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Pulmonary infection after esophageal cancer surgery: impact on the reality, risk factors and development of a predictive nomogram

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Abstract

Background As a major complication after esophageal cancer (EC) surgery, postoperative pulmonary infection (PPI) is speculated to be associated with quality of life and survival after surgery. This study is aimed to explore the influence of PPI on the reality and establish a nomogram to predict PPI.

Methods Data of patients undergoing esophagectomy was collected between January, 2016 and December, 2020 and divided into PPI and without PPI groups. Hospital costs and overall survival (OS) were compared between two groups. Univariate-multivariate analysis and LASSO-multivariate logistic regression were carried out to identify risk factors, and then two models were established based on them. To choose the better one, the receiver operating characteristic (ROC), the area under curve (AUC) and K-fold cross validation were compared between the models.

Results The incidence of PPI in 633 esophageal cancer patients was 30.2% (191/633). PPI caused a total economic burden of RMB11,872.31 yuan on each patient and a poorer overall survival (60.5% vs. 54.0%, $P=0.002$). The final nomogram was established by Univariate-multivariate logistic regression, including four independent risk factors of BMI < 18 kg/m² (OR 2.516, 95%CI 1.264–5.059, $P=0.009$), lung diseases (OR 1.805, 95%CI 0.995–3.259, $P=0.050$), approach to chest (open) (OR 1.182, 95%CI 1.075–1.440, $P<0.001$) and operation time (OR 1.001, 95%CI 1.001–1.002, $P<0.001$).

Conclusion Individual prevention of PPI after esophagectomy would lead a lower financial burden and a better survival for EC patients.

Keywords Esophageal cancer, Pulmonary infection, Economic burden, Survival analysis, Risk factors, Predictive model

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Introduction

Esophageal cancer (EC) remains a worldwide health issue and has become the sixth most common cancer throughout the globe [1]. More seriously in China, EC mortality is surging rapidly from approximately 194,000 in 2016 to over 300,000 in 2020 [2]. Survival from this devastating disease is constantly improving with diversified therapy [3]. Currently, the resection of esophageal cancer in combination with neoadjuvant chemoradiotherapy or postoperative chemoradiotherapy has significantly enhanced the overall survival rate of patients, and has emerged as the mainstream surgical approach for esophageal cancer.

However, as the key step, surgical removal of the esophagus plays the role of a double-edged sword. Since introduced by Czerny in the 1870 s, esophagectomy plagues people due to its troubling postoperative outcomes. The mortality rate after esophagectomy has been declined from a peak of 72% in the 1940 s to 9% in the 1990 s. Recent reviews demonstrate improved, yet formidable, modern 30-day and 90-day mortality rates of 2.4% and 4.5%, respectively [4]. It remains a challenge that more than half of all patients still experience complications after esophagectomy, such as anastomotic leakage, pulmonary infection, recurrent laryngeal nerve injury, cardiac arrhythmia and so on [5].

With the development of operative techniques and increasingly updated instruments, pulmonary infection has replaced anastomotic leakage, becoming the most perilous postoperative complication with an incidence of 10%– 30% [6]. It has been reported that the occurrence of pulmonary infection is associated with increased short-term mortality after surgery [7, 8]. In addition, postoperative complications are also thought to be one of the causes of disease recurrence [9].

In this observational cohort study, we aim to recognize the impact on patients from postoperative pulmonary infection (PPI), containing economical burden and overall survival (OS). We hope to find out the risk factors of PPI and to develop a nomogram to predict the possible PPI after esophagectomy.

Methods

Study participants

In this retrospective study, 633 patients were enrolled during the period between January 2016 and October 2021. All of the patients enrolled were diagnosed with EC by pathological examination and had a definite outcome of either hospital discharge or death. The exclusion criteria for patients are shown in the Fig. 1. This study was approved by the Ethics Committee of Xijing Hospital of Air Force Military Medical University. The hospital's

