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Original Article

Perioperative ΔNLR and ΔPNI independently predict postoperative pulmonary complications in non-small cell lung cancer: a difference analysis-based nomogram

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Abstract: This study investigated whether perioperative dynamic changes in inflammatory and immunonutritional markers could predict postoperative pulmonary complications (PPCs) in non-small cell lung cancer (NSCLC). We retrospectively enrolled 550 NSCLC patients who underwent radical resection, randomly split at a 7:3 ratio into training (n = 384) and validation (n = 166) sets. PPCs occurred in 126 patients (22.91%), with pneumonia being the most common type. Perioperative ΔWBC, ΔNLR, ΔPLR, ΔCAR, ΔLCR, ΔAGR, and ΔPNI were calculated as the values on postoperative day 1 minus the preoperative values. Through univariate screening, Spearman correlation analysis, variance inflation factor testing, LASSO regression, and multivariate logistic regression, five independent predictors were identified: age, lobectomy, number of lymph nodes dissected, ΔNLR, and ΔPNI. A nomogram incorporating these variables was constructed, achieving an AUC of 0.888 (95% CI: 0.843-0.934) in the training set and 0.887 (95% CI: 0.831-0.942) in the validation set, outperforming the ARISCAT score and single ΔPNI. Calibration was satisfactory (validation set Hosmer-Lemeshow test, P = 0.897; Brier score, 0.106), and decision curve analysis confirmed clinical net benefit. Risk stratification using the nomogram cutoff (0.23) effectively discriminated high-risk patients with significantly worse clinical outcomes. Subgroup and sensitivity analyses demonstrated robust predictive stability without obvious overfitting. The nomogram integrating perioperative ΔNLR and ΔPNI provides a practical tool for early identification and risk stratification of PPCs after NSCLC surgery.

Keywords: Non-small cell lung cancer, postoperative pulmonary complications, perioperative inflammation, difference analysis, neutrophil-to-lymphocyte ratio, prognostic nutritional index, nomogram, risk prediction

Introduction

Non-small cell lung cancer (NSCLC) is the major pathological type of lung cancer (LC). Surgical resection remains an important treatment method for resectable NSCLC patients [1]. The safety of LC surgeries has been significantly improved in parallel with continuously developing thoracoscopic techniques, anesthesia management, perioperative monitoring, and the fast-track surgery concept. However, postoperative pulmonary complications (PPCs), inluding pneumonia, atelectasis, pleural effusion (PE), bronchospasm, respiratory failure (RF), and acute respiratory distress syndrome (ARDS), are among the most common and clinically significant issues in perioperative management of thoracic procedures [2]. These events, beyond prolonging chest tube indwelling time and postoperative hospital stays, also increase antibiotic use, intensive care unit (ICU) admission risk, and medical expenses; they may also lead to unplanned readmission, delayed treatment, and decreased quality of life [3, 4]. For NSCLC patients undergoing pneumonectomy, the combined effects of reduced lung parenchyma, one-lung ventilation (OLV), decreased basic pulmonary function (PF) reserve, and surgical trauma predispose them to postoperative oxygenation disorders and infectious/non-infectious pulmonary complications. Therefore, it is of great significance to identify patients at a high risk of PPCs at an early stage and take targeted prevention and intervention measures during the perioperative period, which aid in improving the quality of postopera-

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tive recovery and optimizing medical resource allocation [5].

At present, the risk assessment of PPCs mainly depends on traditional clinical factors such as age, smoking history, chronic obstructive pulmonary disease (COPD), American Society of Anesthesiologists (ASA) classification, PF, surgical approach, resection extent, operative duration (OD), and the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score [6, 7]. Although these markers reflect patients' basic conditions and surgical trauma severity to some extent, limitations persist. First of all, some scoring systems are mainly based on preoperative data or routine perioperative variables, making it difficult to timely reflect changes in acute inflammatory responses and immune states after surgery [8, 9]. Second, the mechanism underlying PPC occurrence in NSCLC is complicated. Besides old age, smoking, COPD, and surgical invasiveness, inflammatory activation, nutrient consumption, immune imbalances, and stress also play important roles [10, 11]. Third, the predictive efficacy of traditional scores may vary across populations, surgical methods, and perioperative management models. Kim et al. [10] reported the limited predictive performance of FEV1 in the specific mild COPD subgroup, which needed to be supplemented by diffusion function (DF) parameters (e.g., Diffusing capacity of the lungs for carbon monoxide [DLCO]/alveolar volume [VA]), and Lee et al. [11] confirmed that the COPD Assessment Test (CAT) score could further refine the risk stratification of PPCs in this population. Yet, these indicators are still essentially an extension of preoperative static assessment. In addition, with the widespread application of neoadjuvant therapy (NAT) in locally advanced NSCLC, Zhang et al. [12] showed that the predictive value of traditional risk factors in this emerging surgical population needs further verification [13]. Even if more detailed preoperative physiological indexes such as cardiopulmonary exercise testing (CPET) are included, the predictive CPET parameter-based nomogram constructed by Li et al. [13] indicated a Concordance Index (C-index) of only 0.790 for PPCs, suggesting limited incremental space of preoperative static evaluation systems. Therefore, relying solely on traditional clinical scores may not fully meet the needs of individualized risk prediction. There is an urgent need to explore new predictive indicators that can reflect early postoperative pathophysiological changes, and integrate them with clinical factors to establish a more accurate, intuitive, and clinically practical predictive model.

Inflammatory and aimmunonutritional status are closely related to postoperative recovery in tumor patients [14]. Surgical trauma, OLV, lung tissue traction, ischemia-reperfusion, and perioperative infections can all induce systemic inflammatory response, characterized by dynamic changes in leukocytes, neutrophils, lymphocytes, platelets, C-reactive protein (CRP), and albumin (ALB) [15]. Inflammatory or Aimmunonutritional markers derived from these routine laboratory indicators, such as white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), CRP-to-ALB ratio (CAR), lymphocyte-to-CRP ratio (LCR), ALB-to-globulin ratio (AGR), and Prognostic Nutritional Index (PNI), can reflect inflammatory load, immunosuppression, and nutrient reserves from different dimensions. De Frunt (WBC) et al. [16] found that preoperative inflammatory ratios, like NLR and PLR, could not effectively predict the occurrence of major complications post-lobectomy, further suggesting the limited predictive power of single preoperative static indices. In contrast, the difference in perioperative indicators, that is, the difference between the level on day 1 post-operation and the preoperative level, may more intuitively reflect an individual's inflammation level in response to surgical trauma as well as immunonutrition decline extents. Therefore, dynamic analysis based on Δ values is expected to provide more sensitive risk information for PPCs than single-time point measurements.

Against the above background, this study systematically analyzed the association between dynamic changes in perioperative inflammatory markers and PPC occurrence in NSCLC patients undergoing surgery, focusing on the roles of ΔWBC, ΔNLR, ΔPLR, ΔCAR, ΔLCR, ΔAGR, and ΔPNI in predicting PPCs. In the variable screening process, univariate analysis, correlation analysis, multicollinearity testing, Least Absolute Shrinkage and Selection Operator (LASSO) regression, and multivariate Logistic regression (LR) were combined to screen

independent predictors for PPCs for individualized nomogram model construction. The nomogram can integrate dynamic changes in clinical features, surgical factors, and inflammatory markers into a visual risk scoring tool, which is convenient for clinicians to quickly estimate the probability of PPCs after surgery. The model's discrimination, calibration, and clinical net benefits are further evaluated across training and validation sets, and compared with single indices or traditional scores like ΔNLR, ΔPNI, and ARISCAT score; risk stratification, subgroup, and sensitivity analyses are further carried out to verify the nomogram's stability and applicability. By constructing a PPC prediction model based on difference analysis, this study aims to provide a reference for early identification, risk stratification, and accurate perioperative management of PPCs in surgically-treated NSCLC patients.

Materials and methods

Study design

This is a single-center retrospective cohort study, retrospectively including 550 NSCLC patients who underwent radical LC surgery in The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture from January 2022 to December 2025. The study protocol was approved by the Medical Ethics Committee of The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture. Due to the retrospective design, with all data retrieved from previous medical record and inspection systems, the requirement for informed consent was waived by the Ethics Committee.

Sample size calculation

It was based on $N = Z^2 \times [P \times (1\text{-}P)]/E^2$, the formula for estimating a single proportion, where $Z = 1.96$ and the allowable error $E = 0.05$. In previous systematic review and meta-analysis [8], the PPCs combined happened with an incidence of about 18.4% (5833/31696). A minimum sample size of 231 cases was determined based on this prevalence, and the minimum required sample size was about 257 cases after accounting for about 10% with missing or invalid data. A number of 550 cases were finally included, which was sufficient to meet the power requirements.

