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ORIGINAL RESEARCH

Analysis of Influencing Factors and Construction of Predictive Model for Persistent Cough After Lung Cancer Resection Under Thoracoscopy

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Objective: This study aims to explore the influencing factors of cough after pulmonary resection (CAP) after thoracoscopic lung resection in lung cancer patients and to develop a predictive model.

Methods: A total of 374 lung cancer patients who underwent lung resection in our hospital from March 2020 to October 2023 were randomly divided into a modeling group (n=262) and a validation group (n=112). Based on the occurrence of CAP in the modeling group, the patients were divided into a CAP group (n=85) and a non-CAP group (n=177). Multivariate Logistic regression analysis was used to identify the influencing factors of CAP in lung cancer patients. A nomogram model for predicting the risk of CAP was constructed using R4.3.1. The consistency of the model's predictions was evaluated, and a clinical decision curve (DCA) was drawn to assess the clinical utility of the nomogram. The predictive performance of the model was evaluated using ROC curves and the Hosmer-Lemeshow test.

Results: Multivariate Logistic regression analysis showed that smoking history (OR=6.285, 95% CI: 3.031–13.036), preoperative respiratory function training (OR=20.293, 95% CI: 7.518–54.779), surgical scope (OR=20.667, 95% CI: 7.734–55.228), and peribronchial lymph node dissection (OR=5.883, 95% CI: 2.829–12.235) were significant influencing factors of CAP in lung cancer patients (P<0.05). ROC curves indicated good discriminatory power of the model, and the Hosmer-Lemeshow test showed a high degree of agreement between predicted and actual probabilities. The DCA curve revealed that the nomogram model had high clinical value when the high-risk threshold was between 0.08 and 0.98.

Conclusion: The nomogram model based on smoking history, preoperative respiratory function training, surgical scope, and peribronchial lymph node dissection has high predictive performance for CAP in lung cancer patients. It is useful for clinical prediction, guiding preoperative preparation, and postoperative care.

Keywords: lung cancer, thoracoscopic resection, persistent cough, influencing factors, prediction model

Introduction

Lung cancer has high incidence and mortality rates globally, and surgical resection remains the primary treatment method.[1] Traditional open thoracotomy involves large incisions, strong patient stress responses, and high postoperative pain levels. With the advancement of medical equipment, thoracoscopic surgery has emerged.[2,3] Thoracoscopic surgery is a minimally invasive technique that allows complex procedures to be performed through small incisions, using advanced imaging technology and specialized instruments. This approach provides surgeons with enhanced, magnified views of the surgical area, leading to greater precision and typically faster recovery times for patients.[4,5] Cough after pulmonary resection (CAP) is one of the complications following thoracoscopic lung resection, with an incidence rate of 25% to 50%. The occurrence of CAP can increase pain, disrupt sleep and eating, and hinder recovery, making it crucial to identify influencing factors and intervene promptly.[6,7] The study highlights that factors such as the extent of surgical resection, the number of lymph nodes removed, and smoking history may influence the likelihood of CAP. However,

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there remains a gap in clinical practice, as reliable models for providing individualized predictions are still lacking.[8]. A nomogram is a model developed based on the results of multivariate regression analysis, visually representing the contribution of various variables to the outcome. It holds significant potential for clinical application. Therefore, this study collected clinical data from 374 patients who underwent thoracoscopic lung resection and constructed a nomogram prediction model based on the influencing factors of CAP. This study aims to provide a reference for the prevention and treatment of postoperative CAP in lung cancer patients, and the report is as follows.

Study Subjects and Methods

Study Subjects

A retrospective study was conducted on 374 lung cancer patients who underwent lung resection surgery at our hospital between March 2020 and October 2023.Using a random number table method (modeling group: validation group = 7:3), they were divided into a modeling group (n=262) and a validation group (n=112), as shown i Figure 1. Inclusion criteria: (1) postoperative pathological diagnosis of lung cancer; (2) first-time thoracoscopic lung cancer resection; (3) complete medical records; (4) age ≥18 years; (5) no preoperative radiotherapy or chemotherapy. Exclusion criteria: (1) pre-existing chronic cough or conditions such as bronchiectasis or pneumonia that could cause coughing; (2) conversion from thoracoscopic to open surgery; (3) preoperative use of cough-inducing medications; (4) communication disorders; (5) postoperative complications like pulmonary embolism; (6) follow-up duration of less than one month. See follow Figure 1. This study was approved by the hospital's medical ethics committee.

