Original Article

Risk factor analysis and nomogram prediction model construction of postoperative complications of thoracoscopic non-small cell lung cancer

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Background: A series of complications will inevitably occur after thoracoscopic pulmonary resection. How to avoid or reduce postoperative complications is an important research area in the perioperative treatment of thoracic surgery. This study analyzed the risk factors for thoracoscopic postoperative complications of non-small cell lung cancer (NSCLC) and established a nomogram prediction model in order to provide help for clinical decision-making.

Methods: Patients with NSCLC who underwent thoracoscopic surgery from January 2017 to December 2021 were selected as study subjects. The relationship between patient characteristics, surgical factors, and postoperative complications was collected and analyzed. Based on the results of the statistical regression analysis, a nomogram model was constructed, and the predictive performance of the nomogram model was evaluated.

Results: A total of 872 patients who met the study criteria were included in the study. A total of 171 patients had complications after thoracoscopic surgery, accounting for 19.6% of the study population. Logistic regression analysis showed that thoracic adhesion, history of respiratory disease, and lymphocyte-monocyte ratio (LMR) were independent risk factors for complications after thoracoscopic surgery (P<0.05). Variables with P<0.1 in logistic regression analysis were included in the nomogram model. The verification results showed that the area under curve (AUC) of the model was 0.734 [95% confidence interval (CI): 0.693–0.775], and the calibration curve showed that the model had good differentiation. The decision curve analysis (DCA) curve showed that this model has good clinical application value. In subgroup analysis of complications, gender, history of respiratory disease, body mass index (BMI), type of surgical procedure, thoracic adhesion, and Time of operation were identified as significant risk factors for prolonged air leak (PAL) after surgery. Tumor location and forced expiratory volume in the first second (FEV_1) were identified as important risk factors for postoperative pulmonary infection. N stage and thoracic adhesion were identified as significant risk factors for postoperative pleural effusion. The AUC for PAL was 0.823 (95% CI: 0.768–0.879). The AUC of postoperative pulmonary infection was 0.714 (95% CI: 0.627–0.801). The AUC of postoperative pleural effusion was 0.757 (95% CI: 0.650–0.864). The calibration curve and DCA curve indicated that the model had good predictive performance and clinical application value.

Conclusions: This study analyzed the risk factors affecting the postoperative complications of NSCLC through thoracoscopic surgery, and the nomogram model built based on the influencing factors has certain significance for the identification and reduction of postoperative complications.

Keywords: Non-small cell lung cancer (NSCLC); thoracoscope; complications; nomogram model

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Introduction

Lung cancer is one of the malignancies with the highest incidence and mortality in China, with an estimated 820,000 new cases of lung cancer and 715,000 lung cancer-related deaths in China in 2020, according to global cancer statistics (1,2). Non-small cell lung cancer (NSCLC) is the predominant form of lung cancer, comprising approximately 80–85% of all instances of lung cancer (3). The primary and crucial treatment for early-stage lung cancer is surgical resection. Video-assisted thoracoscopic surgery (VATS) has been increasingly utilized for diagnosing and treating thoracic diseases since the 1990s. It has gradually replaced conventional thoracotomy due to its numerous benefits, such as minimizing surgical trauma, providing a clear view during the operation, and facilitating rapid postoperative recovery (4,5). Nevertheless, thoracoscopic surgery will unavoidably result in a range of postoperative problems, including postoperative lung leakage, lung infection, pleural effusion, atelectasis, and chylothorax, among others. The presence of these complications will significantly prolong the patient's duration of hospitalization and escalate their medical costs (6). The reported rate of complications following thoracoscopic surgery ranges from 6% to 34% (7-9). How to successfully avoid or reduce postoperative complications is an important research area in the perioperative period of thoracic surgery. Utilizing precise and efficient risk stratification assessment instruments during the perioperative phase can help identify individuals who are susceptible to postoperative complications. And carry out active preoperative intervention and postoperative prevention for such patients. As a result, these interventions contribute to better surgical decision-making, a lower incidence of postoperative complications, and the provision of personalized patient care. In contrast to simplistic models and scoring systems that incorporate a limited number of binary variables, the nomogram model offers a more comprehensive analysis of the risk factors and interaction effects linked to postoperative complications. This is critical in providing guidance for perioperative patient management. Therefore, this study retrospectively analyzed the clinical data of patients with NSCLC who underwent thoracoscopic surgery in the Department of Thoracic Surgery of our hospital from 2017 to 2021 and constructed a nomogram model of postoperative complications in patients with NSCLC in order to provide help for clinical decision-making. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-113/rc).

Highlight box

Key findings

- The probability of postoperative complications can be predicted according to the perioperative baseline characteristics of lung cancer patients.

What is known and what is new?

- Complications after lung cancer surgery affect quality of life and increase medical costs.
- By constructing a nomogram prediction model for postoperative complications of thoracoscopy, risk factors can be observed more directly.

What is the implication, and what should change now?

- The nomogram model based on the results of multi-factor regression is of great significance for the identification and reduction of postoperative complications.