Study population

Case eligibility required: (1) NSCLC diagnosed by pathology after the operation; (2) radical surgery for LC; (3) age ≥18; (4) complete perioperative clinical, surgical, and laboratory testing data before and on the first day after the operation. Study exclusion was indicated by: (1) preoperative pulmonary infection, atelectasis, PE, RF, or other active pulmonary complications; (2) lack of perioperative data, laboratory indicators, or primary endpoint-associated information; (3) additional malignant tumors; (4) repeat lung surgery due to recurrence, metastasis, or postoperative complications; (5) or emergency or non-radical surgeries. Finally, a random allocation with a 7:3 split was carried out (random seed: 2026), dividing 384 cases to the training and 166 to the validation set; (6) patients whose PPCs were clinically diagnosed on postoperative day 1 were excluded to ensure that all blood-based predictor measurements preceded the outcome in time.

Data collection and variable definition

The patients' demographics, basic diseases, tumor characteristics, operation-related data, perioperative inflammatory markers, and postoperative clinical outcomes were collected through the electronic medical record system. Demographics covered age, sex, and body mass index (BMI); past history recorded smoking, drinking, COPD, hypertension, diabetes, coronary heart disease (CHD), cerebrovascular disease (CVD), and NAT. Perioperative risk assessments included the ASA classification and the ARISCAT risk score; the latter was calculated according to age, preoperative oxygen saturation, recent respiratory infection, preoperative anemia, surgical incision site, OD, and emergency operation, and categorized as low, intermediate, or high risk.

Tumor and operation-related variables assessed tumor stage, pathological type, maximum tumor diameter (MTD), surgical approach, resection extent, surgical laterality, OD, anesthesia duration, OLV time, intraoperative blood loss (IBL), intraoperative fluid volume (IFV), number of lymph nodes dissected, and postoperative analgesia mode. Tumor stage followed the TNM staging system, 8th edition. MTD was recorded according to the postoperative pathological report. Surgical methods

were classified as thoracoscopic surgery or thoracotomy. The resection extent was broken down into lobectomy, segmentectomy, or wedge resection, which could be combined into lobectomy or sublobectomy according to the needs of subsequent model analysis.

Perioperative laboratory indicators were derived from the routine test results of the clinical laboratory of our hospital. Blood testing was based on morning fasting venous blood, with samples collected within 3 days before the operation and on the first day post-operation. The test items included WBC, neutrophil count, lymphocyte count, platelet count, CRP, ALB, and globulin. Blood cell-related indexes were detected with the use of an automatic hematology analyzer (Sysmex XN-9000, Sysmex Corporation, Japan), while biochemical indices were measured with an automatic biochemical analyzer (Roche Cobas 8000 c702 module, Roche Diagnostics, Switzerland). All tests were carried out with the original reagents provided with the instruments, in strict accordance with the manufacturer's instructions; the testing was completed by standardized and trained inspectors, with the laboratory quality control conforming to the national clinical laboratory quality control standards. The derived inflammatory and immunonutritional indicators were calculated as follows: NLR = neutrophil count/lymphocyte count; PLR = platelet count/lymphocyte count; CAR = CRP/ALB; LCR = lymphocyte count/CRP; AGR = ALB/globulin; PNI = ALB × 10 + lymphocyte count × 5. The Δ value of each index was defined as the value on the first day post-operation minus the preoperative value, that is, Δ = postoperative day 1 value - preoperative value.

Outcomes

The primary endpoint was the occurrence of PPCs. The PPCs monitored included pneumonia, atelectasis, PE requiring intervention, bronchospasm, RF, and ARDS. Among them, mild PPCs referred to pneumonia and atelectasis, while the rest (PE requiring intervention, bronchospasm, RF, and ARDS) were severe PPCs. Pneumonia was diagnosed based on postoperative new-onset or progressive pulmonary infiltration on imaging, combined with clinical evidence such as pyrexia, cough, expectoration, purulent sputum, leukocyte disorder, or the need for anti-infection treatment. The diagnosis of atelectasis was made by imaging evidence of pulmonary lobe or segmental atelectasis with corresponding clinical manifestations. Intervention-requiring PE was defined as the presence of pleural fluid confirmed by imaging that required thoracic puncture, catheter drainage, or other therapeutic intervention. Bronchospasm was indicated by postoperative wheezing, increased airway resistance, or the need for bronchodilator treatment. RF was defined as postoperative oxygenation disorder and the need for noninvasive or invasive ventilation support. ARDS diagnosis followed the Berlin definition. Secondary endpoints included postoperative hospital stay, chest tube indwelling time, time to initial postoperative ambulation, antibiotic use duration, total hospitalization expenses, ICU admission rate, unplanned 30-day hospital readmission rate, and reoperation rate.

Statistical analysis

Data were imported into SPSS 27.0 and R 4.5.1 for statistical analysis. For normally distributed continuous variables, the mean ± standard deviation was utilized for statistical description, and the independent sample t-test was used for comparison between groups. If non-Gaussian distributed, the continuous variables were represented by the median [quartile], with between-group comparisons made using the Mann-Whitney U tests. Categorical variables, expressed by frequencies and percentages, were comparatively assessed with the χ^2 test or Fisher's exact test. All tests were two-tailed and employed a $P<0.05$ threshold.

For modeling, variable screening was first performed in the training set. The candidate variables were those with $P<0.1$ screened by univariate LR. Subsequently, how the candidate variables were correlated was assessed by Spearman correlation analysis, with a high correlation indicated by $|r|\geq0.7$; variable retention was determined by combining univariate results and clinical significance. Then came multicollinearity evaluation with the variance inflation factor (VIF), with VIF<5 indicating no obvious collinearity. Following the above steps, the glmnet package was used for LASSO regression analysis, and the optimal penalty parameters were determined by 10-fold cross-

validation, with variables screened by the lambda.min criterion. The variables obtained by LASSO screening were included in multivariate LR analysis, and the results were expressed by odds ratios (ORs) and 95% confidence intervals (CIs).

Based on the independent predictors, namely those with P<0.05 in the multivariate LR, the nomogram model for predicting the risk of PPCs was constructed by the rms package. Receiver operating characteristic (ROC) curve, area under the curve (AUC), C-statistic, Youden index, sensitivity, and specificity were used to evaluate the model discrimination. The calibration degree of the model was evaluated by the calibration curve, Hosmer-Lemeshow (HL) test, and Brier score. Clinical practicability was evaluated by decision curve analysis (DCA). ROC curve plotting and DeLong test were carried out by using the pROC package, and AUC differences between the nomogram and ΔNLR, ΔPNI, and the ARISCAT score were assessed.

Furthermore, 550 patients in the training and validation sets were merged for subgroup analysis. The adjusted OR and 95% CI across subgroups were calculated with each 0.1 increase in nomogram prediction risk as the effect unit; the predictive consistency of the model in subgroups stratified by age, gender, surgical method, resection extent, COPD, tumor stage, and ARISCAT risk stratification was evaluated by the test for interaction. Sensitivity analysis consisted of three parts: first, variable screening by the lambda.1se criterion and reconstruction of a conservative model; second, risk stratification verification using 0.20, 0.25, and 0.30 as alternative risk thresholds; third, internal stability and over-fitting risk assessments of the main model using Bootstrap resampling with 1000 iterations.

Results

Basic characteristics of the research participants and the occurrence of PPCs

550 surgically-treated NSCLC patients were included, among whom 126 (22.91%) developed PPCs and 424 (77.09%) did not. In the PPCs group, mild complications (pneumonia and atelectasis) dominated (63.49%), while severe complications (PE requiring intervention, RF, and ARDS) accounted for 36.51%. Among individual complications, pneumonia ranked first in prevalence, followed by atelectasis and intervention-requiring PE.

Baseline data comparison showed that PPC patients was significantly older than their non-PPC counterparts (P = 0.001), together with higher proportions of smoking history (P = 0.019), comorbid COPD (P = 0.001), ASA grade III-IV (P = 0.006), and the ARISCAT high-risk category (P<0.001). Concerning tumor characteristics, this study found a greater MTD in PPC patients compared with non-PPC cases (P<0.001). Among operation-related factors, the PPCs group showed a greater number of patients undergoing thoracotomy (P = 0.028) and lobectomy (P = 0.025), alongside longer operative (P<0.001), anesthesia (P<0.001), and OLV duration time (P<0.001), as well as greater IFV (P<0.001), a greater number of lymph nodes dissected (P<0.001), and greater IBL (P = 0.039).

Gender (P = 0.072), BMI (P = 0.155), drinking history (P = 0.421), comorbidities (hypertension, P = 0.340; diabetes, P = 0.064; CHD, P = 0.069; CVD, P = 0.364), NAT history, (P = 0.223), tumor stage (P = 0.155), pathological type (P = 0.825), surgical laterality (P = 0.631), and postoperative analgesia method (P = 0.072) did not differ significantly between the groups (all P>0.05; **Table 1**).

