Original Article

Predicting complication risks after sleeve lobectomy for non-small cell lung cancer

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Background: Sleeve lobectomy is a challenging procedure with a high risk of postoperative complications. To facilitate surgical decision-making and optimize perioperative treatment, we developed risk stratification models to quantify the probability of postoperative complications after sleeve lobectomy.

Methods: We retrospectively analyzed the clinical features of 691 non-small cell lung cancer (NSCLC) patients who underwent sleeve lobectomy between July 2016 and December 2019. Logistic regression models were trained and validated in the cohort to predict overall complications, major complications, and specific minor complications. The impact of specific complications in prognostic stratification was explored via the Kaplan-Meier method.

Results: Of 691 included patients, 232 (33.5%) developed complications, including 35 (5.1%) and 197 (28.5%) patients with major and minor complications, respectively. The models showed robust discrimination, yielding an area under the receiver operating characteristic (ROC) curve (AUC) of 0.853 [95% confidence interval (CI): 0.705–0.885] for predicting overall postoperative complication risk and 0.751 (95% CI: 0.727–0.762) specifically for major complication risks. Models predicting minor complications also achieved good performance, with AUCs ranging from 0.78 to 0.89. Survival analyses revealed a significant association between postoperative complications and poor prognosis.

Conclusions: Risk stratification models could accurately predict the probability and severity of complications in NSCLC patients following sleeve lobectomy, which may inform clinical decision-making for future patients.

Keywords: Sleeve lobectomy; non-small cell lung cancer (NSCLC); postoperative complication; predictive models

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Introduction

For centrally located non-small cell lung cancer (NSCLC), sleeve lobectomy is a well-established and preferred alternative to pneumonectomy (1). This operative technique not only facilitates the preservation of lung function in patients but also ensures the complete oncologic resection of tumors (2). Studies have highlighted the favorable outcomes of sleeve resection, including improved overall survival, recurrence rate, and disease-free survival (1,3,4). Sleeve lobectomy can be a technically complex procedure with notable morbidity and mortality. According to previous publications, mortality rates after sleeve lobectomy can be as high as 3%, with morbidity ranging from 21% to 50% (1,2,4-11). Complications may incur a negative impact on short-term outcomes after lung surgery, including prolonged hospitalization, reduced quality of life, and increased readmissions, leading to increased healthcare costs and worsened long-term survival (12-17).

To better understand complication risks, predictive models have been constructed following pneumonectomy, some of which have the potential to support surgical decision-making (18,19). However, to date, there are no effective tools for sleeve lobectomy to estimate anticipated risk of complication. Thus, we sought to develop models to predict the risk of complications after sleeve lobectomy, aiming to support health care teams in making surgical decisions and implementing optimized perioperative management. We present this article in accordance with the TRIPOD reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-325/rc).

Highlight box

Key findings

- Risk stratification models could accurately predict the probability and severity of complications in non-small cell lung cancer patients who underwent sleeve lobectomy.

What is known and what is new?

- Sleeve lobectomy is a challenging procedure with high mortality and morbidity, and there is a lack of effective tools to predict complications.
- This study identified risk factors that exist in the preoperative and intraoperative phases and developed risk stratification models.

What is the implication, and what should change now?

- The models may help doctors make medical decisions and offer accurate therapy and individualized recommendations for patients receiving sleeve lobectomy.

Methods

Patients

The records of consecutive patients who underwent sleeve lobectomy for centrally located NSCLC with complete data between July 2016 and December 2019 in Shanghai Pulmonary Hospital were reviewed and retrospectively analyzed. Patients who underwent sleeve lobectomy for small cell lung cancer and metastasis were excluded (*Figure 1*). All patients received full preoperative examinations, including flexible bronchoscopy, chest X-ray, pulmonary function tests, computed tomography (CT) scan/contrast-enhanced CT, abdominal/brain CT scan, bone scan, and related laboratory examinations. Positron emission tomography (PET) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) were conducted upon suspicion of mediastinal involvement on CT scans. Characteristics of the patients such as comorbidities, demographics, lab results, and pulmonary function test data were obtained from electronic medical records.

