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ORIGINAL RESEARCH

Risk factors and predictive model construction for acute respiratory distress syndrome/acute lung injury following lung resection

Xiaochen Lu[1,†], Ziyi He[1,†], Jiajia Lu[2,*]

[1]Department of Thoracic Surgery, The First Affiliated Hospital of Soochow University, 215006 Suzhou, Jiangsu, China
[2]Department of Pharmacy, The First Affiliated Hospital of Soochow University, 215006 Suzhou, Jiangsu, China

***Correspondence**
ljj4121901@163.com
(Jiajia Lu)

† These authors contributed equally.

Abstract

Background: To identify risk factors for acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) after lung resection and develop an effective risk prediction model. **Methods**: A retrospective analysis was conducted on clinical data from patients who underwent lung resection between January 2021 and January 2024. Patients were categorized into two groups: ARDS/ALI (observation group) and non-ARDS/ALI (control group). General characteristics, lung function parameters, surgical indicators, and postoperative laboratory findings were compared between groups. Binary Logistic regression was used to determine independent risk factors for ARDS/ALI, and a prediction model was constructed based on these factors. Model performance was evaluated using the receiver operating characteristic (ROC) curve. **Results**: The observation group included older patients with a higher proportion of smoking index $\geq$400, elevated forced vital capacity (FVC), prolonged surgical duration and one-lung ventilation (OLV) time, higher one-lung airway pressure, and significantly increased postoperative interleukin-6 (IL-6) and white blood cell (WBC) levels (all $p < 0.05$). Multivariate logistic regression analysis identified OLV duration, one-lung airway pressure, postoperative IL-6, postoperative WBC, and age as independent risk factors for ARDS/ALI (all $p < 0.05$). The prediction model, based on these factors, exhibited excellent diagnostic performance with an area under the curve (AUC) of 0.967, sensitivity of 84.80%, and specificity of 97.30%. **Conclusions**: OLV duration, one-lung airway pressure, postoperative IL-6, postoperative WBC, and age are independent risk factors for ARDS/ALI following lung resection. The prediction model, constructed based on these factors, offers high diagnostic accuracy and provides valuable guidance for early identification and intervention of postoperative ARDS/ALI.

Keywords

Lung resection; Acute respiratory distress syndrome; Acute lung injury; Risk factors; Prediction model

1. Introduction

Lung cancer remains a major global health challenge, with surgical treatment serving as the primary therapeutic approach. Advancements in medical technology have reduced the mortality rate of lung cancer and improved patient survival; however, postoperative complications remain a significant issue that demands attention [1, 2]. Among these complications, postoperative pulmonary complications, particularly those associated with general anesthesia during thoracic surgery, are of notable concern. General anesthesia can induce atelectasis, which often progresses to more severe pulmonary complications [3]. These complications are the primary cause of morbidity and mortality following lung resection [4].

Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) are among the severe complications associated with lung cancer resection. These conditions are characterized by a sudden onset, rapid progression and high mortality rates, significantly affecting quality of life in postoperative patients [5, 6]. The incidence of ARDS/ALI following lung cancer resection is alarmingly high, ranging from 2.5% to 11.4% following pneumonectomy and 1.0% to 5.5% following lobectomy, with mortality rates reaching up to 50% [7]. Given their profound impact on patient outcomes, it is imperative to thoroughly analyze the risk factors for ARDS/ALI and develop effective predictive models.

While several scoring systems, such as the Lung Injury Prediction Score (LIPS), Lung Injury Score (LIS), and Acute Physiology and Chronic Health Evaluation (APACHE) II score, have been proposed to assess the risk of postoperative complications, their application specifically to ARDS/ALI following lung cancer surgery remains limited. Current domestic and international studies have yet to comprehensively address the unique risk factors and predictive modeling for ARDS/ALI in the context of pulmonary resection. This study aims to bridge this gap by conducting an in-depth exploration of the risk factors for ARDS and ALI following pulmonary resection, utilizing a combination of retrospective and prospective approaches. Furthermore, this study seeks to construct an effective predictive model to aid in early identification and intervention. By providing a robust framework for clinical decision-making, this research aspires to offer novel insights and strategies for clinical practice and patient management.