Characteristics of dynamic changes in perioperative inflammatory markers

Table 2 is a visualization of the dynamic changes in perioperative inflammatory markers. The comparison of baseline (preoperative) levels of each marker revealed significant inter-group differences in AGR (P = 0.001) and PNI (P = 0.042), with lower levels in the PPCs group versus the non-PPCs group. No statistically significant between-group differences were observed for preoperative WBC, NLR, PLR, CAR, and LCR (all P>0.05). On day 1 post operation, all inflammatory markers changed markedly compared with their baseline levels, with statistical significance identified between groups (P<0.001). Compared with non-PPC patients, WBC, NLR, PLR, and CAR in PPC patients increased significantly on the first postoperative day, while LCR, AGR, and PNI decreased significantly; this suggests that patients who developed PPCs had a more

Table 1. Comparison of baseline clinical characteristics (PPCs group vs. non-PPCs group)

Variable	Categories	Total (n=550)	PPCs group (n=126)	Non-PPCs group (n=424)	Statistic	P
PPC severity stratification		-	(n = 126, used for the description within the PPCs group only)	-(Not applicable to non-PPCs)	-	-
	Mild	-	80 (63.49%)	-		
	Severe	-	46 (36.51%)	-		
PPC types		-	(n = 126, used for the description within the PPCs group only)	-(Not applicable to non-PPCs)	-	-
-	Pneumonia	-	46 (36.51%)	-		
	Atelectasis	-	34 (26.98%)	-		
	Pleural effusion requiring intervention	-	26 (20.63%)	-		
	Bronchospasm	-	12 (9.52%)	-		
	Respiratory failure	-	6 (4.76%)	-		
	ARDS	-	2 (1.59%)	-		
Age (years)	(Continuous variable)	61.93±8.97	64.19±9.02	61.25±8.86	t = -3.256	0.001
BMI (kg/m^2)	(continuous variable)	24.05 [21.40, 26.20]	23.65 [21.12, 25.90]	24.10 [21.50, 26.20]	Z = 1.421	0.155
Sex					χ^2 = 3.231	0.072
	Male	302 (54.91%)	78 (61.90%)	224 (52.83%)		
	Female	248 (45.09%)	48 (38.10%)	200 (47.17%)		
Smoking history					χ^2 = 5.474	0.019
	Yes	264 (48.00%)	72 (57.14%)	192 (45.28%)		
	No	286 (52.00%)	54 (42.86%)	232 (54.72%)		
Drinking history					χ^2 = 0.647	0.421
	Yes	142 (25.82%)	36 (28.57%)	106 (25.00%)		
	No	408 (74.18%)	90 (71.43%)	318 (75.00%)		
Comorbid hypertension					χ^2 = 0.911	0.340
	Yes	190 (34.55%)	48 (38.10%)	142 (33.49%)		
	No	360 (65.45%)	78 (61.90%)	282 (66.51%)		
Comorbid diabetes					χ^2 = 3.437	0.064
	Yes	108 (19.64%)	32 (25.40%)	76 (17.92%)		
	No	442 (80.36%)	94 (74.60%)	348 (82.08%)		
Comorbid coronary heart disease					χ^2 = 3.296	0.069
	Yes	70 (12.73%)	22 (17.46%)	48 (11.32%)		
	No	480 (87.27%)	104 (82.54%)	376 (88.68%)		
Comorbid COPD					χ^2 = 10.542	0.001
	Yes	110 (20.00%)	38 (30.16%)	72 (16.98%)		
	No	440 (80.00%)	88 (69.84%)	352 (83.02%)		
Comorbid cerebrovascular disease					χ^2 = 0.826	0.364
	Yes	42 (7.64%)	12 (9.52%)	30 (7.08%)		
	No	508 (92.36%)	114 (90.48%)	394 (92.92%)		

History of neoadjuvant therapy					χ^2 = 1.483	0.223
	Yes	62 (11.27%)	18 (14.29%)	44 (10.38%)		
	No	488 (88.73%)	108 (85.71%)	380 (89.62%)		
ASA grading					χ^2 = 7.700	0.006
	I-II	354 (64.36%)	68 (53.97%)	286 (67.45%)		
	III-IV	196 (35.64%)	58 (46.03%)	138 (32.55%)		
ARISCAT score					χ^2 = 27.593	<0.001
	Low risk (<26 points)	196 (35.64%)	28 (22.22%)	168 (39.62%)		
	Intermediate risk (26-44 points)	252 (45.82%)	56 (44.44%)	196 (46.23%)		
	High risk (≥45 points)	102 (18.55%)	42 (33.33%)	60 (14.15%)		
Tumor stage					χ^2 = 3.731	0.155
	I	266 (48.36%)	52 (41.27%)	214 (50.47%)		
	II	170 (30.91%)	42 (33.33%)	128 (30.19%)		
	III	114 (20.73%)	32 (25.40%)	82 (19.34%)		
Pathological type					χ^2 = 0.384	0.825
	Adenocarcinoma	336 (61.09%)	74 (58.73%)	262 (61.79%)		
	Squamous cell carcinoma	156 (28.36%)	38 (30.16%)	118 (27.83%)		
	Other	58 (10.55%)	14 (11.11%)	44 (10.38%)		
Maximum tumor diameter (cm)	(Continuous variable)	2.90 [2.10, 3.80]	3.30 [2.42, 4.10]	2.80 [2.00, 3.60]	Z = 3.842	<0.001
Surgical approach					χ^2 = 4.820	0.028
	Thoracoscopic surgery	400 (72.73%)	82 (65.08%)	318 (75.00%)		
	Thoracotomy	150 (27.27%)	44 (34.92%)	106 (25.00%)		
Resection extent					χ^2 = 7.381	0.025
	Lobectomy	364 (66.18%)	96 (76.19%)	268 (63.21%)		
	Segmentectomy	116 (21.09%)	18 (14.29%)	98 (23.11%)		
	Wedge resection	70 (12.73%)	12 (9.52%)	58 (13.68%)		
Surgical laterality					χ^2 = 0.231	0.631
	Left	246 (44.73%)	54 (42.86%)	192 (45.28%)		
	Right	304 (55.27%)	72 (57.14%)	232 (54.72%)		
Operative duration (min)	(Continuous variable)	167.00 [133.00, 200.00]	187.00 [141.25, 221.50]	161.00 [130.75, 194.00]	Z = 4.325	<0.001
Anesthesia duration (min)	(Continuous variable)	189.50 [148.00, 227.75]	207.50 [167.00, 250.75]	182.00 [141.75, 218.25]	Z = 4.809	<0.001
One-lung ventilation time (min)	(Continuous variable)	114.50 [87.00, 137.00]	131.00 [108.25, 157.75]	107.00 [85.00, 131.00]	Z = 5.711	<0.001
Intraoperative blood loss (mL)	(Continuous variable)	179.00 [125.25, 241.00]	178.50 [153.50, 258.00]	179.50 [117.00, 238.00]	Z = 2.066	0.039
Intraoperative fluid volume (mL)	(Continuous variable)	1136.00 [909.25, 1356.00]	1239.00 [1025.75, 1454.75]	1116.00 [878.00, 1319.25]	Z = 3.976	<0.001
Lymph nodes dissected	(Continuous variable)	16.00 [13.00, 19.00]	19.00 [15.00, 22.00]	15.00 [12.00, 19.00]	Z = 5.831	<0.001
Postoperative analgesic method					χ^2 = 5.275	0.072
	Epidural analgesia	186 (33.82%)	32 (25.40%)	154 (36.32%)		
	Patient-controlled intravenous analgesia	298 (54.18%)	76 (60.32%)	222 (52.36%)		
	Others/none	66 (12.00%)	18 (14.29%)	48 (11.32%)		

Note: PPCs, postoperative pulmonary complications; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ARDS, acute respiratory distress syndrome. Continuous variables are presented as mean ± SD for those passing the Shapiro-Wilk normality test and as median [IQR] for non-normally distributed variables.

Table 2. Comparison of dynamic changes in perioperative inflammatory markers

Variable	Total (n = 550)	PPCs group (n = 126)	Non-PPCs group (n=424)	Statistic	P
ΔWBC (×10^9/L)					
Pre-operation	6.60 [5.40, 7.64]	6.82 [5.47, 7.93]	6.58 [5.40, 7.58]	Z = 1.617	0.106
Postoperative 1 day	10.32 [8.65, 12.46]	12.96 [10.82, 14.50]	9.90 [8.34, 11.62]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	3.81 [1.73, 6.28]	5.90 [3.47, 8.62]	3.40 [1.46, 5.65]	Z = 6.657	<0.001
ΔNLR					
Pre-operation	2.29 [1.74, 2.89]	2.39 [1.77, 3.01]	2.25 [1.74, 2.86]	Z = 0.978	0.328
Postoperative 1 day	5.72 [4.13, 7.62]	8.73 [7.01, 11.04]	5.13 [3.81, 6.71]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	3.36 [2.08, 5.22]	6.44 [4.71, 8.20]	2.80 [1.87, 3.95]	Z = 8.222	<0.001
ΔPLR					
Pre-operation	121.45 [90.30, 146.16]	119.94 [89.63, 149.33]	121.53 [91.28, 145.41]	Z = 0.310	0.757
Postoperative 1 day	166.31 [129.30, 202.99]	200.81 [162.81, 236.00]	157.93 [121.94, 191.53]	Z = 6.980	<0.001
Δ value (Postoperative 1 day - pre-operation)	44.69 [3.00, 89.98]	84.29 [33.03, 120.21]	35.59 [-2.91, 71.00]	Z = 6.037	<0.001
ΔCAR					
Pre-operation	0.13 [0.07, 0.18]	0.14 [0.07, 0.19]	0.13 [0.07, 0.18]	Z = 0.744	0.457
Postoperative 1 day	1.44 [0.98, 2.01]	2.21 [1.58, 2.76]	1.31 [0.87, 1.77]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	1.33 [0.86, 1.87]	2.06 [1.43, 2.56]	1.18 [0.76, 1.63]	Z = 8.222	<0.001
ΔLCR					
Pre-operation	0.49 [0.37, 0.63]	0.46 [0.35, 0.62]	0.49 [0.38, 0.63]	Z = 1.299	0.194
Postoperative 1 day	0.16 [0.10, 0.22]	0.09 [0.05, 0.13]	0.18 [0.13, 0.24]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	-0.33±0.19	-0.38±0.19	-0.32±0.19	t = 3.475	<0.001
ΔAGR					
Pre-operation	1.54 [1.40, 1.68]	1.50 [1.35, 1.62]	1.56 [1.42, 1.69]	Z = 3.269	0.001
Postoperative 1 day	1.34 [1.20, 1.49]	1.15 [1.00, 1.29]	1.38 [1.27, 1.51]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	-0.21±0.29	-0.31±0.30	-0.18±0.28	t = 4.437	<0.001
ΔPNI					
Pre-operation	50.16 [45.88, 54.33]	49.37 [44.25, 53.47]	50.56 [46.29, 54.47]	Z = 2.033	0.042
Postoperative 1 day	43.13 [38.84, 47.44]	38.03 [34.23, 41.99]	44.13 [40.81, 48.27]	Z = 8.222	<0.001
Δ value (Postoperative 1 day - pre-operation)	-7.13±8.00	-10.46±8.34	-6.14±7.63	t = 5.451	<0.001

