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A nomogram for postoperative pulmonary infections in esophageal cancer patients: a two-center retrospective clinical study

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Abstract

Background Postoperative pulmonary infections (POPIs) occur in approximately 13–38% of patients who undergo surgery for esophageal cancer, negatively impacting patient outcomes and prolonging hospital stays. This study aims to develop a novel clinical prediction model to identify patients at risk for POPIs early, thereby enabling timely intervention by clinicians.

Methods This study included 910 patients from two hospitals. Of these, 795 patients from one hospital were randomly assigned to the training cohort ($n=556$) and the validation cohort ($n=239$) at a 7:3 ratio. The external test cohort consisted of 115 patients from the second hospital. A nomogram was developed via logistic regression to predict the incidence of POPIs. The model's discrimination, precision and clinical benefit were evaluated by constructing a receiver operating characteristic (ROC) curve, calculating the area under the ROC curve (AUC), performing a calibration plot, conducting decision curve analysis (DCA) and clinical impact curves (CIC).

Results Multivariate logistic regression revealed that age, anemia, neoadjuvant therapy, T stage, thoracic adhesions and duration of surgery were independent risk factors for POPIs. The AUC for the training cohort was 0.8095 (95% CI: 0.7664–0.8527), that for the validation cohort was 0.8039 (95% CI: 0.7436–0.8643), and that for the external test cohort was 0.7174 (95% CI: 0.6145–0.8204). Calibration plots demonstrated good agreement between the predicted and observed probabilities, while DCA and CIC demonstrated good clinical applicability of the model in three cohorts.

Conclusion The nomogram, which incorporates six key factors, effectively predicts the risk of POPIs and can serve as a valuable tool for clinicians in identifying high-risk patients.

Keywords Postoperative pulmonary infections, Esophageal cancer, Nomogram, Risk factors

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Introduction

Esophageal cancer is an extremely aggressive disease with a poor prognosis, as evidenced by its 5-year survival rate of only 20% [1, 2]. It ranks eighth globally in terms of incidence and sixth in terms of mortality [3]. Although minimally invasive techniques are becoming more common, the complexity of esophageal cancer surgery still result in a high incidence of postoperative complications [4–6].

POPIs are frequent complication following esophageal cancer surgery, with studies showing that its incidence ranges from 13 to 38% [7, 8]. Furthermore, research suggests that POPIs can negatively affect long-term survival, extend hospital stays, increase medical costs, and even lead to perioperative mortality in some cases [9]. Therefore, early identification of patients at high risk for POPIs and timely intervention are critical for improving outcomes.

Some studies have focused on identifying risk factors for POPIs based on clinical data [10, 11]. These factors typically include demographic information such as age, gender, and body mass index (BMI, kg/m^2); inflammatory markers such as white blood cell count and C-reactive protein levels; surgical factors such as the type of procedure, duration of surgery, and intraoperative blood loss; and oncological factors such as TNM stage. Although several prediction models for POPIs have been developed [12, 13], their predictive performance varies, and there is no consensus on a unified model. Moreover, only 28.57% of these models have been externally validated, so they are liable to overfitting [14].

To improve clinical utility, the goal of this study was to compile more common perioperative clinical factors for esophageal cancer patients, develop a prediction model based on these factors, and validate the model via an external cohort.

Methods

Patient selection

Patients with esophageal cancer who received surgical treatment at People's Hospital Affiliated to Jiangsu University between January 2019 and August 2024 were chosen as study participants. Additionally, patients with esophageal cancer who received surgical treatment at Dushu Lake Hospital affiliated to Soochow University, between January 2020 and August 2024 were included in the external cohort. The ethics committees of both hospitals gave their approval and consent for this study, our study complies with the relevant provisions of ethics and adheres to the Declaration of Helsinki, the data does not contain any information that discloses the patient's privacy, so the patient's informed consent is exempted. The inclusion criteria were: Patients with a clear pathologic diagnosis of esophageal cancer; Patients who met the indications for surgery in the National Comprehensive Cancer Network (NCCN) guidelines and successfully completed surgery; Complete clinical data. The exclusion criteria of this study were: Lack of clinical data; Preoperative pulmonary infection; Patients with pulmonary infection more than 30 days after surgery; Perioperative death; Other related surgeries were performed during the same period.

Treatment procedures and postoperative courses

Patients with esophageal cancer were admitted to the hospital for multi-disciplinary consultation (MDT) to formulate the best treatment plan. If neoadjuvant therapy was needed, the oncologists will make the neoadjuvant treatment plan, including neoadjuvant immunotherapy, neoadjuvant radiotherapy or chemotherapy, etc. Patients who met the indications for surgery were operated under general anesthesia with double-lumen endotracheal intubation, and the surgical method (the minimally invasive surgery: both the thoracic and abdominal portions were performed by minimally invasive methods, open surgery: one of the thoracic and abdominal portions was performed by open methods or both) was decided by the surgeons before the operation. The nasointestinal tube was placed during the operation, and jejunostomy was performed for those who were difficult to be placed. All postoperative patients were admitted to Surgical Intensive Care Unit (SICU) for 1–3 days of care and treatment, during which enteral nutrition combined with intravenous nutrition was performed on the first postoperative day, and the patients were assisted to turn over and pat their backs to help remove sputum, then they were transferred to the general ward to continue the treatment after the vital signs were stabilized. Patients would be fed by mouth around day 7 postoperatively. Patients were discharged around day 10–14 postoperatively if there was no special complication such as anastomotic leakage, chylothorax, incision infection, etc.

Definition of POPIs

Patients underwent chest X-ray on the first and third postoperative days, blood routine and sputum culture examinations were performed on three consecutive postoperative days, and body temperature were monitored. In case of new onset of fever and increased sputum, chest X-ray with blood routine and sputum culture examinations were performed on the same day. POPIs were diagnosed if the following conditions were met: the presence of new chest X-ray infiltrates plus one of the three clinical variables (fever > 38 °C, leukocytosis or leucopenia and purulent secretions) [15].

Data collection

The following data were collected from the patients: gender, age, BMI, history of smoking, history of drinking,

history of hypertension, history of diabetes mellitus, history of stroke, history of chronic obstructive pulmonary disease (COPD), anemia, neoadjuvant therapy, T stage (T1 + 2, T3 + 4), N stage (N-, N+),site of the tumor (upper, middle, lower), surgical methods, thoracic adhesion, duration of the surgery, intraoperative bleeding, anastomotic method (cervical anastomosis, thoracic anastomosis), anastomotic leakage, PaO_2: arterial blood gas oxygen partial pressure (obtained after admission and before tracheal intubation), $PaCO_2$: arterial blood gas carbon dioxide partial pressure (obtained after admission and before tracheal intubation), forced expiratory volume in one second/ forced vital capacity (FEV1/FEV), white blood cell count (WBC), C-reactive protein(CRP), prealbumin, and albumin. The cohort at People's Hospital affiliated to Jiangsu University was randomly divided into a training cohort and a validation cohort at a 7:3 ratio. The training cohort was used to develop the prediction model and construct the nomogram, and the validation cohort was used for internal validation. Then the cohort from Dushu Lake Hospital affiliated to Soochow University was used for external testing of the nomogram.

