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Original Article

Constructing a Risk Prediction Model for Postoperative Pulmonary Infection in Elderly Patients with Lung Cancer

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SUMMARY

Background: To construct the risk prediction model for postoperative pulmonary infection in elderly patients with lung cancer.
Methods: A retrospective study of 240 elderly patients who underwent lung cancer resection from January to December 2018 at the Sun Yat-sen University Cancer Center in Guangzhou was conducted using a self-designed questionnaire. Basis information was collected. The risk factors were identified by univariate analysis and logistic regression analysis. Prediction model was also constructed using logistic regression analysis. ROC curve was plotted to evaluate the predictive performance of the model.
Results: The incidence of postoperative pulmonary infection in elderly patients with lung cancer was 10.0%. Four independent risk factors including heart disease, need for sputum suctioning, BMI and postoperative WBC count, were entered into the regression equation. The risk prediction equation was Z = 2.562 × heart disease + 2.322 × need for sputum suctioning + 2.963 × emaciation + 1.472 × overweight/obesity + 0.148 × postoperative WBC count-3.747. The area under the ROC curve was 0.827, the Youden index was 0.532, the sensitivity was 70.8%, and the specificity was 82.4%.
Conclusion: Heart disease, need for sputum suctioning, emaciation, overweight/obesity, and increased postoperative WBC count were the risk factors for postoperative pulmonary infection in elderly patients with lung cancer. The risk prediction model constructed in this study had an excellent predictive effect, which was of certain significance for guiding clinical observation and early screening.

1. Introduction

Lung cancer, which originates from trachea, bronchi mucosa or gland, is the most common primary pulmonary malignancy associated with aging. According to the latest Cancer Statistics in China published by the National Cancer Institute, lung cancer ranks the first among malignant tumors in terms of incidence and mortality. Patients with lung cancer account for 20.03% of all malignancy patients, and the deaths incurred by lung cancer account for 26.99% of all tumor-related deaths.[1,2]

The average age at diagnosis of lung cancer is 70 years old, and two-thirds of the patients age over 65 years old. At present, the first and foremost treatment for lung cancer is surgery. However, elderly patients with lung cancer are at a higher risk of postoperative infection due to the decline of somatic and immune functions. Studies have shown that the incidence of postoperative nosocomial infection in elderly patients with lung cancer is 15.3%, and the most common infection is respiratory infection.[3] Besides, pneumonia in elderly patients is usually occult, and the coexistence of multiple diseases may lead to a decrease of reactivity to pathogenic bacteria and drugs. Meanwhile, hidden clinical symptoms or (and) occult lesions may increase the difficulty of making a definitive diagnosis at the first visit, resulting in the missing optimal treatment window and deaths of elderly patients.[4–6]

Therefore, in this study, we established an effective risk prediction model for postoperative pulmonary infection in elderly patients with lung cancer (PPILC) through a comprehensive analysis and assessment of the physical conditions of elderly patients. The predictive effect of this model was evaluated.

2. Materials and methods

2.1. Patients

In this study, a total of 240 elderly patients who underwent lung cancer resection from January to December 2018 at the Sun Yat-sen University Cancer Center were included. This study was approved by the Ethics Committee of Sun Yat-sen University Cancer Center. All patients gave informed written consent to participate in the study. The inclusion criteria were as follows: (1) ≥ 60 years old; (2) pathologically diagnosed with lung cancer; (3) having received thoracoscopy or thoracotomy. The exclusive criteria were as follows: (1) hav-

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ing been infected or been in the latency of infection before surgery; (2) metastases of other malignancies to the lungs.

2.2. Data collection

A retrospective design was adopted, where the patient data were collected by checking the electronic medical records. A self-designed questionnaire was used, which covered the general information of patients (gender, age, BMI, smoking history), disease-related data (history of underlying diseases, including lung disease, heart disease, hypertension, nephrosis, history of anti-tumor therapy, pathological pattern and stage), laboratory test results in perioperative period (12 h preoperative and 2 h postoperative blood-gas (PH), PaO_2, $PaCO_2$, oxygenation index, lactic acid, preoperative and postoperative hemoglobin levels (HGB), serum albumin, postoperative WBC count, C-reactive protein (CRP)), pulmonary function tests (FVC (% pred), FEV1 (% pred), FEV1/FVC, PEF (% pred), MMEF (% pred), MVV, DLCOc (% pred), KCOc (% pred), operation-related information (surgical method, excision extension, surgical duration, intraoperative blood loss, need for secondary surgery), and information about postoperative medication, nursing and treatment (transfusion of blood products, obtundation, use of vasoactive drugs, drainage on the same day of surgery, whether pulmonary function training was undertaken, sputum suctioning, fever). The history of anti-tumor therapy surveyed included the history of chemotherapy, history of radiotherapy, history of targeted therapy, history of immunotherapy, and history of comprehensive therapy.