Note: PPCs, postoperative pulmonary complications; WBC, white blood cell count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; LCR, lymphocyte-to-C-reactive protein ratio; AGR, albumin-to-globulin ratio; PNI, Prognostic Nutritional Index; Δ, delta value. Continuous variables are presented as mean ± SD for those passing the Shapiro-Wilk normality test and as median [IQR] for non-normally distributed variables.

intense inflammatory reaction and a greater decline in nutritional and immune function after the operation. In the Δ value (the level on day 1 postoperation - the level preoperation) analysis, we observed greater changing amplitudes of all markers in the PPCs group versus the non-PPCs group (P<0.001): ΔWBC (P< 0.001), ΔNLR (P<0.001), ΔPLR (P<0.001), and ΔCAR (P<0.001) showed a more pronounced increase in PPC patients, while ΔLCR (P< 0.001), ΔAGR (P<0.001), and ΔPNI (P<0.001) exhibited a greater decline. It indicates that the difference in perioperative changes of inflammatory markers may have stronger predictive value than the measured values at a single time point (**Table 2**).

Comparison of baseline characteristic balance between training and validation sets

The 550 included patients were randomly allocated at a 7:3 ratio, resulting in a training set with 384 cases and a validation set with 166. The baseline characteristic comparison indicated balanced distributions across groups for age, BMI, sex, smoking/drinking history, comorbidities (hypertension, diabetes, CHD, COPD, CVD), history of NAT, ASA grade, tumor stage, pathological type, MTD, surgical approach, resection extent, OD, anesthesia duration, OLV time, IBL, IFV, and lymph nodes dissected (all P>0.05). ARISCAT risk stratification also differed insignificantly (P = 0.071). When assessing differences in perioperative inflammatory markers, we noted compatibility between the training and validation sets in terms of ΔWBC, ΔNLR, ΔPLR, ΔCAR, ΔLCR, ΔAGR, and ΔPNI (P>0.05). It suggests well-balanced variation characteristics of inflammatory indicators across the groups, which supports the reliability of the random allocation scheme and the feasibility of the prediction model established in the training set for the external evaluation of the validation set (**Table 3**).

Comparison of clinical characteristics and perioperative inflammatory markers between PPCs and non-PPCs groups in the training set

88 (22.92%) of the 384 patients included in the training set developed PPCs. In the PPCs group, mild complications (pneumonia and atelectasis) dominated (63.64%), while severe complications (PE requiring intervention, RF, and ARDS) accounted for 36.36%. Pneumonia ranked first in prevalence among individual complications, followed successively by atelectasis and intervention-requiring PE. As shown by the baseline data comparison, PPC patients were significantly older than their non-PPC counterparts (P = 0.015), together with higher proportions of smoking history (P = 0.009), comorbid COPD (P = 0.024), ASA grade III-IV (P = 0.024), and ARISCAT risk stratification (P = 0.001). Concerning tumor characteristics, we identified a greater MTD in PPC patients versus non-PPC cases (P = 0.017). Assessing operation-related factors, the PPCs group was found to have a greater number of patients undergoing thoracotomy (P = 0.004) and lobectomy (P = 0.002), alongside longer operative (P< 0.001), anesthesia (P<0.001), and OLV duration (P<0.001), as well as greater IFV (P = 0.001), lymph nodes dissected (P<0.001), and IBL (P = 0.036). There were no statistically significant differences between the groups in BMI, sex, drinking history, comorbidities (hypertension, diabetes, CHD, and CVD), NAT history, tumor stage, or pathological type (all P>0.05). In the comparison of perioperative inflammatory markers, ΔWBC, ΔNLR, ΔPLR, and ΔCAR presented higher levels in PPC patients than in non-PPC cases (all P<0.001), while ΔLCR, ΔAGR, and ΔPNI showed reduced values (all P<0.001). Thus, perioperative patients who developed PPCs exhibited more intense inflammation as well as a more pronounced decline in immunonutritional status (**Table 4**).

Correlation analysis, multicollinearity testing, and LASSO variable screening of candidate variables

Taking P<0.1 in the univariate LR in the training set as the threshold, 17 candidate variables were screened out for subsequent analysis. Spearman correlation analysis revealed a high correlation between OD and anesthesia duration ($|r|\geq0.7$); OD, with a smaller univariate *P* value, was retained while anesthesia duration was excluded. A high correlation between ΔNLR and ΔCAR was also determined, with ΔNLR retained and ΔCAR eliminated. After correlation-based screening, the remaining 15 variables entered the VIF-based multicollinearity test (**Figure 1A**), which revealed an VIF below 5 for all 15 candidate variables, demonstrating no obvious multicollinearity and thus allowing all 15 variables to be incorporated into the

Table 3. Comparison of baseline characteristics between training and validation sets

Variable	Categories	Total	Training set (n = 384)	Validation set (n = 166)	Statistic	P
Age (years)		61.93±8.97	62.03±8.89	61.69±9.17	t = 0.410	0.682
BMI (kg/m^2)		24.05 [21.40, 26.20]	24.00 [21.40, 26.20]	24.10 [21.40, 26.00]	Z = 0.213	0.831
Sex					χ^2 = 0.600	0.439
	Male	302 (54.91%)	215 (55.99%)	87 (52.41%)		
	Female	248 (45.09%)	169 (44.01%)	79 (47.59%)		
Smoking history					χ^2 = 0.757	0.384
	No	286 (52.00%)	195 (50.78%)	91 (54.82%)		
	Yes	264 (48.00%)	189 (49.22%)	75 (45.18%)		
Drinking history					χ^2 = 1.699	0.192
	No	408 (74.18%)	291 (75.78%)	117 (70.48%)		
	Yes	142 (25.82%)	93 (24.22%)	49 (29.52%)		
Comorbid hypertension					χ^2 = 0.269	0.604
	No	360 (65.45%)	254 (66.15%)	106 (63.86%)		
	Yes	190 (34.55%)	130 (33.85%)	60 (36.14%)		
Comorbid diabetes					χ^2 = 0.009	0.925
	No	442 (80.36%)	309 (80.47%)	133 (80.12%)		
	Yes	108 (19.64%)	75 (19.53%)	33 (19.88%)		
Comorbid coronary heart disease					χ^2 = 0.059	0.808
	No	480 (87.27%)	336 (87.50%)	144 (86.75%)		
	Yes	70 (12.73%)	48 (12.50%)	22 (13.25%)		
Complicated with COPD					χ^2 = 0.779	0.378
	No	440 (80.00%)	311 (80.99%)	129 (77.71%)		
	Yes	110 (20.00%)	73 (19.01%)	37 (22.29%)		
Comorbid cerebrovascular disease					χ^2 = 2.287	0.130
	No	508 (92.36%)	359 (93.49%)	149 (89.76%)		
	Yes	42 (7.64%)	25 (6.51%)	17 (10.24%)		
History of neoadjuvant therapy					χ^2 = 1.189	0.276
	No	488 (88.73%)	337 (87.76%)	151 (90.96%)		
	Yes	62 (11.27%)	47 (12.24%)	15 (9.04%)		
ASA grading					χ^2 = 0.375	0.540
	I-II	354 (64.36%)	244 (63.54%)	110 (66.27%)		
	III-IV	196 (35.64%)	140 (36.46%)	56 (33.73%)		
ARISCAT score					χ^2 = 5.286	0.071
	Low risk	196 (35.64%)	125 (32.55%)	71 (42.77%)		
	High risk	102 (18.55%)	75 (19.53%)	27 (16.27%)		
	Intermediate risk	252 (45.82%)	184 (47.92%)	68 (40.96%)		