Methods

Study population

Retrospectively, we collected clinical data from NSCLC patients who underwent thoracoscopic surgery at the Department of Thoracic Surgery in Qingdao Municipal Hospital between January 2017 and December 2021. The primary result was the occurrence of complications within a 30-day period following lung resection. The postoperative complications, which served as a composite outcome measure, encompassed a range of conditions, including arrhythmias, heart failure, atelectasis, pulmonary infection, chylothorax, prolonged air leak (PAL) lasting for at least 7 days, moderate or higher pleural effusion, severe subcutaneous emphysema, hydropneumothorax, active bleeding, infection or poor wound healing, and pulmonary embolism. The inclusion criteria were as follows: (I) individuals aged 18–90 years; (II) patients diagnosed with stage I–III NSCLC who were undergoing thoracoscopic lobectomy or segmental resection; and (III) patients with comprehensive clinical medical records. The exclusion criteria encompassed the following: (I) NSCLC patients who were deemed unsuitable for surgical intervention or unable to tolerate it; (II) patients with pre-existing infectious diseases, blood system diseases, immune system diseases, or blood abnormalities of unknown origin prior to surgery; (III) cases where thoracoscopic surgery was converted to thoracotomy due to uncontrollable factors or procedures solely for exploration and biopsy purposes; (IV) patients who underwent wedge resection or total pneumonectomy; (V) individuals with poor medical compliance, automatic discharge, an incomplete treatment process, or missing data. This study was a retrospective study. The study was approved by the Institutional Review Committee of Qingdao Municipal Hospital (2023 No. 183), and the study procedure was strictly in accordance with the Declaration of Helsinki (as revised in 2013). Given the retrospective nature of the study, patient's informed consent was considered an exemption.

Clinical treatment process and perioperative management

Upon admission, all patients underwent a comprehensive preoperative assessment, which encompassed laboratory analyses (such as complete blood count, hepatic and renal function tests, etc.), electrocardiography, pulmonary function testing, a chest computed tomography (CT) scan, echocardiography, and other pertinent examinations. Preoperative education of patients and their families in accordance with the principles of enhanced recovery after surgery (ERAS) involved instructing patients to engage in suitable preoperative physical activity, guided deep breathing and cough exercises, and receiving improved nutritional assistance. Patients and their family members were informed about the significance of achieving effective coughing and the production of sputum following surgery. Patients were strongly advised to make an effort to get out of bed as soon as possible after surgery to prevent extended periods of bed rest. Prior to surgery, patients were abstained from eating for a period of 6 to 8 hours. Additionally, patients were not allowed to drink any fluid for a minimum of 2 hours. Furthermore, it was a standard practice to administer antibiotics on the day of surgery in order to prevent any potential infections. The operative is the associate chief physician or chief physician with rich experience.

During the operation, the patient was placed in the lateral position on the healthy side, and the anesthesia method applied was double-lumen tracheal intubation and intravenous general anesthesia. During the operation, the patient underwent single-lung ventilation on the healthy side, and a single thoracoscopic operation was performed. The surgical incision at the 4th or 5th costal space in the midaxillary line with a length of about 3–5 cm was selected as the operating hole. Intraoperative bronchial and hypoplastic lobar clefts were routinely severed by cutting and closing devices. Lymph node sampling, or systematic lymph node dissection, was performed according to National Comprehensive Cancer Network (NCCN) guidelines (10). After pulmonary resection, a water test and the lung expansion method were used to detect whether there was obvious air leakage. Electrical coagulation or suture repair was performed at the air leakage area. A thoracic drainage tube was routinely placed in the chest cavity for drainage after surgery.

Following the surgery, the patient was moved from the anesthesia resuscitation room to the general ward of thoracic surgery, where they received postoperative pain relief and preventive treatment for infection. Following the surgery, the patient was advised to engage in respiratory function exercises and cough exercises. If deemed required, the option of performing bedside sputum aspiration was available to aid in the treatment. Additionally, a postoperative chest radiograph examination was performed, and the thoracic drainage tube was removed according to the patient's condition. Indications for thoracic drainage tube removal included no air leakage, 24 h thoracic drainage flow of less than 200 mL, and imaging findings that indicated good pulmonary re-expansion.

Data collection

The medical records of patients meeting the inclusion criteria were retrospectively collected through the hospital electronic medical record archiving system, quality control registration management system, and laboratory examination report system. The following information was included: age, sex, smoking status, body mass index (BMI), previous respiratory history [such as chronic obstructive pulmonary disease (COPD), bronchial asthma, and bronchiectasis], Eastern Cooperative Oncology Group Performance Status (ECOG PS) before treatment and pulmonary function indicators [forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC], tumor location and diameter, operation plan (lobectomy and segmentectomy), number of lymph nodes (LNs) removed during operation, lymph node metastasis (N stage), operation time, intraoperative blood loss, thoracic adhesion, postoperative retention time of thoracic drainage tube, and laboratory examination results (lymphocytes and monocytes) 1 week before surgery. The lymphocyte-monocyte ratio (LMR) was calculated. BMI was divided into wasting (<18.5 kg/m^2), normal (18.5–23.9 kg/m^2), and obese (>24 kg/m^2). Due to the lack of a unified standard for cutoff values for pulmonary function indicators, this study grouped them based on FEV_1 (%), FVC, and FEV_1/FVC (%) cutoff values and previous findings. The thoracic adhesion was judged by the adhesion area: non-adhesion, or the area of adhesion is limited to a single lung lobe, or the cumulative area of adhesion is less than 30% of the lung surface area, is classified as non-thoracic adhesion. An adhesion area greater than a single lung lobe or a cumulative adhesion area of 30% or more of the lung surface area is classified as thoracic adhesion.

