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Risk factors for postoperative infections in esophageal tumor patients

Mingzhu Lin [a,*], Lu Wang [b], Mengxing Liu [a], Huawei Gu [a], Dan Li [a], Xidong Hou [a], Hongye Yang [a], Yu Shi [a]

[a] *Anyang Tumor Hospital, The Affiliated Anyang Tumor Hospital of Henan University of Science and Technology, Anyang, 455000, China*
[b] *Sanquan College of Xinxiang Medical University, Xinxiang, 453000, China*

A R T I C L E I N F O

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A B S T R A C T

Postoperative infections (PI) are a serious complication after esophageal cancer surgery, as they might be correlated with an elevated risk of death. While several reports discuss risk factors for PI in esophageal tumor surgery, there is a limited amount of research on overall postoperative infections. Therefore, investigating the factors that influence PI holds great clinical significance. We retrospectively reviewed surgical data from a cohort of 902 patients diagnosed with esophageal tumors. The study included esophageal cancer patients treated in the Department of Thoracic Surgery at Anyang Tumor Hospital from January to December 2021. Preoperative and operative risk factors for PI were evaluated using univariable and multivariable analyses. The overall incidence of PI was 28.3% (255/902). Multivariable logistic regression analysis revealed that smoking and preoperative hospital stays are significant risk factors for PI after esophageal tumor surgery. Smoking and preoperative hospital stays are identified as risk factors for PI following esophageal tumor surgery. Based on our results, we predict that certain groups of patients may have a higher risk of PI following esophageal tumor surgery. Preventive measures or closely monitor of these patients may be required to reduce the incidence of postoperative PI.

1. Introduction

Esophageal cancer is a highly aggressive tumor with a significant mortality rate, and surgery remains the mainstay treatment [1,2]. The frequency of postoperative infections (PI) after esophageal tumor surgery is high, particularly in clean contaminated and major surgeries [3,4]. PI may also lead to severe hypoxia, lung injury, and organ failure, ultimately resulting in death among individuals with compromised immune systems [5]. In this study, the definitions of PI are as follows: (1) Positive bacterial cultures in sputum specimens, blood specimens, or other sterile body fluids, (2) Physician-diagnosed infection, primarily based on the incision erythema, tenderness, swelling, fever, or elevated WBC levels, and (3) Purulent secretions from the incision or drain. Previous studies have revealed that the postoperative infection rate in esophageal cancer patients was approximately 10%–30% [6,7]. PI is particularly important in older patients, with several authors reporting higher rates (25.0%–45.44%) in this patient population [8,9].

PI leads to a prolonged hospital stay and increases morbidity and mortality [6]. A postoperative pulmonary infection has been reported to have an incidence ranging from 9.5% to 31.18% following esophageal tumor surgery [10] and is a significant risk factor for

* Corresponding author.
E-mail addresses: ZZHLinmingzhu@163.com (M. Lin), 785462828@qq.com (L. Wang), naylmx@163.com (M. Liu), ayhmghw@163.com (H. Gu), 13783880803@163.com (D. Li), pyhxd2012@126.com (X. Hou), msq4@163.com (H. Yang), shiyuhope@163.com (Y. Shi).

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hospital mortality [11,12]. The serious impact caused by PI and its complications affects patients and is a heavy financial burden to the health care system and families [13,14].

Numerous studies have already focused on the PI of pulmonary after esophageal tumor surgery [9]. Therefore, this study focused on the PI after esophageal tumor surgery, including chest infection, respiratory tract infection, anastomotic fistula and infection of the surgical incision. Hence, identifying these risk factors can enhance the perioperative nursing and treatment of esophageal cancer patients. This retrospective analysis aimed to identify PI in esophageal tumor surgery and examine risk factors that could potentially identify patients at higher risk [15].