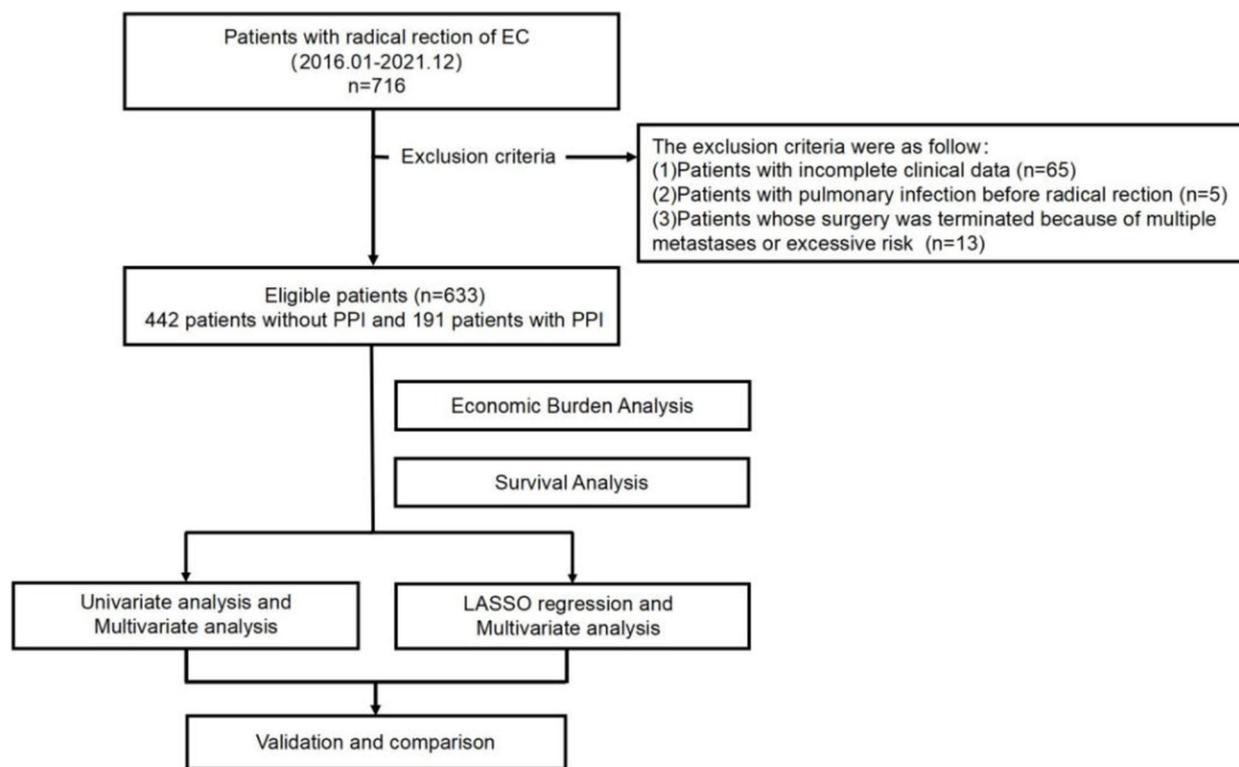


Fig. 1 Flow chart of the study process

ethics committee waived the written informed consent from patients with esophageal cancer.

Data collection

All crude data used in this study were extracted from the Electronic medical record management system. The data entry is carried out by two people in turns, with one person operating and one person supervising to ensure the integrity and reliability of the data. If any inconsistencies or omissions are found, the original medical record is checked and corrected. If there is any objection, a third party shall verify and make a decision. Indeed missing data will be marked as N/A and will be handled by a multiple imputation method [10].

Diagnosis of postoperative pulmonary infection

Referring to the clinical diagnostic criteria of the Guidelines for the Diagnosis and Treatment of Acquired pneumonia and ventilator-related pneumonia in Adult Hospitals in China (2018 edition) revised by the Infectious Diseases Group of the Respiratory Diseases Department of the Chinese Medical Association. Chest X-ray or CT shows new or progressive infiltrative shadows, consolidation shadows, or ground glass shadows, plus two or more of the following three clinical symptoms, a clinical diagnosis can be established: ① Body temperature $>38^{\circ}\text{C}$; ② Purulent airway secretions; ③ Peripheral blood white blood cell count $>10.0 \times 10^9/\text{L}$ or $<4.0 \times 10^9/\text{L}$ [11]. Patients were divided into PPI group and without PPI group according to this criteria.

Statistical analysis

Continuous variables are expressed as mean \pm SD, while categorical variables are presented as frequencies and percentages (%). To compare the difference between groups, we performed univariate exploratory analysis on the data set with SPSS 26.0. Pearson χ^2 test or Fisher exact test were performed for the categorical variables, with t or F test for continuous variables.

Propensity score matching (PSM) was used between the PPI and non-PPI groups in a 1:1 manner to reduce potential confounding bias [12]. The caliper width for PSM was set at 0.20. Sex, age, diabetes, hypertension, coronary heart disease, anastomotic methods and minimally invasive were included in PSM.

Stepwise multivariate logistic regression was performed to assess the most parsimonious combination of risk factors predictive of pneumonia, thus creating the full model. P values less than 0.05 were considered statistically significant in all statistical analysis.

Least absolute shrinkage and selection operator (LASSO) regression was used as another way to screen potential factors, and the selected factors were further

analyzed in stepwise multivariate logistic regression to identify the significant factors associated with pulmonary infection after esophagectomy.

Subsequently, the selected meaningful factors were utilized to build a predictive model and a nomogram was used to visualize the model.

Evaluation and validation of the model

A receiver operating characteristic (ROC) curve was drawn, and area under the ROC curve (AUC) was used to assess discrimination of the model, while the calibration plot was used to graphically evaluate the calibration of the nomogram in both training and validation cohorts. The value of the C-index ranges from 0.5 to 1.0, with 0.5 indicating random chance and 1.0 demonstrating perfect discrimination. All analyses were conducted using R software (version 4.3.0; R Foundation for Statistical Computing), and P values less than 0.05 were considered statistically significant in each statistical analysis.