Tumor stage					χ^2 = 1.674	0.433
	I	266 (48.36%)	185 (48.18%)	81 (48.80%)		
	II	170 (30.91%)	124 (32.29%)	46 (27.71%)		
	III	114 (20.73%)	75 (19.53%)	39 (23.49%)		
Pathological type					χ^2 = 1.188	0.552
	Squamous cell carcinoma	156 (28.36%)	109 (28.39%)	47 (28.31%)		
	Other	58 (10.55%)	44 (11.46%)	14 (8.43%)		
	Adenocarcinoma	336 (61.09%)	231 (60.16%)	105 (63.25%)		
Maximum tumor diameter (cm)	Continuous variable	2.90 [2.10, 3.80]	2.80 [2.00, 3.80]	3.10 [2.20, 3.70]	Z = 0.772	0.440
Surgical approach					χ^2 = 1.209	0.271
	Thoracotomy	150 (27.27%)	110 (28.65%)	40 (24.10%)		
	Thoracoscopic surgery	400 (72.73%)	274 (71.35%)	126 (75.90%)		
Resection extent					χ^2 = 1.018	0.313
	Lobectomy	364 (66.18%)	249 (64.84%)	115 (69.28%)		
	Sublobectomy	186 (33.82%)	135 (35.16%)	51 (30.72%)		
Operative duration (min)		167.00 [133.00, 200.00]	165.00 [131.00, 199.00]	171.00 [138.50, 201.75]	Z = 1.261	0.207
Anesthesia duration (min)		189.50 [148.00, 227.75]	187.00 [144.00, 226.25]	195.50 [157.75, 230.50]	Z = 1.284	0.199
One-lung ventilation time (min)		114.50 [87.00, 137.00]	114.00 [87.00, 136.00]	116.50 [89.00, 138.75]	Z = 0.044	0.965
Intraoperative blood loss (mL)		179.00 [125.25, 241.00]	176.00 [121.50, 239.00]	187.50 [145.00, 248.75]	Z = 1.823	0.068
Intraoperative fluid volume (mL)		1136.00 [909.25, 1356.00]	1136.00 [880.75, 1352.25]	1137.50 [979.00, 1364.50]	Z = 1.151	0.250
Lymph nodes dissected		16.10±4.90	16.01±4.93	16.31±4.85	t = -0.657	0.511
ΔWBC		3.81 [1.73, 6.29]	3.84 [1.75, 6.22]	3.77 [1.69, 6.55]	Z = 0.305	0.760
ΔNLR		3.36 [2.08, 5.22]	3.34 [2.10, 5.00]	3.54 [2.08, 5.37]	Z = 0.637	0.524
ΔPLR		46.47±64.81	43.03±65.78	54.43±61.97	t = -1.897	0.058
ΔCAR		1.33 [0.86, 1.87]	1.32 [0.91, 1.85]	1.35 [0.78, 1.90]	Z = 0.551	0.582
ΔLCR		-0.33±0.19	-0.33±0.20	-0.32±0.19	t = -0.665	0.506
ΔAGR		-0.21±0.29	-0.21±0.29	-0.20±0.31	t = -0.191	0.848
ΔPNI		-7.13±8.00	-7.46±7.85	-6.37±8.30	t = -1.466	0.143

Note: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; WBC, white blood cell count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; LCR, lymphocyte-to-C-reactive protein ratio; AGR, albumin-to-globulin ratio; PNI, Prognostic Nutritional Index; Δ, delta value. Continuous variables are presented as mean ± SD for those passing the Shapiro-Wilk normality test and as median [IQR] for non-normally distributed variables.

Table 4. Comparison of clinical characteristics and perioperative inflammatory markers between PPCs and non-PPCs groups in the training set

Variable	Categories	Total training set size	PPCs group (n = 88)	Non-PPCs group (n = 296)	Statistic	P
PPC severity stratification			n = 88, used for the description within the PPCs group only	-	-	-
	Mild		56 (63.64%)	-		
	Severe		32 (36.36%)	-		
PPC types				-	-	-
	Pneumonia		34 (38.64%)	-		
	Atelectasis		22 (25.00%)	-		
	Pleural effusion		14 (15.91%)	-		
	Bronchospasm		12 (13.64%)	-		
	Respiratory failure		4 (4.55%)	-		
	ARDS		2 (2.27%)	-		
Age (years)		62.03±8.89	64.05±9.23	61.43±8.71	t = -2.439	0.015
BMI (kg/m^2)		23.90±3.38	23.36±3.39	24.07±3.36	t = 1.726	0.085
Sex					χ^2 = 1.338	0.247
	Male	215 (55.99%)	54 (61.36%)	161 (54.39%)		
	Female	169 (44.01%)	34 (38.64%)	135 (45.61%)		
Smoking history					χ^2 = 6.737	0.009
	No	195 (50.78%)	34 (38.64%)	161 (54.39%)		
	Yes	189 (49.22%)	54 (61.36%)	135 (45.61%)		
Drinking history					χ^2 = 0.038	0.846
	No	291 (75.78%)	66 (75.00%)	225 (76.01%)		
	Yes	93 (24.22%)	22 (25.00%)	71 (23.99%)		
Comorbid hypertension					χ^2 = 0.678	0.410
	No	254 (66.15%)	55 (62.50%)	199 (67.23%)		
	Yes	130 (33.85%)	33 (37.50%)	97 (32.77%)		
Comorbid diabetes					χ^2 = 0.308	0.579
	No	309 (80.47%)	69 (78.41%)	240 (81.08%)		
	Yes	75 (19.53%)	19 (21.59%)	56 (18.92%)		
Comorbid coronary heart disease					χ^2 = 1.213	0.271
	No	336 (87.50%)	74 (84.09%)	262 (88.51%)		
	Yes	48 (12.50%)	14 (15.91%)	34 (11.49%)		
Complicated with COPD					χ^2 = 5.062	0.024
	No	311 (80.99%)	64 (72.73%)	247 (83.45%)		
	Yes	73 (19.01%)	24 (27.27%)	49 (16.55%)		
Comorbid cerebrovascular disease					χ^2 = 1.249	0.264
	No	359 (93.49%)	80 (90.91%)	279 (94.26%)		
	Yes	25 (6.51%)	8 (9.09%)	17 (5.74%)		
History of neoadjuvant therapy					χ^2 = 1.431	0.232
	No	337 (87.76%)	74 (84.09%)	263 (88.85%)		
	Yes	47 (12.24%)	14 (15.91%)	33 (11.15%)		

ASA grading					χ^2 = 5.059	0.024
	I-II	244 (63.54%)	47 (53.41%)	197 (66.55%)		
	III-IV	140 (36.46%)	41 (46.59%)	99 (33.45%)		
ARISCAT score					χ^2 = 13.353	0.001
	Low risk	125 (32.55%)	22 (25.00%)	103 (34.80%)		
	High risk	75 (19.53%)	29 (32.95%)	46 (15.54%)		
	Intermediate risk	184 (47.92%)	37 (42.05%)	147 (49.66%)		
Tumor stage					χ^2 = 2.347	0.309
	I	185 (48.18%)	38 (43.18%)	147 (49.66%)		
	II	124 (32.29%)	28 (31.82%)	96 (32.43%)		
	III	75 (19.53%)	22 (25.00%)	53 (17.91%)		
Pathological type					χ^2 = 0.339	0.844
	Squamous cell carcinoma	109 (28.39%)	23 (26.14%)	86 (29.05%)		
	Other	44 (11.46%)	11 (12.50%)	33 (11.15%)		
	Adenocarcinoma	231 (60.16%)	54 (61.36%)	177 (59.80%)		
Maximum tumor diameter (cm)	Continuous variable	2.80 [2.00, 3.80]	3.15 [2.20, 4.10]	2.80 [2.00, 3.70]	Z = 2.380	0.017
Operation mode					χ^2 = 8.399	0.004
	Thoracotomy	110 (28.65%)	36 (40.91%)	74 (25.00%)		
	Thoracoscopic surgery	274 (71.35%)	52 (59.09%)	222 (75.00%)		
Resection extent					χ^2 = 9.215	0.002
	Lobectomy	249 (64.84%)	69 (78.41%)	180 (60.81%)		
	Sublobectomy	135 (35.16%)	19 (21.59%)	116 (39.19%)		
Operative duration (min)		165.00 [131.00, 199.00]	188.50 [150.50, 222.00]	158.00 [127.00, 191.50]	Z = 4.114	<0.001
Anesthesia duration (min)		187.00 [144.00, 226.25]	207.50 [168.25, 251.50]	178.00 [137.00, 216.50]	Z = 4.550	<0.001
One-lung ventilation time (min)		114.00 [87.00, 136.00]	133.00 [110.00, 161.00]	107.00 [84.50, 130.25]	Z = 5.404	<0.001
Intraoperative blood loss (mL)		176.00 [121.50, 239.00]	178.50 [152.75, 258.00]	173.00 [112.50, 233.25]	Z = 2.093	0.036
Intraoperative fluid volume (mL)		1136.00 [880.75, 1352.25]	1202.50 [1021.50, 1456.50]	1111.00 [848.25, 1315.50]	Z = 3.208	0.001
Lymph nodes dissected		16.00 [13.00, 19.00]	19.00 [15.75, 23.00]	15.00 [12.00, 18.00]	Z = 5.507	<0.001
ΔWBC		4.12±3.30	6.04±4.07	3.55±2.80	t = -6.529	<0.001
ΔNLR		3.34 [2.10, 5.00]	6.55 [4.43, 8.51]	2.76 [1.88, 3.89]	Z = 8.222	<0.001
ΔPLR		43.03±65.78	73.69±74.88	33.92±60.00	t = -5.143	<0.001
ΔCAR		1.32 [0.91, 1.85]	2.10 [1.43, 2.66]	1.19 [0.79, 1.63]	Z = 8.100	<0.001
ΔLCR		-0.33±0.20	-0.40±0.20	-0.32±0.19	t = 3.553	<0.001
ΔAGR		-0.21±0.29	-0.32±0.31	-0.18±0.27	t = 4.257	<0.001
ΔPNI		-7.46±7.85	-11.59±7.65	-6.23±7.50	t = 5.851	<0.001