2. Materials and methods

2.1. *Study design and samples*

The patient data was obtained from our hospital's Healthcare Information System (HIS) database, which includes previous medical records and postoperative follow-up details. The research sample consisted of 902 patients who underwent esophageal tumor surgery at the Department of Thoracic Surgery between January 2021 and December 2021. The exclusion criteria for our study are as follows: patients under the age of 18; patients who had an infection before admission; patients who administrated antimicrobial drugs before admission; patients with severe liver, kidney, and brain diseases; immunocompromised patients; pregnant or lactating patients; patients with a diagnosis of any other type of cancer; patients who died within one month after surgery; patients who underwent other combined procedures.

2.2. *Demographics and clinical data*

Data collected from medical records included demographic distribution, preoperative characteristics, and perioperative or postoperative characteristics. A total of 25 potential risk factors were recorded in each patient, and statistical analysis was performed to investigate PI-related factors. Demographic distribution characteristics such as age, sex, smoking, drinking, diabetes mellitus, hypertension, and hyperlipidemia were considered. The preoperative parameters included the patient's history of previous radiotherapy and chemotherapy, duration of preoperative hospital stays, preoperative white blood cell (WBC) count, albumin count, tumor recurrence, TNM stage (UICC/AJCC, 8th edition 2017) and tumor site. Perioperative and postoperative characteristics were evaluated, including hemoglobin levels, surgical duration, surgical procedure, postoperative fever, white blood cell count after surgery, intraoperative blood loss, intraoperative transfusion, pulmonary disease, postoperative blood glucose levels, and duration of hospitalization. Drinking was defined as regular alcohol consumption by the participants (i.e., at least once a week regularly) during the past 12 months, otherwise were regarded as non-drinkers [16]. The survival curves were plotted utilizing the Kaplan-Meier method and compared utilizing the log-rank test.

2.3. *Statistical analysis*

SPSS 23.0 was utilized to analyze and process the data. The statistical results were reported as percentages (%). Univariable and multivariable logistic regression were used for analysis. Multivariable analysis was not conducted if there were fewer than 10 cases for each variable due to insufficient statistical power. A $p < .05$ was considered statistically significant.

3. Results

3.1. *Demographic distribution characteristics of the patients*

The study included 569 male patients and 333 female patients. A total of 902 patients were enrolled in this study with a mean age of 66.55 ± 7.33 years (mean $\pm$ SD, range: 31–87 years). Of these patients, 255 (28.3%) experienced PI (Table 1), including 201 cases of lung PI (22.3%), 14 cases of incisional PI (1.6%), 36 cases of leakages/fistulas PI (4.0%), and 10 cases of PI at other sites (1.1%). Among the 902 patients, tumor sites were distributed as follows: 136 patients had upper-thoracic esophageal tumors, 574 had mid-thoracic esophageal tumors, and 192 had lower-thoracic esophageal tumors.

Table 1
Incidence of site infection relative to the tumor site.

Site of tumor	Total No. (%)	Site infection, No. of patients (%)					P[a]
		Lung	Incision	Leakage/fistula	Other sites	Total	
Upper-thoracic(n = 136)	136(15.1)	30(22.1)	3(2.2)	2(1.5)	1(0.7)	36(26.5)	0.611
Mid-thoracic(n = 574)	574(63.6)	121(21.1)	10(1.7)	24(4.2)	7(1.2)	162(28.2)	0.813
Lower-thoracic(n = 192)	192(21.3)	50(26.0)	1(0.5)	10(5.2)	2(1.0)	63(32.8)	0.297
Total	902(100.0)	201(22.3)	14(1.6)	36(4.0)	10(1.1)	261(28.9)	

[a] Total number of surgical site infections was compared using the Fisher exact test.

3.2. Univariable analysis of PI risk factors in esophageal tumor patients

The cross tabulation with chi-squared testing was employed to assess the parameter difference between groups. The patient-related demographic characteristics are displayed in Table 2. The univariable analysis revealed a significantly higher incidence of PI in patients who smoked (***$P < .001$) and drinking (***$P < .001$). Furthermore, the findings indicate a significant association between the male gender and an elevated risk of PI after esophageal tumor surgery (*$P < .05$).

Table 3 presents a summary of the association between PI and preoperative characteristics. A statistically significant association was observed between PI and preoperative hospital stays (days) (*$P < .05$), and TNM grade (***$P < .001$).