Statistical analysis

The collected continuous variables were transformed into categorical variables based on clinical significance or according to whether they followed a normal distribution (mean) or a nonnormal distribution (median). Pearson's chi-square test or Fisher's exact test was used to compare categorical variables. Variables were first screened through univariate analysis, followed by multivariate logistic regression to identify the final variables, which were then used to construct a predictive model and plot a nomogram. Data analysis was performed via R software (version 4.3.0), SPSS (Statistical Product and Service Solutions) software (version26.0), and GraphPad Prism (version 8.0.2), with a statistical significance threshold set at $p < 0.05$ (two-tailed).

Nomogram performance

We assessed the performance of the nomogram through discrimination, precision and clinical benefit in three cohorts. Discrimination refers to the ability of a model to correctly distinguish between events and nonevents. The receiver operating characteristic (ROC) curve was used to evaluate the discriminatory performance of the predictive nomogram [16]. Calibration curves were then plotted to assess the calibration of the model, which is a scatterplot of actual and predicted incidence, a visualization of the results of the Hosmer-Lemeshow goodness-of-fit test [17]. Additionally, decision curve analysis (DCA) and clinical impact curves (CIC) were performed to evaluate the clinical benefit of the predictive nomogram. DCA is a method of assessing the value of predictive models for application in real-world clinical decision-making. It does so by comparing the net benefit of different decision scenarios over a specific range of thresholds. The term "net gain" refers to the net effect after taking into account the benefits and losses of false-positive and false-negative results [18].

Results

Patient characteristics

A total of 795 patients were included from the People's Hospital affiliated to Jiangsu University, with an incidence of POPIs of 26.3% (209/795), and 115 patients were included Dushu Lake Hospital affiliated to Soochow University, where the incidence of POPIs was 33.2% (37/115). The 795 patients were randomized into a training group ($n = 556$) and a validation group ($n = 239$) at a 7:3 ratio, while the 115 patients composed the external test cohort. The detailed flowchart is shown in Fig. 1. The overall variables of the three cohorts are shown in Table 1. The incidence of POPIs in the training cohort was 25.4% (141/556), the validation cohort was 28.5% (68/239), and there was no statistically significant difference between the training and validation cohorts in terms of the variable data. The data of the external test cohort was only used to validate the model, so we did not statistically compare it with the training cohort and the validation cohort.

Identification of risk factors for POPIs

The training group was divided into POPIs and non-POPIs groups based on the occurrence of POPIs. Univariate analysis (Chi-square test) was first performed to screen the variables, which revealed that age, BMI, anemia, neoadjuvant therapy, T stage, N stage, surgical method, thoracic adhesions, duration of surgery, intraoperative blood loss, PaO_2, CRP, and prealbumin were potential risk factors for POPIs ($p < 0.05$). Further multivariate logistic regression analysis revealed the following independent risk factors for POPIs: age [odds ratio (OR) = 2.241; 95% confidence interval (CI): 1.055–4.760; $p = 0.036$], anemia [OR = 2.216; 95% CI: 1.289–3.506; $p = 0.003$], neoadjuvant therapy [OR = 4.283; 95% CI: 2.345–7.823; $p < 0.001$], T stage [OR = 2.533; 95% CI: 1.355–4.734; $p < 0.001$], thoracic adhesions [OR = 5.311; 95% CI: 2.850–9.900; $p < 0.001$], and duration of surgery [OR = 1.841; 95% CI: 1.080–3.140; $p = 0.025$], Table 2 shows the detailed statistical results, and a forest plot (Fig. 2) is also drawn to show the results.

Nomogram construction

The six independent risk factors identified above were included in the final logistic regression model. A nomogram was then constructed via the "rms" package in R statistical software which is shown in Fig. 3. As shown in