K-Fold Cross-Validation (CV) was employed to prevent the overfitting problem in this study [13]. The performance of the model will be improved when the K-Fold cross-validation is used because the bias can be eliminated due to the random selection of training and testing from datasets. Through K-Fold cross-validation, 10 iterations were applied. For each iteration, by randomly divided the training dataset, the individual subset is generated, in which one subset is used for testing while 09 remaining subsets are used to train the model.

Results

Comparisons of patients' economic burden between patients with PPI and without PPI after propensity score matching

The present study was conducted on a total of 633 patients, of which 191 patients got PPI. In order to calculate the economic burden of PPI, the effect of other confounding factors on the economic results was reduced by propensity score matching (PSM) (Table S1). By utilizing PSM to mitigate data bias, 112 pairs of patients were employed to compare the length of stay and the cost of hospitalization (Table 1).

It turns out that the length of stay after surgery in patients with PPI is 2.39 days longer than those without PPI ($P<0.001$), and the total length of stay in patients with PPI is 2.26 days longer than those without PPI ($P<0.001$). Total cost ($P<0.002$), room charges ($P<0.001$), radiation ($P<0.002$), nurses ($P<0.006$), laboratory exam ($P<0.006$), examination ($P<0.02$), blood transfusion ($P<0.05$), drugs ($P<0.001$) and consultation ($P<0.03$) were significantly different between PPI group and non-PPI group, which demonstrates a direct economic burden (DEBD) of RMB11,441.49 yuan due to PPI.

Table 1 Comparisons of stay and cost between patients with PPI and without PPI after propensity score matching

Variables	PPI (-) (n = 112)	PPI (+) (n = 112)	t	P value
Total length of stay, days	10.09 ± 2.95	12.48 ± 6.23	- 3.676	<0.001
Stay after surgery, days	7.93 ± 2.28	10.19 ± 6.14	- 3.649	<0.001
Total cost, RMB yuan	99,601.89 ± 17,313.08	112,984.55 ± 38,953.09	- 3.322	<0.002
Room Charges, RMB yuan	622.50 ± 211.42	796.07 ± 429.46	- 3.837	<0.001
Radiation, RMB yuan	2010.58 ± 911.93	2503.79 ± 1267.46	- 3.343	<0.002
Nurses, RMB yuan	416.85 ± 197.40	662.09 ± 887.63	- 2.854	<0.006
Laboratory Exam, RMB yuan	4331.79 ± 1467.01	5449.20 ± 3832.99	- 2.881	<0.006
Examination, RMB yuan	6955.10 ± 1956.33	7988.39 ± 3722.69	- 2.600	<0.02
Operation, RMB yuan	14,226.55 ± 9328.27	533.47 ± 1850.63	0.775	0.439
Blood Transfusion, RMB yuan	155.39 ± 728.17	533.47 ± 1850.53	- 2.012	<0.05
Drugs, RMB yuan	20,746.74 ± 6926.11	29,379.95 ± 17,614.80	- 4.827	<0.001
Consultation, RMB yuan	304.78 ± 159.88	384.55 ± 327.27	- 2.318	<0.03
Treatment, RMB yuan	46,997.64 ± 10,749.30	48,550.49 ± 15,725.56	- 0.863	0.389

To calculate indirect economic burden (IEBD), the quantity of individuals lost labor productivity due to PPI should be considered. So, we divided patients into two parts, less than 60 years old and older, meaning loss of production of two persons and only one. Data of per capita income was collected from the yearbook of Shaanxi Province. With 2.39 days of extended postoperative stay, IEBD was about RMB430.82 yuan for one patient with PPI (Table S2).

To sum up, the economic expenditure attributable to PPI, which includes both DEBD and IEBD, is more than 1/3 of disposable income per capita, or estimated at 16.4% of gross domestic product (GDP) in China, 2020. More attention and measures ought to be devoted to the prevention and control of PPI in order to reduce economic losses on it.

Comparisons of patients' overall survival between patients with PPI and without PPI

To explore whether PPI is related with OS of EC patients after surgery, we developed a follow-up survey of 633 patients. 25 patients were lost to follow-up, and 608 patients' living condition were recorded. For the entire cohort, the median follow-up periods were 32.0 months (IQR 1.0–84.0 months) in the non-PPI group and 28.0 months (IQR 1.0–87.0 months) in the PPI group, showing a longer 5-year OS in non-PPI group than PPI group (60.5% vs. 54.0%, $P = 0.002$) (Fig. 2A).

It is probably because of the small sample size that no difference was found between the groups with upper EC (81.8% vs. 71.3%, $P = 0.831$) (Fig. 2B). However, the 5-year OS for middle EC showed a significant difference between the non-PPI group and the PPI group (80.0% vs. 61.2%, $P < 0.001$) (Fig. 2C). Given the clinical

practicalities, the middle part of the esophagus is closer to the trachea, which is prone to infection. In addition, lower EC patients without PPI appeared to have a better prognosis in terms of OS than those with PPI, but this difference was not statistically significant (55.9% vs. 47.8%, $P = 0.108$) (Fig. 2D).