The surgery-related characteristics of esophageal tumor patients are listed in Table 4. These results indicate that patients who undergo longer surgical durations are more likely to develop PI (*$P < .05$).

3.3. Multivariable logistic regression analysis of risk factors of PI in esophageal tumor patients

Multiple logistic regression analysis examined the association between PI and the significant factors identified in the previous univariable analyses (Table 5). Multiple logistic regression analysis included the following 7 variables: sex, smoking, drinking, preoperative hospital stays (days), TNM grade, and surgical duration. In this model, smoking (OR = 0.53, 95% CI [0.36–0.78], *P = .01) and preoperative hospital stays (OR = 1.38, 95% CI [1.02–1.86], *P = .04) were significant independent predictors of PI. Forest plot reveals that non-smoking reduces the ODDS of PI occurring by almost half compared to smokers. Meanwhile, preoperative hospital stays (> 8) increase the ODDS of PI occurring by 1.38 times compared to preoperative hospital stays(≤8). As illustrated in Fig. 1, the forest plot summarizes the findings of these studies.

3.4. Effect of infection status on Kaplan-Meier survival analysis

The patients were stratified into two groups based on their infection status: those with PI and those without PI in the cohort (Fig. 2). Among these, 8 cases were lost to follow-up, and 894 cases were included in this study. This study's 2-year survival rate for non-PI patients was 95.3%, while 88.5% for the 252 PI patients. The results revealed a statistically significant difference between PI and non-PI groups ($P < .05$).

4. Discussion

The study found that the prevalence of PI was 28.3%. This higher prevalence supports the findings of previous observational and meta-analysis studies. Univariable analysis was conducted to identify the risk factors associated with PI, including smoking, drinking, preoperative hospital stays, TNM grade, and surgical duration. Multivariable analysis of the identified risk factors revealed smoking and preoperative hospital stays as significant. The smoking incidence in our study was 47%, and preoperative hospital stays (>8) increased the ODDS of PI occurring by 1.38 times compared to preoperative hospital stays(≤8). Specifically, lung PI (22.3%) is the most common infection occurring in PI compared with other sites PI, comparable to previous studies [17,18]. These findings demonstrated a significant decrease in the overall survival rate for patients with PI than those with non-PI complications.

Previous studies have shown that smoking is an independent risk factor [19,20]. We found that smoking was an independent risk factor of PI in esophageal tumor patients. Smoking has been shown to disrupt the mucociliary clearance process [21] and reduce mucociliary clearance efficiency, which may contribute to the reproduction of pathogens and increase the risk of developing pneumonia [22]. Akutsu Y et al. [23] have shown that smoking has been reported to be a risk factor for pulmonary complications, and it was also indicated that tobacco cessation and preoperative respiratory rehabilitation were expected to reduce the occurrence of complications. Preoperative hospital stays were also independent predictors of PI. Previous studies [24] have established a strong correlation between preoperative hospital stays and postoperative nosocomial infection. Patients who undergo prolonged hospitalization tend to

Table 2
Results of univariable analysis of the patient-related demographic parameters.

Variable		PI(−)	PI(+)	P
Age (years)	> 60 (n = 733)	518	215	0.14
	≤60 (n = 169)	129	40	
Sex	Male (n = 569)	392	177	0.01
	Female (n = 333)	255	78	
Smoking	Yes (n = 362)	231	131	< 0.001
	No (n = 540)	416	124	
Drinking	Yes (n = 173)	115	58	< 0.001
	No (n = 729)	532	197	
Diabetes mellitus	Yes (n = 117)	81	36	0.52
	No (n = 785)	566	219	
Hypertension	Yes (n = 298)	211	87	0.67
	No (n = 604)	436	168	
Hyperlipidemia	Yes (n = 38)	27	11	0.93
	No (n = 864)	620	244	

Table 3
Results of univariable analysis of the preoperative characteristics.