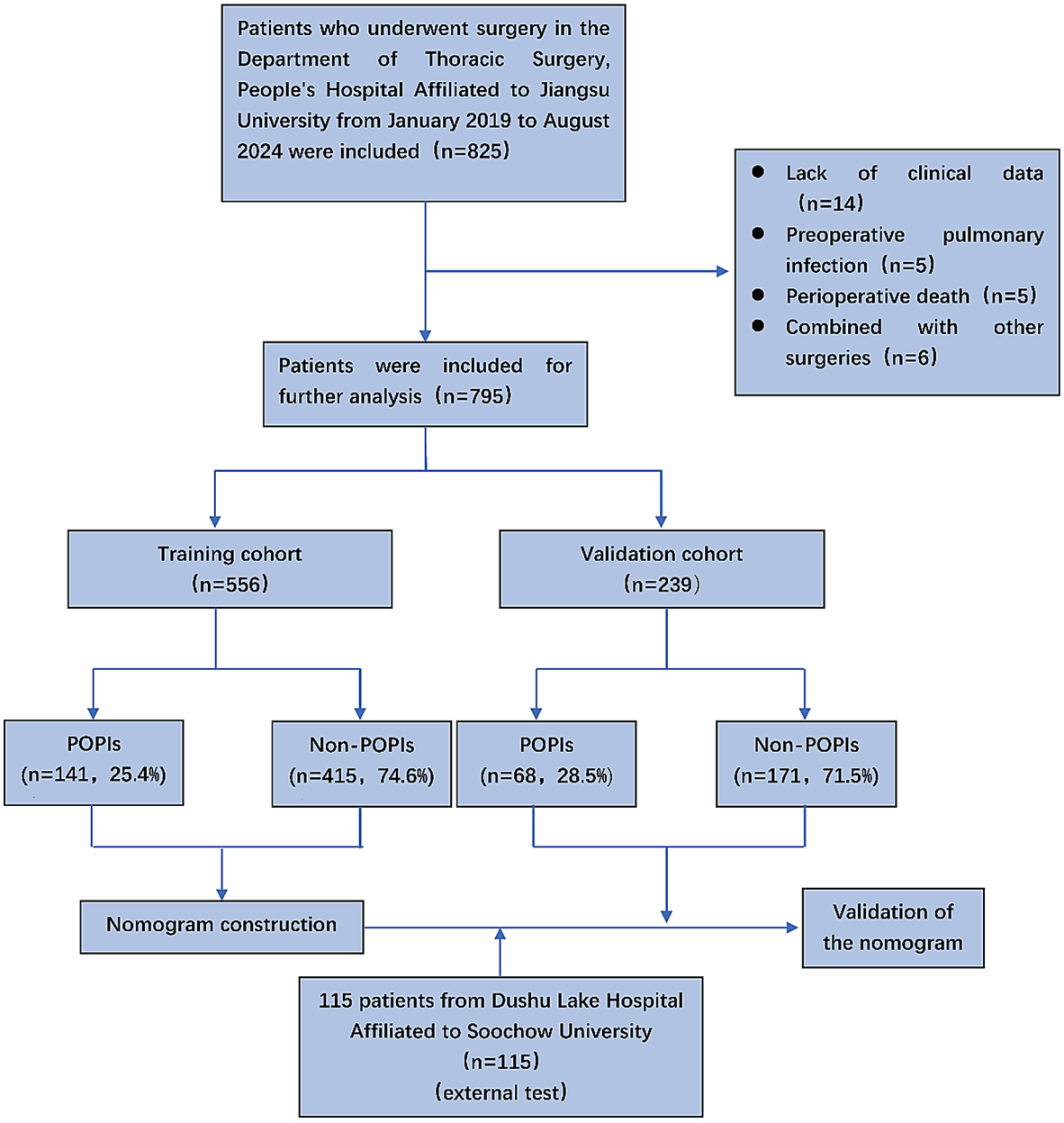

Fig. 1 This flow diagram shows the collection and processing of data. Postoperative Pulmonary Infections (POPIs)

the figure, the nomogram consists of 10 horizontal axes, with axes 2–7 representing the individual risk factors. The estimated score for each risk factor can be calculated by drawing a perpendicular line to the axis corresponding to the highest scores, which are then summed to obtain a total score. This total score can be used to predict the probability of POPIs.

Performance and clinical benefits of the nomogram of POPIs in three cohorts

The discriminative ability of the nomogram was evaluated by plotting ROC curves for the training, validation, and external test cohorts. The AUC for the three cohorts were 0.8095 (95% CI: 0.7664–0.8527), 0.8039 (95% CI: 0.7436–0.8643), and 0.7174 (95% CI: 0.6145–0.8204), respectively (Fig. 4). Calibration curves were also plotted for the three cohorts, we internally validated the model by Bootstrap repeated self-sampling method, and the calibration curves obtained after repeating Bootstrap self-sampling for 1000 times showed that the absolute error between the simulated curve and the actual curve of the three cohorts were 0.034, 0.014, 0.018, respectively. And the trends of the three curves were basically the same, with a strong consistency (Fig. 5).Then, DCAs were performed, and the results showed that the model offered superior net benefits compared to full intervention or no

Table 1 Patients' characteristics of the three cohorts

Variables	All cohorts($n=795$)	Training cohort ($n=556$)	Validation cohort ($n=239$)	χ^2	*P* Value	External test cohort ($n=115$)
POPIs, n (%)				0.825	0.364	
Yes	209(26.3)	141(25.4)	68(28.5)			37(33.2)
No	586(73.7)	451(74.6)	171(71.5)			78(67.8)
Gender, n (%)				0.950	0.330	
Female	184(23.1)	134(24.1)	50(20.9)			24(20.9)
Male	611(76.9)	422(75.9)	189(79.1)			91(79.1)
Age (year), n (%)				0.367		
<65	143(18.0)	97(17.4)	46(19.2)		0.544	59(51.3)
≥ 65	642(82.0)	459(82.6)	193(80.8)			56(48.7)
BMI (Kg/m2), n (%)				1.057	0.625	
<18	31(3.9)	22(4.0)	9(3.8)			6(5.2)
18–24	598(75.2)	423(76.0)	175(73.2)			75(65.2)
>24	166(20.9)	111(20)	55(23.0)			34(29.6)
Hypertension, n (%)				3.227	0.072	
No	431(54.2)	313(56.3)	118(49.4)			69(60.0)
Yes	364(45.8)	243(43.7)	121(50.6)			46(40.0)
Diabetes, n (%)				2.135	0.144	
No	696(87.5)	493(88.7)	203(84.9)			99(86.1)
Yes	99(12.5)	63(11.3)	36(15.1)			16(13.9)
History of stroke, n (%)				0.038	0.846	
No	716(90.1)	500(89.9)	216(90.3)			106(92.2)
Yes	79(9.9)	56(10.1)	23(9.6)			9(7.8)
COPD, n (%)				0.081	0.776	
No	580(73.0)	404(72.7)	176(73.6)			83(72.2)
Yes	215(27.0)	152(27.3)	63(26.4)			32(27.8)
Smoking, n (%)				0.707	0.401	
No	588(74.0)	416(74.8)	172(72.0)			84(73.0)
Yes	207(26.0)	140(25.2)	67(28.0)			31(27.0)
Drinking, n (%)				0.097	0.755	
No	667(83.9)	465(83.6)	202(84.5)			98(85.2)
Yes	128(16.1)	91(16.4)	37(15.5)			17(14.8)
Anemia, n (%)				1.242	0.265	
No	516(64.9)	354(63.7)	162(67.8)			86(74.8)
Yes	279(35.1)	202(36.3)	77(32.2)			29(25.2)
Neoadjuvant therapy, n (%)				0.006	0.938	
No	644(81.0)	450(80.9)	194(81.2)			92(80.0)
Yes	151(19.0)	106(19.1)	45(18.8)			23(20.0)
T stage, n (%)				1.023	0.312	
T1 + T2	287(36.1)	207(37.2)	80(33.5)			71(61.7)
T3 + T4	508(63.9)	349(62.8)	159(66.5)			44(38.3)
N stage, n (%)				1.035	0.309	
N-	421(53.1)	301(54.1)	120(50.2)			73(60.4)
N+	374(47.1)	255(45.9)	119(49.8)			42(36.5)
Site of the tumor, n (%)				1.491	0.475	
Upper	64(8.1)	44(7.9)	20(8.4)			9(7.8)
Middle	372(46.8)	268(48.2)	104(43.5)			55(47.8)
Lower	359(45.2)	244(43.9)	115(48.1)			51(44.3)
Surgical methods, n (%)				0.966	0.326	
Minimally invasive	699(87.9)	493(88.7)	206(86.2)			22(19.1)
Open surgery	96(12.1)	63(11.3)	33(13.8)			93(80.9)
Thorax adhesions, n (%)				1.459	0.227	

Table 1 (continued)