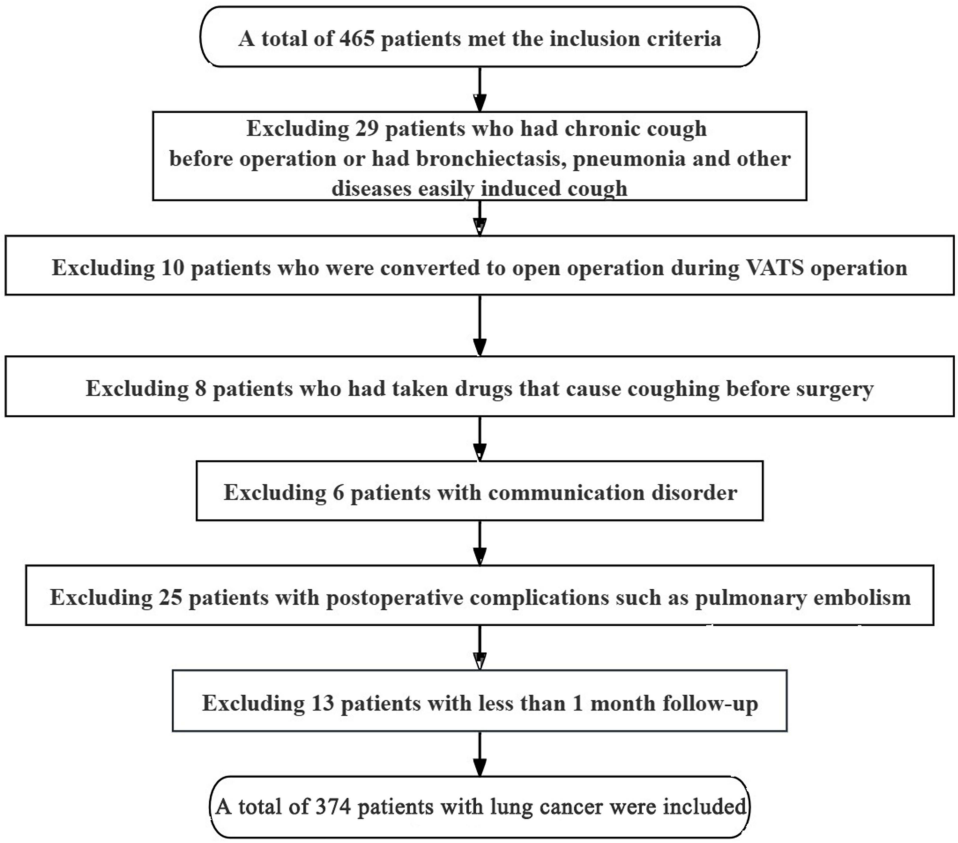

Figure 1 Flow chart of case collection.
Abbreviation: VATS, video-assisted thoracic surgery.

Methods

Diagnosis of CAP

Referring to the diagnostic criteria for CAP[9] (cough lasting ≥2 weeks within one month after surgery, no abnormalities on chest X-ray, excluding cough caused by recurrence or infection), The occurrence of CAP in the modeling group was divided into the CAP group (n=85) and the non-CAP group (n=177).

Clinical Data Collection

Data were collected from 374 patients on the following variables: age, gender, smoking history, TNM stage, pathological type, whether preoperative respiratory function training was conducted, the side and scope of surgery, whether peribronchial lymph node dissection was performed, history of underlying conditions (eg, hyperlipidemia, coronary heart disease, diabetes, hypertension), body mass index, surgery duration, and intraoperative blood loss. Smoking history was defined as smoking at least one cigarette per day for a minimum of six consecutive or cumulative months.