Note: PPCs, postoperative pulmonary complications; ARDS, acute respiratory distress syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; WBC, white blood cell count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; LCR, lymphocyte-to-C-reactive protein ratio; AGR, albumin-to-globulin ratio; PNI, Prognostic Nutritional Index; Δ, delta value. Continuous variables are presented as mean ± SD for those passing the Shapiro-Wilk normality test and as median [IQR] for non-normally distributed variables.

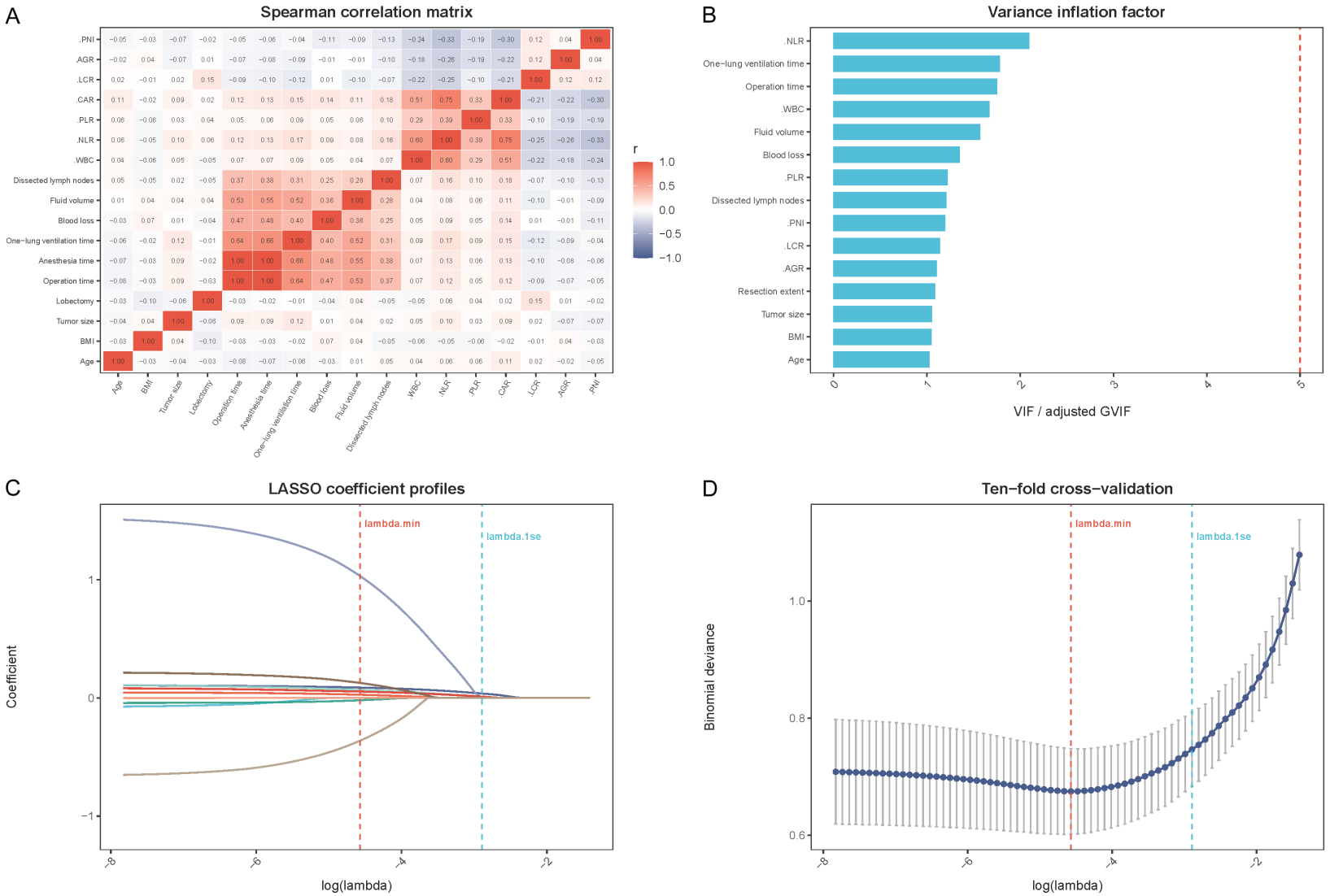

Figure 1. Spearman correlation matrix of candidate variables, VIF testing, and LASSO variable screening. A: Spearman correlation heat map of 17 candidate variables (after dummy coding) obtained by univariate screening; B: The bar chart of the VIF of 15 candidate variables, with the red dotted line representing the VIF = 5 threshold; C: The path diagram of the variations of LASSO regression coefficients with log(lambda), with the red and blue dotted lines corresponding to lambda.min and lambda.1se, respectively; D: The log loss variation curve of 10-fold cross-validation with log(lambda), with the error bar indicating standard error, and the red and blue dotted lines corresponding to lambda.min and lambda.1se.1se, respectively. Note: VIF, variance inflation factor; LASSO, Least Absolute Shrinkage and Selection Operator; NLR, neutrophil-to-lymphocyte ratio; LCR, lymphocyte-to-C-reactive protein ratio; AGR, albumin-to-globulin ratio; PNI, Prognostic Nutritional Index; Δ, delta value.

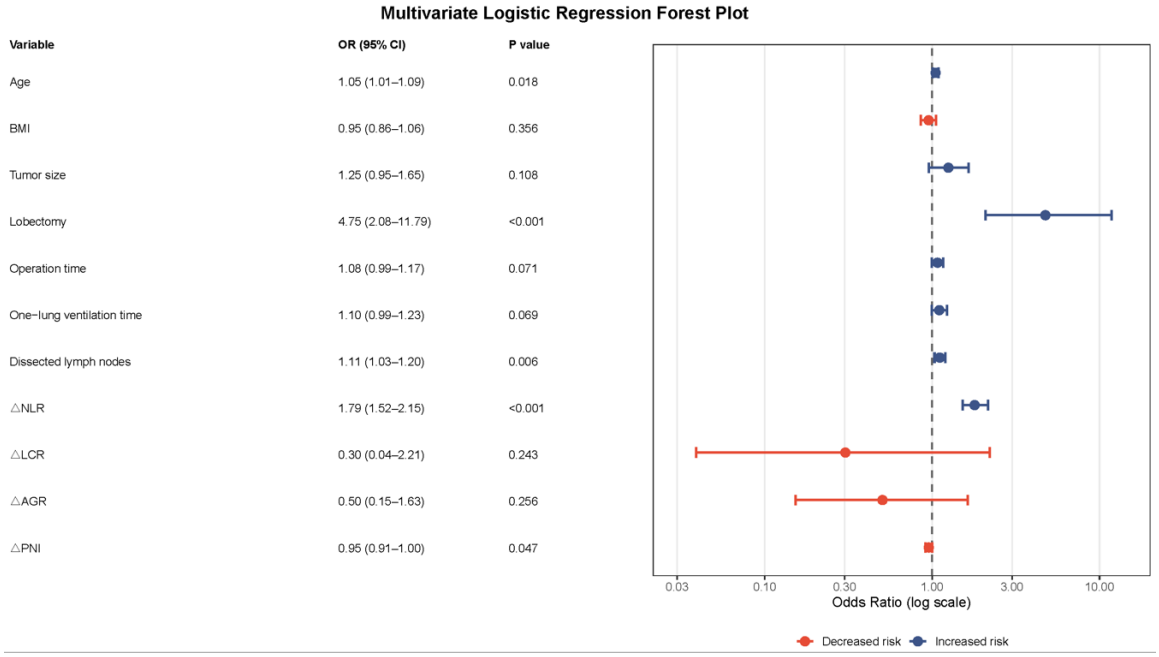

Figure 2. Multivariate Logistic regression forest plot. The forest plot shows the OR values and 95% CIs of 11 candidate variables in multivariate Logistic regression analysis. Red and blue dots indicate risk reduction (OR<1) and increase factors (OR>1), respectively, dotted lines are reference lines (OR = 1), and the horizontal axis adopts a logarithmic scale. Note: OR, odds ratio; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio; LCR, lymphocyte-to-C-reactive protein ratio; AGR, albumin-to-globulin ratio; PNI, Prognostic Nutritional Index; Δ, delta value; PPCs, postoperative pulmonary complications.