Variables	All cohorts($n=795$)	Training cohort ($n=556$)	Validation cohort ($n=239$)	χ^2	*P* Value	External test cohort ($n=115$)
No	691(86.9)	478(86.0)	213(89.1)			82(71.3)
Yes	104(13.1)	78(14.0)	26(10.9)			33(28.7)
Duration of surgery (min), n (%)				0.411	0.522	
<330	373(46.9)	265(47.7)	108(45.2)			69(60.0)
≥330	422(53.1)	291(53.3)	131(54.8)			46(40.0)
Intraoperative blood loss (ml), n (%)				0.009	0.925	
<50	168(21.1)	117(21.0)	51(21.3)			50(43.5)
≥50	627(78.9)	439(79.0)	188(78.7)			65(56.5)
Method of anastomosis, n (%)				1.404	0.236	
Cervical anastomosis	683(85.9)	483(86.9)	200(83.7)			16(13.9)
Intrathoracic anastomosis	112(14.1)	73(13.1)	39(16.3)			99(86.1)
Anastomotic leakage, n (%)				0.2	0.655	
No		519(93.4)	221(92.5)			103(89.6)
Yes		37(6.6)	18(7.5)			12(10.4)
PaO_2, n (%)				1.795	0.180	
≥80mmHg	565(71.1)	403(72.5)	162(67.8)			82(71.3)
<80mmHg	230(28.9)	153(27.5)	77(32.2)			33(28.7)
$PaCO_2$, n (%)				3.489	0.062	
≤45mmHg	684(86.0)	470(84.5)	214(89.5)			95(82.6)
>45mmHg	111(14.0)	86(15.5)	25(10.5)			20(17.4)
FEV1/FVC, n (%)				0.351	0.553	
≥0.7	659(82.9)	458(82.4)	201(84.1)			88(76.5)
<0.7	136(17.1)	98(17.6)	38(15.9)			27(23.5)
WBC, n (%)				0.003	0.955	
≤10×10^9/L	749(94.2)	524(94.2)	225(94.1)			111(96.5)
>10×10^9/L	46(5.8)	32(5.8)	14(5.9)			4(3.5)
CRP, n (%)				0.693	0.405	
Normal	662(83.3)	467(84.0)	195(81.6)			86(74.8)
Higher	133(16.7)	89(16.0)	44(18.4)			29(25.2)
Prealbumin, n (%)				0.293	0.588	
Normal	94(11.8)	68(12.2)	26(10.9)			10(8.7)
Lower	701(88.2)	488(87.8)	213(89.1)			105(91.3)
Albumin, n (%)				0.776	0.379	
Normal	566(71.2)	401(72.1)	165(69.0)			109(94.8)
Lower	229(28.8)	155(27.9)	74(31.0)			6(5.2)

BMI (Kg/m^2), body mass index; COPD, chronic obstructive pulmonary disease; PaO_2, arterial blood gas oxygen partial pressure; $PaCO_2$, arterial blood gas carbon dioxide partial pressure; FEV1/FEV, forced expiratory volume in one second/ forced vital capacity; WBC, white blood cell count; CRP, C-reactive protein, Normal<10 mg/L, Higher ≤ 10 mg/L; Prealbumin, Normal ≥ 280 mg/L, Lower<280 mg/L; Albumin, Normal ≥ 35 g/L, Lower<35 g/L

intervention strategies in training and validation cohorts if the threshold probability of patients was 7–74%. Although the model performed slightly worse in the external validation cohort, it still provided good clinical benefits within a large threshold probability range (about 14–70%) (Fig. 6). Finally, CICs were performed in Fig. 7 to evaluate clinical applicability of the nomogram. CICs showed that the nomogram had a superior overall net benefit within the wide and practical ranges of threshold probabilities in the three cohorts. Overall, the model had a good predictive performance and good degree of generalizability across all three cohorts, which could assist clinicians in making decisions when managing patients.

Discussion

Esophageal cancer is a common malignancy of the upper gastrointestinal tract, and China is a high-incidence region for this disease [19]. The main treatment for esophageal cancer is a comprehensive approach, which is primarily based on surgical intervention. However, surgery is associated with significant trauma and a high incidence of postoperative complications, which severely

Table 2 Results of difference analysis and multivariate logistic regression analysis

Variables	Training cohort ($n=556$)		χ^2	p	Multivariate analysis		p
	Non- POPIs ($n=415$)	POPIs ($n=141$)			OR	95%CI	
Gender, n (%)			0.212	0.646			
Female	98(23.6)	36(25.5)					
Male	317(76.4)	105(74.5)					
Age (years), n (%)			8.876	0.03			0.036
<65	84(20.2)	13(9.2)			reference		
≥65	331(79.8)	128(90.8)			2.241	(1.055–4.760)	
BMI (Kg/m^2), n (%)			8.605	0.01			0.363
<18	10(2.4)	12(8.5)			reference		
18–24	329(79.3)	94(66.7)			0.502	(0.173–1.456)	
>24	76(18.3)	35(24.8)			0.634	(0.199–2.013)	
Hypertension, n (%)			1.685	0.193			
No	227(54.7)	86(61.0)					
Yes	188(45.3)	55(39.0)					
Diabetes, n (%)			1.496	0.221			
No	364(87.7)	129(91.5)					
Yes	51(12.3)	12(8.5)					
History of stroke, n (%)			2.838	0.092			
No	368(88.7)	132(93.6)					
Yes	47(11.3)	9(6.4)					
COPD, n (%)			3.418	0.064			
No	310(74.7)	94(66.7)					
Yes	105(25.3)	47(33.3)					
Smoking, n (%)			0.113	0.737			
No	312(75.2)	104(73.8)					
Yes	103(24.8)	37(26.2)					
Drinking, n (%)			1.154	0.283			
No	343(82.7)	122(86.5)					
Yes	72(17.3)	19(13.5)					
Anemia, n (%)			31.685	<0.001			0.003
No	292(70.4)	62(44.0)			reference		
Yes	123(29.6)	79(56.0)			2.126	(1.289–3.506)	
Neoadjuvant therapy, n (%)			32.913	<0.001			<0.001
No	359(86.5)	91(64.5)			reference		
Yes	56(13.5)	50(35.5)			4.283	(2.345–7.823)	
T stage, n (%)			35.371	<0.001			<0.001
T1 + T2	184(44.3)	23(16.3)			reference		
T3 + T4	231(55.7)	118(83.7)			2.533	(1.355–4.734)	
N stage, n (%)			35.211	<0.001			
N-	255(61.4)	46(32.6)			reference		0.613
N+	160(38.6)	95(67.4)			1.153	(0.664–2.001)	
Site of the tumor, n (%)			5.76	0.056			
Upper	36(8.7)	8(5.7)					
Middle	188(45.3)	80(56.7)					
Lower	191(46)	53(37.6)					
Surgical methods, n (%)			6.088	0.014			0.297
Minimally invasive	376(90.6)	117(83.0)			reference		
Open surgery	39(9.4)	24(17.0)			1.411	(0.725–2.863)	
Thorax adhesions, n (%)			42.475	<0.001			<0.001
No	380(91.6)	98(69.5)			reference		
Yes	35(8.4)	43(30.5)			5.311	(2.850–9.900)	
Duration of surgery (min), n (%)			39.503	<0.001			0.025
<330	230(55.4)	35(24.8)			reference		

