

# Risk factor analysis and predictive model development for air leakage after thoracoscopic pulmonary wedge resection

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**Background:** The rate of postoperative complications in wedge resection is low because it does not involve major structures. However, postoperative air leakage (AL) is common. This research sought to determine the risk factors associated with AL following thoracoscopic pulmonary wedge resection and to create a predictive model for identifying patients suitable for tubeless procedures.

**Methods:** This study included individuals who underwent thoracoscopic pulmonary wedge resection at Fujian Medical University Union Hospital from January 2015 to December 2020. Univariate and multivariate logistic regression analyses were conducted to identify independent risk factors and construct relevant models. Concurrent data from two other centers were collected as validation sets for external validation.

**Results:** A total of 2,503 patients meeting the inclusion criteria were included in the study, with an overall incidence of AL at 11.35% (284/2,503). The development dataset included 2,006 cases, and columnar plots were drawn based on the outcomes of the multivariate logistic regression analysis. The final model included age >70, forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio (FEV1%) <80%, nodule size, benignity/malignancy, and pleural adhesions (none, focal, diffuse). In the development dataset, the C-index was 0.829. The external validation set included 497 cases, with a C-index of 0.833.

**Conclusions:** The AL prediction model performed well and may be clinically useful for assessing AL and identifying patients who can benefit from tubeless strategies.

**Keywords:** Postoperative air leak (postoperative AL); predictive model; pulmonary wedge resection; thoracoscopic; tubeless strategy

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## Introduction

The advent of high-resolution computed tomography (CT) has markedly improved the detection rate of lung nodules. Surgical resection remains the definitive treatment for lung nodules (1-3). The increase in the number of pulmonary surgical procedures (4) underscores the need to expedite postoperative recovery and minimize the associated surgical burden. Enhanced Recovery After Surgery (ERAS) (3,5) has gained considerable attention because it reduces the postoperative stress-induced reactions of the body through effective perioperative management (6,7). Postoperative chest tube drainage is a routine postoperative management strategy performed following thoracic surgery (8). However, postoperative chest tube drainage can cause pain and inflammation and impair early patient movement (9). Compared to conventional chest tube drainage, patients without tubes have better perioperative outcomes (7,10).

Wedge resection of the lung is the main surgical procedure for early-stage lung cancer and benign lung lesions (11,12). Owing to the limited extent of resection and involvement of the large bronchi or blood vessels, the rate of postoperative complications with the tubeless strategy is low (13-16). However, several techniques can be used to perform wedge resection. Wedge resection is associated with air leakage (AL) rates of 5.9–40%. Additionally, a prospective randomized controlled study by Zhang *et al.* involving 96 pulmonary wedge resections reported a 10% incidence of postoperative pneumothorax in patients without chest tubes after pulmonary wedge surgery, even after water testing, and the patients required repeat surgical intervention or retubing (4,10,15,17-19). AL after pulmonary wedge resection is a significant challenge; thus, a method for identifying

# Highlight box

#### Key findings

• This study established a prediction model with good performance that can aid in implementing the tubeless strategy.

#### What is known and what is new?

- Air leakage (AL) after pulmonary wedge resection can indeed be a significant challenge in thoracic surgery.
- This is the first extensive multi-center study aiming at developing a predictive model for AL after pulmonary wedge resection.

#### What is the implication, and what should change now?

 The AL prediction model demonstrated robust performance and holds potential clinical utility for evaluating AL risk and identifying patients suitable for tubeless management strategies. patients suitable for tubeless strategies is urgently needed.

Therefore, this study aimed to identify risk factors for postoperative pulmonary AL in patients undergoing thoracoscopic pulmonary wedge resection and establish a predictive model. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd. amegroups.com/article/view/10.21037/jtd-24-1090/rc).

# Methods

#### Patients

We retrospectively analysed demographic and clinical data from patients who had thoracoscopic pulmonary wedge resection at Fujian Medical University Union Hospital, the First Affiliated Hospital of Xiamen University, and Quanzhou First Hospital between January 2015 and December 2020. The inclusion/exclusion criteria were as follows: (I) CT imaging suggestive of peripheral-type lung nodules with a maximum nodule diameter of <3.0 cm; (II) availability of preoperative biochemical indices, coagulation function, cardiopulmonary function, and other tests and examinations consistent with surgical requirements, and the ability to tolerate general anesthesia and one-lung ventilation; (III) patient underwent thoracoscopic wedge resection; (IV) availability of complete perioperative data; and (V) no significant AL on the water test after wedge resection. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Ethics Committees of Fujian Medical University Union Hospital (2024KY182) and patient consent was waived because of the retrospective nature of the study.

#### Surgical procedures and perioperative management

Preoperative preparation encompassed various critical steps aiming at ensuring patient safety and enhancing surgical outcomes. These steps included psychological counseling to alleviate anxiety, urging smokers to cease smoking at least 2 weeks before the operation, discontinuing anticoagulant and antiplatelet medications one week prior, and engaging in respiratory exercises and infection treatments. Additionally, conditions such as hypertension, diabetes, and coronary artery disease were stabilized, and patients must adhere to an 8-hour fasting and a 6-hour water restriction before surgery.