LASSO regression analysis (**Figure 1B**). Further screening of these candidate variables was conducted by employing LASSO regression with 10-fold cross-validation (**Figure 1C** and **1D**). Using the lambda.min function, the coefficients of 11 variables, namely age, BMI, MTD, lobectomy, OD, OLV time, number of lymph nodes dissected, ΔNLR, ΔLCR, ΔAGR, and ΔPNI, were non-zero. According to lambda.1se, only four variables had non-zero coefficients (OD, OLV time, number of lymph nodes dissected, and ΔNLR). Considering the model's predictive power and variable coverage, the 11 variables corresponding to lambda.min were finally used to enter the multivariate LR analysis.

Multivariate LR analysis and screening of independent predictors

Eleven variables selected by LASSO (lambda.min) were included in multivariate LR. The results showed that age (P = 0.018), lobectomy (P<0.001), number of lymph nodes dissected (P = 0.006), ΔNLR (P<0.001), and ΔPNI (P = 0.047) were independent risk factors (age, lobectomy, lymph nodes dissected, ΔNLR) or a protective factor (ΔPNI) for PPCs. Of these, lobectomy had the largest OR, suggesting that it has the most significant influence on PPCs. For each unit increase in ΔNLR, the PPC risk increased significantly. The risk of PPCs was lowered with a one-unit increase in ΔPNI. BMI (P = 0.356), MTD (P = 0.108), OD (P = 0.071), OLV time (P = 0.069), ΔLCR (P = 0.243), and ΔAGR (P = 0.256) did not reach statistically significant levels in multivariate analysis (**Figure 2**).

Nomogram construction based on independent predictors

Based on the five independent predictors (P< 0.05) in multivariate LR, i.e. age, lobectomy, lymph nodes dissected, ΔNLR, and ΔPNI, a predictive nomogram for PPCs was constructed by rms package. The model showed good overall fitting, with the likelihood-ratio test χ^2 = 169.80 (P<0.001), C-statistic = 0.888, Dxy = 0.777, and Brier score = 0.093, which indicates the model's good distinguishing ability. In the nomogram, each variable corresponded to an integral corresponding to its regression

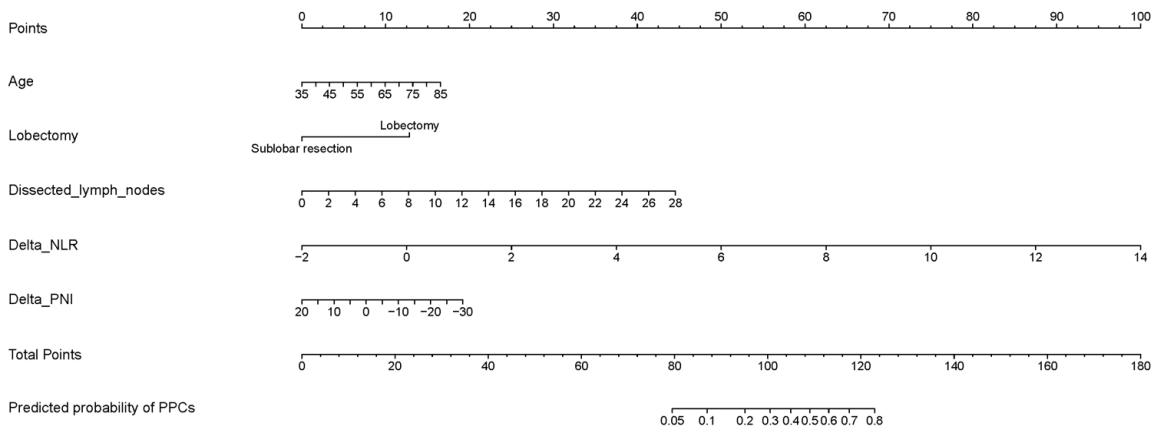

Figure 3. Nomogram for predicting the risk of PPCs in NSCLC. The nomogram includes five independent predictive variables: age, lobectomy, lymph nodes dissected, ΔNLR, and ΔPNI. Each predictor corresponds to the Points axis. Summing up the integrals of each variable yields the total score (Total Points), and corresponding to the bottom probability axis, the predicted probabilities of PPCs can be read. Note: PPCs, postoperative pulmonary complications; NSCLC, non-small cell lung cancer; NLR, neutrophil-to-lymphocyte ratio; PNI, Prognostic Nutritional Index; Δ, delta value.

coefficient. ΔNLR and the number of lymph nodes dissected contribute most to the total integral, while lobectomy significantly increased the integral compared with sublobectomy. Summing up the integrals of each variable yielded the total integral, which can be read on the bottom predicted probability axis to obtain the predicted probability of individual PPC occurrence (**Figure 3**).

ROC curve analysis and DeLong test of the nomogram and single indices

A ROC curve analysis of ΔNLR, ΔPNI, ARISCAT risk score, and nomogram in both training and validation sets was conducted, followed by a pairwise comparison of AUC between various single markers and the nomogram model by the DeLong method. In the training set, the nomogram had an AUC of 0.888 (95% CI: 0.843-0.934), with 84.1% sensitivity, 84.1% specificity, and a Youden index of 0.682 at the corresponding optimal cutoff value. The AUC was 0.848 (95% CI: 0.795-0.900) for ΔNLR, 0.695 (95% CI: 0.631-0.759) for ΔPNI, and 0.598 (95% CI: 0.533-0.663) for the ARISCAT risk score. The DeLong test results indicated a superior AUC of the nomogram in training set to ΔNLR (P = 0.008), ΔPNI (P<0.001), and the ARISCAT risk score (P<0.001). In the validation set, the nomogram achieved an AUC of 0.887 (95% CI: 0.831-0.942), with 73.7% sensitivity, 88.3% specificity, and a Youden index of 0.620. The AUC of ΔNLR, ΔPNI, and the ARISCAT score was 0.900 (95% CI: 0.839-0.962), 0.583 (95% CI: 0.472-0.695), and 0.713 (95% CI: 0.628-0.798), respectively. The DeLong test showed no statistical significance difference in AUC between the nomogram and ΔNLR (P = 0.544) in the validation set, but the model performed significantly better than ΔPNI (P<0.001) and the ARISCAT score (P = 0.001; **Figure 4** and **Table 5**).

Calibration curve and DCA of the nomogram model

Calibration curve evaluation and DCA of the nomogram were carried out across the training and validation sets. According to the calibration curve, the nomogram had a concordance index (C-index) = 0.888 (95% CI: 0.843-0.934), a Brier score = 0.093, and an HL test χ^2 = 18.44 (P = 0.018) in the training set, which indicates acceptable calibration of the model upon training but a certain fitting bias. During validation, the relevant parameters were 0.887 (95% CI: 0.831-0.942) for the C-index, 0.106 for the Brier score, and χ^2 = 3.525 for the HL test (P = 0.897). The calibration curve of the validation set agreed rigorously with the ideal diagonal, indicating that the model has satisfactory calibration performance in external validation (**Figure 5A** and **5B**). In both training and validation sets, the DCA indicated that the nomogram had a net benefit curve that was