2. Methods

2.1 Study population

The study population consisted of patients who underwent lung resection in the thoracic surgery department of our hospital between January 2021 and January 2024.

Inclusion criteria comprised of following patients: ① Those who underwent lung resection, including lobectomy, pneumonectomy, or other lung parenchyma resection surgeries at our hospital; ② Aged ≥18 years; ③ Exhibited preoperative cardiopulmonary function assessment indicating surgical tolerance; ④ Had complete preoperative, intraoperative, and postoperative follow-up data; and ⑤ Provided informed consent for the study.

Exclusion criteria encompassed patients with severe dysfunction of important organs such as the heart, liver, and kidneys, as well as those with preexisting ARDS or ALI before surgery.

After applying the inclusion and exclusion criteria, 330 patients were included and divided into two groups: the observation group (n = 33), comprising those who developed postoperative ARDS/ALI, and the control group (n = 297), consisting of those without these complications. The diagnostic criteria for ARDS/ALI were based on the American-European Consensus Conference (AECC) guidelines, which, despite being superseded in part by the Berlin Definition, remain clinically relevant for this study. While the Berlin Definition refines the AECC criteria and eliminates the ALI classification, the AECC criteria provide indicators that are easier to obtain and assess in clinical practice. For patients undergoing lung resection, the AECC criteria are particularly suitable for better reflecting the actual situation of their postoperative pulmonary complications. According to the AECC criteria, the diagnostic criteria for ARDS/ALI include the following: ① Acute onset within 1 week after exposure to risk factors; ② Chest X-ray or Computed Tomography(CT) showing bilateral lung infiltration shadows, indicating non-cardiac pulmonary edema; ③ A ratio of arterial oxygen partial pressure (PaO_2) to fraction of inspired oxygen (FiO_2) (PaO_2/FiO_2) ≤300 mmHg for ALI and ≤200 mmHg for ARDS; and ④ Pulmonary capillary wedge pressure (PCWP) ≤18 mmHg, or no clinical evidence of significant left atrial pressure elevation, ruling out cardiac pulmonary edema [8].

2.2 Data collection

Comprehensive data were collected for all patients, encompassing general patient information, lung function indicators, surgical parameters, and postoperative laboratory findings. General information included gender, age, body mass index (BMI), history of diabetes, history of hypertension, alcohol consumption history, smoking index (number of cigarettes smoked per day × number of years smoked), obtained from the hospital information system. Lung function indicators included forced vital capacity (FVC) and forced expiratory volume in one second (FEV1), obtained through lung function test. Surgical indicators included the proportion of open surgical procedures, operation duration, intraoperative infusion volume, intraoperative blood loss, oxygen saturation, carbon dioxide partial pressure, duration of one-lung ventilation, and mean one-lung airway pressure, recorded by operating room nurses. Postoperative laboratory findings included serum interleukin (IL)-6, white blood cell (WBC) count, and procalcitonin (PCT) levels. These were measured from venous blood samples drawn 1 day after surgery.

2.3 Statistical methods

Data analysis was conducted using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, and comparisons between groups were performed using either independent samples *t*-test or Mann-Whitney U test. Categorical variables were presented as frequency and percentage, and comparisons between groups were performed using the chi-square test or Fisher's exact test as appropriate. Binary Logistic regression analysis was used to identify independent risk factors for the occurrence of ARDS/ALI. A multivariate prediction model for predicting the risk of ARDS/ALI was established based on the results of multivariate logistic regression analysis. The model's discriminative ability was evaluated using receiver operating characteristic (ROC) curve analysis, with area under the curve (AUC) serving as the primary metric. The significance of the test was set at $\alpha = 0.05$ (two-sided), and *p*-value < 0.05 was considered statistically significant.