Patient characteristics

The baseline clinical characteristics of 442 patients without PPI and 191 patients with PPI were compared in Table 2. For the entire cohort, there were more males than females (ratio, 5.96:1). The median age was 62 years (range, 20–87 years). Most patients presented with no history of alcohol abuse (82.3%), no history of smoking (57.6%), BMI < 18 kg/m² (54.6%), no lung diseases (90.3%), no diabetes (91.4%), no hypertension (80.6%), no CHD (93.3%), T3 - 4 (69.2%), N0 - 1 (61.3%), adenocarcinoma (68.2%), and moderate to poor differentiation (91.1%). Before esophagectomy, only a little part of patients received adjuvant treatment, including chemotherapy (13%) and radiotherapy (0.5%).

Identification of risk factors for PPI by univariate combined multivariate analysis

The involved 26 variables were subjected to univariate Logistic regression analysis, and 11 variables were found to be potentially associated with PPI, including BMI < 18 kg/m², lung diseases, (FEV1/FVC)/prediction, neck incision, approach to chest, ostomy, nutritional vessel, operation time, site of tumor, pathology type and TNM stage. Subsequently, these variables were further analyzed by introducing them in the multivariate logistic regression model. It is found that BMI < 18 kg/m² (OR 2.516, 95%CI 1.264–5.059, $P = 0.009$), lung diseases (OR 1.805, 95%CI

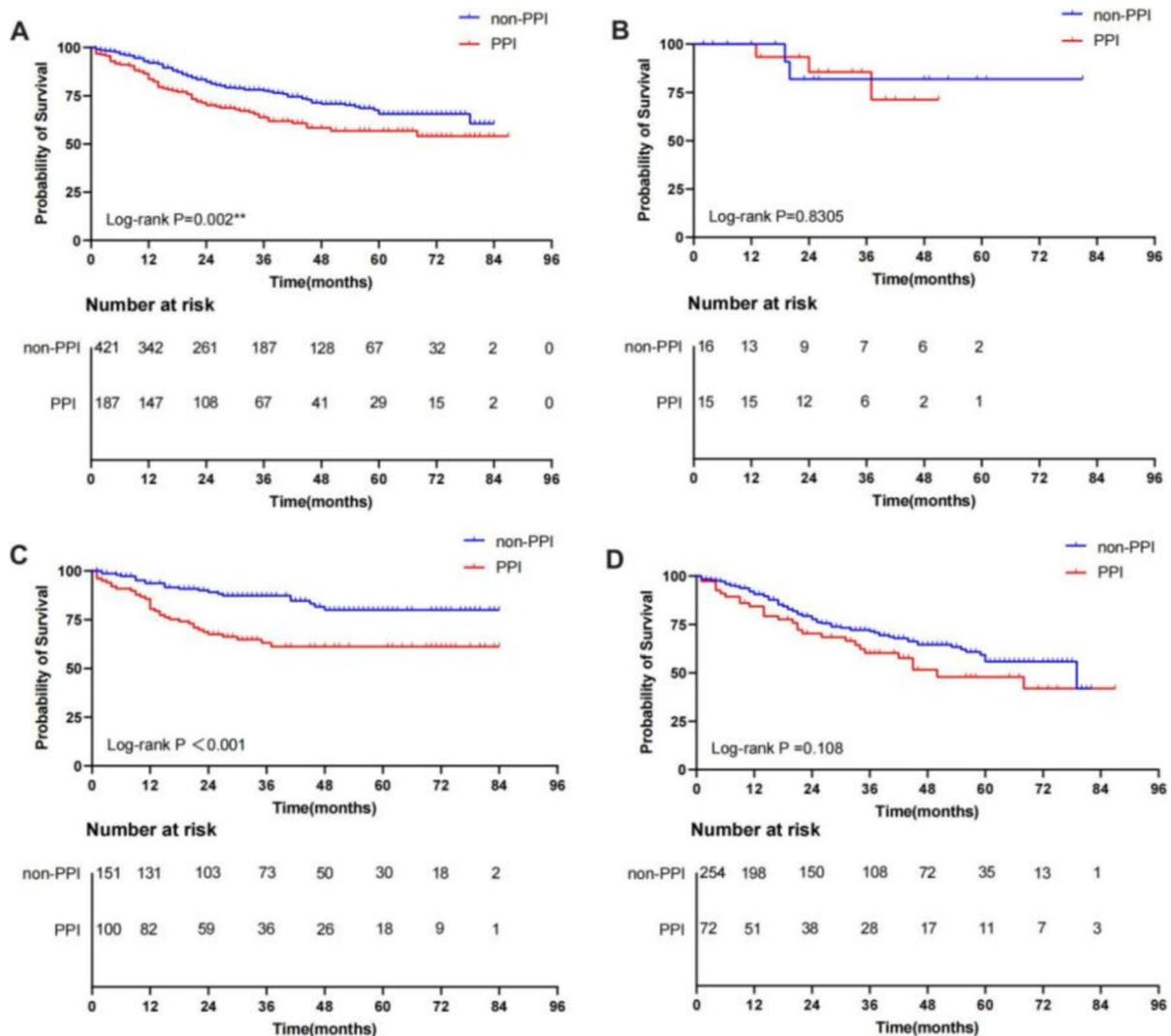


Fig. 2 Comparison of OS between non-PPI and PPI groups. **A** OS of the whole cohort; **B** OS of upper EC patients; **C** OS of middle EC patients; **D** OS of lower EC patients

0.995–3.259, $P = 0.050$), approach to chest (open) (OR 1.182, 95%CI 1.075–1.440, $P < 0.001$) and operation time (OR 1.001, 95%CI 1.001–1.002, $P < 0.001$) were independent risk factors of PPI in patients after esophagectomy (Table 3). Based on the four screened variables, we established a model named model-log to predict the probability of PPI in patients after esophagectomy.