Postoperative complications were tabulated individually, and patients were classified into two groups based on whether they had developed complications or not. For this study, complications (prolonged air leak, pneumonia, cardiac arrhythmia, postoperative blood transfusion, pulmonary embolism, chylothorax, bronchopleural fistula, pyothorax, hemothorax, heart failure, respiratory failure, and death within 30 days after surgery) were classified using the Clavien-Dindo Classification system (20). Major complications were defined as grade III-V and minor complications were defined as grade I–II. All tumors were reclassified based on the eighth edition of the TNM staging system for lung cancer. (21). Comorbidities were evaluated using the Charlson Comorbidity Index (CCI) (22). A prolonged air leak was considered to be one lasting over five days postsurgery. Follow-up was conducted through telephone calls or outpatient visits, comprising interval medical history, physical examination, and enhanced contrast whole-body CT scans every six months for the initial three years, followed by annual assessments. Overall survival (OS) was measured from the surgery date until death from any cause, or until the final follow-up date. Recurrence-free survival (RFS) was calculated from the surgical resection date to disease progression (relapse or metastasis), death from any cause, or the final follow-up.

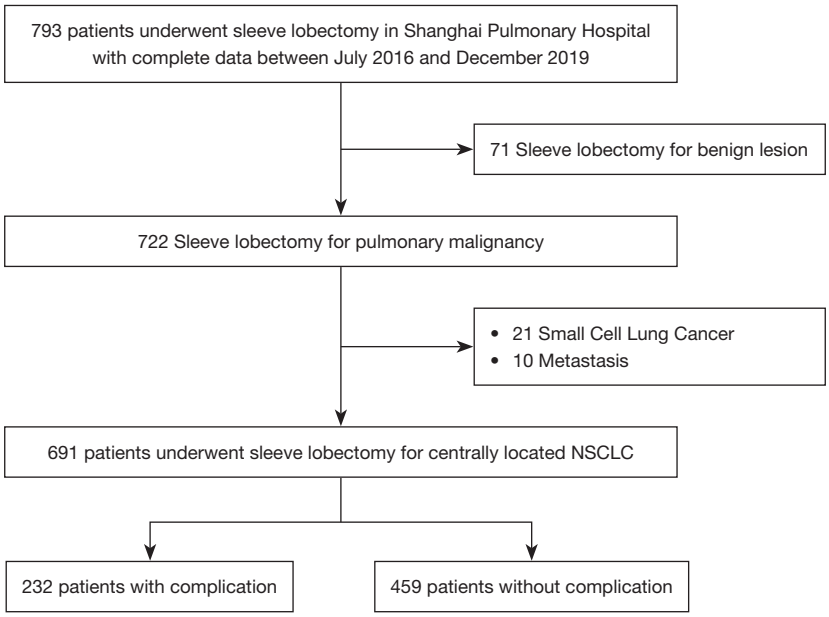


Figure 1 Flowchart showing which patients were included and excluded. NSCLC, non-small cell lung cancer.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Shanghai Pulmonary Hospital (No. K22-793; 15 December 2022) and individual consent for this retrospective analysis was waived.

Model development

The models were crafted utilizing the logistic regression method, ensuring that all variables from the structured dataset were incorporated for the multivariable regression models, aimed at predicting the risks of overall, major, or specific minor complications. The variable inclusion was grounded on a thorough univariable analysis conducted between groups, where variables with a significance level of $P<0.10$ were selected. Furthermore, the derivation cohort was systematically divided into two subsets: a training cohort comprising 60% of the data, dedicated to training the predictive models, and a validation cohort with 40% of the data, used to rigorously test the developed models on unseen data, thereby validating their accuracy and reliability.

Feature weight analysis

To determine the major predictors for complication risks in the cohort, we measured the importance of each feature using coefficients derived from the predictive model designed for predicting complication risks. Scaled importance was calculated as the ratio of the relative importance of each feature to the highest relative importance among all features. The feature's importance weight in the overall complication risk prediction was determined by the ratio of its relative importance to the sum of the relative importance of all features.

Statistical analysis

The discriminative ability of the models for the evaluation of complication risks in centrally located NSCLC was quantified using the area under the receiver operating characteristic (ROC) curve (AUC).

Categorical data are presented as frequency (percentage) and was analyzed using Chi-square analysis. Continuous data with a normal distribution are shown as mean ± standardized deviation and evaluated using the Student's *t*-test. For skewed distribution, continuous data are summarized by median and interquartile range (IQR) and analyzed with the Mann-Whitney *U* test. Survival analyses (OS and RFS) among groups without complications, with minor complications, and with major complications were assessed using the Kaplan-Meier method along with the log-rank test. All statistical analyses and model construction were performed using IBM SPSS 20.0 (IBM Corporation,

Armonk, NY, USA) and R version 3.2.4 (https://www.rstudio.com/products/rstudio/).