3. Results

3.1 Comparison of clinical data

The clinical data revealed significant differences between the observation and control groups. Patients in the observation group were notably older ($p < 0.05$) and a higher proportion of them had a smoking index ≥400 ($p < 0.05$). Additionally, the observation group also exhibited higher forced vital capacity (FVC) ($p < 0.05$), longer operation duration ($p < 0.05$), extended duration of one-lung ventilation ($p < 0.05$), and a higher one-lung airway pressure ($p < 0.05$). They also had higher postoperative serum levels of interleukin-6 (IL-6) and white blood cell (WBC) count ($p < 0.05$) compared to the control group (Table 1).

TABLE 1. Comparison of clinical data between the observation and control groups.

Project	Observation group (n = 33)	Control group (n = 297)	t/χ^2	*p*-value
General Information				
Males, n (%)	23 (69.70)	196 (65.99)	0.183	0.669
Age (yr), Mean ± SD	65.25 ± 5.42	62.50 ± 5.71	2.642	0.009
Body Mass Index (kg/m^2), Mean ± SD	21.88 ± 3.10	22.14 ± 2.88	0.489	0.625
History of diabetes, n (%)	3 (9.09)	29 (9.76)	0.015	0.901
History of hypertension, n (%)	10 (30.30)	95 (31.99)	0.039	0.844
Proportion of drinking history, n (%)	14 (42.42)	130 (43.77)	0.022	0.882
TNM stage ≥ stage III, n (%)	15 (45.45)	170 (57.24)	1.674	0.196
Smoking index ≥400, n (%)	14 (42.42)	70 (23.57)	5.565	0.018
Pulmonary function indicators				
FEV1 (%), Mean ± SD	64.19 ± 6.82	67.01 ± 6.88	2.239	0.026
FVC (%), Mean ± SD	90.09 ± 5.74	92.47 ± 4.68	2.705	0.007
FEV1/FVC, Mean ± SD	0.71 ± 0.07	0.72 ± 0.06	1.021	0.308
Surgical indicators				
Cases with open surgical procedures, n (%)	1 (3.03)	10 (3.37)	0.010	0.919
Surgical duration (min), Mean ± SD	97.38 ± 14.62	84.89 ± 11.69	4.743	<0.001
Intraoperative infusion volume (mL), Mean ± SD	249.72 ± 55.59	243.50 ± 58.10	0.587	0.558
Intraoperative bleeding volume (mL), Mean ± SD	412.32 ± 100.27	421.32 ± 87.39	0.553	0.581
Oxygen saturation, Mean ± SD	89.75 ± 4.81	90.17 ± 5.28	0.447	0.655
Partial pressure of carbon dioxide (mmHg), Mean ± SD	29.15 ± 2.84	30.02 ± 2.94	1.625	0.105
Duration of single lung ventilation (min), Mean ± SD	89.95 ± 9.26	80.21 ± 5.85	5.910	<0.001
Single lung airway pressure (cmH_2O), Mean ± SD	29.75 ± 3.16	26.97 ± 2.58	4.878	<0.001
Postoperative laboratory indicators				
Postoperative IL-6 (pg/mL), Mean ± SD	29.24 ± 8.94	19.99 ± 5.65	5.814	<0.001
Postoperative WBC ($\times 10^9$/L), Mean ± SD	18.28 ± 2.48	14.97 ± 2.29	7.803	<0.001
Postoperative PCT (ng/mL), Mean ± SD	0.79 ± 0.34	0.84 ± 0.36	0.810	0.419

FEV1: forced expiratory volume in one second; FVC: forced vital capacity; IL: interleukin; WBC: white blood cell; PCT: procalcitonin; TNM: tumor-node-metastasis; SD: standard deviation.

3.2 Multivariate analysis

A binary logistic regression analysis was performed to identify independent risk factors for postoperative ARDS/ALI in patients undergoing lung resection surgery. Clinically relevant variables with significant differences between the observation and control groups were included as independent variables, while group assignment served as the dependent variable. The results indicated that age, duration of one-lung ventilation, one-lung airway pressure, postoperative IL-6 levels and postoperative WBC count were independent risk factors for postoperative ARDS/ALI in patients undergoing lung resection surgery (Table 2).