Statistical Analysis

Data were processed using SPSS 25.0. Count data such as TNM staging, surgical side, and surgical range were expressed as n (%), and the X^2 test was used. Measurement data were expressed as ($\overline{X} \pm s$) and analyzed using the *t*-test. Multivariate logistic regression analysis in SPSS was used to assess the factors influencing the development of CAP in lung cancer patients, followed by the Hosmer-Lemeshow test for model evaluation. The rms package in R 4.3.1 was used to construct a nomogram model for predicting the risk of CAP, with internal validation performed using the Bootstrap method, and a calibration curve was plotted. The rmda package in R 4.3.1 was used to draw a clinical decision curve (DCA) to assess the clinical application value of the nomogram. ROC analysis in SPSS was performed to evaluate the predictive discrimination of the nomogram model for CAP and non-CAP. A P-value <0.05 was considered statistically significant.

Results

Comparison of Clinical Data Between the Modeling and Validation Groups

There were no significant differences in smoking history, TNM staging, surgical range, and other factors between the modeling and validation groups (P > 0.05). See Table 1.

Univariate Analysis of CAP Occurrence in the Modeling Group Patients

Univariate analysis showed that, compared to the non-CAP group, the CAP group had a significantly higher proportion of patients with a smoking history (X^2=4.963), no preoperative respiratory function training (X^2=5.959), lobectomy as the surgical range (X^2=6.198), and a higher percentage of bronchial tree perilymphatic dissection (X^2=8.648) (*P*<0.05). There were no significant differences in gender, surgical side, and surgery duration between the two groups (*P > 0.05*). See Table 2.

Multifactorial Logistic Regression Analysis of CAP Occurrence in the Modeling Group Patients

Taking the occurrence or non-occurrence of CAP in the modeling group as the dependent variable (occurrence=1, non-occurrence=0) and the factors with statistically significant differences in Table 2 as independent variables, multifactorial logistic regression analysis showed that smoking history (*OR=6.285, 95% CI: 3.03113.036*), lack of preoperative respiratory function training (OR=20.293, 95% CI: 7.51854.779), surgical range (*OR=20.667, 95% CI: 7.73455.228*), and bronchial tree perilymphatic dissection (*OR=5.883, 95% CI: 2.82912.235*) were all influencing factors for the occurrence of CAP of in lung cancer patients (P < 0.05). See Table 3.

Nomogram Model for Predicting the Risk of CAP in Lung Cancer Patients

A nomogram model for predicting the risk of postoperative CAP in lung cancer patients was developed using R software, incorporating the four influencing factors identified through multivariate analysis. The results indicated that smoking

Table 1 Comparison of Clinical Data Between Modeling Group and Validation Group[($\overline{X} \pm s$), n (%)]

Item	Total cases	Model group (n=262)	Validation group (n=112)	t/X^2	*P*
Age				0.745	0.388
≥60	213	153 (58.40)	60 (53.57)		
<60	161	109 (41.60)	52 (46.43)		
Gender				0.103	0.748
Male	209	145 (55.34)	64 (57.14)		
Female	165	117 (44.66)	48 (42.86)		
Smoking history				0.315	0.575
Yes	145	104 (39.69)	41 (36.61)		
No	229	158 (60.31)	71 (63.39)		
TNM staging				0.115	0.735
I	212	150 (57.25)	62 (55.36)		
II~IIIa	162	112 (42.75)	50 (44.64)		
Pathological pattern				1.305	0.521
Squamous carcinoma	68	51 (19.47)	17 (15.18)		
Adenocarcinoma	269	187 (71.37)	82 (73.21)		
Other	37	24 (9.16)	13 (11.61)		
Preoperative respiratory function training				0.915	0.339
Yes	144	105 (40.08)	39 (34.82)		
No	230	157 (59.92)	73 (65.18)		
Operative side				0.992	0.319
Left side	169	114 (43.51)	55 (49.11)		
Right side	205	148 (56.49)	57 (50.89)		
Scope of surgery				0.501	0.479
Lobe	164	119 (45.04)	46 (41.07)		
Subpulmonary lobe	210	143 (54.96)	66 (58.93)		
Lymph node dissection around bronchial tree				0.511	0.475
Yes	220	151 (57.63)	69 (61.61)		
No	154	111 (42.37)	43 (38.39)		
Underlying disease history					
History of hyperlipidemia	98	71 (27.10)	27 (24.11)	0.363	0.547
History of coronary heart disease	64	40 (15.27)	24 (21.43)	2.100	0.147
History of diabetes	77	49 (18.70)	28 (25.00)	1.903	0.168
History of hypertension	129	88 (33.59)	41 (36.61)	0.317	0.574
Body mass index (kg/m^2)	–	22.68±1.90	22.97±2.03	1.324	0.186
Time of operation (min)	–	136.41±17.75	133.56±17.17	1.436	0.152
Intraoperative blood loss (mL)	–	122.82±15.85	124.38±16.09	0.868	0.386