Variable		PI(−)	PI(+)	P
Previous radiotherapy	Yes (n = 21)	19	2	0.05
	No (n = 881)	628	253	
Previous chemotherapy	Yes (n = 217)	167	50	0.06
	No (n = 685)	480	205	
Preoperative hospital stays (days)	> 8 (n = 461)	314	147	0.01
	≤8 (n = 441)	333	108	
WBC count	Normal (n = 859)	615	244	0.69
	Abnormal (n = 43)	32	11	
Albumin count	Normal (n = 860)	618	242	0.69
	Low (n = 42)	29	13	
Tumor recurrence	Yes (n = 5)	4	1	0.68
	No (n = 897)	643	254	
TNM grade	I–II (n = 505)	373	132	< 0.001
	III–IV (n = 397)	274	123	
Tumor site	upper-thoracic(n = 136)	102	34	0.31
	mid-thoracic(n = 574)	414	159	
	Lower-thoracic(n = 192)	130	62	

Table 4
Results of univariable analysis of the surgery-relate variables.

Variable		PI(−)	PI(+)	P
Hemoglobin	Normal (n = 592)	434	158	0.97
	High (n = 2)	2	0	
	Low (n = 308)	211	97	
Surgical duration (h)	> 4 (n = 428)	291	137	0.02
	≤4 (n = 474)	356	118	
Surgical method	Endoscopic (n = 589)	413	176	0.14
	Thoracotomy (n = 313)	234	79	
Post-operative fever	> 38.5 (n = 12)	6	6	0.09
	≤38.5 (n = 890)	641	249	
Post-operative WBC count	Normal (n = 228)	163	65	0.84
	High (n = 664)	476	188	
	Low (n = 10)	8	2	
Intraoperative blood loss(ml)	< 200 (n = 728)	517	211	0.61
	200-400 (n = 157)	117	40	
	> 400 (n = 17)	13	4	
Intraoperative transfusion	< 200 (n = 892)	641	251	0.37
	200-400 (n = 9)	5	4	
	> 400 (n = 1)	2	0	
Pulmonary disease	Yes (n = 127)	88	39	0.51
	No (n = 775)	559	216	
Postoperative blood glucose	Yes (n = 679)	488	191	0.87
	No (n = 223)	159	64	
Hospitalization times	> 1 (n = 411)	306	105	0.10
	1 (n = 491)	341	150	

Table 5
Risk factors for PI according to multivariable logistic regression analysis.

Variable		PI(−)	PI(+)	OR(95% CI)	P
Sex	Male (n = 569)	392	177	1.03(0.69–1.53)	0.88
	Female (n = 333)	255	78		
Smoking	Yes (n = 362)	231	131	0.53(0.36–0.78)	0.01
	No (n = 540)	416	124		
Drinking	Yes (n = 173)	115	58	1.04(0.70–1.55)	0.84
	No (n = 729)	532	197		
Preoperative hospital stays (days)	> 8 (n = 461)	314	147	1.38(1.02–1.86)	0.04
	≤8 (n = 441)	333	108		
TNM grade	I–II (n = 505)	373	132	1.25(0.93–1.68)	0.15
	III–IV (n = 397)	274	123		
Surgical duration (h)	> 4 (n = 428)	291	137	1.33(0.98–1.79)	0.06
	≤4 (n = 474)	356	118		

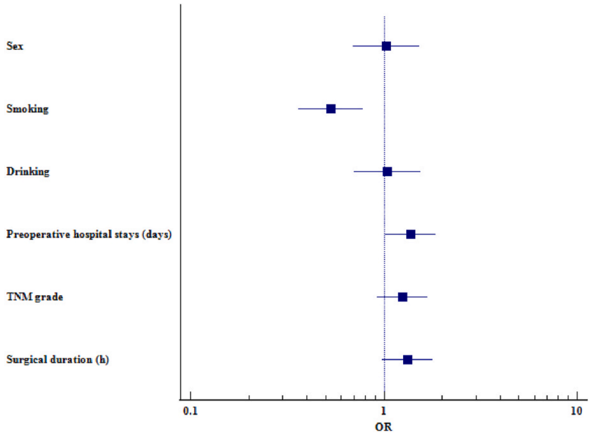

Fig. 1. The forest plot between PI and independent risk factors of independent risk factors.