During the procedure, all patients underwent combined

intravenous general anesthesia with double-lumen endotracheal intubation for unilateral lung ventilation and were positioned laterally on the healthy side. The surgery entailed a single-port thoracoscopic wedge resection, with an incision measuring between 3.0 and 4.0 cm located between the anterior and mid-axillary lines at the 4th intercostal space. The surgeon located the target lung tissue and utilized surgical staplers to excise a wedge-shaped section precisely. The resection boundaries were carefully selected to ensure complete lesion removal while preserving as much healthy lung tissue as possible. Once the specimen was excised, it was immediately sent to the pathology department for rapid intraoperative frozen section analysis, which typically confirmed preliminary determinations of nodule characteristics intraoperatively. Following this, a water test and lung expansion method using a pressure of 15 cmH<sub>2</sub>O were utilized to check for AL. Any detected leaks were addressed through electrical coagulation or suturing without fibrin glue or reinforcement materials. At the end of the surgery, two types of tubes were installed. One large-bore (22-24 F) chest tube, attached to a chest drainage bottle without extra negative pressure suction, was positioned higher to evacuate air and was removed if there was no significant AL. Another smaller 8 F disposable drainage catheter placed lower was used to drain fluid and was removed when fluid output was less than 150 mL daily.

Postoperatively, patients received fluid and nutrition, pain management, and other symptomatic treatments. They were encouraged to mobilize early and actively expel sputum. For those with obstructed sputum, fiberoptic bronchoscopy was employed for aspiration. Patients suffering from lung infections were treated with appropriate antibiotics. AL was specifically identified if the chest tube could not be removed within 24 hours post-surgery due to air bubbles observed during intentional coughing. The chest tube removal was contingent upon the absence of air bubbles in the drainage system following continuous intentional coughing (20).

#### Data collection

We gathered comprehensive demographic and clinical data encompassing various variables, including age, sex, body mass index, American Society of Anesthesiologists (ASA) score, respiratory disease history, cardiovascular disease history (such as arrhythmia and heart valve issues), history of other oncological conditions, underlying medical conditions such as hypertension and diabetes, thoracic surgery records, as well as smoking and alcohol consumption habits (both past and present smokers/drinkers, as well as those who have never smoked or consumed alcohol). During the preoperative assessment, we gathered comprehensive data, including CT imaging, cardiac ultrasound examinations, lung function measurements [specifically forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio (FEV1%)], albumin levels, and absolute lymphocyte counts. Additionally, we collected intraoperative data pertaining to the surgical site, total operative time, intraoperative bleeding volume, pathological findings, and pleural adhesions, ranging from no adhesions to focal or diffuse adhesions (20). Lastly, we collected data on postoperative variables such as pain score, duration of hospital stay, and drainage details.

# Statistical analysis

Patients from Fujian Medical University Union Hospital were used as the model development cohort, and those from the other two hospitals were used as the external validation cohorts. Baseline characteristics were assessed using nonparametric methods for continuous data and Chi-squared tests for categorical data. Univariate and multivariate logistic regression analyses were employed to identify independent predictors of postoperative AL. Statistically significant variables (P<0.05) in the multivariate logistic regression analyses were included in the prediction model. Nomograms were developed using R programming language based on the findings from multivariate logistic regression analyses. The scores for each variable were derived from regression coefficient values. Each patient's total score, derived from summing individual variable scores, was used to estimate the probability of postoperative AL. The model was validated using external validation cohorts, and calibration curves were plotted to measure model performance. Goodness-of-fit was evaluated using Hosmer-Lemeshow test. All analyses were conducted using R version 2.8.1 (R Foundation for Statistical Computing).

# **Results**

#### Patient characteristics

From January 2015 to December 2020, 2,068 patients who underwent thoracoscopic pulmonary wedge resection at Fujian Medical University Union Hospital were initially enrolled. However, 62 patients were excluded due to

significant AL detected during the water test following the procedure, resulting in 2,006 patients ultimately being included in the study. The overall incidence of postoperative AL was 11.57% (232/2,006), and the patients were grouped according to the presence or absence of AL (AL and non-AL groups). Table 1 presents demographic and clinical characteristics of the study cohort. Among the AL patients, 59.91% (139/232) were male, with a median age of 60 [53, 68] years. Among patients >70 years, the incidence of AL was 20.69% (48/232 patients). Patients without pleural adhesions were less likely to develop AL [147/1,782 (8.25%) vs. 85/224 (37.95%), P<0.001]. Postoperative pathological findings were benign in 1,025 [1,025/2,006 (51.10%)] and malignant in 981 [981/2,006 (48.90%)] cases, and there was a higher risk of malignancy than benignity [163/981 (16.62%) vs. 69/1,025 (6.73%)]. The median tumor diameter was 0.90 (0.80, 1.30) cm and was significantly larger in the AL group compared to the non-AL group (1.40 vs. 0.90 cm, P<0.001). Patients with FEV1% values  $\geq 80\%$ were less likely to have AL [104/1,475 (7.05%) vs. 128/531 (24.11%), P<0.001].

# Univariate and multivariate analyses of risk factors for AL

The risk factors for AL were identified using univariate logistic regression analysis for each variable (Table 2). Surgical duration was excluded because it was influenced by pleural adhesions and the presence or absence of multiple wedge resections. Among the analyzed variables, sex, age, pleural adhesions, FEV1%, surgical site, pathological benignity, pathological type, tumor diameter, ASA score, respiratory disease, history of thoracic surgery, history of hypertension, and history of smoking were significantly correlated with AL. However, multivariate logistic regression analyses revealed that age [ $\leq 70 vs. > 70$  years, 0.642 (0.413, 0.998)], pleural adhesions [focal adhesions vs. no adhesions, 0.066 (0.036, 0.122), diffuse adhesions vs. no adhesions 0.282 (0.143, 0.559)], pathologically benignancy and malignancy [0.418 (0.295, 0.593)], tumor diameter [1≤ diameter <1.5 vs. <1 cm, 0.247 (0.155, 0.396); 1.5≤ diameter  $<2 vs. <1 cm, 0.272 (0.161, 0.459); \geq 2 vs. <1 cm, 0.649 (0.396,$ 1.066)], and FEV1% [50%≤ FEV1% <80% vs. ≥80%,  $33.186 (8.176, 134.705); <50\% vs. \geq 80\%, 3.835 (2.779,$ 5.292)] were independently associated with AL development (Table 3).