2.3. Diagnostic criteria

Diagnostic criteria for pulmonary infection: The Healthcare Industry Standard of the People's Republic of China (WS 382-2012): The Diagnosis Criteria for Pneumonia, implemented since February 1, 2013, was adopted as the basis for the diagnosis of postoperative pulmonary infection. The diagnosis of hospital-acquired pneumonia should meet the following three criteria: (1) having received chest X-ray examination at least twice (only one chest X-ray was required for patients without underlying cardiac and pulmonary diseases such as respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, chronic obstructive pulmonary disease or congestive heart-failure), with the results conforming to at least one of the following criteria: a) newly appeared or progressive and persistent pulmonary infiltrates, b) consolidation, c) cavitation; (2) conforming to at least one of the following criteria: a) fever (body temperature > 38 °C) of unknown cause, b) peripheral WBC count $> 12 \times 10^9$/L or $< 4 \times 10^9$/L, c) mind change of unknown cause in patients aged ≥ 70 years; (3) conforming to at least two of the following criteria: a) expectoration or change in the characteristics of sputum, or increased respiratory secretions, or increased frequency of sputum suctions; b) cough, breathing difficulty or increased respiratory rate, or aggravation of existing cough, breathing difficulty or polypnea; c) rales or bronchial breath sounds; d) deterioration of gas exchange, increasing oxygen demand or demand for mechanical ventilation.

2.4. Statistical analysis

SPSS 21.0 software was used for statistical analyses. For continuous variables with a percentage of missing value < 10, the mean value was used to fill the missing value, and the other missing values were not processed. The measurement data were expressed as mean ± standard deviation, and enumeration data were expressed in frequency and percentage. In univariate analysis, the measurement data conforming to normal distribution were analyzed through the t-test, and not-normal distribution were analyzed through the rank-sum test. The enumeration data were analyzed through chi-square test. Then, the variables with statistical significance were entered into the multivariate analysis. Logistic binary regression was performed for multivariate analysis and construction of the risk prediction model for postoperative pulmonary infection. The ROC curve was plotted to evaluate the predictive performance of the model. $p < 0.05$ was considered as statistically significant difference. All data in this study have been recorded at Sun Yat-sen University Cancer Center for further reference (number RDDA2020001587).

3. Results

3.1. Basic characteristics

A total of 240 elderly patients with lung cancer were included in this study. The general information of the patients is shown in Table 1. There were 77 females and 163 males.

Among them, 24 patients were diagnosed with PPILC, the incidence was 10.0%. 198 patients aged between 60 and 69 years old, which accounted for 82.5% of total patients.

3.2. Univariate analysis for PPILC

There were significant differences of fever, heart disease, need for sputum suctioning, BMI, postoperative PaO_2, postoperative oxygenation index, postoperative WBC count, and postoperative CRP between the PPILC and non-PPILC patents ($p < 0.05$). The patients with PPILC were more likely to have fever, heart disease, need for sputum suctioning, lower BMI, lower postoperative PaO_2 and postoperative oxygenation index, higher postoperative WBC count and postoperative CRP (Table 2).

3.3. PPILC multiple factors analysis

With the occurrence of PPILC as the dependent variable, the variables with statistical significance in the univariate analysis were

Table 1
Basic characteristics.

Characteristics	N	Percentage (%)
Gender		
Female	77	32.1
Male	163	67.9
Age (years)		
60–69	198	82.5
70–79	39	16.2
80–92	3	1.3
Pathological type		
Adenocarcinoma	164	68.3
Squamous cell carcinoma	62	25.9
Other[a]	14	5.8
Pathological stage		
Carcinoma in situ	1	0.4
I	110	45.8
II	98	40.8
III	21	8.8
IV	10	4.2
Choice of operation		
Endoscopy	120	50.0
Open surgery	120	50.0

[a] Others include adenosquamous carcinoma, lymphoepithelioma like carcinoma, sarcomatoid carcinoma and neuroendocrine carcinoma.