Abbreviation: TNM, tumor node metastasis.

history contributed 61 points, lack of preoperative respiratory function training contributed 99 points, lobectomy as the surgical range contributed 100 points, and bronchial perilymphatic dissection contributed 59 points. The total score for the four factors is summed to obtain the overall score, and by drawing a vertical line from the total score axis to the prediction probability axis, the corresponding probability of CAP occurrence can be determined. For example, a total score of 223 corresponds to a 0.7 risk of postoperative CAP, while a score of 267 corresponds to a 0.9 risk. See Figure 2.

Evaluation of the Nomogram Prediction Model

In the Hosmer-Lemeshow (H-L) goodness-of-fit test, the modeling group had a X^2=4.125, P=0.660, and the validation group had a X^2=11.980, P=0.101. The calibration curves (Figure 3A and B) showed slopes close to 1 for both the modeling and validation groups. The ROC curves (Figure 3C and D) showed that the AUC for the modeling group was 0.794 (95% CI: 0.737–0.851), while the AUC for the validation group was 0.751 (95% CI: 0.652–0.851). In the DCA

Table 2 Univariate Analysis of CAP Occurrence in the Modeling Group[($\overline{X} \pm s$), n (%)]

Item	Total cases	CAP group (n=85)	Non-CAP group (n=177)	t/X^2	P
Age				2.902	0.088
≥60	153	56 (65.88)	97 (54.80)		
<60	109	29 (34.12)	80 (45.20)		
Gender				0.617	0.432
Male	145	50 (58.82)	95 (53.67)		
Female	117	35 (41.18)	82 (46.33)		
Smoking history				4.963	0.026
Yes	104	42 (49.41)	62 (35.03)		
No	158	43 (50.59)	115 (64.97)		
TNM staging				0.197	0.657
I	150	47 (55.29)	103 (58.19)		
II~IIIa	112	38 (44.71)	74 (41.81)		
Pathological pattern				1.156	0.561
Squamous carcinoma	51	15 (17.65)	36 (20.34)		
Adenocarcinoma	187	60 (70.59)	127 (71.75)		
Other	24	10 (11.76)	14 (7.91)		
Preoperative respiratory function training				5.959	0.015
Yes	105	25 (29.41)	80 (45.20)		
No	157	60 (70.59)	97 (54.80)		
Operative side				1.760	0.185
Left side	114	32 (37.65)	82 (46.33)		
Right side	148	53 (62.35)	95 (53.67)		
Scope of surgery				6.198	0.013
Lobe	119	48 (56.47)	71 (40.11)		
Subpulmonary lobe	143	37 (43.53)	106 (59.89)		
Lymph node dissection around bronchial tree				8.648	0.003
Yes	151	60 (70.59)	91 (51.41)		
No	111	25 (29.41)	86 (48.59)		
Underlying disease history					
History of hyperlipidemia	71	25 (29.41)	46 (25.99)	0.341	0.559
History of coronary heart disease	40	11 (12.94)	29 (16.38)	0.526	0.468
History of diabetes	49	18 (21.18)	31 (17.51)	0.507	0.477
History of hypertension	88	30 (35.29)	58 (32.77)	0.164	0.685
Body mass index (kg/m^2)	–	22.94±1.95	22.56±1.87	1.519	0.130
Time of operation (min)	–	137.63±18.55	135.82±17.36	0.773	0.440
Intraoperative blood loss (mL)	–	125.28±16.71	121.64±15.43	1.740	0.083