#### Development and validation of the predictive nomogram

We employed five significant variables (age, pleural adhesions, pathologically benignancy and malignancy, tumor diameter, and FEV1%) from the multifactorial analysis to develop a nomogram for predicting AL. As depicted in *Figure 1*, the cumulative score for these risk factors varied between 0 and 100 points, correlating with a risk rate fluctuating from 0.05 to 0.99. The score from the top row aligned with each predictor's vertical line was summed to derive the total score, providing a straightforward method to estimate AL risk following pulmonary wedge resection. A higher total score indicated an increased likelihood of AL.

The internal calibration curve demonstrated no significant deviation from the ideal curve, indicating good accuracy between the column line plot predictions and the actual observations for AL, with a C-index of 0.829 for the development dataset. The demographic and clinical characteristics of the external validation cohort were presented in *Table 4*. The overall incidence of postoperative AL was 10.46% (52/497). Of these, 51 patients (10.26%) were aged over 70, and 258 (51.91%) were male. The external calibration curve showed model validation using an external validation set, with no significant deviation from the reference line and a C-index of 0.833 for the validation dataset. The goodness-of-fit test for both model development and validation was not significant (*Table 5*).

*Figure 2* illustrates the receiver operating characteristic (ROC) curve of the nomogram. The optimal cutoff value for the total nomogram score was 68 points, corresponding to an estimated AL probability of approximately 20%. The sensitivity and specificity were 81.7% and 68.1% at this cutoff, respectively.

#### Discussion

Following wedge resection, inserting a postoperative chest tube allows for effective drainage of fluid and gas, thereby minimizing early postoperative complications (15). However, a postoperative chest tube can lead to pain, decreased lung function, and restricted mobility, hindering patients' early functional exercise (9,17,21). Minimally invasive surgery represents a novel approach to treating lung nodules. Its advancement has heightened clinical emphasis on ERAS, which aims to minimize postoperative complications and shorten hospital stays (22-24). Tubeless strategies are

Table 1 Clinical characteristics of the 2,006 patients after wedge resection

Variables	Total (n=2,006)	AL [n=232 (11.57%)]	Non-AL [n=1,774 (88.43%)]	Р
Age >70 years				<0.001
Yes	205 (10.22)	48 (20.69)	157 (8.85)	
No	1,801 (89.78)	184 (79.31)	1,617 (91.15)	
Sex				0.002
Male	1,016 (50.65)	139 (59.91)	877 (49.44)	
Female	990 (49.35)	93 (40.09)	897 (50.56)	
BMI (kg/m²)	22.83 (20.90, 24.95)	22.86 (20.45, 24.61)	22.83 (20.96, 24.97)	0.32
Operation time (min)	80.00 (60.00, 102.00)	97.00 (75.00, 129.75)	78.00 (60.00, 99.25)	<0.001
Blood loss (mL)	20.00 (15.00, 50.00)	20.00 (15.00, 50.00)	20.00 (15.00, 50.00)	0.42
Multiple wedge resection				0.91
Yes	368 (18.34)	42 (18.10)	326 (18.38)	
No	1,638 (81.66)	190 (81.90)	1,448 (81.62)	
Location of surgery				0.27
Left	807 (40.23)	101 (43.53)	706 (39.80)	
Right	1,199 (59.77)	131 (56.47)	1,068 (60.20)	
ASA score				0.001
1	1,116 (55.63)	103 (44.40)	1,013 (57.10)	
2	638 (31.80)	90 (38.79)	548 (30.89)	
3	252 (12.56)	39 (16.81)	213 (12.01)	
Pleural adhesions				<0.001
None	1,782 (88.83)	147 (63.36)	1,635 (92.16)	
Focal	160 (7.98)	48 (20.69)	112 (6.31)	
Diffuse	64 (3.19)	37 (15.95)	27 (1.52)	
Benign and malignant				<0.001
Benign	1,025 (51.10)	69 (29.74)	956 (53.89)	
Malignant	981 (48.90)	163 (70.26)	818 (46.11)	
Nodule diameter (cm)				<0.001
<1	1,098 (54.74)	73 (31.47)	1,025 (57.78)	
1≤ diameter <1.5	434 (21.64)	44 (18.97)	390 (21.98)	
1.5≤ diameter <2	315 (15.70)	63 (27.16)	252 (14.21)	
≥2	159 (7.93)	52 (22.41)	107 (6.03)	
Diabetes				0.31
Yes	286 (14.26)	28 (12.07)	258 (14.54)	
No	1,720 (85.74)	204 (87.93)	1,516 (85.46)	
Hypertension				0.009
Yes	453 (22.58)	68 (29.31)	385 (21.70)	
No	1,553 (77.42)	164 (70.69)	1,389 (78.30)	

Table 1 (continued)

Table 1 (continued)