Table 2
Univariate analysis of PPILC in patients with different characteristics.

Characteristics	Pneumonia		$\chi^2/t/Z$	*p*
	Without (n = 216)	With (n = 24)		
Smoking [n(%)]			2.779	0.249
No	110 (50.9)	8 (33.3)		
Yes	69 (31.9)	11 (45.8)		
Stop	37 (17.1)	5 (20.8)		
Fever [n (%)]			5.307	0.021*
No	171 (79.2)	14 (58.3)		
Yes	45 (20.8)	10 (41.7)		
Respiratory diseases [n (%)]			0.000	1.000
No	200 (92.6)	22 (91.7)		
Yes	16 (7.4)	2 (8.3)		
Hypertension [n (%)]			0.455	0.500
No	158 (73.1)	16 (66.7)		
Yes	58 (26.9)	8 (33.3)		
Diabetes mellitus [n (%)]			0.000	1.000
No	192 (88.9)	21 (87.5)		
Yes	24 (11.1)	3 (12.5)		
Heart disease [n (%)]			a	0.024*
No	212 (98.1)	21 (87.5)		
Yes	4 (1.9)	3 (12.5)		
Nephropathy [n (%)]			a	1.000
No	210 (97.2)	24 (100)		
Yes	6 (2.8)	0 (0)		
History of cancer treatment [n (%)]			0.000	1.000
No	195 (90.3)	22 (91.7)		
Yes	21 (9.7)	2 (8.3)		
Pathological type [n (%)]			2.537	0.281
Adenocarcinoma	150 (69.4)	14 (58.3)		
Squamous cell carcinoma	55 (25.5)	7 (29.2)		
Others	11 (5.1)	3 (12.5)		
Stage [n (%)]			1.937	0.804
Carcinoma in situ	1 (0.5)	0 (0)		
I	100 (46.3)	10 (41.7)		
II	86 (39.8)	12 (50)		
III	20 (9.3)	1 (4.2)		
IV	9 (4.2)	1 (4.2)		
Reoperation [n (%)]			a	0.080
No	213 (98.6)	22 (91.7)		
Yes	3 (1.4)	2 (8.3)		
Choice of operation [n (%)]			0.185	0.667
Endoscopy	107 (49.5)	13 (54.2)		
Open surgery	109 (50.5)	11 (45.8)		
Blood transfusion products [n (%)]			0.304	0.581
No	177 (81.9)	18 (75)		
Yes	39 (18.1)	6 (25)		
Use of painkillers [n (%)]			3.210	0.073
No	46 (21.3)	9 (37.5)		
Yes	170 (78.7)	15 (62.5)		
Use of vasoactive drugs [n (%)]			0.507	0.476
No	167 (77.3)	17 (70.8)		
Yes	49 (22.7)	7 (29.2)		
Pulmonary respiratory exercise [n (%)]			0.002	0.965
No	127 (58.8)	14 (58.3)		
Yes	89 (41.2)	10 (41.7)		
Sputum suctioning [n (%)]			23.457	< 0.001**
No	212 (98.1)	18 (75)		
Yes	4 (1.9)	6 (25)		
Number of hemostatic drugs [n (%)]			2.353	0.460
0	158 (73.1)	18 (75)		
1	5 (2.3)	0 (0)		
2	51 (23.6)	5 (20.8)		
Above 3	2 (0.9)	1 (4.2)		
Method of operation [n (%)]			3.464	0.205
wedge excision	33 (15.3)	4 (16.7)		
Lobectomy	182 (84.3)	19 (79.2)		
Pneumonectomy	1 (0.5)	1 (4.2)		
Age (years, $\bar{x} \pm s$)	65.67 ± 4.91	64.88 ± 3.40	-0.300	0.764
BMI ($\bar{x} \pm s$)	22.93 ± 2.94	23.93 ± 3.96	-1.528	0.128

Table 2 Continued.