3.3 Establishment of regression model

The correlation analysis showed that the maximum correlation coefficient between the model variables was 0.565, and all variance inflation factors (VIFs) were below 2, indicating the absence of significant autocorrelation among the variables (Table 3). Based on the independent risk factors for postoperative ARDS/ALI in patients undergoing lung resection surgery, a logistic regression model was constructed.

The probability (P) of developing postoperative ARDS/ALI was calculated using following equation:

$$P = 0.230x_1 + 0.290x_2 + 0.413x_3 + 0.285x_4 + 0.439x_5 - 67.283$$

Where x_1, x_2, x_3, x_4 and x_5 represent the independent variables included in the model. Specific details are provided in Table 4.

3.4 ROC curve analysis of the regression model

The ROC curve analysis revealed that the sensitivity and specificity of the model for predicting postoperative ARDS/ALI in patients undergoing lung resection surgery were 84.80% and 97.30%, respectively. The model's AUC was 0.967, indicating a high diagnostic performance and a strong ability to effectively distinguish between patients who developed

TABLE 2. Multivariate logistic regression analysis for postoperative ARDS/ALI in patients undergoing lung resection surgery.

Project	β	SE	Wald χ^2	p	OR	95% CI
Age	0.262	0.086	9.281	0.002	1.299	1.098–1.538
FEV1	0.041	0.065	0.392	0.531	1.042	0.917–1.183
FVC	−0.175	0.100	3.060	0.080	0.839	0.689–1.021
Surgical Duration	0.017	0.029	0.341	0.559	1.017	0.961–1.076
Ventilation Duration	0.298	0.076	15.391	<0.001	1.348	1.161–1.564
Airway Pressure	0.414	0.149	7.686	0.006	1.513	1.129–2.028
IL-6	0.327	0.094	12.054	0.001	1.386	1.153–1.667
WBC	0.570	0.195	8.581	0.003	1.769	1.208–2.591
Smoking Index	1.107	0.807	1.881	0.170	3.024	0.622–14.700

FEV1: forced expiratory volume in one second; FVC: forced vital capacity; IL: interleukin; WBC: white blood cell; SE: standard error; OR: odds ratio; CI: confidence interval.

TABLE 3. Results of collinearity diagnosis of regression model parameters.

	Age	Ventilation Duration	Airway Pressure	IL-6	WBC	VIF
Age	1.000	0.483	0.281	0.342	0.027	1.030
Ventilation Duration	0.483	1.000	0.243	0.565	−0.038	1.100
Airway Pressure	0.281	0.243	1.000	0.041	0.243	1.069
IL-6	0.342	0.565	0.041	1.000	−0.022	1.085
WBC	0.027	−0.038	0.243	−0.022	1.000	1.154

IL: interleukin; WBC: white blood cell; VIF: variance inflation factors.

TABLE 4. Logistic regression model for postoperative ARDS/ALI in patients undergoing lung resection surgery.

Project	Symbol	β	SE	Wald χ^2	p	OR	95% CI
Age	x_1	0.230	0.072	10.043	0.002	1.258	1.092–1.450
Ventilation Duration	x_2	0.290	0.065	19.700	<0.001	1.336	1.176–1.519
Airway Pressure	x_3	0.413	0.138	8.912	0.003	1.511	1.152–1.981
IL-6	x_4	0.285	0.072	15.591	<0.001	1.329	1.154–1.531
WBC	x_5	0.439	0.157	7.854	0.005	1.551	1.141–2.108

IL: interleukin; WBC: white blood cell; SE: standard error; OR: odds ratio; CI: confidence interval.

ARDS/ALI postoperatively and those who did not. Detailed results are presented in Table 5, with the corresponding ROC curve illustrated in Fig. 1.

4. Discussion

Postoperative ARDS/ALI is a common and severe complication in thoracic surgery, especially in patients undergoing lung resection surgery, with a relatively high incidence rate [9]. The pathogenesis of postoperative ARDS/ALI is complex, encompassing systemic inflammatory responses triggered by surgical trauma, lung injury induced by mechanical ventilation, improper postoperative fluid management, and infections [10]. Currently, there is no specific consensus on the diagnosis of postoperative ARDS/ALI in thoracic surgery. As a result, diagnosis often rely on clinical experience, lacking standardized criteria and evidence-based guidelines [11]. While imaging examinations such as CT and X-rays are important means for assessing ARDS/ALI, their complexity, reliance on advanced equipment, and time-intensive nature make them unsuitable for rapid screening or early diagnosis. This situation underscores the importance of developing standardized diagnostic models and early prediction tools to improve patient outcomes.