Variables	Total (n=2,006)	AL [n=232 (11.57%)]	Non-AL [n=1,774 (88.43%)]	Р
Cardiovascular disease				0.10
Yes	88 (4.39)	15 (6.47)	73 (4.11)	
No	1,918 (95.61)	217 (93.53)	1,701 (95.89)	
History of other tumors				0.62
Yes	236 (11.76)	25 (10.78)	211 (11.89)	
No	1,770 (88.24)	207 (89.22)	1,563 (88.11)	
History of respiratory disease				<0.001
Yes	104 (5.18)	37 (15.95)	67 (3.78)	
No	1,902 (94.82)	195 (84.05)	1,707 (96.22)	
History of thoracic surgery				<0.001
Yes	21 (1.05)	11 (4.74)	10 (0.56)	
No	1,985 (98.95)	221 (95.26)	1,764 (99.44)	
Smoking				0.005
Yes	774 (38.58)	109 (46.98)	665 (37.49)	
No	1,232 (61.42)	123 (53.02)	1,109 (62.51)	
Drinking				0.03
Yes	546 (27.22)	77 (33.19)	469 (26.44)	
No	1,460 (72.78)	155 (66.81)	1,305 (73.56)	
High pulmonary artery pressure				0.71
Yes	204 (10.17)	22 (9.48)	182 (10.26)	
No	1,802 (89.83)	210 (90.52)	1,592 (89.74)	
EF value (%)	68.00 (65.00, 72.00)	68.00 (65.00, 71.00)	68.00 (64.00, 72.00)	0.71
FEV1%				<0.001
≥80%	1,475 (75.53)	104 (44.83)	1,371 (77.28)	
50%≤ FEV1% <80%	517 (25.77)	117 (50.43)	400 (22.55)	
<50%	14 (0.70)	11 (4.74)	3 (0.17)	
Preoperative albumin (g/L)	44.00 (41.40, 46.00)	44.25 (41.90, 46.10)	43.90 (41.40, 46.00)	0.18
Postoperative albumin (g/L)	37.00 (35.00, 39.50)	36.80 (35.10, 39.68)	37.00 (35.00, 39.50)	0.64
Preoperative lymphocyte count (10 <sup>9</sup> /L)	1.82 (1.51, 2.28)	1.79 (1.47, 2.18)	1.83 (1.51, 2.30)	0.15
Postoperative lymphocyte count (10 <sup>9</sup> /L)	1.09 (0.80, 1.50)	1.02 (0.75, 1.45)	1.09 (0.80, 1.50)	0.20

Data are presented as n (%) or median (IQR). Nodule diameter, refers to the largest nodule size. BMI, body mass index; ASA, American Society of Anesthesiologists; EF, ejection fraction; FEV1%, FEV1/FVC ratio; AL, air leakage; IQR, interquartile range; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

a crucial component of ERAS, supported by extensive evidence demonstrating feasibility and safety (15,17,18,25). However, the risk of postoperative residual pneumothorax stemming from extubation ranges from 8% to 59% of cases (16,26), necessitating re-tubing interventions in certain instances (15,16,27). Re-tubing can lead to secondary injury and negatively impact the patient's postoperative recovery.

Wedge resection has become a prevalent treatment for pulmonary nodules, with a relatively low risk of postoperative complications (25). No large-scale studies Table 2 Univariate logistic regression analysis of AL presence

Variables	OR (95% CI)	Р
Age >70 years (yes vs. no)	0.372 (0.260, 0.532)	<0.001
Sex (male vs. female)	1.529 (1.157, 2.020)	0.003
BMI (kg/m²)	0.973 (0.930, 1.018)	0.23
Operation time (min)	1.016 (1.012, 1.019)	<0.001
Blood loss (mL)	1.001 (0.998, 1.005)	0.42
_ocation of surgery (left vs. right)	1.166 (0.885, 1.538)	0.28
Multiple wedge resection (yes vs. no)	0.982 (0.688, 1.400)	0.92
ASA score		0.001
2 points vs. 1 point	0.555 (0.373, 0.826)	0.004
3 points vs. 1 point	0.897 (0.597, 1.348)	0.60
Pleural adhesions		<0.001
Focal vs. none	0.066 (0.039, 0.111)	<0.001
Diffuse vs. none	0.313 (0.172, 0.570)	<0.001
Benign vs. malignant	0.362 (0.269, 0.487)	<0.001
Nodule diameter (cm)	1.906 (1.679, 2.164)	<0.001
1≤ diameter <1.5 <i>vs.</i> <1	0.147 (0.097, 0.220)	<0.001
1.5≤ diameter <2 <i>vs.</i> <1	0.232 (0.147, 0.366)	<0.001
≥2 <i>vs.</i> <1	0.514 (0.334, 0.792)	0.003
Diabetes (yes <i>vs.</i> no)	0.807 (0.532, 1.223)	0.31
Hypertension (yes <i>v</i> s. no)	1.496 (1.103, 2.028)	0.010
Cardiovascular disease (yes vs. no)	1.611 (0.908, 2.858)	0.10
History of other tumors (yes vs. no)	0.895 (0.577, 1.388)	0.62
History of respiratory disease (yes vs. no)	4.834 (3.151, 7.416)	<0.001
History of thoracic surgery (yes vs. no)	8.780 (3.687, 20.909)	<0.001
Smoking (yes <i>vs.</i> no)	1.478 (1.122, 1.946)	0.005
Drinking (yes vs. no)	1.382 (1.031, 1.853)	0.03
High pulmonary artery pressure (yes vs. no)	0.916 (0.575, 1.459)	0.71
EF value (%)	0.738 (0.068, 8.001)	0.80
EV1%		<0.001
50%≤ FEV1% <80% <i>vs.</i> ≥80%	48.337 (13.278, 175.960)	<0.001
<50% <i>v</i> s. ≥80%	3.856 (2.895, 5.136)	<0.001
Preoperative albumin (g/L)	1.026 (0.988, 1.067)	0.18
Postoperative albumin (g/L)	1.002 (0.983, 1.021)	0.83
Preoperative lymphocyte count (10 <sup>9</sup> /L)	0.844 (0.676, 1.054)	0.14
Postoperative lymphocyte count (10 <sup>9</sup> /L)	0.896 (0.679, 1.182)	0.44

Nodule diameter, refers to the largest nodule size. AL, air leakage; BMI, body mass index; ASA, American Society of Anesthesiologists; EF, ejection fraction; FEV1%, FEV1/FVC ratio; OR, odds ratio; CI, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 3 Multivariable logistic regression analysis of AL presence