Results

Patient characteristics

The clinical and therapeutic characteristics of patients are shown in *Table 1*. A total of 691 patients were included. The median age was 63 (range, 25–83) years, and 89.7% (n=620) of the patients were male. Five hundred and seventeen patients (74.8%) had a smoking history, and 81 patients (11.7%) underwent neoadjuvant therapy (typically with at least 2 cycles of platinum-based 2-drug regimens). Procedures for 150 patients (21.7%) necessitated pulmonary artery reconstruction, while 319 patients (46.2%) underwent video-assisted thoracic surgery (VATS). The

Table 1 Patient characteristics

Characteristics	All patients (n=691)	Without complication (n=459)	With complications (n=232)	P value
Age, years	63 [25–83]	62 [25–83]	64 [46–80]	0.11
Sex				0.04
Male	620 (89.7)	404 (88)	216 (93.1)	
Female	71 (10.3)	55 (12.0)	16 (6.9)	
BMI (kg/m^2)	23.4±2.9	23.5±2.8	23.1±2.9	0.045
Smoking				0.13
Ever	517 (74.8)	279 (60.8)	147 (63.4)	
Never	174 (25.2)	180 (39.2)	85 (36.6)	
Charlson Comorbidity Index				0.007
0	26 (3.8)	23 (5.0)	3 (1.3)	
1	118 (17.1)	82 (17.9)	36 (15.5)	
2	258 (37.3)	183 (39.9)	75 (32.3)	
3	232 (33.6)	135 (29.4)	97 (41.8)	
4	54 (7.8)	34 (7.4)	20 (8.6)	
5	3 (0.4)	2 (0.4)	1 (0.4)	
Pulmonary function				
FEV1, L	2.3 [1.9–2.6]	2.6 [2.3–3.3]	2.2 [1.9–2.6]	0.23
FEV1% of predicted	82.3 [73.0–92.1]	93.1 [82.3–101.3]	82.3 [71.3–89.8]	0.08
Neoadjuvant chemotherapy				0.29
Yes	81 (11.7)	58 (12.6)	23 (9.9)	
No	610 (88.3)	401 (87.4)	209 (90.1)	
Preoperative laboratory parameters				
WBC (10^9/L)	6.9 [5.7–8.6]	8.6 [6.9–7.1]	6.9 [5.5–8.7]	0.97
PLT (10^9/L)	229 [185–280]	279 [226–245]	236.5 [183.3–285.0]	0.24
LYM (10^9/L)	1.8 [1.4–2.2]	2.2 [1.8–2.3]	1.7 [1.3–2.3]	0.77
NEUT (10^9/L)	4.4 [3.3–5.7]	5.7 [4.3–4.4]	4.5 [3.2–5.7]	0.93
Pulmonary artery reconstruction				<0.001
Yes	150 (21.7)	78 (17.0)	72 (31.0)	
No	541 (78.3)	381 (83.0)	160 (69.0)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	All patients (n=691)	Without complication (n=459)	With complications (n=232)	P value
Surgical approach				<0.001
Thoracotomy	372 (53.8)	223 (48.6)	149 (64.2)	
VATS	319 (46.2)	236 (51.4)	83 (35.8)	
Operation time, min	200 [165–245]	195 [160–235]	222 [174–270]	<0.001
Estimated blood loss, mL	100 [100–200]	200 [100–200]	200 [100–300]	<0.001
Intraoperative blood transfusion				<0.001
No	586 (84.8)	450 (98.0)	136 (58.6)	
Yes	105 (15.2)	9 (2.0)	96 (41.4)	
Lymph nodes				
Total stations	6 [4–8]	6 [4–8]	6 [4–8]	0.67
Total numbers	12 [6–18]	13 [7–19]	12 [7–17]	0.47
Tumor location				0.54
Left	327 (47.3)	221 (48.1)	106 (45.7)	
Right	364 (52.7)	238 (51.9)	126 (54.3)	
Tumor size, cm	3.5 [2.5–4.5]	4.5 [3.5–5.0]	3.5 [2.5–5.0]	0.27
pT stage				0.03
1	36 (5.2)	26 (5.7)	10 (4.3)	
2	496 (71.8)	334 (72.8)	162 (69.8)	
3	117 (16.9)	80 (17.4)	37 (15.9)	
4	42 (6.1)	19 (4.1)	23 (9.9)	
pN stage				0.51
0	405 (58.6)	267 (58.2)	138 (59.5)	
1	129 (18.7)	91 (19.8)	38 (16.4)	
2	157 (22.7)	101 (22)	56 (24.1)	
Pathologic stage				0.43
IA	27 (3.9)	23 (4.1)	4 (3.0)	
IB	245 (35.5)	199 (35.7)	46 (34.3)	
IIA	46 (6.7)	34 (6.1)	12 (9.0)	
IIB	156 (22.6)	132 (23.7)	24 (17.9)	
IIIA	175 (25.3)	138 (24.8)	37 (27.6)	
IIIB	42 (6.1)	31 (5.6)	11 (8.2)	
Pathologic type				0.37
Squamous cell carcinoma	521 (75.4)	349 (76.0)	172 (74.1)	
Adenocarcinoma	134 (19.4)	90 (19.6)	44 (19.0)	
Other NSCLCs	36 (5.2)	20 (4.4)	16 (6.9)	
Death within 30 days				0.07
Yes	3 (0.4)	0 (0)	3 (1.3)	
No	688 (99.6)	459 (100.0)	229 (98.7)	