The results of this study indicated that, compared with the control group, the observation group had significantly higher age ($p < 0.05$), a greater proportion of individuals with a smoking index ≥400 ($p < 0.05$), a higher FVC ($p < 0.05$), a longer operative duration ($p < 0.05$), extended one-lung ventilation ($p < 0.05$), higher one-lung airway pressure ($p < 0.05$), and higher postoperative serum levels of IL-6 and WBC ($p < 0.05$). These findings can be attributed to several underlying mechanisms. Elderly patients experience a decline in lung reserve function and weakened lung tissue repair capacity, resulting in poor tolerance to surgical trauma,

TABLE 5. Diagnostic value of risk factors in the model.

Project	Cut-off	AUC	SE	p	95% CI	Sensitivity	Specificity
Age	62.155	0.633	0.047	0.012	0.541–0.724	0.758	0.508
Ventilation Duration	89.650	0.794	0.049	<0.001	0.698–0.890	0.576	1.000
Airway Pressure	29.545	0.739	0.051	<0.001	0.640–0.838	0.606	0.815
IL-6	26.765	0.802	0.045	<0.001	0.713–0.890	0.636	0.859
WBC	17.460	0.825	0.037	<0.001	0.754–0.897	0.667	0.808
Combined Diagnosis	0.259	0.967	0.015	<0.001	0.937–0.997	0.848	0.973

IL: interleukin; WBC: white blood cell; AUC: area under the curve; SE: standard error; CI: confidence interval.