Identification of risk factors for PPI by LASSO combined multivariate logistic regression

The most important variables related to PPI identified by LASSO logistic regression are presented in the simplified model (Fig. 3; Table S3). The logistic LASSO regression results showed that BMI $< 18 \text{ kg/m}^2$, lung diseases, ostomy, approach to abdomen, Hb, approach to chest,

(FEV1/FVC)/prediction, pathology type and TNM stage contributed to PPI. And in the stepwise multivariate regression analysis, BMI $< 18 \text{ kg/m}^2$ (OR 2.486, 95%CI 1.250–5.000, $P = 0.010$), lung diseases (OR 1.726, 95%CI 0.951–3.115, $P = 0.007$) and approach to chest (open) (OR 1.224, 95%CI 1.105–1.464, $P < 0.001$) were considered as independent risk factors associated with PPI.

With the same procedure of the first model, we get another one called model-lasso based on the results from LASSO combined multivariate logistic regression.

Validation and comparison between models

In Figure S1 A, the horizontal coordinate indicates the predicted probability of PPI after surgery, the ordinate represents the probability of actual PPI in EC patients,

Table 2 Comparisons of patients' clinical factors between patients with PPI and without PPI

Variables	PPI (-) (n = 442)	PPI (+) (n = 191)	p value
Sex, male, n (%)	364 (82.4)	155 (81.2)	0.736
Age, mean \pm SD (years)	61.88 \pm 7.83	61.99 \pm 6.88	0.978
Drink, yes, n (%)	79 (17.9)	38 (19.9)	0.577
Smoke, yes, n (%)	180 (40.7)	82 (42.9)	0.660
BMI, \leq 18 kg/m ² , n (%)	22 (5.0)	22 (11.5)	0.006
Lung diseases, yes, n (%)	39 (8.8)	28 (14.7)	0.034
Diabetes, yes, n (%)	29 (6.6)	6 (3.1)	0.091
Hypertension, yes, n (%)	79 (17.9)	28 (14.7)	0.357
CHD, yes, n (%)	21 (4.8)	6 (3.1)	0.401
Neoadjuvant radiochemotherapy, yes, n (%)	87 (19.7)	39 (20.4)	0.829
(FEV1/FVC)/prediction, n (%)			
< 70%	12 (2.3)	2 (1.8)	0.132
70–80%	20 (3.8)	10 (8.9)	
80–90%	92 (17.7)	21 (18.8)	
\geq 90%	397 (76.2)	79 (70.5)	
Hb, < 100 g/L, n (%)	21 (4.8)	6 (3.1)	0.401
ALB, < 35 g/L, n (%)	25 (5.7)	4 (2.1)	0.061
Neck incision, yes, n (%)	233 (52.7)	156 (81.7)	< 0.001
Approach to chest, n (%)			
Thorascopic	284 (64.3)	165 (86.4)	< 0.001
Transdiaphragmatic-hiatal	138 (31.2)	10 (5.2)	
Open	20 (4.5)	16 (8.4)	
Approach to abdomen, n (%)			
Laparoscopic	32 (7.2)	21 (11.0)	0.121
Open	410 (92.8)	170 (89.0)	
Ostomy, yes, n (%)	214 (48.4)	144 (75.4)	< 0.001
Nutritional Vessel, yes, n (%)	181 (41.0)	126 (66.0)	< 0.001
Operation time, mean \pm SD (min)	273.71 \pm 90.95	308.09 \pm 89.38	< 0.001
Blood loss, mean \pm SD (g/L)	234.66 \pm 557.43	201.68 \pm 239.81	0.432
Blood transfusion, yes, n (%)	22 (5.0)	9 (4.7)	1
Site of tumor, n (%)			
Upper	17 (3.8)	15 (7.9)	< 0.001
Middle	160 (36.2)	101 (52.9)	
Lower	265 (60.0)	75 (39.3)	
Size of tumor, median [IQR](cm)	4.00 [3.00, 5.38]	4.00 [3.00, 5.00]	0.262
Anastomotic methods, n (%)			
Hand-sewn closure	105 (23.8)	74 (38.7)	< 0.001
Instrumental anastomosis	337 (76.2)	117 (61.3)	
Pathology type, n (%)			
Adenocarcinoma	189 (42.8)	27 (14.1)	< 0.001
Squamous cell carcinoma	230 (52.0)	155 (81.2)	
Others	23 (5.2)	9 (4.7)	
TNM stage, n (%)			
I	84 (19.0)	43 (22.5)	0.003
II	129 (29.2)	62 (32.5)	
III	135 (30.5)	68 (35.6)	
IV	94 (21.3)	18 (9.4)	

