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Original Article

Evaluation of Risk Factors for Anastomotic Leakage and Mortality Following Esophageal Cancer Surgery

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ABSTRACT

Objective: Postoperative anastomotic leakage is one of the most severe complications of esophageal surgery, significantly increasing patient morbidity and mortality risk. This study aims to evaluate the impact of the anastomosis level on postoperative leakage and stricture rates in esophageal cancer surgery.

Methods: A total of 104 patients operated on for esophageal cancer at the General Surgery Department of Istanbul Dr. Lütfi Kırdar City Hospital between January 2010 and February 2023 were included.

Results: Mortality occurred in 47 patients during follow-up. Among the patients who developed mortality, the rates of McKeown operation, hand-sewn anastomosis, and lymphovascular invasion were significantly higher than in those who did not develop mortality.

Conclusion: Identifying risk factors and selecting the appropriate technique can reduce complication rates and improve postoperative outcomes.

INTRODUCTION

Esophageal cancer is a significant global health issue characterized by high mortality rates, with approximately 600,000 new cases diagnosed annually, most of which are detected at advanced stages.[1] Surgical treatment, particularly esophagectomy, is one of the most effective treatments for localized esophageal cancer. However, determining the anastomosis level post-surgery is critical for postoperative complications.

Postoperative anastomotic leakage (AL) is one of the most severe complications of esophageal surgery, significantly increasing patient morbidity and mortality risk. The literature reports anastomotic leakage rates ranging from 1.4% to 17%.[2] Anastomotic stricture is also a common complication that can negatively impact patients' quality of life. Cervical anastomoses are reported to have higher stricture rates compared to thoracic anastomoses.[1]

Recent years have seen intraoperative and postoperative interventions effectively reduce anastomotic leakage and stricture rates. The intraoperative frozen section method provides high accuracy in assessing surgical margins, potentially reducing the need for repeat surgeries and complication rates.[3] Additionally, advancements in perioperative management and early feeding protocols can accelerate recovery and reduce complication risks.[4,5]

This study aims to evaluate the risk factors affecting anastomotic leakage and mortality in esophageal cancer surgery. For this purpose, data from 104 patients operated on between 2010 and 2023 at our clinic were retrospectively analyzed and compared with existing literature.

MATERIALS AND METHODS

Study Design

This study was designed as a retrospective cohort study. 104 patients who were operated on for esophageal cancer at a tertiary reference hospital between January 2010 and February 2023 were included in the study. The study protocol was approved by the Kartal Dr. Lütfi Kırdar City Hospital (approval number 2024/010.99/2/34).

Inclusion and Exclusion Criteria

Patients aged >18 years who underwent surgery in the general surgery clinic were included. Patients whose data were inaccessible or who were operated on for reasons other than esophageal cancer were excluded.

Data Collection

Data were obtained from patient files, surgery reports, and pathology reports. Age, gender, type of surgery, postoperative pathology results, tumor characteristics, and