Characteristics	Pneumonia		$\chi^2/t/Z$	*p*
	Without (n = 216)	With (n = 24)		
BMI n(%)			13.692	0.001**
< 18.5 (Emaciation)	14 (6.5)	4 (16.7)		
18.5–24 (Normal)	129 (59.7)	5 (20.8)		
> 24 (Overweight/obesity)	73 (33.8)	15 (62.5)		
Length of operation (min, $\bar{x} \pm s$)	171.04 ± 82.03	189.17 ± 93.35	-0.910[b]	0.363
Postoperative drainage (ml, $\bar{x} \pm s$)	432.37 ± 246.58	402.50 ± 286.57	-1.015[b]	0.310
Intraoperative blood loss (ml, $\bar{x} \pm s$)	102.32 ± 78.38	116.67 ± 150.09	-0.007[b]	0.995
FVC (pred%) ($\bar{x} \pm s$)	102.12 ± 15.86	98.29 ± 18.13	1.106[c]	0.270
FEV1 (pred%) ($\bar{x} \pm s$)	95.85 ± 16.87	90.64 ± 16.34	1.440[c]	0.151
FEV1/FVC ($\bar{x} \pm s$)	89.26 ± 10.22	87.20 ± 10.77	-0.893[b]	0.372
PEF (pred%) ($\bar{x} \pm s$)	87.57 ± 18.20	83.15 ± 23.02	1.098[c]	0.273
MMEF (pred%) ($\bar{x} \pm s$)	62.00 ± 25.43	58.45 ± 24.00	-0.452[b]	0.651
MVV ($\bar{x} \pm s$)	92.17 ± 53.07	82.11 ± 19.07	-1.746[b]	0.081
DLCOc ($\bar{x} \pm s$)	95.30 ± 16.52	98.16 ± 20.13	-0.333[b]	0.739
KCOc ($\bar{x} \pm s$)	107.82 ± 15.92	109.84 ± 24.22	-0.243[b]	0.808
Preoperative PH ($\bar{x} \pm s$)	7.42 ± 0.05	7.43 ± 0.02	-1.939[b]	0.053
Preoperative PaO2 ($\bar{x} \pm s$)	86.96 ± 12.53	85.69 ± 7.11	-0.282[b]	0.778
Preoperative PaCO2 ($\bar{x} \pm s$)	38.35 ± 2.84	37.72 ± 2.42	-0.815[b]	0.415
Preoperative HGB ($\bar{x} \pm s$)	138.15 ± 14.48	134.62 ± 17.14	1.111[c]	0.268
Preoperative lactic acid ($\bar{x} \pm s$)	1.84 ± 0.97	2.04 ± 1.13	-0.360[b]	0.719
Preoperative oxygenation index ($\bar{x} \pm s$)	413.23 ± 43.91	409.21 ± 33.99	-0.347[b]	0.728
Preoperative ALB ($\bar{x} \pm s$)	43.20 ± 3.52	42.41 ± 4.01	-0.832[b]	0.405
Postoperative PH ($\bar{x} \pm s$)	7.35 ± 0.04	7.39 ± 0.13	-1.411[b]	0.158
Postoperative PaO2 ($\bar{x} \pm s$)	110.14 ± 30.53	91.90 ± 26.53	-2.785[b]	0.005**
Postoperative PaCO2 ($\bar{x} \pm s$)	43.82 ± 5.18	42.43 ± 6.81	-1.045[b]	0.296
Postoperative lactic acid ($\bar{x} \pm s$)	2.03 ± 1.03	1.97 ± 0.80	-0.091[b]	0.927
Postoperative HGB ($\bar{x} \pm s$)	121.78 ± 14.97	122.87 ± 14.70	-0.341[c]	0.733
Postoperative oxygenation index ($\bar{x} \pm s$)	335.79 ± 98.53	268.75 ± 98.13	-2.619[b]	0.009**
Postoperative WBC ($\bar{x} \pm s$)	12.52 ± 3.54	15.63 ± 4.57	-3.318[b]	0.001**
Postoperative ALB ($\bar{x} \pm s$)	34.11 ± 3.44	33.69 ± 3.83	0.550[c]	0.583
Postoperative CRP ($\bar{x} \pm s$)	103.41 ± 64.94	141.11 ± 81.62	-2.351[b]	0.019*

Note: a: Fisher's exact test statistic value. b: *Z* value. c: *t* value. Respiratory diseases included acute respiratory distress syndrome, pulmonary hypertension, pulmonary tuberculosis and silicosis.
* $p < 0.05$, ** $p < 0.01$.

entered into the binary logistic regression analysis as independent variables. It was found that heart disease, need for sputum suctioning, BMI and postoperative WBC count were independent influence factors of PPILC (Table 3). The risk prediction equation was Z = 2.562 × heart disease + 2.322 × need for sputum suctioning + 2.963 × emaciation + 1.472 × overweight/obesity + 0.148 × postoperative WBC counts-3.747 (Table 4).