Hb hemoglobin; ALB Albumin

Table 3 Univariate and Multivariate Analyses of Risk Factors for PPI

Variables	Univariate analysis		p value	Multivariate analysis		p value
	OR	95% CI		OR	95% CI	
Sex						
Male	1					
Female	0.916	0.520–1.545	0.751			
Age	1.007	0.981–1.035	0.596			
Drink						
No	1					
Yes	1.141	0.736–1.746	0.548			
Smoke						
No	1					
Yes	1.341	0.888–2.021	0.161			
BMI						
> 18 kg/m ²	1			1		
≤ 18 kg/m ²	4.502	2.370–8.481	< 0.001	2.516	1.264–5.059	0.009
Lung diseases						
No	1			1		
Yes	2.383	1.336–4.139	0.002	1.805	0.995–3.259	0.050
Diabetes						
No	1					
Yes	0.585	0.171–1.518	0.323			
Hypertension						
No	1					
Yes	0.788	0.429–1.367	0.416			
CHD						
No	1					
Yes	0.361	0.058–1.235	0.170			
Neoadjuvant radiochemotherapy						
No	1					
Yes	1.120	0.668–1.824	0.656			
(FEV1/FVC)/prediction						
≥ 90%	1			1		
80–90%	2.456	1.074–5.290	0.026	2.445	1.031–5.822	0.061
70–80%	1.076	0.623–1.791	0.784			
< 70%	0.748	0.479–1.188	0.209			
Hb						
≥ 100 g/L	1					
< 100 g/L	1.006	0.996–1.017	0.244			
ALB						
≥ 35 g/L	1					
< 35 g/L	0.357	0.122–1.040	0.049			
Neck incision						
No	1			1		
Yes	3.037	1.879–5.104	< 0.001	0.850	0.365–1.992	0.706
Approach to chest						
Thoracoscopic	1			1		
Transdiaphragmatic-hiatal	1.863	0.709–4.395	0.174			
Open	1.171	1.082–1.319	< 0.001	1.182	1.075–1.440	< 0.001
Approach to abdomen						
Laparoscopic	1					

Table 3 (continued)

Variables	Univariate analysis		p value	Multivariate analysis		p value
	OR	95% CI		OR	95% CI	
Open	0.712	0.372–1.459	0.326			
Ostomy						
No	1			1		
Yes	2.560	1.640–4.098	< 0.001	1.634	0.895–2.973	0.108
Nutritional Vessel						
No	1			1		
Yes	2.795	1.968–4.000	< 0.001	0.835	0.455–1.536	0.561
Operation time	1.004	1.002–1.006	< 0.001	1.001	1.001–1.002	< 0.001
Blood loss	1.000	0.999–1.000	0.451			
Blood transfusion						
No	1					
Yes	0.944	0.405–2.027	0.887			
Site of tumor						
Upper	1			1		
Middle	1.978	1.403–2.794	< 0.001	0.602	0.278–1.312	0.197
Lower	0.432	0.304–0.610	< 0.001	0.666	0.291–1.527	0.333
Size of tumor	0.961	0.863–1.064	0.454			
Anastomotic methods						
Hand-sewn closure	1					
Instrumental anastomosis	0.688	0.448–1.069	0.091			
Pathology type						
Adenocarcinoma	1			1		
Squamous cell carcinoma	3.969	2.666–6.038	< 0.001	1.609	0.860–3.066	0.141
Others	0.901	0.388–1.922	0.796			
TNM stage, n (%)						
I	1					
II	1.428	0.925–2.184	0.103			
III	1.163	0.751–1.780	0.492			
IV	0.264	0.109–0.546	0.001	1.206	0.614–2.333	0.580

Hb hemoglobin; ALB Albumin

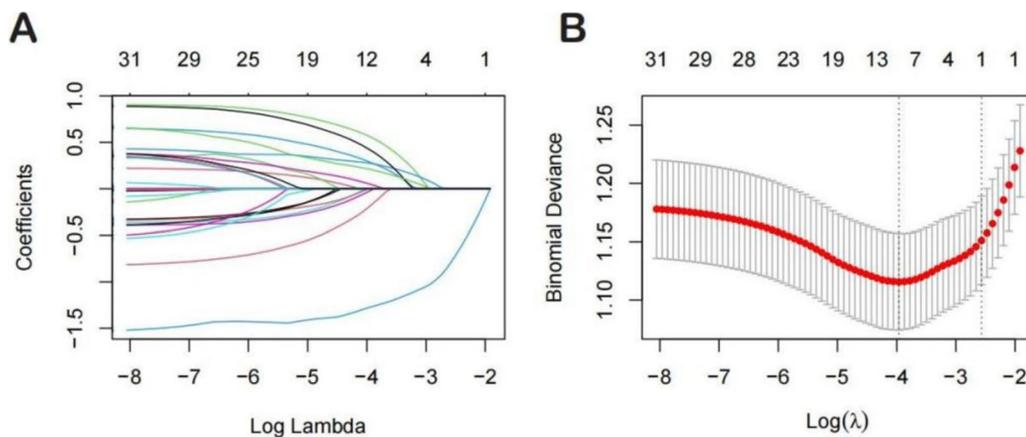


Fig. 3 LASSO logistic regression model construction. **A** LASSO coefficients of 34 features; **B** Selection of tuning parameter (k) for the LASSO model