Table 1. Evaluation of patients who are alive and ex as a result of follow-up

	Total	Alive	Ex	p
Variable	n=104	n=57	n=47	
	n (%)	n (%)	n (%)	
Gender				
Female	58 (55.8)	36 (63.2)	22 (46.8)	0.095*
Male	46 (44.2)	21 (36.8)	25 (53.2)	
Age [median (IQR)]	57.5 (50.25-64.75)	57 (48-63)	58 (52-66)	0.209**
Preoperative Biopsy Result				
Squamous Cell Carsinoma	94 (90.4)	51 (89.5)	43 (91.5)	1.00f
Leiomyoma	1 (1.0)	1 (1.8)	0 (0)	
Adenocarcinoma	9 (8.7)	5 (8.8)	4 (8.5)	
Localization				
Distal esophagus	75 (72.1)	40 (70.2)	35 (74.5)	0.828f
Middle esophagus	27 (26.0)	16 (28.1)	11(23.4)	
Proximal esophagus	2 (1.9)	1 (1.8)	1 (2.1)	
Tumor Size	4 (3-5)	4 (2-5)	4 (3-5)	0.597**
Operation Type				
Transhiatal	24 (23.1)	16 (28.1)a	8 (17.0)a	0.018*
Mckeown	44 (42.3)	17 (29.8)a	27 (57.4)b	
Ivor Lewis	36 (34.6)	24 (42.1)a	12 (25.5)a	
Type of Anastomosis				
Hand Sewn	48 (46.2)	20 (35.1)a	28 (59.6)b	0.018f
Stapler	55 (52.9)	36 (63.2)a	19 (40.4)b	
Cervical	1 (1.0)a	1 (1.8)a	0 (0)a	
Site of Anastomosis				
Intrathoracic	37 (35.6)	24 (42.1)	13 (27.7)	0.126*
Cervical	67 (64.4)	33 (57.9)	34 (72.3)	
Surgical margin				
Negative	98 (94.2)	55 (96.5)	43 (91.5)	0.406f
Positive	6 (5.8)	2 (3.5)	4 (8.5)	
Pathology				
No residue tumor	39 (37.5)	24 (42.1)	15 (31.9)	0.544*
Squamous Cell Carsinoma	54 (51.9)	27 (47.4)	27 (57.4)	
Adenocarcinoma	11 (10.6)	6 (10.5)	5 (10.6)	
Total Lymph Nodes	12 (8.25-17)	11 (7-17)	14 (9-17)	0.218**
Pathological Lymph Nodes	0 (0-1)	0 (0-5)	0 (0-2)	0.052**
Lymphovascular Invasion	25 (24.0)	9 (15.7)	16 (34)	0.030*
Perineural Invasion	27 (26.0)	13 (22.8)	14 (29.8)	0.419*

*Chi square test, **Mann-whitney U test, fFisher's exact test. IQR: Interquartile range.

postoperative complications were recorded.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (version 24.0, IBM Corp., Armonk, NY, USA). Descriptive statistical methods (median, frequency, percent, minimum, and maximum) were used to present the data. The Pearson chi-square test was used to compare qualitative data, and Fisher's exact test was applied when the number of subgroups was low. The normal distribution of quantitative data was assessed by the Kolmogorov–Smirnov and Shapiro–Wilk tests. Quantitative data without normal distribution were compared using the Mann–Whitney U test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 104 patients were operated on for esophageal cancer in our clinic between 2010 and 2023. The distribution of patients by year is shown in Figure 1.

Of the patients, 55.8% were female, with a mean age of 57.32±10.69 years. The characteristics of the patients are presented in Table 1. Mortality occurred in 47 patients during follow-up. Among the patients who developed mortality, the rates of McKeown operation, hand-sewn anastomosis, and lymphovascular invasion were significantly higher than in those who did not develop mortality.

The most common comorbidities in patients were hypertension, diabetes, and coronary artery disease, respectively. Intraoperative bleeding occurred in 2 patients (Table 2).

Among the patients who developed mortality, 16 died within the first month postoperatively, and 25 died within the first year postoperatively. Postoperative stricture occurred in 21.2% of patients, and postoperative leakage occurred in 7.7%, as shown in Table 3. There was no statistically significant difference between patients who developed and did not develop mortality in terms of postoperative stricture and leakage. Patients who developed postoperative leakage had longer operation and hospitalization times (p=0.030 and p<0.001, respectively). Among those who developed postoperative stricture, the proportion of males (63.9%) was significantly higher than those who did not develop stricture (39%) (p=0.039). There was no statistically significant difference between other factors and the development of postoperative stricture or leakage.