Table 2 (continued)

Variables	Training cohort ($n=556$)		χ^2	p	Multivariate analysis		p
	Non- POPIs ($n=415$)	POPIs ($n=141$)			OR	95%CI	
≥ 330	185(44.6)	106(75.2)			1.841	(1.080–3.140)	
Intraoperative blood loss (ml), n (%)			4.3	0.038			0.766
<50	96(23.1)	21(14.9)			reference		
≥ 50	319(76.9)	120(85.1)			1.104	(0.576–2.116)	
Method of anastomosis, n (%)			2.509	0.113			
Cervical anastomosis	366(88.2)	117(83.0)					
Intrathoracic anastomosis	49(11.8)	24(17.0)					
Anastomotic leakage (%)			0.293	0.589			
No	386(93.1)	133(94.4)					
Yes	29(6.9)	8(5.6)					
PaO_2, n (%)			4.956	0.026			0.425
≥ 80mmHg	311(74.9)	92(65.2)			reference		
<80mmHg	104(25.1)	49(34.8)			1.249	(0.723–2.158)	
$PaCO_2$, n (%)			0.103	0.748			
≤ 45mmHg	352(84.8)	118(83.7)					
>45mmHg	63(15.2)	23(16.3)					
FEV1/FVC, n (%)			1.734	0.188			
≥ 0.7	347(83.6)	111(78.7)					
<0.7	68(16.4)	30(21.3)					
WBC, n (%)			0.218	0.641			
≤ 10*10^9/L	390(94.0)	134(95.0)					
>10*10^9/L	25(6.0)	7(5.0)					
CRP, n (%)			9.233	0.002			0.223
Normal	360(86.7)	107(75.9)			reference		
Higher	55(13.3)	34(24.1)			1.465	(0.793–2.704)	
Prealbumin, n (%)			4.646	0.031			0.076
Normal	58(14.0)	10(7.1)			reference		
Lower	357(86.0)	131(92.9)			2.143	(0.922–4.979)	
Albumin, n (%)			3.571	0.059			
Normal	308(74.2)	93(66.0)					
Lower	107(25.8)	48(34.0)					

BMI (Kg/m^2), body mass index; COPD, chronic obstructive pulmonary disease; PaO_2, arterial blood gas oxygen partial pressure; $PaCO_2$, arterial blood gas carbon dioxide partial pressure; FEV1/FEV, forced expiratory volume in one second/ forced vital capacity; WBC, white blood cell count; CRP, C-reactive protein, Normal<10 mg/L, Higher ≤ 10 mg/L; Prealbumin, Normal ≥ 280 mg/L, Lower<280 mg/L; Albumin, Normal ≥ 35 g/L, Lower<35 g/L

affect both the quality of life and the prognosis of patients [20]. POPIs are common complication in patients with esophageal cancer. This may result from surgical disruption of the chest wall and intercostal muscles, particularly the diaphragm, leading to impaired respiratory function and a reduced ability to expectorate sputum [21]. Previous studies have shown that the risk factors for POPIs are associated with various clinical factors, such as tumor size, history of smoking, history of COPD, duration of surgery and intraoperative blood loss [22, 23]. In our study, we identified age, anemia, neoadjuvant therapy, T stage thoracic adhesions and duration of surgery as independent risk factors for POPIs.

Elderly patients are more prone to pulmonary complications after surgery, a finding that is consistent with those of previous study [24]. Research has shown that the risk of postsurgical pulmonary complications (PPCs) increases with age [7]. Specifically, the risk ratio for PPCs was 2.1 (95% CI: 1.7–2.6) for patients aged 60 to 69 years, 3.1 (95% CI: 2.1–4.4) for patients aged 70 to 79 years, and the risk ratio for patients aged 80 years or older increased further to 5.1 (95% CI: 1.9–13.3). Our study also revealed that in patients who underwent surgery for esophageal cancer, those aged ≥ 65 years had a 1.241-fold greater risk of developing POPIs than those aged < 65 years [OR = 2.241; 95%CI: 1.055–4.760; $p = 0.036$]. This may be attributed to the decline in various physiological functions in elderly patients, as well as a weakened immune system that reduces their ability to combat pathogenic bacteria. Furthermore, elderly patients often have additional underlying conditions, such as hypertension and diabetes, which can affect their overall health and increase the risk of infection [25, 26].

Variable	OR(95%CI)	*P* value
Age≥65	2.241(1.055-4.760)	0.036
BMI:18-24	0.502(0.173-1.456)	0.363
BMI: > 24	0.634(0.199-2.013)	0.363
Anemia:Yes	2.126(1.289-3.506)	0.003
Neoadjuvant therapy:Yes	4.283(2.345-7.823)	< 0.001
T stage:T3+T4	2.533(1.355-4.734)	< 0.001
N stage:N+	1.153(0.664-2.001)	0.613
Surgical methods :open surgery	1.411(0.725-2.863)	0.297
Thorax adhesions:Yes	5.311(2.850-9.900)	< 0.001
Duration of surgery:≥330	1.841(1.080-3.140)	0.025
Intraoperative blood loss:≥50	1.104(0.576-2.116)	0.766
PaO2: < 80mmHg	1.249(0.723-2.158)	0.425
CRP:Higher	1.465(0.793-2.704)	0.223
Prealbumin:Lower	2.143(0.922-4.979)	0.076

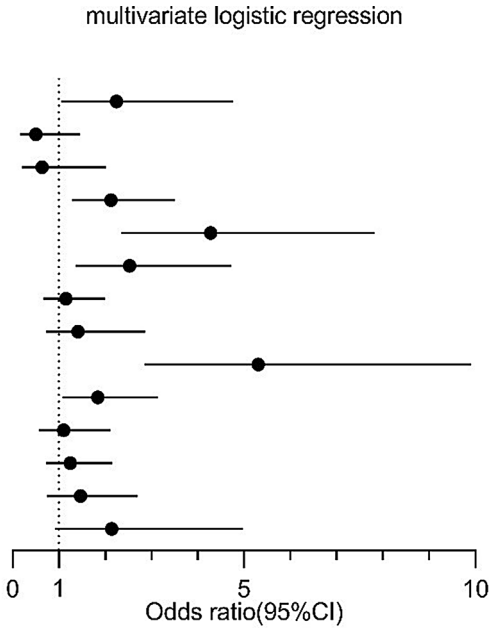

Fig. 2 The forest plot shows the results of multivariate logistic regression analysis