Continuous data are presented as the median [interquartile range] or mean ± standardized deviation, and categorical data are presented as n (%). BMI, body mass index; FEV1, forced expiratory volume in 1 second; WBC, white blood cell; PLT, platelet; LYM, lymphocyte; NEUT, neutrophil; VATS, video-assisted thoracic surgery; NSCLC, non-small cell lung cancer.

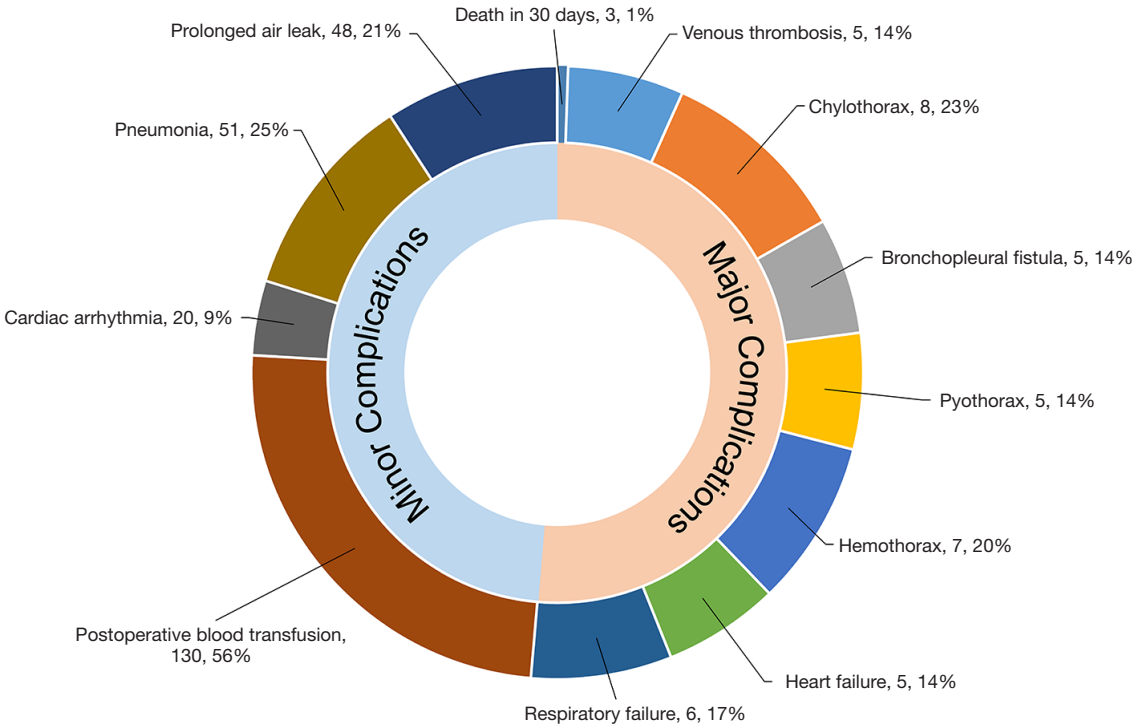


Figure 2 Classification of complications after sleeve lobectomy. The numerator is the number of specific complications, the denominator is the number of patients with minor complications (n=232, 100% of the patients with complications) or the number of patients with major complications (n=35, 15% of the patients with complications).

median operation time and estimated intraoperative blood loss were 200 (IQR, 165–245) minutes and 100 (IQR, 100–200) mL, respectively. Complications developed among 232 patients (33.6%), including 35 patients (5.1%) suffering major complications and 197 (28.5%) with minor complications. Regarding pathologic stage, 27 patients (3.9%) were classified as stage IA, 245 patients (35.5%) as stage IB, 46 patients (6.7%) as stage IIA, 156 patients (22.6%) as stage IIB, 175 (25.3%) as stage IIIA, and 42 (6.1%) as stage IIIB. Surgical pathologic histology revealed 521 patients (75.4%) with squamous cell carcinoma, 134 (19.4%) with adenocarcinoma, and 36 (5.2%) with other NSCLCs.