Types and grades of complications

- ❖ Arrhythmia: diagnosed based on electrocardiogram (ECG) reports, the main types of concern are atrial fibrillation and premature ventricular beats.
- ❖ Cardiac failure: combined with the patient's symptoms (such as chest tightness, dyspnea, inability to lie flat at night, dyspnea, etc.) and auxiliary examination (such as: heart color ultrasound indicates decreased systolic function of the heart, ejection fraction value <50%).
- ❖ Pulmonary atelectasis: chest radiograph results suggest poor pulmonary reexpansion.
- ❖ Pulmonary infection: chest CT examination suggests new or progressive solid, infiltrating, or ground glass shadows with two or more of the following symptoms or signs: (I) body temperature greater than 38 ℃; (II) peripheral blood white blood cell counts greater than 10×10^9/L; (III) clinical symptoms of lung infection, such as cough, yellow phlegm or thick phlegm, and lung moist rales.
- ❖ Chylothorax: the pleural effusion was large and milk-like, and the pleural effusion chyle test was positive.
- ❖ PAL: a large number of bubbles appear in the chest bottle when coughing persists after surgery, which can assist in the diagnosis of chest radiography. Air leakage lasts for 7 days or more.
- ❖ Pleural effusion: combined with the patient's symptoms (palpitation, dyspnea, cough, chest pain, etc.), physical signs (full chest, accompanied by diminished or disappeared breathing sounds, etc.), and imaging examination. The main concern is moderate or higher pleural effusion (≥500 mL).
- ❖ Pneumoderm: extensive subcutaneous emphysema involving the chest area, neck, face, or two or more of the limbs.
- ❖ Hydropneumothorax: the presence of both fluid and air in the chest cavity, which can be diagnosed by imaging.
- ❖ Active hemorrhage: (I) mainly including pulse and blood pressure changes, blood pressure instability after blood volume supplementation, abnormal blood routine, etc.; (II) closed thoracic drainage volume >200 mL/h for 3 hours; (III) the hemoglobin, red blood cell count, and hematocrit decreased progressively.
- ❖ Incision infection or poor healing: there is purulent fluid oozing from the incision, and the bacterial culture of the secretion indicates that the bacterial infection is diagnosed. Postoperatively, delayed incision healing or excessive fluid seepage at the incision, which is light yellow in color, is the diagnosis of fat liquefaction.
- ❖ Pulmonary embolism: combined with typical clinical symptoms (sudden chest pain, dyspnea, hemoptysis), physical signs (pulmonary valve second auscultation area heart sound hyperactivity or division, tricuspid systolic murmur), and auxiliary examination (plasma D-dimer, ECG, chest film, echocardiography, pulmonary angiography, etc.).

Those who had one or more of the above complications were classified as complication groups, and those who did not have the above complications were classified as no complication groups.

The severity of complications was assessed using Clavien-Dindo (11). The Clavien-Dindo scale classifies postoperative complications into five grades. Grade I: abnormal changes requiring antiemetic, antipyretic, painkillers, electrolytes, and physical therapy that do not require surgery, endoscopy, or radiation but include wound infections requiring open drainage; Grade II: requires blood transfusion, total parenteral nutrition, and drug therapy in addition to the drugs used in class I;

Grade IIIa: no intervention such as surgery, endoscopy, or radiation therapy under general anesthesia is required; Grade IIIb: intervention such as surgery, endoscopy, or radiation therapy under general anesthesia is required; Grade IVa: life-threatening complications, single organ dysfunction (including dialysis); Grade IVb: life-threatening complications, multiple organ dysfunction; Grade V: death.

To avoid bias, this study focused only on objective complications identified by laboratory or imaging auxiliary tests and recorded by the attending physician during the course of the disease.

Statistical analysis

SPSS 27.0 software and R4.2.1 software were used for data processing and analysis. The Kolmogorov-Smirnov test is used to evaluate whether continuous variables are normal, and the mean value and positive and negative standard deviation are used to represent the normal distribution. The median, 25th percentile, and 75th percentile are used to represent non-normal distributions. Differences between continuous variables with a normal distribution were compared using the *t*-test, while differences with a skewed distribution were compared using the Mann-Whitney *U* test. Counting data were represented by an example (%), and a chi-squared test was used for comparison between groups. Binary logistic regression analysis was used to screen out the factors with P<0.1, and the nomogram model was constructed with the RMS package in R software. If the nomogram model has less than three variables, it is plotted by correcting for the age factor. A bootstrap test with repeated sampling 1,000 times was used to validate the nomogram model internally. The concordance index (C-index) and calibration graph method were used to evaluate the predictive performance and accuracy of the model. P<0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 872 patients were included in this study, including 396 males (45.4%) and 476 females (54.6%). Patients' median age was 62 years. Most patients had a BMI ≥24 kg/m^2. A total of 269 patients (30.8%) had a smoking history. 212 patients (24.3%) had a history of respiratory disease. In addition, 164 patients (18.8% of the sample) exhibited an ECOG PS score of 2 or above. In this study, 576 patients underwent a pulmonary lobectomy. The most common tumor locations were in the right lung, accounting for 58.6% of the population. The median tumor diameter was 1.5 cm. The median operative time and intraoperative blood loss were 135 min and 20 mL, respectively. The median LMR value was 4.37. The characteristics of other patients are shown in *Table 1*.

Postoperative complications

Postoperative complications were observed in 171 patients, or 19.6% of the study population. There were 24 cases of grade I, 142 cases of grade II, 40 cases of grade IIIa, 3 cases of grade IIIb, and 1 case of class IVb. The most common postoperative complications were PAL (>7 days, 7.0%), pulmonary infection (4.5%), and pleural effusion (3.0%). Details are shown in *Table 2*.

Univariate analysis of thoracoscopic postoperative complications

The results of single factor analysis showed that postoperative complications were more likely to be related to age (P=0.046), gender (P<0.001), smoking status (P<0.001), history of respiratory disease (P<0.001), type of surgical procedure (P<0.001), FEV_1 (P<0.001), FEV_1/FVC (P=0.002), N stage (P<0.001), thoracic adhesion (P<0.001), tumor diameter (P<0.001), LNs (P<0.001), time of operation (P=0.001), intraoperative blood loss (P<0.001), and LMR level (P<0.001). The difference was statistically significant (P<0.05) (*Table 1*).

