adverse consequences, including prolonged hospital stay and high postoperative mortality. PSM showed that IAL was a significant risk factor for postoperative mortality. Infection and high BMI were significantly associated with postoperative IAL after esophageal cancer resection. These findings suggested that special care should be taken when treating such patients.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-024-02562-5.

Supplementary Material 1

Acknowledgements

The authors would like to thank all participating investigators.

Author contributions

Jian Zhu designed and wrote the manuscript. Tianxiao Tao, Gengxin Zhang collected and analyzed the data. Shenhui Dai reviewed and edited the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by Science Plan Project of Huainan City (2021175).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical committee of the first Affiliated Hospital of Anhui University of Science & Technology(Huainan First People's Hospital) and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent(2019-ethics-054).

Consent to participate and publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 23 May 2024 / Accepted: 5 September 2024
Published online: 13 September 2024

References

1. Watanabe M, Otake R, Kozuki R, Toihata T, Takahashi K, Okamura A, Imamura Y. Recent progress in multidisciplinary treatment for patients with esophageal cancer. Surg Today. 2020;50(1):12–20. https://doi.org/10.1007/s00595-019-01878-7. Epub 2019 Sep 18. Erratum in: Surg Today. 2020;50(4):425. PMID: 31535225; PMCID: PMC6952324.
2. Liu K, Zhao T, Wang J, Chen Y, Zhang R, Lan X, Que J. Etiology, cancer stem cells and potential diagnostic biomarkers for esophageal cancer. Cancer Lett. 2019;458:21–8. https://doi.org/10.1016/j.canlet.2019.05.018. Epub 2019 May 21. PMID: 31125642; PMCID: PMC6597177.