Complications and classifications

Postoperative complications and their classification are listed in *Figure 2* and Table S1. The overall morbidity was 33.6%. The most frequent complications in this cohort were postoperative blood transfusion (n=130, 18.8%), followed by pneumonia (n=57, 8.3%). Among patients who experienced these two common complications, 14 patients (14/130, 10.8%) with postoperative blood transfusion and six patients (6/57, 10.5%) with pneumonia also developed major complications. Prolonged air leak (n=48, 7.0%) was also a notable adverse event, after which 12.5% (n=6) of patients developed major complications. Five patients in the major complication group experienced bronchopleural fistula (n=5, 0.7%). Additionally, cardiac arrhythmia (n=21, 3.0%), chylothorax (n=8, 1.2%), hemothorax (n=7, 1.0%), respiratory failure (n=6, 0.9%), pyothorax (n=5, 0.7%), and heart failure (n=5, 0.7%) were recorded individually (Table S1).

Risk factors of complications

Table 1 shows that several variables could serve as predictors for complications after sleeve lobectomy. In the complication group (n=232, 33.6%), patients were predominantly male (93.1% *vs.* 88.0%, P=0.04) with a higher CCI score (P=0.007). Meanwhile, lower body mass index (BMI) scores (P=0.045), pulmonary artery reconstruction (P<0.001), thoracotomy (P<0.001), longer operation time (P<0.001), more estimated blood loss (P<0.001), and intraoperative

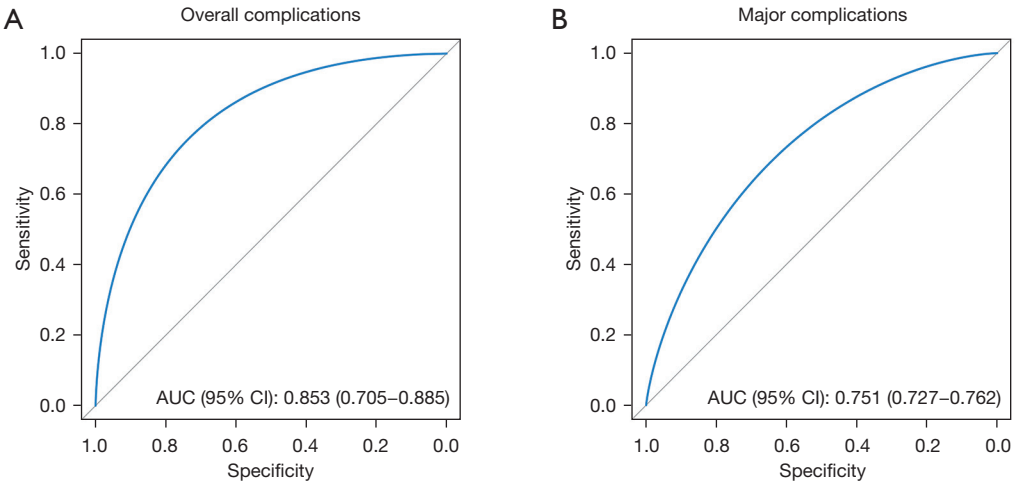


Figure 3 Predictive performance of the logistic regression models. Receiver operating characteristic curves of the models predicting overall complications (A), and major complications (B) in the validation cohorts. AUC, area under the curve; CI, confidence interval.

blood transfusion (P<0.001) were also significantly associated to postoperative complications.