The results of the relationship between patient characteristics, surgical factors, and PAL after surgery are shown in Table S1. PAL after surgery was more likely to be associated with gender (P<0.001), smoking status (P<0.001), history of respiratory disease (P<0.001), BMI (P=0.003), type of surgical procedure (P<0.001), FEV_1 (P=0.001), FEV_1/FFVC (P=0.003), N stage (P=0.02), thoracic adhesion (P<0.001), tumor diameter (P=0.001), LNs (P=0.001), time of operation (P=0.004), intraoperative blood loss (P<0.001), and LMR level (P=0.01) relevant.

The results of the relationship between patient characteristics, surgical factors, and postoperative pulmonary infection are shown in Table S2. Postoperative pulmonary infection was more likely to be associated with history of respiratory disease (P=0.003), tumor location (P=0.03), FEV_1 (P=0.003), intraoperative blood loss (P=0.04), and LMR level (P=0.01).

Table 1 The relationship between patient characteristics or surgical factors and postoperative complications

Characteristic	Total	Complication		P value
		No	Yes	
Age (years)	62 [55–67]	62 [55–67]	63 [58–67]	0.046
Gender				
Male	396 (45.4)	281 (40.1)	115 (67.3)	<0.001
Female	476 (54.6)	420 (59.9)	56 (32.7)	
Smoking history				
No	603 (69.2)	520 (74.2)	83 (48.5)	<0.001
Yes	269 (30.8)	181 (25.8)	88 (51.5)	
History of respiratory disease				
No	660 (75.7)	562 (80.2)	98 (57.3)	<0.001
Yes	212 (24.3)	139 (19.8)	73 (42.7)	
ECOG PS score				
0–1	708 (81.2)	575 (82.0)	133 (77.8)	0.23
≥2	164 (18.8)	126 (18.0)	38 (22.2)	
BMI (kg/m^2)				0.25
<18.5	22 (2.5)	15 (2.1)	7 (4.1)	
18.5–23.9	354 (40.6)	281 (40.1)	73 (42.7)	
≥24	496 (56.9)	405 (57.8)	91 (53.2)	
Tumor location				
Left lung	361 (41.4)	284 (40.5)	77 (45.0)	0.30
Right lung	511 (58.6)	417 (59.5)	94 (55.0)	
Type of surgical procedure				
Segmentectomy	296 (33.9)	264 (37.7)	32 (18.7)	<0.001
Pulmonary lobectomy	576 (66.1)	437 (62.3)	139 (81.3)	
FVC (%)				
<80	86 (9.9)	66 (9.4)	20 (11.7)	0.39
≥80	786 (90.1)	635 (90.6)	151 (88.3)	
FEV_1 (%)				
<80	163 (18.7)	113 (16.1)	50 (29.2)	<0.001
≥80	709 (81.3)	588 (83.9)	121 (70.8)	
FEV_1/FVC (%)				
<70	154 (17.7)	109 (15.5)	45 (26.3)	0.002
≥70	718 (82.3)	592 (84.5)	126 (73.7)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	Total	Complication		P value
		No	Yes	
N staging				<0.001
N_0	725 (83.1)	602 (85.9)	123 (71.9)	
N_1	56 (6.4)	36 (5.1)	20 (11.7)	
N_2	87 (10.0)	60 (8.6)	27 (15.8)	
N_3	4 (0.5)	3 (0.4)	1 (0.6)	
Thoracic adhesion				
No	671 (76.9)	566 (80.7)	105 (61.4)	<0.001
Yes	201 (23.1)	135 (19.3)	66 (38.6)	
Diameter of tumor (cm)	1.5 [1.0–2.4]	1.5 [1.0–2.2]	2.0 [1.2–3.1]	<0.001
LNs (number)	9 [5–14]	9 [4–14]	11 [7–19]	<0.001
Time of operation (min)	135 [90–180.75]	130 [90–180]	150 [100–205]	0.001
Peroperative bleeding (mL)	20 [10–50]	20 [10–50]	20 [20–50]	<0.001
LMR	4.37 [3.28–5.69]	4.48 [3.35–5.85]	3.71 [3.02–5.04]	<0.001

Data are presented as median [interquartile range] or number (%). ECOG PS, Eastern Cooperative Oncology Group Performance Status; BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; LNs, number of lymph nodes; LMR, lymphocyte/monocyte ratio.

Table 2 Types and incidence of postoperative complications

Types	I	II	IIIa	IIIb	IVb	Incidence rate (%)
Arrthythmia	0	22	0	0	0	2.5
Cardiac failure	0	2	0	0	0	0.2
Pulmonary atelectasis	10	0	0	0	0	1.1
Pulmonary infection	0	39	0	0	0	4.5
Chylothorax	0	14	0	0	0	1.6
Prolonged air leak	0	61	0	0	0	7.0
Pleural effusion (medium or higher)	0	0	26	0	0	3.0
Pneumoderm	9	0	0	0	0	1.0
Hydropneumothorax	0	0	14	0	0	1.6
Active hemorrhage	0	0	0	3	0	0.3
Incision infection or poor healing	5	4	0	0	0	1.0
Pulmonary embolism	0	0	0	0	1	0.1

Table 3 Multivariate analysis of risk factors for postoperative complications

Factor	B	SE	Wals	P	OR	95% CI
History of respiratory disease	0.659	0.206	10.290	0.001	1.934	1.292–2.893
Thoracic adhesion	0.639	0.207	9.565	0.002	1.894	1.264–2.840
LNs	0.024	0.013	3.313	0.07	1.024	0.998–1.051
Time of operation	0.002	0.001	3.113	0.08	1.002	1.000–1.005
LMR	–0.136	0.057	5.659	0.02	0.873	0.780–0.976

B, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; LNs, lymph nodes; LMR, lymphocyte/monocyte ratio.