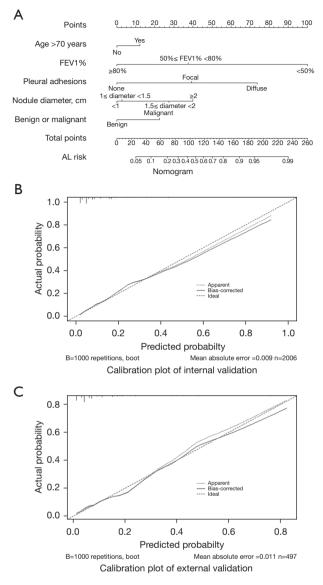
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Factors	В	OR (95% CI)	Р
Age >70 years (yes <i>vs.</i> no)	-0.443	0.642 (0.413, 0.998)	0.045
Pleural adhesions			<0.001
Focal vs. none	-2.713	0.066 (0.036, 0.122)	<0.001
Diffuse vs. none	-1.265	0.282 (0.143, 0.559)	<0.001
Nodule diameter (cm)			<0.001
1≤ diameter <1.5 vs. <1	-1.397	0.247 (0.155, 0.396)	<0.001
1.5≤ diameter <2 <i>vs.</i> <1	-1.304	0.272 (0.161, 0.459)	<0.001
≥2 <i>v</i> s. <1	-0.432	0.649 (0.396, 1.066)	0.09
Benign vs. malignant	-0.871	0.418 (0.295, 0.593)	<0.001
FEV1%			<0.001
50%≤ FEV1% <80% <i>vs.</i> ≥80%	3.502	33.186 (8.176, 134.705)	<0.001
≤50% <i>vs.</i> ≥80%	1.344	3.835 (2.779, 5.292)	<0.001
Sex	0.153	1.165 (0.796, 1.707)	0.43
ASA score			0.66
2 points vs. 1 point	0.228	1.255 (0.766, 2.057)	0.37
3 points vs. 1 point	0.192	1.212 (0.742, 1.980)	0.44
Smoking (yes vs. no)	-0.095	0.910 (0.629, 1.316)	0.62
Drinking (yes vs. no)	-0.065	0.937 (0.625, 1.407)	0.76

Nodule diameter, refers to the largest nodule size. AL, air leakage; FEV1%, FEV1/FVC ratio; OR, odds ratio; Cl, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

have investigated the risk factors for postoperative AL, and there is currently no standardized assessment process for classifying patients as beneficiaries of tubelessness after surgery. The method proposed by Nakashima et al. is still used for tubeless screening (16). The criteria include (I) absence of preoperative pulmonary bullae, emphysema, and significant pleural effusion; (II) lack of severe intraoperative pleural adhesions; (III) absence of AL detected during intraoperative water tests; and (IV) low risk of postoperative bleeding. The intraoperative water test for detecting AL is considered the most critical aspect. However, several studies have suggested that water tests are not sufficiently reliable. Yang et al. compared the outcomes of 30 tubeless wedge resections with those of 30 conventional resections utilizing chest tube drainage (17). The findings revealed that by day 14, 6.6% of the tubeless group still exhibited residual



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**Figure 1** The nomogram and the calibration plots. (A) The nomogram for the preoperative prediction of AL risk after wedge resection. (B,C) The calibration plot of internal and external validation. Nodule diameter, refers to the largest nodule size. FEV1%, FEV1/FVC ratio; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; AL, air leakage.

pneumothorax. Liu *et al.* retrospectively analyzed 135 tubeless pulmonary wedge resection cases in a dual center and found that 13 (9.6%) patients required interventions for postoperative chest drainage (4,17,28).

Attaar *et al.* conducted a meta-analysis of 26 studies on postoperative AL up to 2017, identifying smoking history, low FEV1%, pleural adhesions, and major pulmonary

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Table 4 Clinical characteristics of the 497	patients after wedge resection (data of external validation)
	putternes unter weage resection (auta or enternar variaution)

Variables	Total (n=497)	AL [n=52 (10.46%)]	Non-AL [n=445 (89.54%)]
Age >70 years			
Yes	51 (10.26)	11 (21.15)	40 (8.99)
No	446 (89.74)	41 (78.85)	405 (91.01)
Sex			
Male	258 (51.91)	32 (61.54)	226 (50.79)
Female	239 (48.09)	20 (38.46)	219 (49.21)
BMI (kg/m²)	22.86 (20.82, 24.91)	22.85 (20.72, 25.03)	22.86 (20.83, 24.92)
Operation time (min)	78.00 (63.00, 101.00)	80.50 (70.25, 109.25)	77.00 (62.00, 101.00)
Blood loss (mL)	30.00 (10.00, 50.00)	30.00 (10.00, 50.00)	27.50 (10.00, 50.00)
Multiple wedge resection			
Yes	88 (17.71)	8 (15.38)	73 (16.40)
No	409 (82.29)	44 (84.62)	372 (83.60)
Location of surgery			
Left	199 (40.04)	21 (40.38)	178 (40.00)
Right	298 (59.96)	31 (59.62)	267 (60.00)
ASA score			
1	299 (60.16)	25 (48.08)	274 (61.57)
2	142 (28.57)	21 (40.38)	121 (27.19)
3	56 (11.27)	6 (11.54)	50 (11.24)
Pleural adhesions			
None	442 (88.93)	32 (61.54)	410 (92.13)
Focal	39 (7.85)	11 (21.15)	28 (6.29)
Diffuse	16 (3.22)	9 (17.31)	7 (1.57)
Benign and malignant			
Benign	255 (51.31)	15 (28.85)	240 (53.93)
Malignant	242 (48.69)	37 (71.15)	205 (46.07)
Nodule diameter, cm			
<1	273 (54.93)	16 (30.77)	257 (57.75)
1≤ diameter <1.5	108 (21.73)	10 (19.23)	98 (22.02)
1.5≤ diameter <2	77 (15.49)	14 (26.92)	63 (14.16)
≥2	39 (7.85)	12 (23.08)	27 (6.07)
Diabetes			
Yes	53 (10.66)	5 (9.62)	48 (10.79)
No	444 (89.34)	47 (90.38)	397 (89.21)
Hypertension			
Yes	108 (21.73)	17 (32.69)	91 (20.45)
No	389 (78.27)	35 (67.31)	354 (79.55)