3. Ashok A, Niyogi D, Ranganathan P, Tandon S, Bhaskar M, Karimundackal G, Jiwnani S, Shetmahajan M, Pramesh CS. The enhanced recovery after surgery (ERAS) protocol to promote recovery following esophageal cancer resection. Surg Today. 2020;50(4):323–334. https://doi.org/10.1007/s00595-020-01956-1. Epub 2020 Feb 11. Erratum in: Surg Today. 2020;: PMID: 32048046; PMCID: PMC7098920.
4. Kasai F, Kobayashi T, Hoshi E, Nagai T, Yamashita T, Otsuka K, Murakami M, Kawate N. Does Prehabilitation reduce postoperative length of Hospital stay after esophageal Cancer surgery? Prog Rehabil Med. 2024;9:20240013. https://doi.org/10.2490/prm.20240013. PMID: 38601861; PMCID: PMC11001495.
5. Kundel Y, Kurman N, Sulimani O, Gavrielli S, Nachalon Y, Moore A, Kashtan H, Fenig E, Brenner B, Popovtzer A, Fredman E. The effect of gastric fundus radiation dose on postoperative anastomotic leakage in esophageal cancer. Front Oncol. 2023;13:1080089. https://doi.org/10.3389/fonc.2023.1080089. PMID: 36925923; PMCID: PMC10011689.
6. de Groot EM, Bronzwaer SFC, Goense L, Kingma BF, van der Horst S, van den Berg JW, Ruurda JP, van Hillegersberg R. Management of anastomotic leakage after robot-assisted minimally invasive esophagectomy with an intrathoracic anastomosis. Dis Esophagus. 2023;36(6):doac094. https://doi.org/10.1093/dote/doac094. PMID: 36636758; PMCID: PMC10226267.
7. Verstegen MHP, Bouwense SAW, van Workum F, Ten Broek R, Siersema PD, Rovers M, Rosman C. Management of intrathoracic and cervical anastomotic leakage after esophagectomy for esophageal cancer: a systematic review. World J Emerg Surg. 2019;14:17. https://doi.org/10.1186/s13017-019-0235-4. PMID: 30988695; PMCID: PMC6449949.
8. Ubels S, Klarenbeek B, Verstegen M, Bouwense S, Griffiths EA, van Workum F, Rosman C, Hannink G. TENTACLE—Esophagus Collaborative Group. Predicting mortality in patients with anastomotic leak after esophagectomy: development of a prediction model using data from the TENTACLE-Esophagus study. Dis Esophagus. 2023;36(5):doac081. https://doi.org/10.1093/dote/doac081. PMID: 36461788; PMCID: PMC10150169.
9. Froiio C, Berlth F, Capovilla G, Tagkalos E, Hadzijusufovic E, Mann C, Lang H, Grimminger PP. Robotic-assisted surgery for esophageal submucosal tumors: a single-center case series. Updates Surg. 2022;74(3):1043–54. https://doi.org/10.1007/s13304-022-01247-z. Epub 2022 Feb 11. PMID: 35147859; PMCID: PMC9213313.
10. He G, Wang J, Chen B, Xing X, Wang J, Chen J, He Y, Cui Y, Chen M. Feasibility of endoscopic submucosal dissection for upper gastrointestinal submucosal tumors treatment and value of endoscopic ultrasonography in pre-operation assess and post-operation follow-up: a prospective study of 224 cases in a single medical center. Surg Endosc. 2016;30(10):4206–13. https://doi.org/10.1007/s00464-015-4729-1. Epub 2016 Jan 28. PMID: 26823060.
11. Zhu H, Ma X, Ye T, Wang H, Wang Z, Liu Q, Zhao K. Esophageal cancer in China: Practice and research in the new era. Int J Cancer. 2023;152(9):1741–1751. https://doi.org/10.1002/ijc.34301. Epub 2022 Oct 5. PMID: 36151861.
12. Gao P, Yang X, Suo C, Yuan Z, Cheng H, Zhang Y, Jin L, Lu M, Chen X, Ye W. Socioeconomic status is inversely associated with esophageal squamous cell carcinoma risk: results from a population-based case-control study in China. Oncotarget. 2018;9(6):6911–23. https://doi.org/10.18632/oncotarget.24003. PMID: 29467939; PMCID: PMC5805525.
13. Sobrino-Cossío S, Soto-Pérez JC, Coss-Adame E. Post-fundoplication symptoms and complications: Diagnostic approach and treatment. Rev Gastroenterol Mex. 2017;82(3):234–247. English, Spanish. https://doi.org/10.1016/j.rgmx.2016.08.005. Epub 2017 Jan 5. PMID: 28065591.
14. Weir CB, Jan A, BMI Classification Percentile And Cut Off Points. 2023 Jun 26. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 31082114.
15. Huang FL, Yu SJ. Esophageal cancer: risk factors, genetic association, and treatment. Asian J Surg. 2018;41(3):210–5. https://doi.org/10.1016/j.asjsur.2016.10.005. Epub 2016 Dec 13. PMID: 27986415.
16. Liu CQ, Ma YL, Qin Q, Wang PH, Luo Y, Xu PF, Cui Y. Epidemiology of esophageal cancer in 2020 and projections to 2030 and 2040. Thorac Cancer. 2023;14(1):3–11. https://doi.org/10.1111/1759-7714.14745. Epub 2022 Dec 8. PMID: 36482832; PMCID: PMC9807450.
17. Uhlenhopp DJ, Then EO, Sunkara T, Gaduputi V. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. Clin J Gastroenterol. 2020;13(6):1010–21. https://doi.org/10.1007/s12328-020-01237-x. Epub 2020 Sep 23. PMID: 32965635.
18. Bardol T, Ferre L, Aouinti S, Dupuy M, Assenat E, Fabre JM, Picot MC, Souche R. Survival after Multimodal Treatment including surgery for metastatic esophageal Cancer: a systematic review. Cancers (Basel). 2022;14(16):3956. https://doi.org/10.3390/cancers14163956. PMID: 36010949; PMCID: PMC9405894.