Abbreviations: TNM, tumor node metastasis; CAP, cough after pulmonary resection.

curve (Figure 4), the horizontal line along the x-axis indicates that none of the patients developed CAP or received intervention, resulting in a net benefit rate of 0. The gray diagonal line represents the scenario where all patients developed CAP and received intervention. The further the red curve is from these two lines, the higher the net benefit rate. From the graph, it is evident that the nomogram model shows high clinical application value when the predicted high-risk threshold is between 0.08 and 0.98.

Discussion

Clinically, it is believed that moderate coughing after lung cancer surgery is beneficial for expectoration and promoting lung re-expansion, reducing the chances of lung infection. However, prolonged coughing is detrimental to recovery and may develop into chronic cough, affecting the quality of life later on.[10,11] In our study, 32.44% of the 262 patients in the modeling group developed CAP postoperatively. Lu et al[12] reported that 36.6% of 112 patients who underwent lobectomy experienced

Table 3 Multivariate Logistic Regression Analysis of CAP Occurrence in the Modeling Group

Variate	The way of assign	*β*	*SE*	Wald X^2	*P*	*OR*	*95% CI*	
							Lower Limit	Upper Limit
Smoking history	Yes =1, No =0	1.838	0.372	24.395	<0.001	6.285	3.031	13.036
Preoperative respiratory function training	No=1, Yes=0	3.010	0.507	35.302	<0.001	20.293	7.518	54.779
Scope of surgery	Lobe =1, Subpulmonary lobe =0	3.029	0.501	36.47	<0.001	20.667	7.734	55.228
Lymph node dissection around bronchial tree	Yes =1, No =0	1.772	0.374	22.504	<0.001	5.883	2.829	12.235
Constant term	–	−5.894	0.765	59.311	<0.001	0.003	–	–

refractory cough after surgery. In a study by Xie et al[13] 39.77% (68/171) of lobectomy patients developed chronic cough postoperatively. These high rates of postoperative cough among lung cancer patients highlight the need for clinical attention, and understanding the factors influencing postoperative CAP is crucial for reducing its incidence.

In our study, by comparing clinical data of patients in the CAP and non-CAP groups, we found that a history of smoking, preoperative respiratory function training, surgical range, and bronchial tree perilymphatic dissection are influencing factors for the development of CAP in lung cancer patients. Mu et al[14] reported that the occurrence of postoperative CAP in lung cancer patients was related to resection of the right upper lobe. In a study by Wu et al[15] postoperative acid reflux and female gender were also identified as independent risk factors for CAP after lung resection. However, these findings were not observed in our study and require further investigation.

The development of predictive models has become a key focus of clinical research in recent years, but there are still few reports on CAP risk prediction models for lung cancer patients. Based on the above influencing factors, a nomogram prediction model for assessing the risk of CAP occurrence in lung cancer patients was developed. This model, being a visual graph, offers better readability and enables individualized predictions for patients. The model shows that a smoking history contributes 61 points. However, some studies suggest that preoperative smoking may reduce cough