Table 4 (continued)

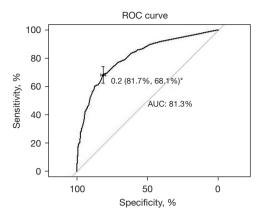
Table 4 (continued)

Variables	Total (n=497)	AL [n=52 (10.46%)]	Non-AL [n=445 (89.54%)]
Cardiovascular disease			
Yes	31 (6.24)	3 (5.77)	28 (6.29)
No	466 (93.76)	49 (94.23)	417 (93.71)
History of other tumors			
Yes	66 (13.28)	5 (9.62)	61 (13.71)
No	431 (86.72)	47 (90.38)	384 (86.29)
History of respiratory disease			
Yes	37 (7.44)	6 (11.54)	31 (6.97)
No	460 (92.56)	46 (88.46)	414 (93.03)
History of thoracic surgery			
Yes	5 (1.01)	1 (1.92)	14 (0.90)
No	492 (98.99)	51 (98.08)	441 (99.1)
Smoking			
Yes	204 (41.05)	20 (38.46)	184 (41.35)
No	293 (58.95)	32 (61.54)	261 (58.65)
Drinking			
Yes	133 (26.76)	17 (32.69)	116 (26.07)
No	364 (73.24)	35 (67.31)	329 (73.93)
High pulmonary artery pressure			
Yes	15 (3.02)	0 (0.00)	15 (3.37)
No	482 (96.98)	52 (100.00)	430 (96.63)
EF value (%)	68.30 (64.70, 71.20)	68.00 (65.00, 71.00)	68.00 (64.00, 72.00)
FEV1%			
≥80%	366 (73.64)	23 (44.23)	343 (77.08)
50%≤ FEV1% <80%	129 (25.96)	27 (51.92)	102 (22.92)
<50%	2 (0.40)	2 (3.85)	0 (0.00)
Preoperative albumin (g/L)	44.00 (41.70, 46.05)	43.75 (41.33, 46.20)	44.00 (41.70, 46.05)
Postoperative albumin (g/L)	36.70 (34.90, 39.25)	36.50 (34.75, 38.15)	36.80 (35.00, 39.50)
Preoperative lymphocyte count (10 <sup>9</sup> L)	1.87 (1.51, 2.30)	1.75 (1.55, 2.10)	1.88 (1.50, 2.31)
Postoperative lymphocyte count (10 <sup>9</sup> /L)	1.10 (0.80, 1.51)	1.06 (0.75, 1.44)	1.10 (0.81, 1.53)

Data are presented as n (%) or median (IQR). Nodule diameter, refers to the largest nodule size. BMI, body mass index; ASA, American Society of Anesthesiologists; EF, ejection fraction; FEV1%, FEV1/FVC ratio; AL, air leakage; IQR, interquartile range; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 5 Performance measures for the definitive model

Aspect	Measure	Development data set	Validation data set
Discrimination	C-index	0.829	0.833
Goodness-of-fit test	Hosmer-Lemeshow	χ²=3.935, P=0.79	χ <sup>2</sup> =7.945, P=0.24



**Figure 2** The receiver operating characteristic curve of the nomogram. \*, data are expressed as an estimated AL probability at the cut-off value (sensitivity, specificity). ROC, receiver operating characteristic; AUC, area under the curve; AL, air leakage.

resection as the key risk factors (29). However, most of the studies focused on lobectomy, and large studies on pulmonary wedge resection were lacking (30-32). For instance, Pompili *et al.* included all patients who underwent lobectomy at their institution from January 2007 to August 2015 (33). Additionally, Murakami excluded wedge resection from the study on the effect of emphysema index on postoperative AL (34).

Our study identified age, low FEV1%, pathological benignity, tumor diameter, and pleural adhesions as risk factors for AL after pulmonary wedge resection. Postoperative lung recovery is greatly affected by age, which has been recognized as a risk factor for AL in several studies (31,35,36). A low FEV1% indicates deteriorated lung function, encompassing higher airway resistance, reduced lung compliance, and an escalated emphysema index (37-39). The tumor diameter determines the extent of the operation, requiring sufficient lung tissue removal to ensure adequate margins. Pathological findings indicate that malignant tumors are more likely to infiltrate the surrounding lung tissue compared to confined benign nodules. This distinction is also an important factor in assessing lung quality (38,40,41). It is important to note that including factors identifiable only postoperatively is inappropriate. However, routine intraoperative frozen section analysis at our center is conducted during wedge resection, with the accuracy of diagnosing benignity or malignancy nearing 100%. This high level of precision enables us to use intraoperative frozen section analysis as a substitute for postoperative pathology in the real-time application of the predictive model. All the above mentioned factors are directly related to the healing process (42,43). Additionally, pleural adhesions lead to increased trauma to lung tissue during surgery and increased pleural pressure levels, which may lead to an increased incidence of postoperative AL (44). Another noteworthy point is that while a "History of thoracic surgery" showed statistical significance in our univariate analysis, we excluded it from the multivariate analysis for several reasons. First, previous thoracic surgeries could cause structural changes such as scarring and pleural adhesions, complicating subsequent surgeries and potentially biasing the study's outcomes. Second, the number of patients in our dataset with a history of thoracic surgery was relatively small-only 21 cases, representing 1.05% of our sample. This small subset could potentially skew the results and reduce the generalizability of our findings. Focusing on factors affecting a larger portion of the patient population, our model aims to provide more reliable and universally applicable predictions.