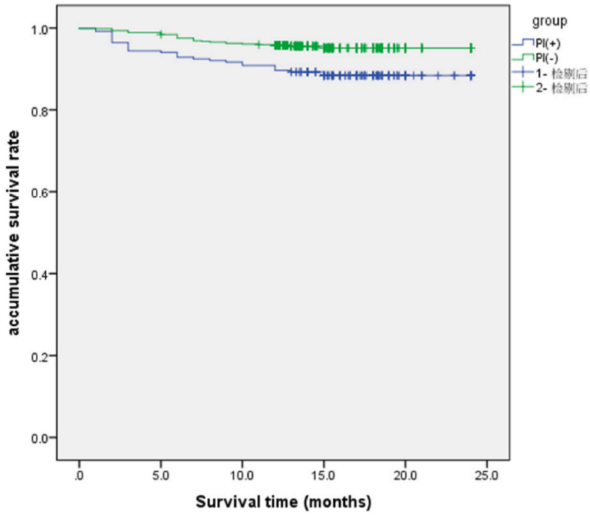

Fig. 2. Kaplan-Meier survival analysis of between PI and non-PI patients with esophageal tumors.

have more severe illnesses, resulting in slower body recovery and increased exposure to the bacterial environment. The probability of patient infection increases with extended hospitalization.

In addition, previous studies [25,26] have demonstrated that diabetes mellitus patients may have a higher risk of PI. However, our research indicated no significant difference in the incidence of PI between diabetic and non-diabetic patients. This finding suggests that patients are strongly aware of the significance of glycemic control in preventing diabetic complications. Moreover, patients in the preoperative period are typically subjected to closer monitoring for hyperglycemia, potentially leading to more rigorous glycemic control. Various other factors require further investigation in future research.

This study aimed to identify risk factors of PI after esophagectomy for esophageal cancer. A combination of factors influences PI. This study solely analyzes the risk factors associated with PI and conducts a simple survival rate analysis. Therefore, the findings of this study need to be considered when implementing targeted intervention strategies to address the identified risk factors. We eagerly anticipate additional studies and reports in this area, encompassing the screening of pathogenic bacteria in patients with PI, the analysis of drug sensitivity results for pathogenic bacteria, PI treatment, and the examination of prophylactic use of antimicrobial drugs during the perioperative period in esophageal cancer patients.

This study has several strengths, including optimal sample size and the inclusion of 25 risk factors for a more comprehensive analysis. The limitations of the current study are as follows. Firstly, due to the limitations of observational studies, causal relationships cannot be inferred, and there is a lack of treatment data for infections. Furthermore, all the sites included in this study were located in China. It was a single-center observational cohort study, so the generalizability of the results and conclusions may be limited. Moreover, the duration of follow-up in this study was insufficient to fully assess PI's survival or conduct prognostic studies. In the future, it remains crucial to undertake multi-center, large-scale collaborations and conduct prospective research and evidence-based medical demonstrations to achieve a compelling and conclusive result.

Ethics approval

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Anyang Tumor Hospital (No.2023WZ08K01).

Consent to participate

Informed consent included in the study was obtained from all individual participants.

Data availability

The data has been used is confidential due to restrictions, their containing information that could compromise the privacy of research participants and some of the relevant data is being studied. Therefore, data associated with study cannot be stored in publicly available repositories.

CRediT authorship contribution statement

Mingzhu Lin: Conceptualization, Data curation, Formal analysis, Project administration, Resources, Software, Writing – original draft, Writing – review & editing. **Lu Wang:** Data curation, Methodology, Software. **Mengxing Liu:** Formal analysis, Investigation, Project administration. **Huawei Gu:** Data curation, Formal analysis, Investigation. **Dan Li:** Data curation, Resources, Software. **Xidong Hou:** Methodology, Software, Supervision. **Hongye Yang:** Data curation, Investigation, Software. **Yu Shi:** Data curation, Methodology, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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