Table 4 Multivariate analysis of risk factors for postoperative complications (subgroup analysis)

Subgroup analysis	Factor	B	SE	Wals	P	OR	95% CI
Prolonged air leak	Gender	–1.258	0.454	7.696	0.006	0.284	0.117–0.691
	History of respiratory disease	0.674	0.308	4.786	0.03	1.963	1.073–3.591
	BMI (18.5–23.9 kg/m^2)	–1.722	0.662	6.774	0.009	0.179	0.049–0.654
	Type of surgical procedure	1.641	0.543	9.113	0.003	5.158	1.778–14.964
	Thoracic adhesion	0.744	0.309	5.804	0.02	2.103	1.149–3.851
	Time of operation	0.005	0.002	7.352	0.007	1.005	1.001–1.008
Pulmonary infection	History of respiratory disease	0.683	0.352	3.777	0.052	1.980	0.994–3.944
	Tumor location	–0.741	0.340	4.757	0.03	0.477	0.245–0.928
	FEV_1	–0.818	0.357	5.254	0.02	0.441	0.219–0.888
	Peroperative bleeding	0.001	0.001	3.531	0.06	1.001	1.000–1.002
	LMR	–0.210	0.109	3.706	0.054	0.811	0.654–1.004
Pleural effusion	N staging	1.467	0.524	7.853	0.005	4.337	1.554–12.102
	Thoracic adhesion	1.516	0.440	11.854	0.001	4.555	1.921–10.796

B, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; BMI, body mass index; FEV_1, forced expiratory volume in the first second; LMR, lymphocyte/monocyte ratio.

The results of the relationship between patient characteristics or surgical factors and postoperative pleural effusion are shown in Table S3. Postoperative pleural effusion was more likely to be associated with gender (P=0.045), history of respiratory disease (P=0.02), type of surgical procedure (P=0.01), FEV_1 (P=0.04), N stage (P<0.001), thoracic adhesion (P<0.001), tumor diameter (P=0.002), and intraoperative blood loss (P=0.03).

Multivariate analysis of thoracoscopic postoperative complications

The multivariate analysis of risk factors for postoperative complications of thoracoscopic surgery is shown in *Table 3*. Thoracic adhesion (OR 1.894, 95% CI: 1.264–2.840, P=0.002), history of respiratory disease (OR 1.934, 95% CI: 1.292–2.893, P=0.001), and LMR level (OR 0.873, 95% CI: 0.780–0.976, P=0.02) were significant risk factors for postoperative complications.

The multivariate analysis results of risk factors for PAL, pulmonary infection, and pleural effusion are shown in *Table 4*. Gender (OR 0.284, 95% CI: 0.117–0.691, P=0.006), history of respiratory disease (OR 1.963, 95% CI: 1.073–3.591, P=0.03), BMI (OR 0.179, 95% CI: 0.049–0.654, P=0.009), type of surgical procedure (OR 5.158, 95% CI: 1.778–14.964, P=0.003), thoracic adhesion (OR 2.103, 95% CI: 1.149–3.851, P=0.02), and time of operation (OR 1.005, 95% CI: 1.001–1.008, P=0.007) were identified as important