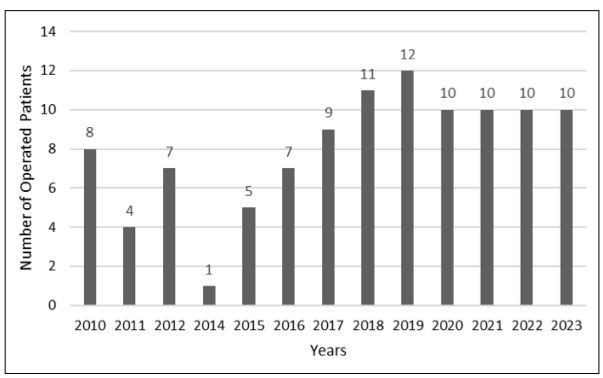

Figure 1. Distribution of the number of patients operated on due to esophageal cancer by years.

Table 2. Comorbidities of patients and preoperative complications

Variables	n	%
Comorbidities		
None	63	60.6
DM	17	16.3
HT	25	24.0
Coroner arter disease	11	10.6
Chronic kidney failure	2	1.9
Chronic heart failure	2	1.9
Chronic obstructive pulmonary disease	3	2.9
FMF	1	1.0
HCV	1	1.0
Complications (perop)		
Bleeding	2	1.9
Spleen Injury	1	1.0
Hepatic Vein Aberrant Branch Repair	1	1.0
Pleural Injury	1	1.0
Left Vocal Cord Sacrification/Tracheostomy	1	1.0

*DM: Diabetes mellitus; HT: Hypertension; CAD: Coroner arter disease; CKD: Chronic kidney failure; CHF: Chronic heart failure; COPD: Chronic obstructive pulmonary disease; FMF: Familial mediterrian fever; HCV: Hepatit C virus.

Table 3. Follow-up results of patients

	Mean±S.D.	Median (IQR)
Hospitalizition	19.04±21.35	12 (9-17)
	n	%
Complications		
Pneumonia	8	7.7
Pleural Injury	6	5.8
Pyloric Dysfunction	6	5.8
Relapse		
	1	1.0
Lymphatic Leakage	1	1.0
Evisceration	1	1.0
Number of patients hospitalized in ICU	90	86.5
Leakage	8	7.7
Stenosis	22	21.2
Results		
Ex in 1 Month	16	15.4
Ex in 1 Year	25	24.0
Ex in 2 Years	3	2.9
Ex in 3 Years	3	2.9

Table 4. Examining the factors affecting the development of mortality using multivariate analysis

	Adjusted O.R.	95% C.I.	p
Gender			116
Male	2.08	0.84-5.19	
Age	1.03	0.99-1.07	204
Type of Operation			17
Ivor Lewis	0.27	0.10-0.75	
Transhiatal	0.25	0.08-0.77	
Lymphovascular invasion	2.96	1.05-8.38	41
Leakage	4.03	0.62-26.10	144
Coronary artery disease	3.44	0.78-15.18	103

Nagelkerke R2: 0.271; Hosmer-Lemeshow Test: 0.325.

When the factors influencing the risk of developing mortality were examined using multivariate regression analysis, it was found that the type of operation and the presence of lymphovascular invasion were associated with mortality (Table 4). Compared to patients undergoing McKeown operation, those undergoing Ivor Lewis and transhiatal operations had a lower likelihood of developing mortality. The presence of lymphovascular invasion had an odds ratio of 2.96 for developing mortality.