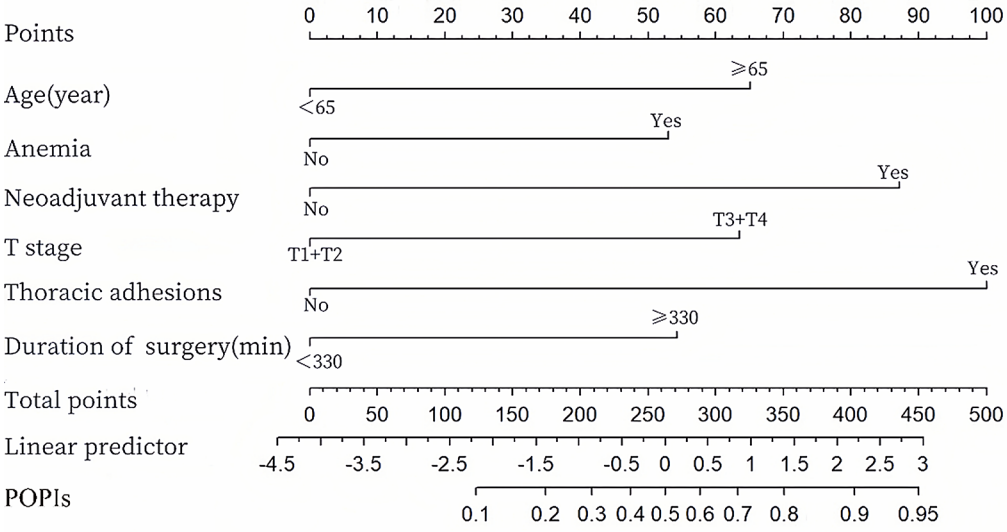

Fig. 3 Nomogram for predicting POPIs. Draw a vertical line from the corresponding axis of each variable to the points axis to acquire the point of this variable. Make a summation of the points for each variable to yield a total score, and the probability of POPIs could be estimated by projecting the total score to the lower total point axis

Study has shown that approximately 1/3 of surgical patients are anemic preoperatively [27].Anemia can affect a patient's body function in many ways, such as the immune system and respiratory system [28]. A meta-analysis has shown that anemia can increase the probability of common postoperative complications, including POPIs [29]. Our study has also shown that anemia can increase the incidence of POPIs, and the incidence of developing POPIs in anemic patients is 1.216 times greater than that in nonanemic patients [OR = 2.216; 95% CI: 1.289–3.506; $p = 0.003$]. Therefore, early intervention and treatment of patients with anemia can help reduce the incidence of postoperative complications.

The long-term follow-up results of two multicenter, prospective, randomized controlled phase III clinical studies, CROSS and NEOCRTEC5010, established preoperative neoadjuvant synchronous radiotherapy as the standard treatment for operable locally advanced esophageal cancer [30, 31]. which has been shown to improve survival rates [32]. However, some studies have also shown that neoadjuvant therapy increases the risk of postoperative complications, such as pulmonary

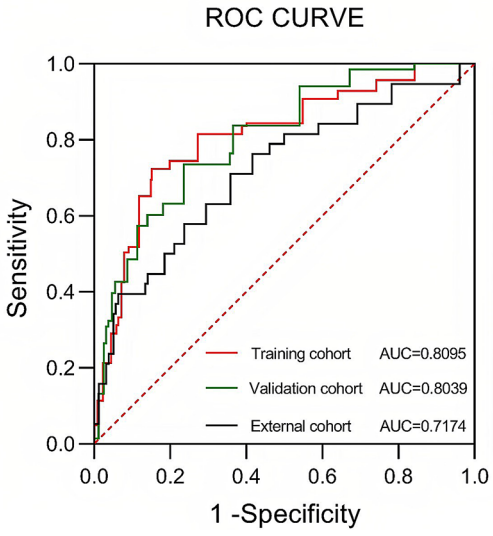

Fig. 4 ROC curves of the nomogram for predicting POPIs in the training, validation and external cohorts. ROC, receiver operating characteristic; AUC, areas under the ROC curve

infection and anastomotic fistula [33]. In our study, neoadjuvant therapy was found to be an independent risk factor for POPIs [OR = 4.283; 95% CI: 2.345–7.823; $p < 0.001$]. Although previous studies have suggested that neoadjuvant therapy does not increase surgical difficulty and does not increase the rate of postoperative complications [34], it may still lead to tissue edema and fibrosis in the surgical area, which presents significant challenges for the surgeon and may increase the operative time. Furthermore, immunotherapy and radiation therapy themselves can increase the risk of pneumonia [35, 36].

Our study also revealed a strong correlation between tumor T stage and POPIs, with the incidence of POPIs being 1.533 times greater in T3 + 4 patients than in T1 + 2 patients[OR = 2.533; 95% CI: 1.355–4.734; $p < 0.001$]. Previous models rarely included the T stage in their models [10, 37]. We believe that the later the T-stage of the tumor is, the closer the tumor is to the surrounding tissues, resulting in increased surgical difficulty and the need for greater intraoperative effort to expose the surgical field, resulting in increased compression of the surrounding tissues, especially the lung tissues, which leads to lung injury and an increase in the incidence of POPIs.

Thoracic surgeons frequently encounter thoracic adhesions during surgery, which can increase surgical trauma and even cause lung tissue damage, resulting in prolonged postoperative air leakage and an elevated risk of infection. Our study revealed that patients with thoracic adhesions had 4.311 times fold greater risk of developing POPIs [OR = 5.311; 95% CI: 2.850–9.900; $p < 0.001$]. However, we did not further stratify the extent of adhesions, such as by classifying them based on the lobes involved.