Wedge resection decreases the damage to lung tissue, as no anatomical manipulation is involved, which reduces the impact of variables such as incomplete lung laceration and anatomical resection (31,39,42,45,46). To enhance compliance with ERAS protocols, we aim to gather additional evidence to reinforce the tubeless strategy. This pioneering multi-center study develops a predictive model for AL following pulmonary wedge resection, marking the first extensive effort in this area. This study sought to create a new predictive model to stratify patients according to their risk of developing postoperative AL. The results of this study are notably reliable, having undergone both internal and external validations with data from multiple centers to ensure its generalizability and practical application across different institutions. This clinical model is useful for clinicians, helping them implement a tubeless strategy in surgeries. By using this model, surgeons can more accurately identify patients who may benefit from less invasive procedures without tubes, leading to quicker and safer recoveries. This approach minimizes complications like pain and infections, and shortens hospital stays, improving both patient outcomes and healthcare efficiency. Furthermore, conducting pulmonary wedge resections as day surgeries embodies the concept of ERAS and reflects the current trend toward optimizing medical resource use. Although most patients undergoing thoracoscopic pulmonary wedge resections are suitable for day surgery, our study helps explicitly target those at high risk of AL, who may not be ideal candidates for such

procedures. Nonetheless, the study's retrospective design is a limitation, highlighting the need for further validation through prospective studies. In the future, we plan to refine the model using more comprehensive data obtained from prospective research, thereby enhancing its applicability in clinical decision-making.

# Conclusions

In summary, we developed and validated a set of nomograms that effectively predict the risk of AL following thoracoscopic pulmonary wedge resection. This robust clinical model assists clinicians in implementing a tubeless strategy, thereby potentially enhancing patient postoperative recovery.

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#### Footnote

*Reporting Checklist:* The authors have completed the TRIPOD reporting checklist. Available at https://jtd. amegroups.com/article/view/10.21037/jtd-24-1090/rc

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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-24-1090/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 received approval from the Ethics Committees of Fujian Medical University Union

Hospital (2024KY182) and patient consent was waived because of the retrospective nature of the study.

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# References

- Saghir Z, Dirksen A, Ashraf H, et al. CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. Thorax 2012;67:296-301.
- Endo C, Sagawa M, Sakurada A, et al. Surgical treatment of stage I non-small cell lung carcinoma. Ann Thorac Cardiovasc Surg 2003;9:283-9.
- Sanchez-Lorente D, Navarro-Ripoll R, Guzman R, et al. Prehabilitation in thoracic surgery. J Thorac Dis 2018;10:S2593-600.
- Zhang JT, Dong S, Chu XP, et al. Randomized Trial of an Improved Drainage Strategy Versus Routine Chest Tube After Lung Wedge Resection. Ann Thorac Surg 2020;109:1040-6.
- Cavallaro P, Bordeianou L. Implementation of an ERAS Pathway in Colorectal Surgery. Clin Colon Rectal Surg 2019;32:102-8.
- Batchelor TJP, Ljungqvist O. A surgical perspective of ERAS guidelines in thoracic surgery. Curr Opin Anaesthesiol 2019;32:17-22.
- Shen C, Che G. No drains in thoracic surgery with ERAS program. J Cardiothorac Surg 2020;15:112.
- Takamochi K, Nojiri S, Oh S, et al. Comparison of digital and traditional thoracic drainage systems for postoperative chest tube management after pulmonary resection: A prospective randomized trial. J Thorac Cardiovasc Surg 2018;155:1834-40.
- Refai M, Brunelli A, Salati M, et al. The impact of chest tube removal on pain and pulmonary function after pulmonary resection. Eur J Cardiothorac Surg 2012;41:820-2; discussion 823.
- 10. Cui F, Liu J, Li S, et al. Tubeless video-assisted

thoracoscopic surgery (VATS) under non-intubated, intravenous anesthesia with spontaneous ventilation and no placement of chest tube postoperatively. J Thorac Dis 2016;8:2226-32.

- Nakamura H, Taniguchi Y, Miwa K, et al. Comparison of the surgical outcomes of thoracoscopic lobectomy, segmentectomy, and wedge resection for clinical stage I non-small cell lung cancer. Thorac Cardiovasc Surg 2011;59:137-41.
- Grills IS, Mangona VS, Welsh R, et al. Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. J Clin Oncol 2010;28:928-35.
- Aiolfi A, Inaba K, Martin M, et al. Lung Resection for Trauma: A Propensity Score Adjusted Analysis Comparing Wedge Resection, Lobectomy, and Pneumonectomy. Am Surg 2020;86:261-5.
- Jacobson MJ, Zand L, Fox RT, et al. A comparison of wedge and segmental resection of the lung. Thorax 1976;31:365-8.
- Watanabe A, Watanabe T, Ohsawa H, et al. Avoiding chest tube placement after video-assisted thoracoscopic wedge resection of the lung. Eur J Cardiothorac Surg 2004;25:872-6.
- Nakashima S, Watanabe A, Mishina T, et al. Feasibility and safety of postoperative management without chest tube placement after thoracoscopic wedge resection of the lung. Surg Today 2011;41:774-9.
- Yang SM, Wang ML, Hung MH, et al. Tubeless Uniportal Thoracoscopic Wedge Resection for Peripheral Lung Nodules. Ann Thorac Surg 2017;103:462-8.
- Luckraz H, Rammohan KS, Phillips M, et al. Is an intercostal chest drain necessary after video-assisted thoracoscopic (VATS) lung biopsy? Ann Thorac Surg 2007;84:237-9.
- Hung MH, Cheng YJ, Chan KC, et al. Nonintubated uniportal thoracoscopic surgery for peripheral lung nodules. Ann Thorac Surg 2014;98:1998-2003.
- Kim WH, Lee HC, Ryu HG, et al. Intraoperative ventilatory leak predicts prolonged air leak after lung resection: A retrospective observational study. PLoS One 2017;12:e0187598.
- 21. Mueller MR, Marzluf BA. The anticipation and management of air leaks and residual spaces post lung resection. J Thorac Dis 2014;6:271-84.
- 22. Jones NL, Edmonds L, Ghosh S, et al. A review of enhanced recovery for thoracic anaesthesia and surgery. Anaesthesia 2013;68:179-89.
- 23. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, et