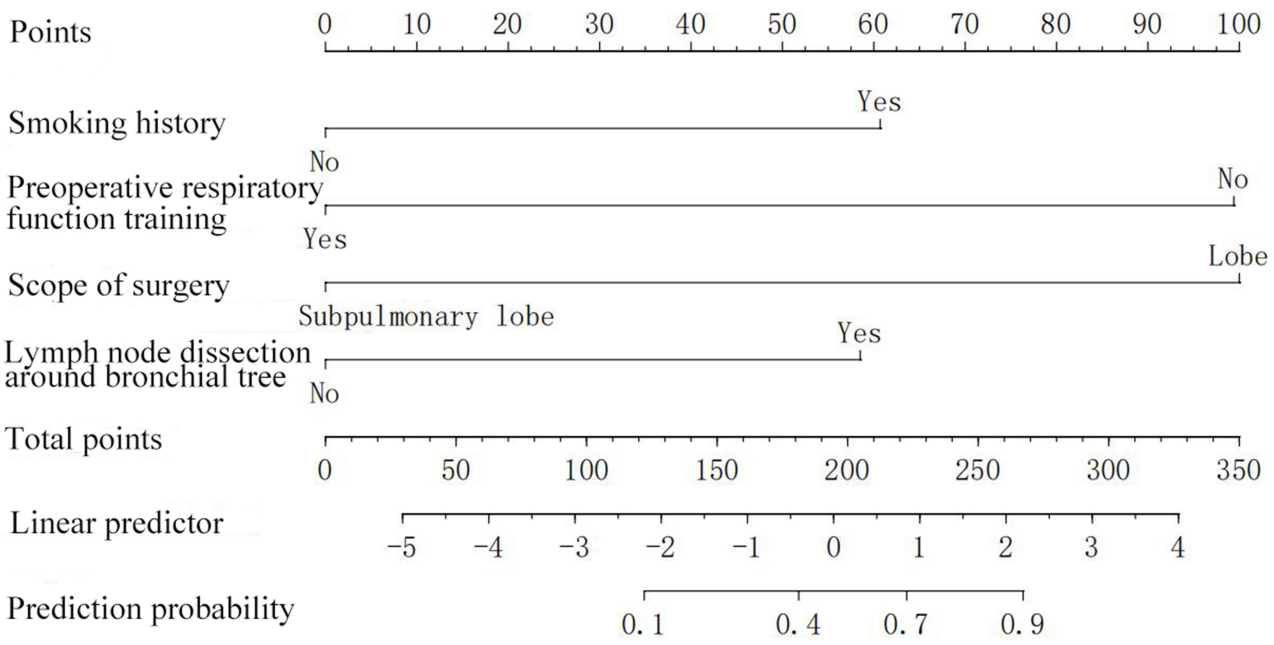

Figure 2 A Nomogram model for predicting the risk of CAP in lung cancer patients.
Abbreviation: CAP, cough after pulmonary resection.