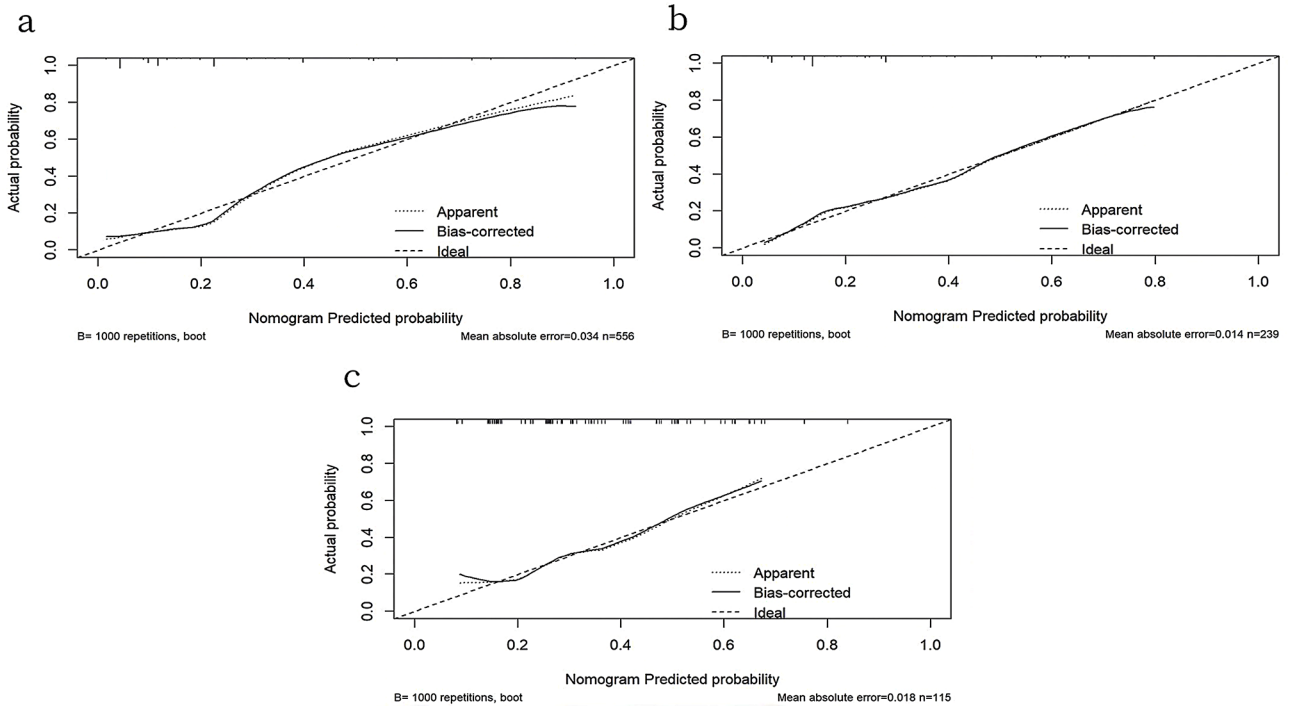

Fig. 5 Calibration plots of the nomogram in the training cohort (**a**), validation cohort (**b**) and external cohort (**c**). The x-axis represents the nomogram's predicted probability, and the y-axis represents the actual probability of POPIs. The long-dotted line represents the ideal curve, the short-dotted line represents the apparent curve, and solid black line represents the bias-correction curve by bootstrapping (B = 1000 repetitions). The calibration plots revealed good predictive accuracy between the actual probability and predicted probability in the three cohorts

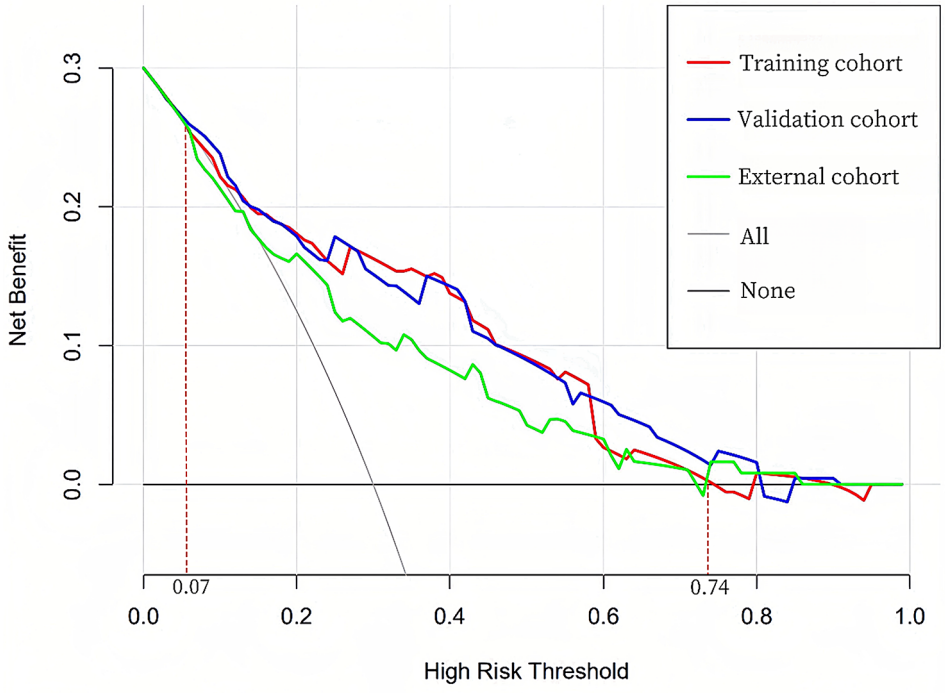

Fig. 6 DCA in the three cohorts. The y-axis measures the net benefit. The black line represents the benefit of not treating all patients, and the gray line represents the benefit of treating all patients, the red line represents the training cohort, the blue line represents the validation cohort, and the green line represents the external cohort. DCA showed that the model's net benefit was higher than both limit lines over a relatively large range of threshold probability in the three cohorts

Future studies could refine this by investigating the relationship between the extent of adhesions and the risk of POPIs, this is one of the limitations of our study.

The duration of surgery has been shown to be significantly correlated with POPIs in previous study [38]. Our study similarly identified duration of surgery as a risk factor for POPIs, with a duration longer than 330 min increasing the risk by 0.841 times [OR = 1.841; 95% CI: 1.080–3.140; $p = 0.025$]. However, the degree of surgical expertise varies among different operators and teams, making it difficult to assess surgical time with a uniform standard. This variability likely contributed to the decreased predictive accuracy of the model in the later stages of validation. In conclusion, our consensus is that shorter operation times, coupled with greater surgical skill, result in less trauma to the patient and a lower risk of POPIs.