Performance of the complication prediction models

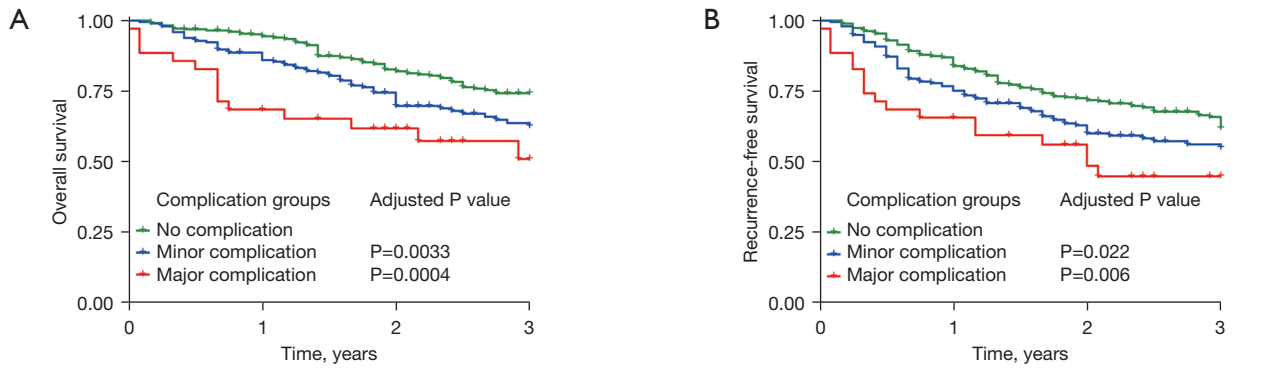
Four preoperative variables [sex, BMI, CCI, the first second of forced expiratory volume FEV1% of predicted (FEV1%pre)] and five surgical-related variables (pulmonary artery reconstruction, surgical approach, operation time, estimated blood loss, intraoperative blood transfusion) were identified and included in the model predicting overall complication risks. The model predicting major complication risks selected three variables (intraoperative blood transfusion, number of lymph node stations dissected, and CCI). In the validation set, the models achieved an AUC of 0.853 (95% CI: 0.705, 0.885) for predicting overall complications and an AUC of 0.751 (95% CI: 0.727, 0.762) for predicting major complications (*Figure 3A*,*3B*). Intraoperative blood transfusion possessed the highest feature importance weight (72.57%) in the model predicting complications (Table S2). The included variables in each minor complication predictive model and their relative importance are shown in Table S2. The models achieved AUCs of 0.78 (95% CI: 0.77, 0.80) for pneumonia, 0.79 (95% CI: 0.73, 0.79) for prolonged air leak, and 0.89 (95% CI: 0.81, 0.89) for predicting cardiac arrhythmia (Figure S1A-S1C).

Impact of postoperative complications on prognosis

Median follow-up time was 29 months. The 3-year OS and 3-year RFS were 76.3% and 66.4% respectively. As shown in *Figure 4A*, different complication levels could significantly stratify patients' prognoses. Patients with minor complications or major complications presented a significantly decreased tendency in 3-year OS, while the major complication group presented the poorest prognosis. Similar to OS, patients with complications showed a tendency for decreased 3-year RFS (*Figure 4B*). In the multivariable analysis (*Tables 2*,*3*), the presence of postoperative complications was independently associated with adverse RFS [hazard ratio (HR) 1.476; 95% CI: 1.141–3.381; P=0.003] and OS (HR 1.548; 95% CI: 1.149–2.084; P=0.004). The long-term analysis of competing risk showed similar results, indicating that major complications were significantly associated with death due to specific causes (Figure S2).

Discussion

Sleeve lobectomy is a widely utilized technique for the resection of centrally located NSCLC (1,2,4). Given the increased complication risks resulting from these procedures, patients who undergo sleeve lobectomy benefit from individualized patient decision-making and healthcare management strategies. In this study, we identified risk factors for complications related to sleeve lobectomy through the presently largest procedure-specific database. Intraoperative blood transfusion, pulmonary artery reconstruction, high CCI, low BMI, thoracotomy, sex male, low FEV1%pre, estimated blood loss, and long



Number at risk				
No complication	459	409	247	117
Minor complication	197	165	110	55
Major complication	35	23	16	7
95% Confidence interval				
No complication	–	0.92–0.97	0.78–0.86	0.70–0.80
Minor complication	–	0.81–0.91	0.63–0.77	0.55–0.71
Major complication	–	0.55–0.86	0.47–0.81	0.35–0.75

Number at risk				
No complication	459	373	210	100
Minor complication	197	142	89	47
Major complication	35	22	15	7
95% Confidence interval				
No complication	–	0.81–0.87	0.68–0.76	0.56–0.68
Minor complication	–	0.81–0.91	0.63–0.77	0.55–0.71
Major complication	–	0.55–0.86	0.47–0.81	0.35–0.75

Figure 4 The relationship between complications and prognosis. Overall survival (A) and recurrence-free survival (B) curves of different complication groups. The green curve refers to the no complication subgroup, the blue curve represents to the minor complication subgroup, and the red curve indicates to the major complication subgroup.

Table 2 Cox regression analysis for recurrence-free survival in the entire cohort