19. Gockel I, Hoffmeister A. Endoscopic or Surgical Resection for Gastro-Esophageal Cancer. Dtsch Arztebl Int. 2018;115(31–32):513–9. https://doi.org/10.3238/arztebl.2018.0513. PMID: 30149830; PMCID: PMC6131362.
20. Chen SB, Liu DT, Chen YP. Surgical resection for esophageal adenosquamous carcinoma: an analysis of 56 cases. World J Surg Oncol. 2022;20(1):143. https://doi.org/10.1186/s12957-022-02607-0. PMID: 35509082; PMCID: PMC9066921.
21. Kudou K, Saeki H, Nakashima Y, Kimura Y, Oki E, Mori M, Shimokawa M, Kakeji Y, Toh Y, Doki Y, Matsubara H. Clinical outcomes of surgical resection for recurrent lesion after curative esophagectomy for esophageal squamous cell carcinoma: a nationwide, large-scale retrospective study. Esophagus. 2022;19(1):57–68. Epub 2021 Sep 12. PMID: 34510325; PMCID: PMC8739466.
22. Hua F, Sun D, Zhao X, Song X, Yang W. Update on therapeutic strategy for esophageal anastomotic leak: a systematic literature review. Thorac Cancer. 2023;14(4):339–47. https://doi.org/10.1111/1759-7714.14734. Epub 2022 Dec 16. PMID: 36524684; PMCID: PMC9891862.
23. Sun ZW, Du H, Li JR, Qin HY. Constructing a risk prediction model for anastomotic leakage after esophageal cancer resection. J Int Med Res. 2020;48(4):300060519896726. https://doi.org/10.1177/0300060519896726. PMID: 32268818; PMCID: PMC7153184.
24. Fan J, Liu Z, Mao X, Tong X, Zhang T, Suo C, Chen X. Global trends in the incidence and mortality of esophageal cancer from 1990 to 2017. Cancer Med. 2020;9(18):6875–87. https://doi.org/10.1002/cam4.3338. Epub 2020 Aug 4. PMID: 32750217; PMCID: PMC7520289.
25. Mazidimoradi A, Banakar N, Khani Y, Allahqoli L, Salehiniya H. Current status and temporal trend in incidence, death, and burden of esophageal cancer from 1990–2019. Thorac Cancer. 2023;14(24):2408–58. https://doi.org/10.1111/1759-7714.15028. Epub 2023 Jul 13. PMID: 37443420; PMCID: PMC10447176.
26. Shridhar R, Takahashi C, Huston J, Doepker MP, Meredith KL. Anastomotic leak and neoadjuvant chemoradiotherapy in esophageal cancer. J Gastrointest Oncol. 2018;9(5):894–902. https://doi.org/10.21037/jgo.2018.04.09. PMID: 30505592; PMCID: PMC6219963.
27. Alqarni A, Aljehaiman F, Almousa SA, Almarshad SA, Alrzouq FK. The relationship between BMI and postoperative complications among Colorectal Cancer patients undergoing surgery. Cureus. 2023;15(11):e48715. https://doi.org/10.7759/cureus.48715. PMID: 38094533; PMCID: PMC10716719.
28. van Kooten RT, Voeten DM, Steyerberg EW, Hartgrink HH, van Berge Henegouwen MI, van Hillegersberg R, Tollenaar RAEM, Wouters MWJM. Patient-related prognostic factors for anastomotic leakage, Major complications, and short-term mortality following esophagectomy for Cancer: a systematic review and Meta-analyses. Ann Surg Oncol. 2022;29(2):1358–73. https://doi.org/10.1245/s10434-021-10734-3. Epub 2021 Sep 5. PMID: 34482453; PMCID: PMC8724192.
29. Wang P, Li Y, Sun H, Liu S, Zhang R, Liu X, Zhu Z. Predictive value of body Mass Index for short-term outcomes of patients with Esophageal Cancer after Esophagectomy: a Meta-analysis. Ann Surg Oncol. 2019;26(7):2090–103. https://doi.org/10.1245/s10434-019-07331-w. Epub 2019 Apr 1. PMID: 30937663.
30. Kim YI, Yu CS, Kim YS, Kim CW, Lee JL, Yoon YS, Park IJ, Lim SB, Kim JC. Clostridium difficile infection after ileostomy closure and anastomotic failure in rectal cancer surgery patients. BJS Open. 2022;6(2):zrac026. https://doi.org/10.1093/bjsopen/zrac026. PMID: 35445239; PMCID: PMC9021405.
31. Biere SS, Maas KW, Cuesta MA, van der Peet DL. Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. Dig Surg. 2011;28(1):29–35. https://doi.org/10.1159/000322014. Epub 2011 Feb 4. PMID: 21293129.
32. Matsuda A, Maruyama H, Akagi S, Inoue T, Uemura K, Kobayashi M, Shiomi H, Watanabe M, Fujita T, Takahata R, Takeda S, Fukui Y, Toiyama Y, Hagiwara N, Kaito A, Matsutani T, Yasuda T, Yoshida H, Tsujimoto H, Kitagawa Y. Survival impact of surgical site infection in esophageal cancer surgery: a multicenter retrospective cohort study. Ann Gastroenterol Surg. 2023;7(4):603–14. https://doi.org/10.1002/ags3.12656. PMID: 37416740; PMCID: PMC10319607.
33. Guo D, Liao F, Yang L, Liu B, Chen L. The influence of minimally invasive esophagectomy on wound infection in patients undergoing esophageal cancer surgery: a meta-analysis. Int Wound J. 2024;21(1):e14598. https://doi.org/10.1111/iwj.14598. PMID: 38272810; PMCID: PMC10789583.
34. Gao S, Liu Y, Duan X, Liu K, Mohammed M, Gu Z, Ren J, Yakoumatos L, Yuan X, Lu L, Liang S, Li J, Scott DA, Lamont RJ, Zhou F, Wang H. Porphyromonas

gingivalis infection exacerbates oesophageal cancer and promotes resistance to neoadjuvant chemotherapy. Br J Cancer. 2021;125(3):433–44. https://doi.org/10.1038/s41416-021-01419-5. Epub 2021 May 12. PMID: 33981017; PMCID: PMC8329259.

Publisher's note