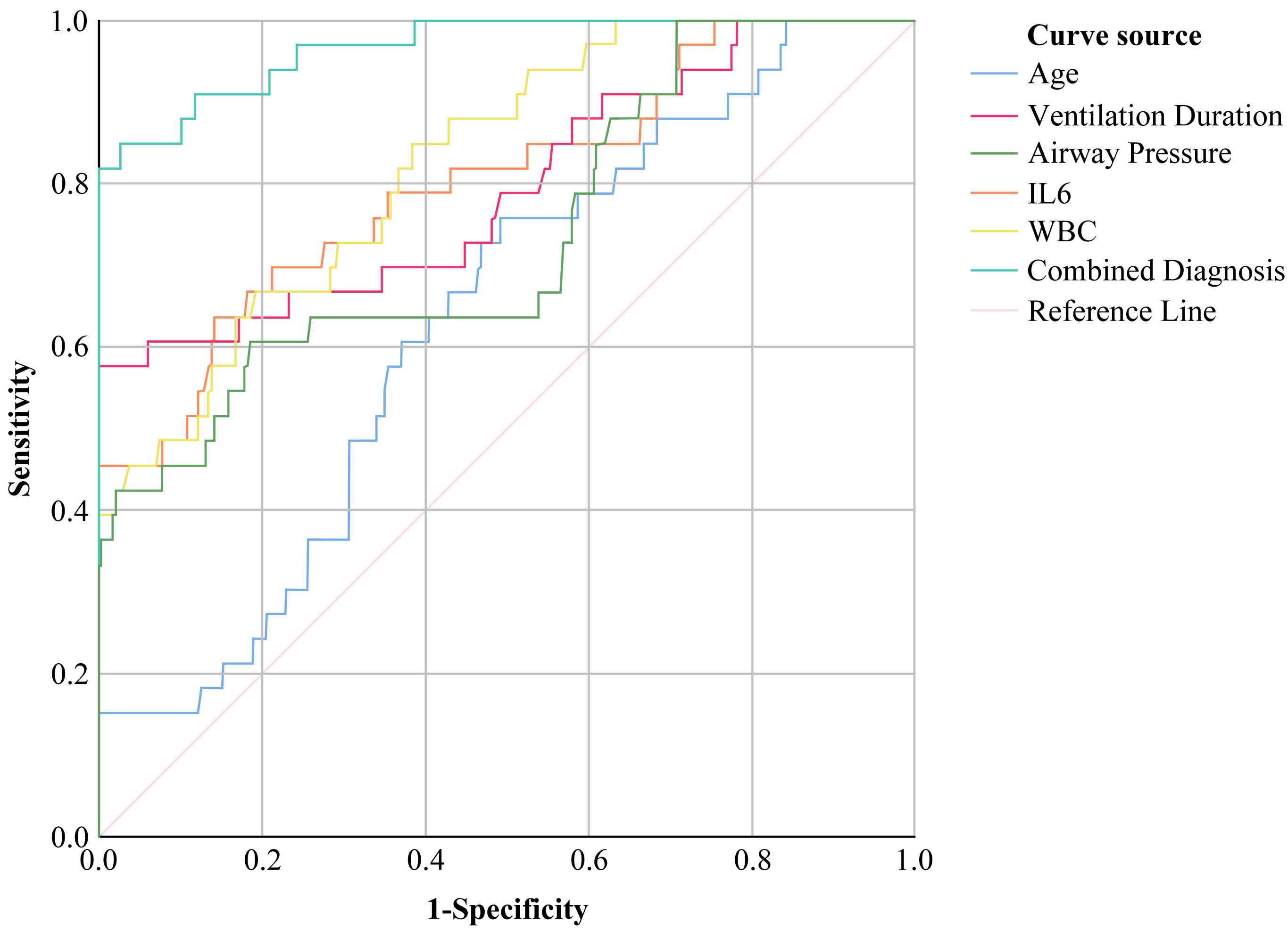

FIGURE 1. ROC curve for independent risk factors in the model. IL6: interleukin-6; WBC: white blood cell.

hypoxia, and postoperative inflammatory responses. A study by Giannakoulis *et al*. [12] showed that advanced age (odds ratio 1.07, 95% confidence interval 1.04–1.09) was associated with increased 90-day mortality in patients with postoperative ARDS. Additionally, comorbid conditions such as chronic obstructive pulmonary disease (COPD) and cardiovascular disease may further elevate the risk of postoperative complications in older patients.

Smoking, a well-established risk factor for lung diseases, exacerbates the risk of postoperative complications. Long-term smoking has been shown to cause lung inflammation, impairs ciliary motility, and increases airway secretions, thereby increasing the risk of postoperative lung infection and respiratory failure. Existing studies have shown that the smoking index is closely related to the incidence of lung diseases such as lung cancer and COPD [13]. A higher FVC may be related to healthier lung parenchyma and larger lung tissue volume. Studies have shown that the decline in preoperative lung function is associated with postoperative pulmonary complications (PPCs) following esophagectomy [14]. Larger lung tissue may be more susceptible to damage due to overinflation or uneven ventilation during one-lung ventilation and mechanical ventilation. Research suggests that open-lung ventilation during cardiopulmonary bypass (CPB) is a potential strategy to alleviate postoperative ARDS [15]. A study by Leng *et al*. [16] involving 1022 esophageal cancer surgery patients, identified operative duration as an independent risk factor for ALI following esophagectomy. Prolonged operative duration increases the duration of anesthetic administration and mechanical ventilation, potentially leading to decreased lung compliance and increased release of inflammatory cytokines [17].

Binary logistic regression analysis in this study revealed that duration of one-lung ventilation, one-lung airway pressure, postoperative IL-6, postoperative WBC, and age were independent risk factors for postoperative ARDS/ALI in patients undergoing lung resection surgery. OLV is widely used technique in thoracic surgery, but its prolonged use is closely associated with the occurrence of ARDS/ALI. Extended OLV may lead to ischemia-reperfusion injury in the operated lung, increasing the release of inflammatory cytokines and subsequently triggering ARDS/ALI. Upon re-ventilation after prolonged hypoxia, the operated lung generates reactive oxygen species (ROS), inducing inflammation and oxidative stress [18]. Studies have also shown that during OLV, the phenotype of alveolar macrophages (AM) in the non-ventilated lung may change, exacerbating the inflammatory response [19]. Additionally, imbalance in ventilation/perfusion (V/Q) ratio, with severe mismatch between ventilation and blood flow can exacerbates hypoxemia. Research has indicated a positive correlation between the duration of OLV and the incidence of postoperative ARDS, suggesting that shortening the duration of OLV can reduce the risk of complications.