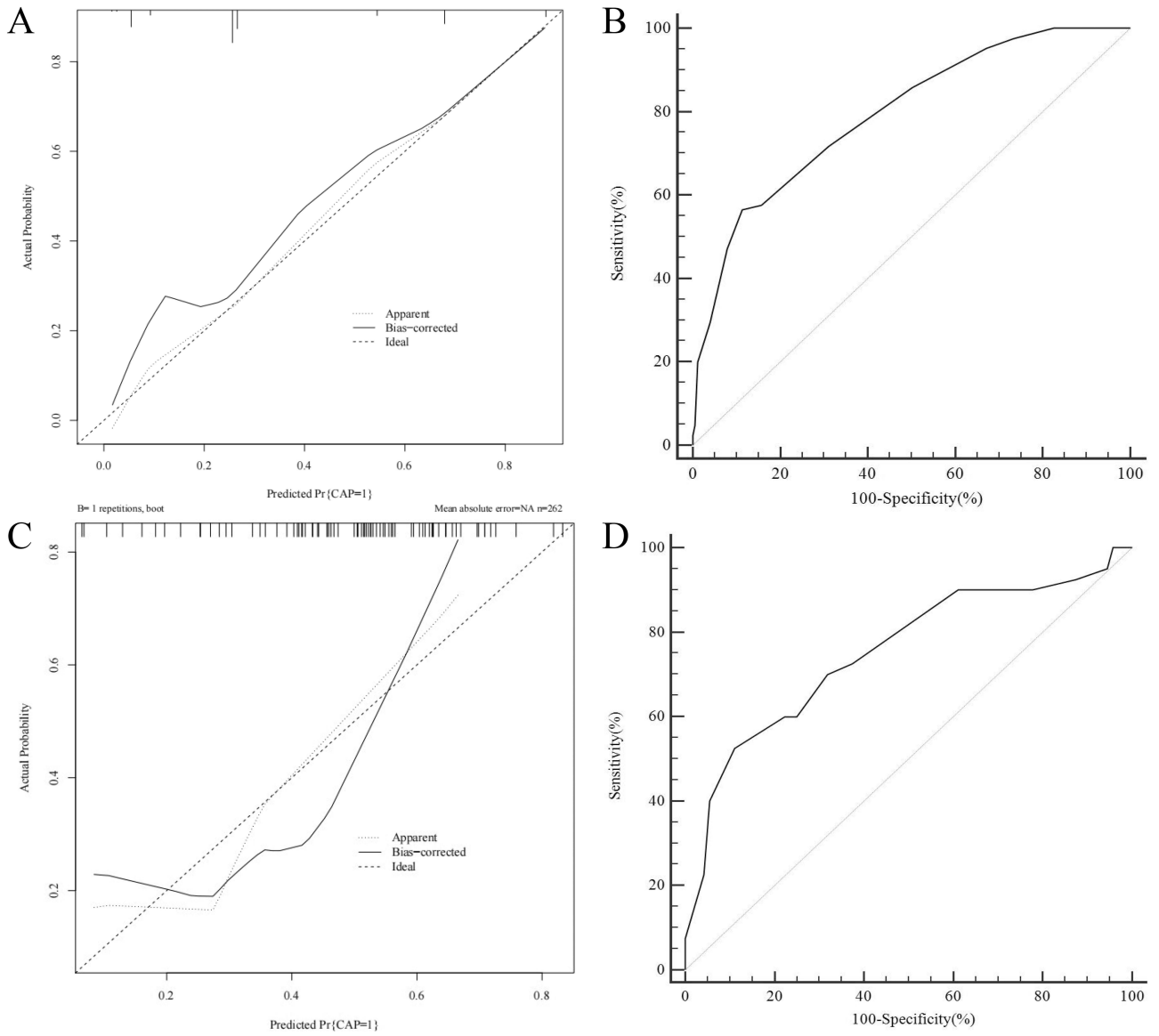

Figure 3 Evaluation of Nomogram prediction model for predicting the risk of CAP after VATS in lung cancer patients (**A**)Calibration curve of model group; (**B**)ROC curve of model group; (**C**) Calibration curve of verify group; (**D**) ROC curve of verify group.
Abbreviations: CAP, cough after pulmonary resection; VATS, video-assisted thoracic surgery; ROC, receiver operating characteristic.

sensitivity, potentially acting as a protective factor against postoperative CAP, which requires further investigation. Lack of preoperative respiratory function training adds 99 points, as such training can improve respiratory muscle strength, enhance pulmonary ventilation and gas exchange, and help prevent postoperative hypoxia and ease respiratory difficulties.[16] Lobectomy as the surgical procedure contributes 100 points, while bronchial perilymphatic dissection adds 59 points. The impact of surgical range and bronchial tree lymph node dissection on CAP is mainly due to surgical trauma. Lobectomy involves the removal of a larger portion of lung tissue, which reduces intrathoracic pressure, alters the thoracic structure, causes bronchial distortion, and changes airflow dynamics.[17] Vagal nerve C-fibers, the primary cough receptors crucial for the cough reflex, are distributed in the larynx, trachea, and bronchi within the lungs.[18] Perilymphatic dissection around the bronchial tree can cause trauma to the tracheal wall, trigger the release of neurogenic inflammatory factors, and damage the vagus nerve, leading to increased cough sensitivity.[19] Clinically, based on the individual patient's condition with regard to the four factors, the corresponding score and prediction probability can be calculated, allowing for preoperative prevention and postoperative care to be planned in advance. It is recommended that patients undergo respiratory function training before