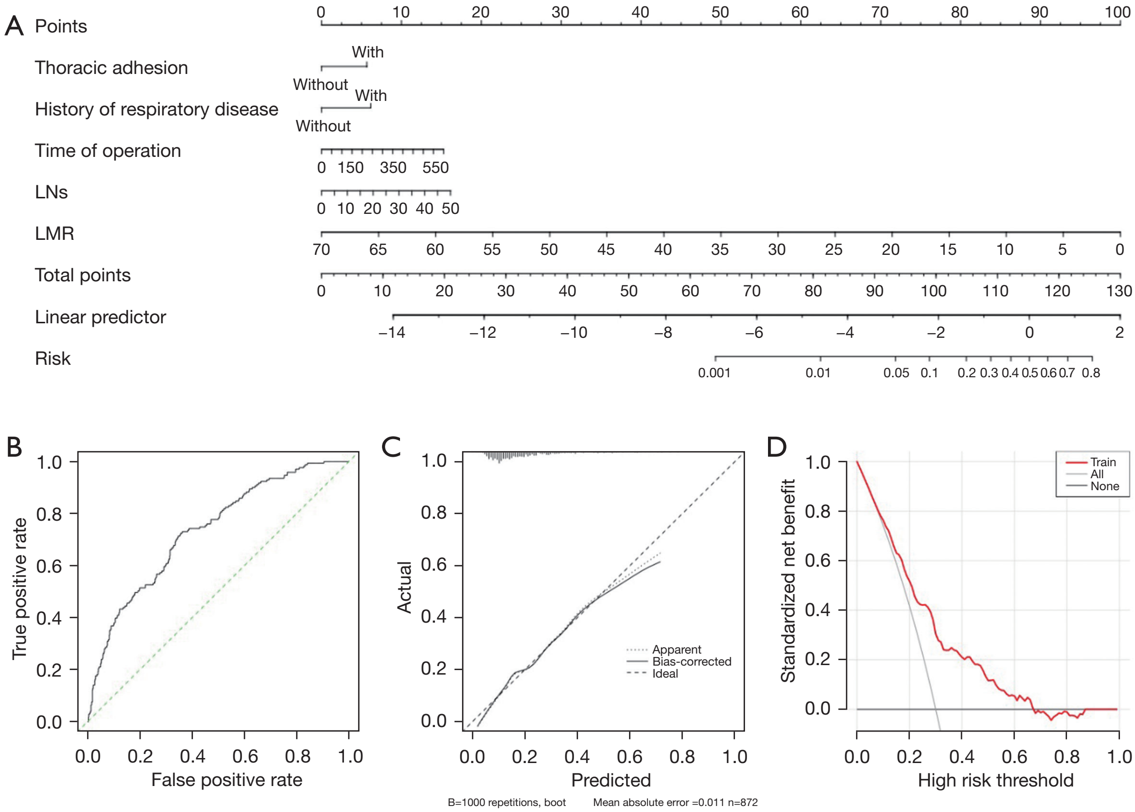

Figure 1 A nomogram prediction model of risk factors for thoracoscopic postoperative complications in lung cancer patients. (A) Nomogram prediction model; (B) ROC curve of prediction model; (C) calibration curve of prediction model; (D) DCA curve of prediction model. LNs, lymph nodes; LMR, lymphocyte/monocyte ratio; ROC, receiver operating characteristic; DCA, decision curve analysis.

risk factors for PAL after surgery (P<0.05). Tumor location (OR 0.477, 95% CI: 0.245–0.928, P=0.03) and FEV_1 (OR 0.441, 95% CI: 0.219–0.888, P=0.02) were identified as important risk factors for postoperative pulmonary infection (P<0.05). N stage (OR 4.337, 95% CI: 1.554–12.102, P=0.005) and thoracic adhesion (OR 4.555, 95% CI: 1.921–10.796, P=0.001) were identified as significant risk factors for postoperative pleural effusion (P<0.05).

Establishment and verification of postoperative PAL prediction model

The establishment of a nomogram

Variables with P<0.1 in logistic regression analysis (thoracic adhesion, history of respiratory disease, time of operation, LNs, and LMR) were included in the nomogram model. which was used to assess the risk of complications after thoracoscopic surgery. As shown in *Figure 1A*, the total score of risk factors ranged from 0 to 130 points. The corresponding risk rate ranges from 0.001 to 0.8. The score of the first row corresponding to the vertical of each indicator was added to obtain the total score, which can intuitively estimate the probability of complications after thoracoscopic pulmonary resection. The higher the total score, the greater the risk of postoperative complications. The ROC curve was used to evaluate the accuracy of the model (*Figure 1B*). The results showed that the area under the curve (AUC) of the model was 0.734 (95% CI: 0.693–0.775). The Bootstrap self-sampling method (B=1,000) was used to verify the model internally, and a calibration curve was drawn (*Figure 1C*). The results showed that there was good consistency between the predicted probability of the model and the actual probability. The decision curve analysis (DCA) shows that this model has good clinical application value, as shown in *Figure 1D*. The nomogram models of risk factors for postoperative PAL, pulmonary infection, and pleural effusion are shown in Figures S1-S3. The AUC for PAL was 0.823 (95% CI: 0.768–0.879).

The AUC of postoperative pulmonary infection was 0.714 (95% CI: 0.627–0.801). The AUC of postoperative pleural effusion was 0.757 (95% CI: 0.650–0.864). The calibration curve and DCA curve indicate that the model has good predictive performance and clinical application value.

Discussion

The occurrence of postoperative complications not only leads to an extension of hospital stay and an increase in medical expenses but it also has a significant impact on the operation effect and postoperative rehabilitation (12). Logistic regression analysis showed that thoracic adhesion, history of respiratory disease, and LMR were independent risk factors for postoperative complications. A number of studies have shown that thoracic adhesion is closely related to postoperative complications, which may be due to the limitations of the surgical field of view and operating space when thoracoscopic surgery encounters with severe thoracic adhesion, thus increasing the complexity and operation time of surgery. The prolongation of operation time leads to the prolongation of anesthesia, mechanical ventilation, and hemodynamic changes, which increases the possibility of cardiopulmonary complications to some extent. Second, prolonged wound exposure increases the risk of incision contamination, which can lead to increased susceptibility to postoperative infection. In addition, severe thoracic adhesion can increase the complexity of intraoperative anatomy, which increases the risk of tissue damage from surgical instruments and intraoperative blood loss, leading to more postoperative problems. However, in the multivariate analysis of this study, no statistically significant relationship was found between operative time, intraoperative blood loss, and the occurrence of postoperative complications ($P>0.05$). This may be because thoracic adhesion not only affects the operative time and intraoperative blood loss but also mechanical ventilation time and anesthesia-related factors. Therefore, compared with the single factors of operative time and intraoperative blood loss, the influence of thoracic adhesion is more extensive, thus masking the influence of the other two on complications.

The presence or absence of a history of respiratory disease is also an influential factor in the occurrence of complications, such as impaired pulmonary ventilation function in patients with bronchial asthma or COPD, and surgery can further reduce lung function reserve, thereby increasing the risk of postoperative respiratory failure.

Markers of inflammation are also associated with complications, and the results of this study showed that a higher lymphocyte/monocyte ratio was associated with a lower incidence of postoperative complications. The activation of lymphocytes and monocytes plays a crucial role in the immune response and can participate in many physiological processes such as immune defense, inflammation, and tissue remodeling. The early stages of inflammation are proinflammatory states mediated by inflammatory factors such as tumor necrosis factor alpha (TNF-α), interleukin-1, and interleukin-6, which are released by neutrophils, macrophages, and monocytes (13,14). LMR is a widely used marker for the assessment of tumor-associated inflammation and a prognostic indicator of malignant tumors (15-17). In addition, studies have shown that the decline of LMR is related to systemic inflammatory responses. Preoperative LMR can also be used as an effective prognostic marker for predicting postoperative complications (18-20). In addition, LMR has the advantages of simple acquisition and effective predictive performance. Therefore, it is of great significance to use LMR as a predictor of postoperative complications.