DISCUSSION

The aim of this study was to identify risk factors for mortality following esophagectomy for esophageal cancer. Anastomotic leaks are the most common complications following esophageal resections. Postoperative surgical sepsis is responsible for the high rates of mortality and morbidity. The frequency of this complication is highly variable, with some studies reporting leakage rates over 30%.[6] The choice of surgical method is important in terms of postoperative morbidity and mortality. The potential advantages of transhiatal resection include being less invasive and faster. The literature indicates that transthoracic approaches lead to higher perioperative morbidity and mortality rates, but there is no significant difference in long-term survival between the two methods.[7] While some studies report higher leakage rates in cervical anastomoses, this is explained by the long intrathoracic segment through which the stomach tube passes and the reduced blood supply to the proximal stomach area.[8,9] In our study, the main findings increasing mortality risk were McKeown operation, hand-sewn anastomosis, and the presence of lymphovascular invasion. Therefore, when planning esophagectomy for esophageal cancer, attention should be paid to patients with these risk factors. Generally, cervical and intrathoracic anastomoses are performed either hand-sewn or with a stapler.[10] Although single-layer continuous suturing is the most commonly applied hand-sewn anastomosis technique, studies have shown lower leakage rates after double-layer anastomosis.[11] While some studies support the superiority of the stapler technique, a definitive comparison in leakage rates is not proven. Similar leakage rates have been observed with different stapler techniques.[12,13] In our study, we found higher leakage rates in cervical anastomoses, especially in hand-sewn anastomoses. We believe that surgical technique choice, experience, and patient comorbidities are important factors. The most common comorbidity in our study group was diabetes mellitus, and the literature supports that diabetes is a risk factor for anastomotic leakage.[14] Previous retrospective studies have shown a relationship between lymph node invasion and dissection status and anastomotic leakage in patients undergoing esophagectomy for esophageal cancer. A meta-analysis indicated that three-field lymph node dissection was significantly associated with higher leakage incidence compared to two-field lymph node dissection. Given the current and previous findings, the lymph node dissection status may have clinical implications in patients undergoing esophagectomy.[15,16] In our study, three-field lymph node dissection and lymphovascular invasion were associated with mortality. Another noteworthy finding in our study was that male gender was significantly more at risk for developing postoperative stricture. There are several limitations to this study. First, it was a retrospective, single-center study with a relatively small sample size. Second, many risk factors evaluated in previous studies, such as nutritional status, BMI, albumin level, and immunity, were not evaluated in this study. Additionally, the results of different surgeons and surgical approaches were analyzed. Given these limitations, the current findings need to be confirmed in other series with a larger number of patients.

Conclusion

Results from this study show that factors such as McKeown surgery and the presence of LVI are associated with increased mortality. As a result, these factors significantly increase mortality and morbidity. It seems that patients with these factors should be closely monitored and necessary precautions should be taken.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City

Hospital Ethics Committee (Date: 27.03.2024, Decision No: 2024/010.99/2/34).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Y.T., H.F.K.; Design: Y.T.; Supervision: A.E.K., G.A.; Materials: C.H., S.P.; Data: F.Y., A.A; Literature search: Y.T., G.A.; Writing: C.H.; Critical revision: A.E.K.

Conflict of Interest

None declared.

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Özofagus Kanseri Cerrahisi Sonrası Anastomoz Kaçağı ve Mortalite Risk Faktörlerinin Değerlendirilmesi

Amaç: Postoperatif anastomoz kaçağı, özofagus cerrahisinin en ciddi komplikasyonlarından biridir ve hasta morbidite ve mortalite riskini önemli ölçüde artırır. Bu çalışmanın amacı, özofagus kanseri cerrahisinde anastomoz seviyesinin postoperatif kaçak ve darlık oranlarına etkisini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Çalışmaya Ocak 2010 ile Şubat 2023 tarihleri arasında İstanbul Dr. Lütfi Kırdar Şehir Hastanesi Genel Cerrahi Bölümü'nde özofagus kanseri nedeniyle ameliyat edilen 104 hasta alındı.

Bulgular: Takip sırasında 47 hastada mortalite meydana geldi. Mortalite gelişen hastalarda McKeown operasyonu, elle yapılan anastomoz ve lenfovasküler invazyon oranları, mortalite gelişmeyenlere göre anlamlı derecede yüksekti.

Sonuç: Risk faktörlerinin belirlenmesi ve uygun tekniğin seçilmesi komplikasyon oranlarını azaltabilir ve ameliyat sonrası sonuçları iyileştirebilir.

Anahtar Sözcükler: Anastomoz kaçağı; McKeown özefajektomi; özefagus kanseri.