Characteristics	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (≥65 years)	1.016 (0.999–1.032)	0.06	1.017 (1.000–1.034)	0.048*
Sex (male)	1.045 (0.701–1.557)	0.83		
BMI (continuous)	0.994 (0.954–1.037)	0.79		
Smoke (former-smokers and actual smokers)	0.751 (0.573–0.984)	0.04*	0.744 (0.563–0.982)	0.04*
CCI (>2)	1.038 (0.914–1.178)	0.57		
Lesion location (right)	1.101 (0.859–1.411)	0.45		
Pulmonary artery reconstruction (presence)	1.090 (0.816–1.458)	0.56		
Surgical approach (thoracotomy)	0.787 (0.607–1.022)	0.07	0.888 (0.667–1.182)	0.42
Operation time (continuous)	1.001 (0.999–1.002)	0.28		
Estimated blood loss (continuous)	1.000 (1.000–1.001)	0.04*	1.000 (1.000–1.001)	0.31
Pathological T stage				
1	Reference		Reference	
2	1.715 (0.844–3.487)	0.14	1.662 (0.817–3.381)	0.16
3	2.642 (1.257–5.554)	0.010*	2.416 (1.144–5.106)	0.02*
4	2.999 (1.335–6.737)	0.008*	2.562 (1.132–5.797)	0.02*
Complication (presence)	1.479 (1.151–1.901)	0.002*	1.476 (1.141–3.381)	0.003*

*, significant P values. Surgical approach: thoracotomy or video-assisted thoracic surgery. HR, hazard ratio; CI, confidence interval; BMI, body mass index; CCI, Charlson Comorbidity Index.

Table 3 Cox regression analysis for overall survival in the entire cohort

Characteristics	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (≥65 years)	1.028 (1.009–1.049)	0.005*	1.029 (1.009–1.05)	0.004*
Sex (male)	0.994 (0.618–1.597)	0.98		
BMI (continuous)	0.995 (0.947–1.045)	0.83		
Smoke (former-smokers and actual smokers)	0.778 (0.568–1.067)	0.12	0.747 (0.539–1.033)	0.08
CCI (>2)	1.141 (0.984–1.323)	0.08	1.000 (0.655–1.526)	0.99
Lesion location (right)	1.109 (0.831–1.48)	0.48		
Pulmonary artery reconstruction (presence)	1.072 (0.769–1.495)	0.68		
Surgical approach (thoracotomy)	0.822 (0.605–1.117)	0.21		
Operation time (continuous)	1.002 (1.000–1.003)	0.044*	1.001 (1.000–1.003)	0.11
Estimated blood loss (continuous)	1.000 (1.000–1.001)	0.056	1.000 (1.000–1.001)	0.19
Pathological T stage				
1	Reference		Reference	
2	1.956 (0.800–4.784)	0.14	1.915 (0.783–4.684)	0.16
3	3.216 (1.272–8.130)	0.01*	2.95 (1.159–7.510)	0.02*
4	3.131 (1.147–8.549)	0.03*	2.684 (0.973–7.405)	0.056
Complication (presence)	1.564 (1.170–2.090)	0.003*	1.548 (1.149–2.084)	0.004*

*, significant P values. Surgical approach: thoracotomy or video-assisted thoracic surgery. HR, hazard ratio; CI, confidence interval; BMI, body mass index; CCI, Charlson Comorbidity Index.

operation time were found to be predictors of postoperative complications after sleeve lobectomy.

By modeling these factors, we developed models aimed at predicting both the probability and severity of postoperative complications. These models exhibited robust performance, boasting an AUC of 0.85 for overall complications and 0.75 for major complications respectively, thus demonstrating their efficacy in clinical prognostication.

In general, mortality and morbidity rates of sleeve lobectomy ranged between 0–3% and 21–50%, respectively (1,2,5-11). In our study, the 30-day mortality and complication rates of sleeve lobectomy were 0.4% and 34%, respectively. Minor complications such as pneumonia, and prolonged air leaks could affect the length of stay and patient readmission (16,23). The most prevalent minor complication in our study was postoperative blood transfusion, with 17% morbidity. Major complications, especially anastomotic complications such as bronchopleural fistulas, could seriously affect patients' postoperative quality of life and even lead to death (24). Previous investigators have shown rates of anastomotic complications following sleeve lobectomy patients of 5.2% (25-27). In our study, the rate of anastomotic complications (bronchopleural fistula) was 0.7%. This difference may be attributed to variations in efficacy of preoperative management (such as correcting malnutrition, treating underlying diseases, and controlling chronic lung infections) and intraoperative protection of the bronchial blood supply.

A previous study considered older age as a risk factor for postoperative complications in centrally located NSCLCs (28). Likewise, in our cohort, older patients were more prone to experiencing complications. The CCI assesses complications based on both the quantity and gravity of diseases. It quantifies complications and can predict the risk of death from diseases (29). In lung cancer patients, a higher CCI score is correlated to a higher risk of 3-year death (30). Blanc *et al.* discovered that the CCI index serves as an independent risk factor for acute respiratory distress syndrome (ARDS) and tracheal intubation following lung surgery (31). Daffrè *et al.* discovered that it was linked

to perioperative mortality (32). In our study, patients with a higher CCI score experienced more postoperative complications, and the severity of these complications was higher than those with a lower CCI index. This result aligns with the above studies. However, it is important to note that the CCI score is only a quantitative index. In our study, one patient died three days after surgery because of severe ventricular fibrillation. This patient had a 21-year history of hypertension with poor blood pressure control. The postoperative stress state, coupled with hypoxia from intense coughing, triggered the ventricular fibrillation. Interestingly, our predictive models indicated no complication or major complication for this patient. We believe this discrepancy arose as the CCI score did not fully reflect the severity and control of hypertension. Therefore, it is critical to assess the patients' fundamental states before surgery.