The advantages of our study are the use of an external cohort for testing, and the model showed good results in the three cohorts. Furthermore, all the predictors were available at the end of the surgical procedure, surgeons can use our model on the first postoperative day to screen high-risk patients for timely intervention and treatment. However, this study still has the following limitations: Because the data were collected retrospectively, some important potential risk factors may have been missed, such as whether sarcopenia is a risk factor for POPIs. The sample size is still small, resulting in a degree of bias in the data and not confirming risk factors that have been confirmed in previous studies, such as anastomotic leakage. In addition, our study converts continuous variables into categorical variables, which simplifies the model but may reduce the statistical efficacy of the data due to the small sample size. Such results also lead to the fact that small changes in variables may lead to large changes in risk of POPIs. So, the Nomogram of this study only provide corresponding reference and auxiliary diagnosis, and clinicians need more personal information for judgment in individuals. Future studies need to collect data prospectively and use multicenter data for training and validation, aiming to improve the accuracy and utility of the model.

Conclusion

Our study ultimately constructed a model with relatively good predictive ability by using indicators that are extremely easy to obtain clinically, validated it with external cohort, and obtained good results, which is worthy of clinical promotion.

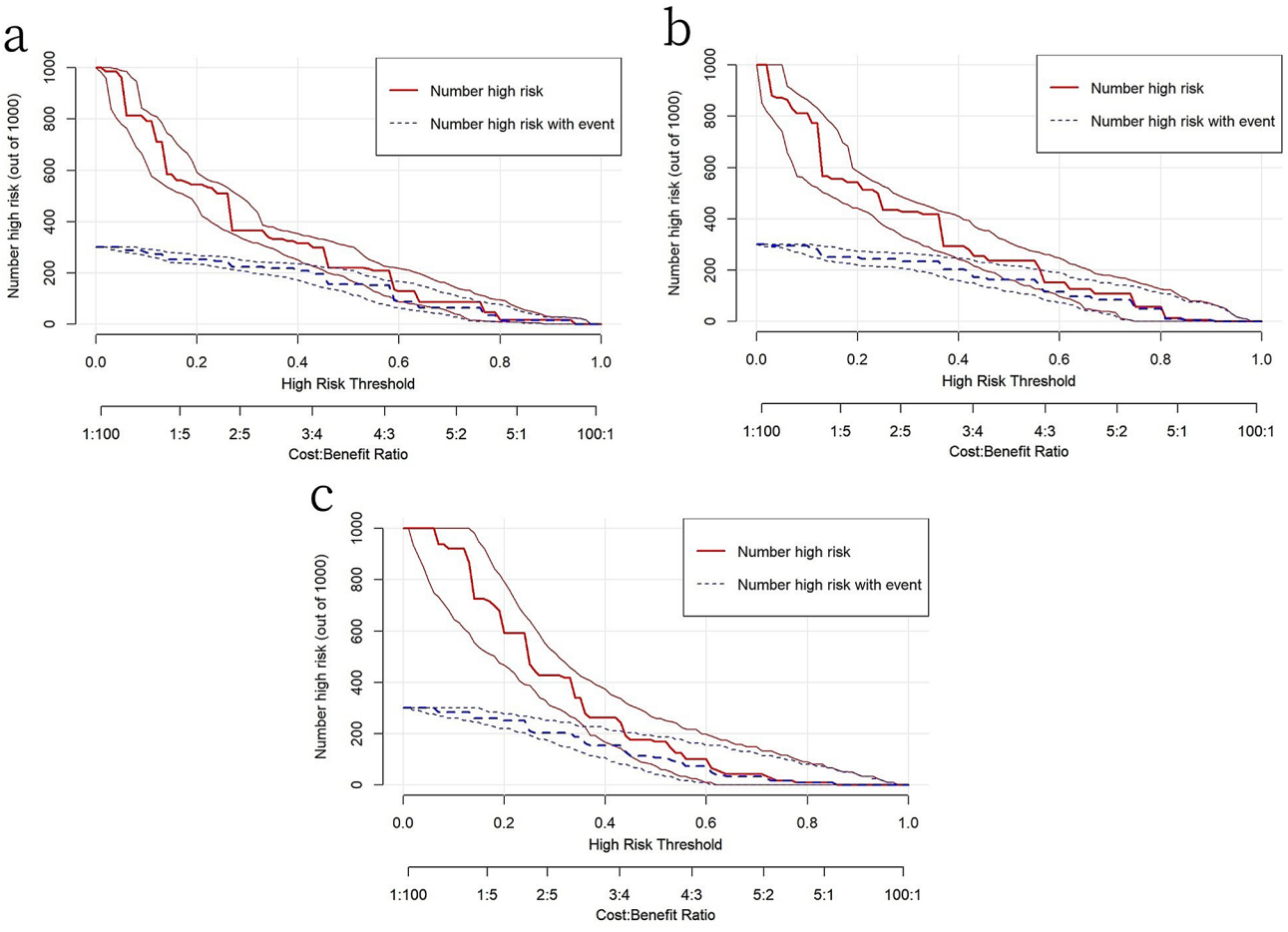

Fig. 7 Clinic impact curve (CIC) of the nomogram in the training cohort (**a**), validation cohort (**b**) and external cohort (**c**). The red curve indicates the number of people who are classified as positive by the model at each threshold probability, the blue curve indicates the number of people who are true positive at each threshold probability. CIC visually showed that the nomogram had a superior overall net benefit within the wide and practical ranges of threshold probabilities in the three cohorts

Abbreviations

POPIs	Postoperative pulmonary infections
ROC	Receiver operating characteristic curve
AUC	Area under the ROC curve
DCA	Decision curve analysis
CIC	Clinical impact curves
BMI	Body mass index
NCCN	National Comprehensive Cancer Network
MDT	Multi-disciplinary consultation
SICU	Surgical Intensive Care Unit
COPD	Chronic obstructive pulmonary disease
PaO_2	Arterial blood gas oxygen partial pressure
$PaCO_2$	Arterial blood gas carbon dioxide partial pressure
FEV1/FEV	Forced expiratory volume in one second/ forced vital capacity
WBC	White blood cell count
CRP	C-reactive protein
SPSS	Statistical Product and Service Solutions
OR	Odds ratio
CI	Confidence interval
PPCs	Postsurgical pulmonary complications

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Author contributions
S.L. designed the study, analyzed the data, and wrote the manuscript. C.F. and Z.T. assisted with data acquisition, analysis, and manuscript revisions. J.Z. provided guidance on the study design and data interpretation. H.M. supervised the study and critically revised the manuscript. All authors approved the final manuscript.

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Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
The ethics committees of People's Hospital Affiliated to Jiangsu University and Dushu Lake Hospital affiliated to Soochow University gave their approval and consent for this study. Our research does not involve human experiments or tissue samples, and is following relevant guidelines and regulations. The data in this study did not include any patient identity information and did not contain any direct or indirect identifiers that could reveal basic patient information.

Consent for publication
All the authors reviewed and approved the final version of the manuscript and agreed to its publication.

Competing interests
The authors declare no competing interests.

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