Mechanical ventilation-induced lung injury (VILI) caused by high airway pressure is an important precipitating factor in ARDS pathogenesis. High airway pressure can cause alveolar overinflation and disruption of the alveolar-capillary barrier, leading to plasma protein leakage and lung edema. Furthermore, mechanical stretching of airway epithelial cells and alveolar epithelial cells under high pressure also induces the release of inflammatory mediators, exacerbating the inflammatory response. Relevant studies have linked high airway pressure during OLV with an increased incidence of postoperative ARDS, underscoring the need for strategies to optimize ventilatory parameters during surgery [20].

Inflammation plays a crucial role in the development of ARDS/ALI. IL-6, a classic proinflammatory cytokine and WBC count, one of the important indicators reflecting the body's inflammatory response, play a central role in the systemic inflammatory response syndrome (SIRS). Mast cells (MCs) and polymorphonuclear neutrophils (PMNs) are the main inflammatory cells that participates in the process of ALI [21]. Studies have shown that circulating extracellular vesicles overexpressing cancer protein-induced transcript 3 can be absorbed by lung epithelial cells, triggering K48 and K63 polyubiquitination through the transfer of cancer protein-induced transcript 3. This inactivates the NOD-like receptor thermal protein domain associated protein 3 (NLRP3) inflammasome, inhibiting the release of lung proinflammatory cytokines and immune cell infiltration, thereby alleviating CPB-induced ALI [22]. Literature also suggests that surgical trauma, ischemia-reperfusion injury, and mechanical ventilation can activate alveolar macrophages and neutrophils, promoting increased secretion of IL-6. Elevated WBC count reflect the body's immune response to lung inflammation, but excessive high levels of WBC may also lead to excessive inflammation and tissue damage, further exacerbating the condition of ARDS/ALI. A comparative study by Kormish *et al*. [23] identified IL-6, WBC, and Tumor Necrosis Factor (TNF)-α as the independent biomarkers for distinguishing the occurrence of ARDS/ALI in patients undergoing lung surgery.

This study indicated that the predictive model for postoperative ARDS/ALI in patients undergoing lung resection surgery, which was constructed based on duration of one-lung ventilation, one-lung airway pressure, postoperative IL-6, postoperative WBC, and age, had high diagnostic value with an AUC of 0.967, sensitivity of 84.80%, and specificity of 96.70%. This model provides clinicians with an effective tool to assess the risk of postoperative ARDS/ALI in patients undergoing lung resection surgery. By calculating the patient's model score, clinicians can identify high-risk individuals who may benefit from enhanced monitoring and early intervention, ultimately improving patient outcomes. This predictive model represents a significant step toward the early identification and management of ARDS/ALI, facilitating evidence-based decision-making and personalized care in thoracic surgery.

5. Conclusions

This study successfully developed a predictive model for ARDS/ALI complications in patients undergoing lung resection, based on the duration of one-lung ventilation, one-lung airway pressure, postoperative IL-6 levels, postoperative WBC count, and smoking index. The model demonstrates high sensitivity, facilitating early identification of high-risk patients for ARDS/ALI following surgery. Additionally, it's reliance on easily accessible variables makes it convenient for clinical application and promotion.

However, it is worth noting that this study is a retrospective analysis, which depends on the collected clinical data, and may introduce selection bias. In addition, the sample size of the included study is relatively limited, resulting in the performance decline of the model when it is extended to a larger or more heterogeneous patient population. Therefore, the validity of the model needs to be further verified in future large sample and prospective studies.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

XCL, ZYH, JJL—designed the study and carried them out; supervised the data collection; analyzed the data; interpreted the data. XCL, ZYH—prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of The First Affiliated Hospital of Soochow University (Approval no. 2024707). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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