al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardiothorac Surg 2019;55:91-115.

- 24. Haro GJ, Sheu B, Marcus SG, et al. Perioperative Lung Resection Outcomes After Implementation of a Multidisciplinary, Evidence-based Thoracic ERAS Program. Ann Surg 2021;274:e1008-13.
- Li S, Jiang L, Ang KL, et al. New tubeless video-assisted thoracoscopic surgery for small pulmonary nodules. Eur J Cardiothorac Surg 2017;51:689-93.
- Holbek BL, Hansen HJ, Kehlet H, et al. Thoracoscopic pulmonary wedge resection without post-operative chest drain: an observational study. Gen Thorac Cardiovasc Surg 2016;64:612-7.
- 27. Satherley LK, Luckraz H, Rammohan KS, et al. Routine placement of an intercostal chest drain during videoassisted thoracoscopic surgical lung biopsy unnecessarily prolongs in-hospital length of stay in selected patients. Eur J Cardiothorac Surg 2009;36:737-40.
- Liu CY, Hsu PK, Leong KI, et al. Is tubeless uniportal video-assisted thoracic surgery for pulmonary wedge resection a safe procedure?. Eur J Cardiothorac Surg 2020;58:i70-i76.
- 29. Attaar A, Tam V, Nason KS. Risk Factors for Prolonged Air Leak After Pulmonary Resection: A Systematic Review and Meta-analysis. Ann Surg 2020;271:834-44.
- Rivera C, Bernard A, Falcoz PE, et al. Characterization and prediction of prolonged air leak after pulmonary resection: a nationwide study setting up the index of prolonged air leak. Ann Thorac Surg 2011;92:1062-8; discussion 1068.
- Brunelli A, Varela G, Refai M, et al. A scoring system to predict the risk of prolonged air leak after lobectomy. Ann Thorac Surg 2010;90:204-9.
- 32. Gilbert S, Maghera S, Seely AJ, et al. Identifying Patients at Higher Risk of Prolonged Air Leak After Lung Resection. Ann Thorac Surg 2016;102:1674-9.
- 33. Pompili C, Falcoz PE, Salati M, et al. A risk score to predict the incidence of prolonged air leak after videoassisted thoracoscopic lobectomy: An analysis from the European Society of Thoracic Surgeons database. J Thorac Cardiovasc Surg 2017;153:957-65.
- Murakami J, Ueda K, Tanaka T, et al. Grading of Emphysema Is Indispensable for Predicting Prolonged Air Leak After Lung Lobectomy. Ann Thorac Surg 2018;105:1031-7.

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- 35. Petrella F, Rizzo S, Radice D, et al. Predicting prolonged air leak after standard pulmonary lobectomy: computed tomography assessment and risk factors stratification. Surgeon 2011;9:72-7.
- Singhal S, Ferraris VA, Bridges CR, et al. Management of alveolar air leaks after pulmonary resection. Ann Thorac Surg 2010;89:1327-35.
- Liang S, Ivanovic J, Gilbert S, et al. Quantifying the incidence and impact of postoperative prolonged alveolar air leak after pulmonary resection. J Thorac Cardiovasc Surg 2013;145:948-54.
- Lee L, Hanley SC, Robineau C, et al. Estimating the risk of prolonged air leak after pulmonary resection using a simple scoring system. J Am Coll Surg 2011;212:1027-32.
- Brunelli A, Monteverde M, Borri A, et al. Predictors of prolonged air leak after pulmonary lobectomy. Ann Thorac Surg 2004;77:1205-10; discussion 1210.
- 40. Attaar A, Winger DG, Luketich JD, et al. A clinical

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- 41. Bardell T, Petsikas D. What keeps postpulmonary resection patients in hospital? Can Respir J 2003;10:86-9.
- Brunelli A, Cassivi SD, Halgren L. Risk factors for prolonged air leak after pulmonary resection. Thorac Surg Clin 2010;20:359-64.
- Loran DB, Woodside KJ, Cerfolio RJ, et al. Predictors of alveolar air leaks. Chest Surg Clin N Am 2002;12:477-88.
- Casha AR, Bertolaccini L, Camilleri L, et al. Pathophysiological mechanism of post-lobectomy air leaks. J Thorac Dis 2018;10:3689-700.
- 45. Abolhoda A, Liu D, Brooks A, et al. Prolonged air leak following radical upper lobectomy: an analysis of incidence and possible risk factors. Chest 1998;113:1507-10.
- Cerfolio RJ, Bass CS, Pask AH, et al. Predictors and treatment of persistent air leaks. Ann Thorac Surg 2002;73:1727-30; discussion 1730-1.