and the diagonal line, also called fitting line, represents the actual value corresponding to the predicted value. The calibration curve showed that model-log is closer to the fitting line and revealed better predictive accuracy than model-lasso. The DCA was shown in Figure S2B, where a red curve represented clinical benefits of patients at different risk levels of PPI which identified that more benefits could be obtained by using the model-log to identify the PPI than model-lasso. In Figure S1 C and S1D, the model-log demonstrated good accuracy for predicting PPI in patients after esophagectomy with an AUC of 0.786 (95% CI: 0.742–0.829), while the AUC of model-lasso was 0.768 (95% CI: 0.723–0.813). K-fold cross validation was used to validate the two models, showing a better validity of model-log (AUC 0.788, Accuracy 0.822, kappa 0.124) than model-lasso (AUC 0.777, Accuracy 0.825, kappa 0.123).

In conclusion, it is found that model-log is the better one through the comparison and evaluation. Hence, we built a predictive nomogram based on model-log by R 4.3.0 software (Fig. 4).

Discussion

As one of the common complications after radical resection of esophageal cancer, pulmonary infection is an important public health problem, which not only hinders the postoperative recovery of patients, prolongs the length of hospital stay, but also increases the financial burden of their families [14–16]. Based on the result of our study that preoperative lung diseases, duration of the operation, BMI < 18 kg/m², and approach to chest (open) were risk factors for PPI in patients after esophagectomy, we could identify high-risk groups quickly and provide

effective measures to prevent PPI, even to improve the quality of patients' life and the reduce economic burden.

Clinical experience suggests that PPI is associated with previous disease history, including susceptibility diseases like diabetes [17]. However, some studies have shown that diabetes is not a risk factor for PPI, which is consistent with our results. Our results show that preoperative lung diseases, including COPD, pulmonary bullae and silicosis, have been identified as important risk factors for PPI in patients, presenting the same trend as previous research results [18, 19]. For patients with pre-existing lung diseases, individualized respiratory system management programs should be developed according to different conditions of lung function before operation, such as evaluating the respiratory function of the patients, advising smokers to quit smoking for more than 4 weeks before surgery, and guiding patients to perform respiratory function exercises like abdominal breathing, lip contraction breathing and eliminating sputum to increase lung function reserve [20]. The original chronic respiratory diseases could be controlled by means of atomizing medication.

While operation time is screened as a risk factor in our study, there are still many other unmeasurable factors hiding behind it, such as the difficulty of individualized tumor resection, the operative proficiency of the surgeon, the duration of surgical anesthesia, the duration of chest exposure and so on. The duration of the operation cannot be artificially shortened, so effective intervention measures cannot be easily taken to reduce the risk of postoperative infection.

In the study of Haruhiko Cho, patient's performance was considered to be an influential factor for postoperative infection [21]. And in our study, validating this view

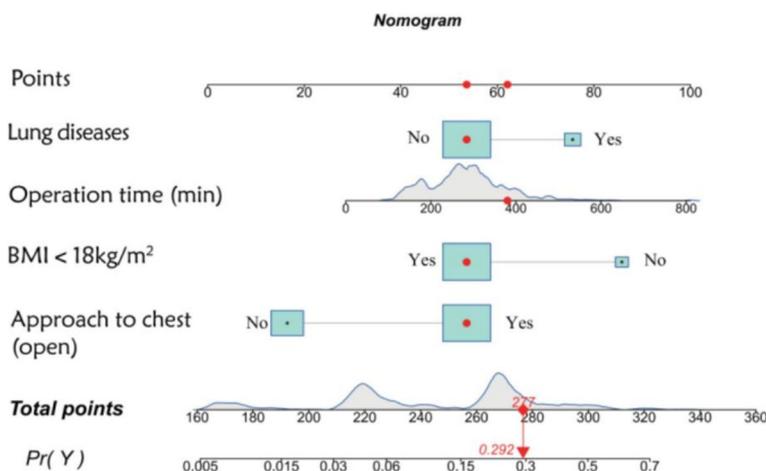


Fig. 4 A nomogram predictive model for PPI in EC patients after surgery. Each factor in the model is given a weighted score and the sum of each factor is used as the total score for the patient

from the perspective of specific indicators, BMI < 18 kg/m² was the screened variable. It is suggested that patients with inadequate nutritional status are more likely to be exposed to PPI. Therefore, it is essential to popularize the nutritional knowledge to patients before surgery, including the importance of nutritional treatment, the way of nutrition management in the hospital, the use of nutritional preparations, the advantages of postoperative nutritional treatment, and the dietary guidance after discharge. Patients should be stopped from eating solid food 6 h before surgery and could take liquid food 2 h before surgery. The diabetic patients could take specially formulated low-glycemic oral liquid to reduce the stress reaction of surgery.