3.4. Evaluation of risk prediction model

The ROC curve was plotted to analyze the predictive performance of the PPILC risk model. The area under the ROC curve was 0.827 (95% CI: 0.734–0.919, $p < 0.001$), suggesting that the predictive performance of the prediction model was good (Figure 1). The maximum Youden index (0.532) was used to determine the optimal cutoff value of the prediction model, which was -0.107, while the sensitivity was 70.8% and the specificity was 82.4%.

4. Discussion

In our study, it was found that showed that heart disease, need for sputum suctioning, emaciation or overweight/obesity, and increased postoperative WBC count were independent influence factors of PPILC. The AUC of the risk prediction model was 0.827, which indicated that the model was able to screen elderly patients with lung cancer who would suffer from a postoperative pulmonary infection.

We found that the concomitant heart disease in elderly patients with lung cancer was the independent risk factor for PPILC (OR = 12.956, $p = 0.004$), which was consistent with results from the previous studies.[7,8] Cardiovascular disease is one of the common underlying diseases in elderly patients, and operative treatment is likely to induce or aggravate cardiac insufficiency and secondary pulmonary infection. The incidence of vascular disease increases with aging, leading to higher mortality of postoperative cardiopulmonary complications. According to the ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Non-cardiac Surgery, the heart risk of intrathoracic surgery ranges from 1 to 5%. For patients aged over 70 years, further examinations shall be administered before moderate- or high-risk surgeries to evaluate their surgical tolerance.[9]

The need for sputum suctioning was a risk factor for PPILC in elderly patients (OR = 10.195, $p = 0.0009$). Infirmity, weakened cough reflex, and postoperative pain of elderly patients were indications of the need for sputum suctioning. Degenerative changes occur in each organ due to aging, and the clearing function of airway cilia, cough ability and sputum excretion ability decline. Therefore, the airway secretions will deposit, which may lead to PPILC. The need for sputum suctioning indicated that the poor postoperative cough ability and sputum excretion ability, thus increasing the risk for PPILC. It was suggested that the inhibition of cough reflex became more obvious with aging.[10] It has shown that training in active circular breathing technique was helpful to remove the respiratory secretions in elderly patients.[11] Therefore, nurses should guide elderly patients to take up active breathing training before surgeries, closely observe them after surgeries, and encourage and help them

Table 3
Assignment of variables into regression model.

Variables	Assignment
Fever	Yes = 1, No = 0
Heart disease	Yes = 1, No = 0
Sputum suctioning	Yes = 1, No = 0
BMI	Taking BMI as a sub variable, X1 = emaciation (0,1), X2 = overweight/obesity (0,1)
Postoperative PaO2, Postoperative oxygenation index, Postoperative WBC, Postoperative CRP	Original value

Table 4
Multivariate analysis of PPILC.

Independent variable	Regression coefficient	Standard error	Wals $\chi 2$	OR	p	95% CI
Heart disease	2.562	0.898	8.134	12.956	0.004	2.228–75.332
Sputum suctioning	2.322	0.893	6.766	10.195	0.009	1.772–58.637
BMI						
Emaciation	2.963	0.842	12.392	19.355	< 0.001	3.718–100.746
Overweight/obesity	1.472	0.607	5.885	4.359	0.015	1.327–14.318
Postoperative WBC	0.148	0.068	4.803	1.160	0.028	1.016–1.325
Constant	-3.747	1.532	5.982	0.024	0.014	