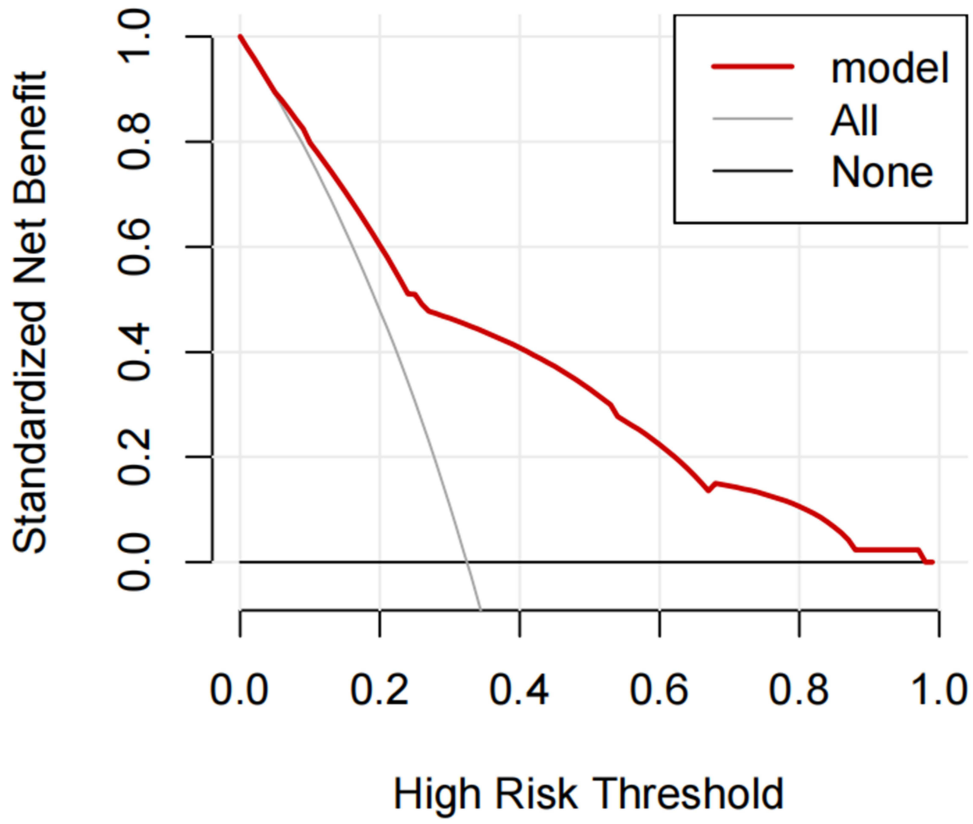

Figure 4 DCA curve of the predictive model for the risk of CAP after VATS in lung cancer patients.
Abbreviations: DCA, decision curve analysis; CAP, cough after pulmonary resection; VATS, video-assisted thoracic surgery.

surgery. For those with a high predicted risk of CAP, patients should be informed prior to surgery and advised to avoid exposure to irritants such as gases, dust, and pollen after surgery to reduce the risk of CAP. Additionally, they should be advised to stay warm and avoid catching colds to prevent worsening CAP symptoms.

To assess the predictive efficacy of this nomogram model, this study verifies the model. The results showed that both passed the Hosmer-Lemeshow goodness-of-fit test, indicating consistency with actual conditions. In ROC analysis, the AUCs for the modeling and validation groups were 0.794 and 0.751. It is suggested that the prediction differentiation between CAP and non-CAP is reasonable. Additionally, the DCA curve demonstrated that the nomogram model provided a higher net clinical benefit when predicting risk values between 0.08 and 0.98, indicating its high value for clinical application.

In summary, smoking history, lack of preoperative respiratory function training, surgical scope, and bronchial perilymphatic dissection are key factors influencing the development of CAP in lung cancer patients. The nomogram model based on these four factors demonstrates strong predictive accuracy and clinical relevance. However, as this is a retrospective, single-center study, there are certain limitations, and the findings need to be validated through multi-center research.

Research Involving Human Participants

The study was approved by Lishui Central Hospital ethics review board and with the 1964 helsinki Declaration. Written informed consent to participate in this study was provided by the participants.

Data Sharing Statement

The original contributions presented in the study are included in the article.

Consent for Publication

All authors give consent for publication.

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Disclosure

Authors declared no conflict of interest.

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