If a patient get score ≥ 300 points on this model (probability $\geq 50\%$), clinicians should pay more attention to his postoperative management. Using patients controlled analgesia if necessary. Nasogastric feeding is the main way after surgery. Patients should be given glucose while patients with diabetes could be fed with saline on the first day; half nutrient solution was used on the second day; full nutrient solution was used on the third day, and a semi-liquid diet was gradually taken after three days. Encourage patients to get out of bed early. Clinicians should observe patients daily for respiratory symptoms, combined with blood routine and chest X-ray examination, to diagnose PPI patients and treat them timely. Perform upper gastrointestinal contrast one week after operation to observe whether there was anastomotic fistula and other adverse conditions.

Although data from multiple studies have shown that neoadjuvant chemoradiotherapy improves OS of EC patients, it is still a controversial factor for PPI. A recent report shows that rate of PPI after neoadjuvant chemoradiotherapy was 33.3% (26/78), much more than the average rate, indicating neoadjuvant chemoradiotherapy contributing to the PPI [22]. In the study of Hayami et al., radiation mode, radiation dose and radiation frequency are probably associated with infection [23, 24]. Immune checkpoint inhibitor-related pneumonitis was the most common cause of immunotreatment-related death, accounting for 10% of immune-related adverse events deaths [25]. More practice find out that the combination of immunization and radiotherapy may increase the incidence of pneumonia [26]. However, neoadjuvant chemoradiotherapy did not become a statistically significant factor in our study, possibly because most patients enrolled did not take neoadjuvant chemoradiotherapy before surgery.

The effect of postoperative pulmonary complications (PPCs) including pulmonary infection on survival remains a controversy. In this study, PPI was found to result in a poorer OS among patients after

esophagectomy, especially middle EC patients [27]. Chaoyang Tong demonstrated that there was no significant difference between patients with and without PPCs [28]. However, some other studies showed that the occurrence of complications after esophageal cancer resection has a negative impact on long-term survival [29]. Furthermore, a recent meta-analysis shows that PPCs truly leads to worse clinical outcomes on long-term OS, cancer specific survival (CSS), and disease free survival (DFS) at 60-month follow-up, which is consistent with our findings in some ways [30].

Chaoyang Tong et al. had developed a nomogram for predicting PPCs with 10 predictors, but considering that PPCs included atelectasis, pulmonary infection and respiratory failure, it's not suitable for predicting PPI specially [28]. At the same time, Shuang Li et al. developed another nomogram for predicting PPI, of which predictive factors are length of stay, albumin, intraoperative bleeding and perioperative blood transfusion [31]. Given that PPI may occur shortly after surgery, we did not take into account the length of hospital stay. Thus, we established a clinical model with indicators easy to access.

We analyzed a large set of samples using the data from Xijing Hospital of Air Force Military Medical University, one of the largest digestive disease centers in China, which represents the characters of populations in this area. We followed the recommendation of the Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement to calculate calibration curves, DCA curves, and AUC. The favorable results were replicated well in the cross-validation cohort. Overall, our nomogram may be a useful tool of evaluating PPI in patients after esophagectomy.

Although the nomogram performed well, the present study had some limitations. For instance, the collected data is insufficient to analyze the relationship between muscularity and PPI, which now is identified as an indicator of PPI [32]. Patients accepted neoadjuvant chemoradiotherapy is not enough in quantity which may affect the whole model. More importantly, multicenter clinical validation is also needed to evaluate the external utility of our nomogram.

Conclusion

PPI has been shown to increase the financial burden on patients and lead a worse long-term survival. We used two methods to screen risk factors for PPI in esophageal cancer patients after surgery, and established a new nomogram on the better one, which may benefit treatment results for patients and clinicians, as well as pre and postoperative intervention strategy-making.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12957-025-03806-1>.

Supplementary Material 1.

Authors' contributions

J Chen: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing -original draft. Y Zhao: Investigation, Project administration, Validation. W Yang: Formal analysis, Investigation, Resources. L Duan: Formal analysis, Investigation, Resources. L Niu: Formal analysis, Investigation, Resources. Z Li: Resources, Software, Visualization. Y Zhang: Project administration, Validation. Y Miao: Resources, Software. A Fan: Data curation, Investigation. S Wei: Data curation, Investigation. H Bai: Data curation, Investigation. Y Li: Methodology. X Wang: Methodology. W Zhou: Methodology. Q Xie: Investigation. C Wang: Investigation. X Chen: Investigation. Y Han: Project administration, Supervision. L Hong: Conceptualization, Supervision, Writing -original draft. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval

This study has been registered on clinicaltrials.gov website (NCT05740852) and has been approved by Xijing Hospital Ethics Committee (KY20232060-C-1).

Competing interests

The authors declare no competing interests.

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