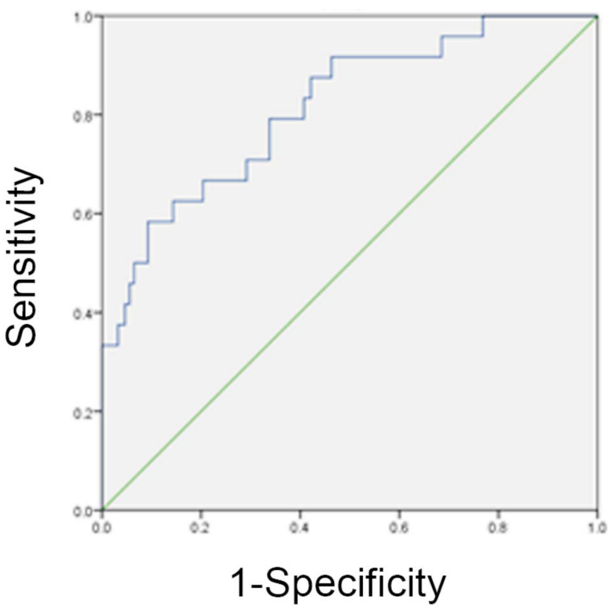

Figure 1. ROC curve of the PPILC risk model.

excrete airway secretions to reduce the incidence of PPILC.

In this study, the emaciated patients were more likely to suffer from PPILC than those with normal BMI (OR = 19.355, $p < 0.001$), which suggested that emaciation and malnutrition were independent risk factors for PPILC in elderly patients. The risk of PPILC in patients with BMI > 24 was 4.359 times of patients with normal BMI ($p = 0.015$), which suggested that overweight or obesity was one of the risk factors for PPILC. This result is consistent with previous study.[12] First, obesity may cause pharyngeal airway stenosis, an increase of upper airway collapse, and a higher risk of respiratory infection, which further lead to pulmonary dysfunction, thus impairing the prognosis of patients.[13,14] Second, excessive fat in overweight/obese patients make the surgical manipulations more difficult, and the duration of surgery and anesthesia is prolonged, which can lead to an increase of the exposure time of surgical field and the number of repeated squeezing and kneading of lung tissues, resulting in a higher probability of contamination. After surgery, overweight/obese patients may have difficulty in turning over in bed or have poor activity endurance, which may also lead to PPILC.[15] It has showed that patients with abdominal obesity usually have a lower pulmonary function and lower lung reserve capacity.[15]

Early postoperative inflammatory reactions can lead to a transient elevation of WBC count and other inflammatory factors, typically within 24 h after surgery. The WBC count and the levels of inflammatory factors fall back after peaking at 72 h after surgery.[16,17] In this study, the peak WBC count of patients at 4–10 days after surgery was evaluated. It indicated that the peak WBC count in the PPILC group was 15.63 ± 4.57, which was higher than that of the non-PPILC group (12.52 ± 3.54). Therefore, the continuous increase of WBC count was an independent risk factor for PPILC, suggesting postoperative inflammatory response. This result is consistent with two previous studies.[18,19] Therefore, it is necessary to dynamically monitor the levels of inflammatory factors, such as postoperative WBC count, to detect infection and intervene as early as possible, which may be helpful to improve the prognosis of PPILC.

A good differentiating ability is considered if the AUC is within the range of 0.8–0.9. In this study, the AUC of this risk prediction model was 0.827, which indicated that the model was able to screen for elderly patients with lung cancer who would suffer from a postoperative pulmonary infection. According to this risk prediction model, when Z-value in the equation ≥ -0.107, elderly patients with lung cancer were at risk for postoperative pulmonary infection. This model might help clinician to identify elderly patients at risk of pulmonary infection, thus conducting early intervention and management to improve their prognosis. A previous study on the the risk factors associated with postoperative pneumonia after lung resection showed that patients with older age, smoking and extent of excision of more than one lobe have a higher risk for pneumonia after lung cancer surgery.[20] The main reason for the difference with our study was that we included the elderly patients ≥ 60 years old, while in that study, the included patients were obvious younger than that in our study.

There were also some limitations in this study. This study was a single-center, retrospective study with limited sample size, and the predictive performance of the model needs to be evaluated in a validation cohort. Multi-center prospective studies were still needed to be conducted with expanded sample size.

In conclusion, the risk prediction model for postoperative pulmonary infection in elderly patients with lung cancer was constructed in this study had a good predictive performance. Our findings might be helpful to the management, monitoring, early screening and intervention among elderly patients in the perioperative period.

Acknowledgements

None.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study is approved by the Ethics Committee of Sun Yat-sen University Cancer Center. Written informed consent was obtained.

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