In this study, PAL, pulmonary infection, and pleural effusion were the most common complications after lung cancer surgery. Studies have shown that the incidence of PAL after pulmonary surgery is about 15% (21). Poor nutritional status before the operation is associated with poor healing of the surgical area (22). Extensive thoracic adhesion will increase the lung parenchymal injury during surgery, and the inevitable air leakage of some needle holes or minor lung tissue damage in the cutting and closing device may lead to PAL after surgery (23). However, the proportion of male patients with a history of smoking and respiratory diseases is larger, and the lung function reserve is poor, which indirectly leads to the incidence of PAL in male patients after lung surgery being higher than that in female patients. However, due to the complexity of the operation of pulmonary lobectomy, it is inevitable that there will be lung tissue injury during the operation. If these potential minor injuries are not found during the operation and the patient's nutritional status is poor, the probability of postoperative lung air leakage will also increase. BMI is also an important factor in the closure of lung damage; on the one hand, low BMI predicts poor nutritional status and poor wound healing (24,25). On the other hand, patients with a low BMI had thinner body types. After surgery, even in the case of complete lung reexpansion, there will still be local residual space, and the visceral pleura and parietal pleura on the lung surface cannot effectively fit to seal the lung surface damage. However, obese patients tend to have a higher respiratory rate, while tidal volume, respiratory compliance, and expiratory reserve are lower. When adjusted according to lung volume, spirometry, gas exchange, and airway resistance are often relatively well preserved, which is conducive to the sealing of the intrathoracic environment with substantial defects, which explains why patients with a higher BMI are less likely to develop PAL (26). Longer operation times were also associated with an increased risk of postoperative PAL complications (27). A study by Dexter *et al.* (28) in patients undergoing lobectomy for early-stage lung cancer showed that longer operation times were associated with atelectasis, increased hospital stay, pneumonia, and PAL, and our results confirm this conclusion. In addition, our study also found that there was a significant correlation between the occurrence of PAL and whether patients had a history of respiratory disease, and the risk of PAL development in patients with a history of respiratory disease was 1.963 times higher than that in patients without a history of respiratory disease. This may be related to poor lung function in patients.

Pulmonary infection after pneumonectomy is also a common complication after surgery. The pain or discomfort of the surgical incision prevents patients from coughing or expectorating effectively, and anesthetic drugs inhibit the cough reflex, thus affecting the clearance function of cilia and resulting in the retention of sputum. Therefore, patients are prone to fever and various bacterial infections after surgery, and complications such as pneumonia and atelectasis may occur in severe cases (29). It has been reported that the incidence of postoperative lung infection is about 6.2% to 14.5% (30-32). In these reports, age, smoking history, chronic obstructive pulmonary disease, and BMI have been reported as risk factors for postoperative pulmonary complications. In this study, tumor site was also an important risk factor for lung infection, which may be related to the anatomical characteristics of the lung. The bronchial structure of the left lung is narrower and steeper than that of the right lung. This anatomical difference makes the left lung more susceptible to retention of secretions in the airway after surgery, which increases the risk of infection. In addition, FEV_1 (%) is also an important risk factor for postoperative lung infection, and the reason is also closely related to lung function reserve.

In this study, the incidence of postoperative pleural effusion was about 3.0%, similar to the previous study (4.1%) (33). Thoracic adhesion and N stage are important risk factors for postoperative pleural effusion, which may be due to the need for careful tissue separation and increased surgical difficulty caused by thoracic adhesion. In patients with lymph node metastasis, the number of lymph nodes increased. However, due to the small number of patients with N3, the results in the nomogram model may be skewed. Based on the above anatomical factors, in the process of postoperative tissue or blood vessel repair, part of the stump fails to close completely or tissue fluid leaks, resulting in fluid leakage and accumulation in the chest cavity, causing pleural effusion.

In terms of the selection of surgical methods, our study did not include patients with VATS wedge-shaped resection and total pneumonectomy because the incidence of complications after wedge-shaped resection is low and the operation time is short, while the incidence of complications after total pneumonectomy is high and has strong interfering factors. Therefore, in order to reduce the deviation caused by surgical factors, only thoracoscopic patients with lobectomy and segmental resection were analyzed in this study to ensure the stability of the study. Since the model was established based on a retrospective study conducted in a single center, future studies with larger sample sizes in multiple centers are needed to verify this result.