Intraoperative blood transfusion is frequently associated with intraoperative bleeding problems then that have a deep impact on the post-operative course. Among our patients, intraoperative blood transfusion was significantly associated with postoperative complications and possessed the highest feature importance weight in the predictive complication model. A study has also identified intraoperative blood transfusion as a predictor of postoperative complications, such as atrial fibrillation in lung cancer lobectomy (33). Another study has found that blood transfusion is related to unfavorable short-term or long-term outcomes in surgical patients (34). It is reasonable to control the surgical risk and ensure the quality of surgery to reduce the occurrence of intraoperative blood transfusion.

We also developed models to predict minor complications, such as pneumonia, prolonged air leaks, and cardiac arrhythmia. These minor complications could prolong hospitalization, impair the patient's quality of life, and increase hospital readmissions and medical costs (16). Some prior studies have constructed models to predict these complications in lung cancer patients. Song *et al.* developed an algorithm to predict postoperative pneumonia with an AUC of 0.71 (35). Kim *et al.* used intraoperative ventilatory leaks to predict prolonged air leaks after lung resection, and the AUC of the model was 0.80 (36). Another study conducted by Nojiri *et al.* predicted postoperative atrial fibrillation by analyzing preoperative tissue Doppler echocardiography and achieved an AUC of 0.83 (37). In our study, the models achieved an AUC of 0.78 for predicting pneumonia, an AUC of 0.78 for predicting prolonged air leaks, and an AUC of 0.89 for predicting cardiac arrhythmia. In the validation cohort, one patient died of severe pneumonia and chylothorax after surgery. The models for predicting overall complications or major complications did not assign the right signatures to this patient. However, the occurrence of pneumonia was successfully predicted by the pneumonia model. These minor complication models could be used as a complement to the overall complication and major complication models.

We also conducted a prognosis analysis to investigate the impact of postoperative complications after sleeve lobectomy. The results showed that the complications were associated with adverse outcomes. Pieces of evidence about the relationship between postoperative complications and prognosis in NSCLC are similar to our results. A study conducted by Lugg *et al.* showed that postoperative complications were an independent predictor of worse 5-year cancer-specific survival in stage I NSCLC (14). Nakada *et al.* concluded that postoperative complications were significantly related to a poor prognosis in NSCLC patients who underwent lobectomy (15). Lugg *et al.* and Wang *et al.* found that a postoperative pulmonary complication after thoracic surgery is associated with a poorer long-term outcome (14,38). We recognize that postoperative complications can have a direct impact on patient outcomes, including recurrence and survival. However, it is also important to consider that these complications may be indicative of an underlying fragility or predisposition of the patient to adverse events. In this context, the predictive models for complications could serve as a valuable tool to help identify and correct preoperative risk factors, thus optimizing patients before surgery. By reducing the risk of postoperative complications, we may be able to improve patient outcomes and reduce the burden of adverse events.

We acknowledge that this study is limited by its retrospective nature, and as a result, the incidence of complications in patients may be underestimated. Second, our models were developed based on a single-center database, making it difficult to further verify the robustness and generalization of the models. Therefore, there is a need for future prospective, multi-center studies to validate our findings and further refine the predictive models. Third, because of the small sample size of major complications, our models only offer a broad estimation of major complication risks without specific information on the types of postoperative major complications. Finally, it should be noted that the median follow-up duration of 29 months is slightly shorter than the full three-year period for which OS and RFS were reported. This discrepancy may introduce

a degree of bias into our results, and thus, the three-year OS and RFS estimates should be interpreted with caution. However, given the nature of our study and the current data available, we believe that these estimates still provide valuable insights for clinical practice and future research.

Conclusions

We created models to predict the probability and severity of postoperative complications for patients undergoing sleeve lobectomy. These models may help future healthcare teams in making medical decisions, thereby ensuring that patients who are being considered for sleeve lobectomy receive appropriate workup, informed discussions of risk, and individualized recommendations.

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Footnote

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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 board of Shanghai Pulmonary Hospital (No. K22-793; 15 December 2022) and individual consent for this retrospective analysis was waived.

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