Conclusions

In this study, a nomogram model for postoperative complications of thoracoscopy was constructed, and its accuracy and predictive performance were evaluated, which has good clinical application value. Based on this nomogram model, a patient's risk of postoperative complications can be assessed.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-113/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Committee of Qingdao Municipal Hospital (2023 No. 183). Given the retrospective nature of the study, patient's informed consent was considered an exemption.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Cao W, Chen HD, Yu YW, et al. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. Chin Med J (Engl) 2021;134:783-91.
3. Mantovani A, Allavena P, Sica A, et al. Cancer-related inflammation. Nature 2008;454:436-44.
4. Giudicelli R, Thomas P, Guillen JC, et al. Video-assisted pulmonary resection surgery. Technique, indications and first results. Ann Chir 1993;47:707-11.
5. Ismail NA, Elsaegh M, Dunning J. Novel Techniques in Video-assisted Thoracic Surgery (VATS) Lobectomy. Surg Technol Int 2015;26:206-9.
6. Shapiro M, Swanson SJ, Wright CD, et al. Predictors of major morbidity and mortality after pneumonectomy utilizing the Society for Thoracic Surgeons General Thoracic Surgery Database. Ann Thorac Surg 2010;90:927-34; discussion 934-5.
7. Wang Z, Zhang J, Cheng Z, et al. Factors affecting major morbidity after video-assisted thoracic surgery for lung cancer. J Surg Res 2014;192:628-34.
8. Brunelli A, Salati M, Rocco G, et al. European risk models for morbidity (EuroLung1) and mortality (EuroLung2) to predict outcome following anatomic lung resections: an analysis from the European Society of Thoracic Surgeons database. Eur J Cardiothorac Surg 2017;51:490-7.
9. Estors-Guerrero M, Lafuente-Sanchis A, Quero-Valenzuela F, et al. Risk factors for the development of complications after surgical treatment for bronchopulmonary carcinoma. Cir Esp (Engl Ed) 2020;98:226-34.
10. Ettinger DS, Wood DE, Aisner DL, et al. NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2.2021. J Natl Compr Canc Netw 2021;19:254-66.
11. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
12. Sabaté S, Mazo V, Canet J. Predicting postoperative pulmonary complications: implications for outcomes and costs. Curr Opin Anaesthesiol 2014;27:201-9.
13. Grossman Z, Paul WE. Dynamic tuning of lymphocytes: physiological basis, mechanisms, and function. Annu Rev Immunol 2015;33:677-713.
14. Geissmann F, Manz MG, Jung S, et al. Development of monocytes, macrophages, and dendritic cells. Science 2010;327:656-61.
15. Chen J, Wei S, Zhao T, et al. Clinical Significance of Serum Biomarkers in Stage IV Non-Small-Cell Lung Cancer Treated with PD-1 Inhibitors: LIPI Score, NLR, dNLR, LMR, and PAB. Dis Markers 2022;2022:7137357.
16. Jin J, Yang L, Liu D, et al. Prognostic Value of Pretreatment Lymphocyte-to-Monocyte Ratio in Lung Cancer: A Systematic Review and Meta-Analysis. Technol Cancer Res Treat 2021;20:1533033820983085.
17. Yan H, Cai L, Chen S, et al. Preoperative lymphocyte-to-monocyte ratio versus platelet-to-lymphocyte ratio as a prognostic predictor for non-small cell lung cancer patients. J Med Biochem 2020;39:160-4.
18. Zhao Q, Gao R, Liu C, et al. Dynamic Change of

Lymphocyte-to-Monocyte Is Associated With the Occurrence of POCD After Cardiovascular Surgery: A Prospective Observational Study. Front Behav Neurosci 2021;15:646528.
19. Ginesu GC, Paliogiannis P, Feo CF, et al. Inflammatory Indexes as Predictive Biomarkers of Postoperative Complications in Oncological Thoracic Surgery. Curr Oncol 2022;29:3425-32.
20. Xia LJ, Li W, Zhai JC, et al. Significance of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio and prognostic nutritional index for predicting clinical outcomes in T1-2 rectal cancer. BMC Cancer 2020;20:208.
21. Zheng Q, Ge L, Zhou J, et al. Risk factors for prolonged air leak after pulmonary surgery: A systematic review and meta-analysis. Asian J Surg 2022;45:2159-67.
22. Okada S, Shimada J, Kato D, et al. Prolonged air leak following lobectomy can be predicted in lung cancer patients. Surg Today 2017;47:973-9.
23. Pan H, Chang R, Zhou Y, et al. Risk factors associated with prolonged air leak after video-assisted thoracic surgery pulmonary resection: a predictive model and meta-analysis. Ann Transl Med 2019;7:103.
24. Gooseman MR, Brunelli A, Chaudhuri N, et al. Prolonged air leak after segmentectomy: incidence and risk factors. J Thorac Dis 2023;15:858-65.
25. Konstantinidis K, Woodcock-Shaw J, Dinesh P, et al. Incidence and risk factors for 90-day hospital readmission following video-assisted thoracoscopic anatomical lung resection†. Eur J Cardiothorac Surg 2019;55:666-72.
26. Littleton SW. Impact of obesity on respiratory function. Respirology 2012;17:43-9.
27. Daley BJ, Cecil W, Clarke PC, et al. How slow is too slow? Correlation of operative time to complications: an analysis from the Tennessee Surgical Quality Collaborative. J Am Coll Surg 2015;220:550-8.
28. Dexter E, Attwood K, Demmy T, et al. Does Operative Duration of Lobectomy for Early Lung Cancer Increase Perioperative Morbidity? Ann Thorac Surg 2022;114:941-7.
29. Charles MP, Easow JM, Joseph NM, et al. Incidence and risk factors of ventilator associated pneumonia in a tertiary care hospital. Australas Med J 2013;6:178-82.
30. Agostini PJ, Lugg ST, Adams K, et al. Risk factors and short-term outcomes of postoperative pulmonary complications after VATS lobectomy. J Cardiothorac Surg 2018;13:28.
31. Lee JY, Jin SM, Lee CH, et al. Risk factors of postoperative pneumonia after lung cancer surgery. J Korean Med Sci 2011;26:979-84.
32. Agostini P, Cieslik H, Rathinam S, et al. Postoperative pulmonary complications following thoracic surgery: are there any modifiable risk factors? Thorax 2010;65:815-8.
33. King M, Kerr A, Dixon S, et al. Multicentre review of readmission rates within 30 days of discharge following lung cancer surgery. Br J Nurs 2019;28:S16-22.

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