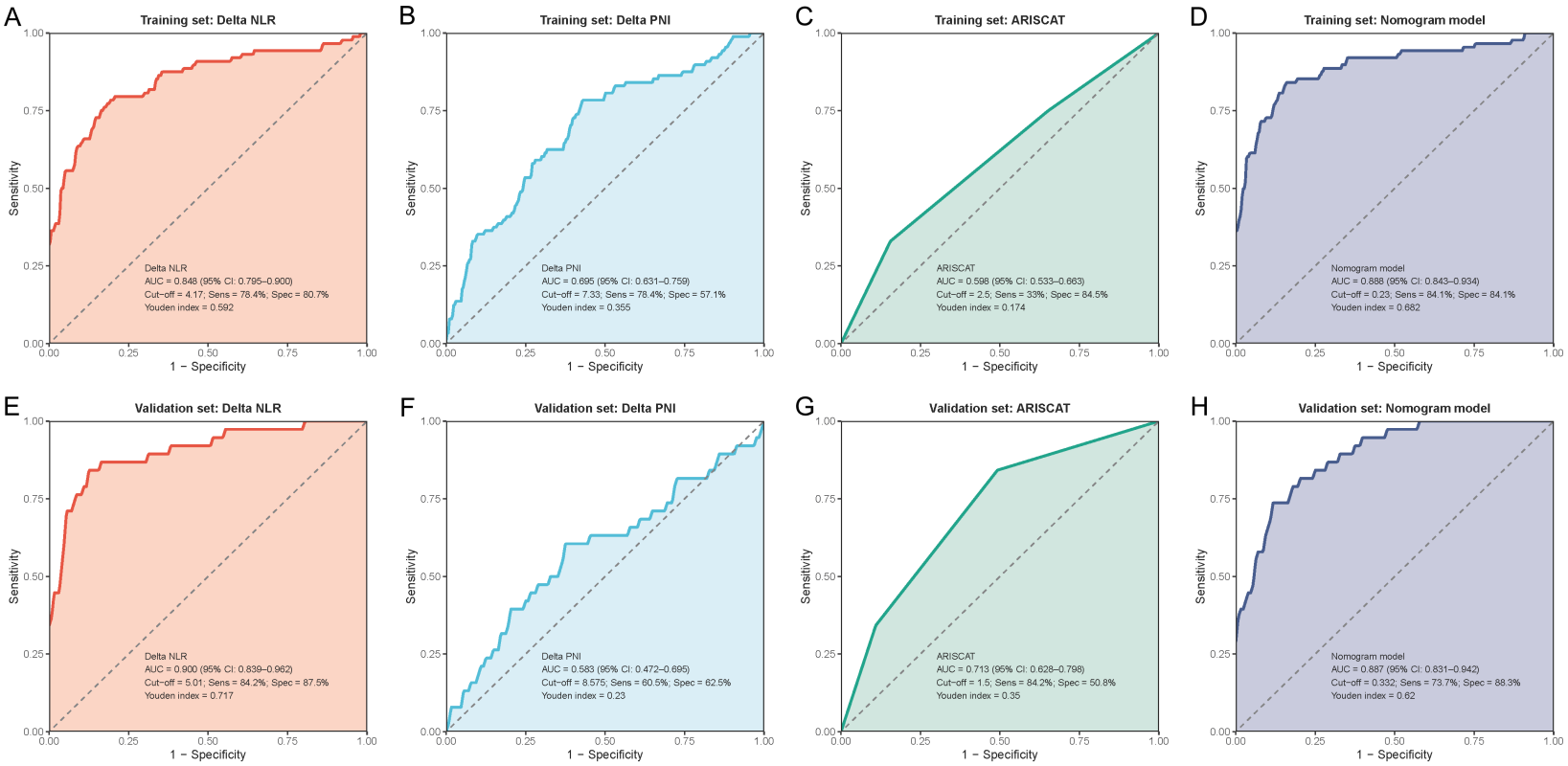

Figure 4. ROC curves of various indices and the nomogram in training and validation sets. A: ROC curve of ΔNLR in the training set; B: ROC curve of ΔPNI in the training set; C: ROC curve of the ARISCAT score in the training set; D: ROC curve of the nomogram in the training set; E: ROC curve of ΔNLR in the validation set; F: ROC curve of ΔPNI in the validation set; G: ROC curve of the ARISCAT score in the validation set; H: ROC curve of the nomogram in the validation set. Note: AUC, area under the curve; CI, confidence interval; Sens, sensitivity; Spec, specificity; NLR, neutrophil-to-lymphocyte ratio; PNI, Prognostic Nutritional Index; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; Δ, delta value.

Table 5. AUC comparison between various markers and the nomogram by the DeLong test

Dataset	Comparison	AUC_1	AUC_2	Z	*P*_value_format
Training set	ΔNLR vs. Nomogram model	0.848	0.888	-2.632	0.008
Training set	ΔPNI vs. Nomogram model	0.695	0.888	-6.046	<0.001
Training set	ARISCAT vs. Nomogram model	0.598	0.888	-6.761	<0.001
Validation set	ΔNLR vs. Nomogram model	0.9	0.887	0.607	0.544
Validation set	ΔPNI vs. Nomogram model	0.583	0.887	-6.361	<0.001
Validation set	ARISCAT vs. Nomogram model	0.713	0.887	-3.277	0.001

Note: AUC, area under the curve; NLR, neutrophil-to-lymphocyte ratio; PNI, Prognostic Nutritional Index; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; Δ, delta value.

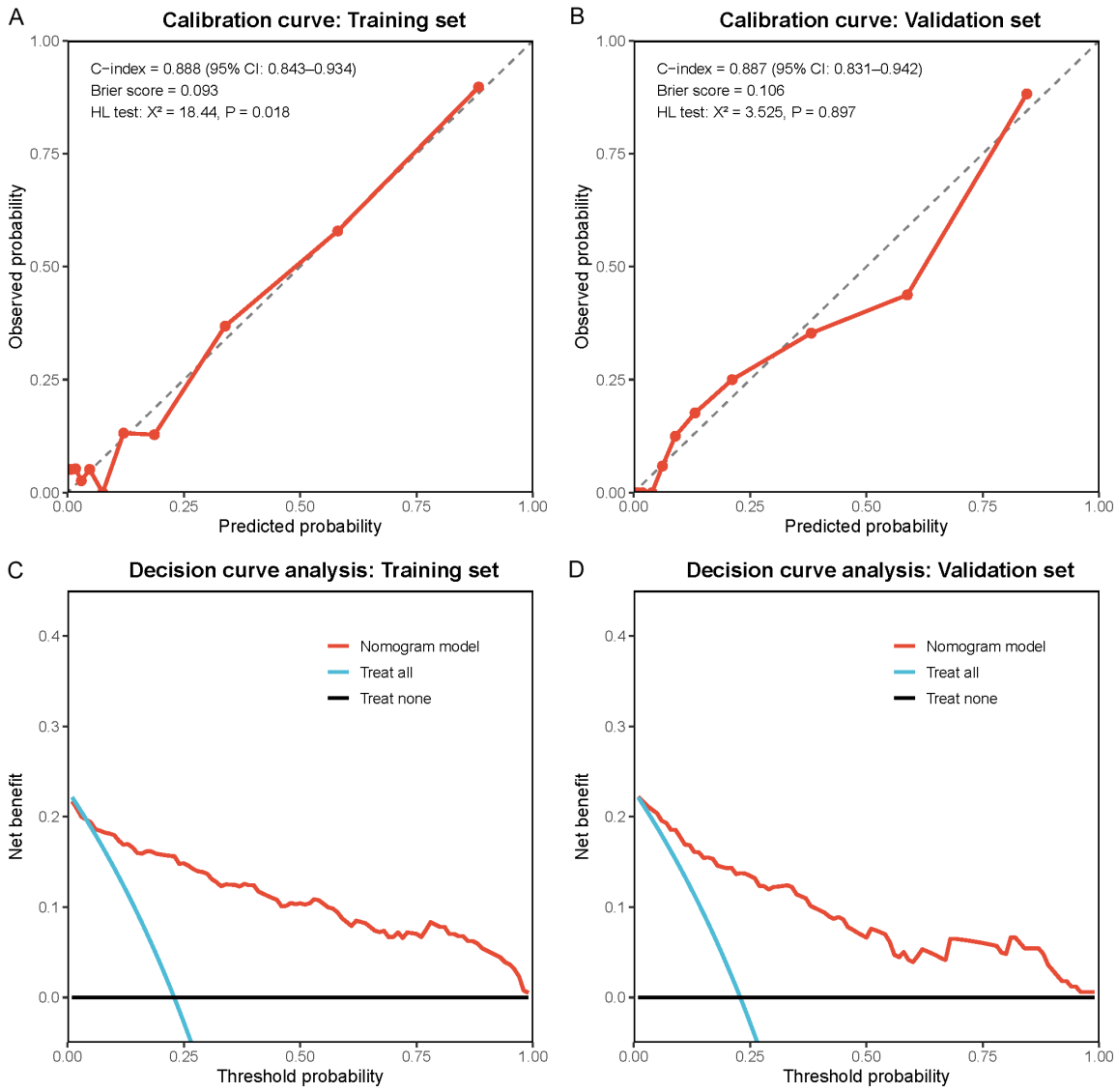

Figure 5. Calibration curve and DCA of the nomogram model in training and validation sets. A: Calibration curve of the training set, with the horizontal axis representing predicted probabilities, the vertical axis showing actually observed probabilities, and the dotted line indicating the ideal calibration line; B: Calibration curve of the validation set; C: Decision curve of the training set, with red solid line as the nomogram model, cyan solid line as the treat all strategy, and black solid line as the treat none strategy; D: Decision curve of the validation set. Note: DCA, decision curve analysis; C-index, concordance index; CI, confidence interval; HL test, Hosmer-Lemeshow test; PPCs, postoperative pulmonary complications.

Table 6. Comparison of clinical outcome indexes between high- and low-risk groups in the training set

Clinical outcome-associated indices	High-risk group (n = 121)	Low-risk group (n = 263)	Statistic	P
Postoperative hospital stay (days)	10.94±4.16	7.43±2.16	t = 8.779	<0.001
Chest tube indwelling time (days)	4.66±2.08	2.81±1.19	t = 9.134	<0.001
Time to initial postoperative ambulation (days)	2.97±1.36	1.90±0.77	t = 8.048	<0.001
Duration of antibiotic use (days)	7.05±3.27	4.38±1.94	t = 8.330	<0.001
Total hospitalization expenses	63504.21±17075.09	45613.03±11283.96	t = 10.517	<0.001
ICU admission			χ^2 = 5.383	0.020
Yes	18 (14.88%)	18 (6.84%)		
No	103 (85.12%)	245 (93.16%)		
Reoperation			χ^2 = 2.500	0.114
Yes	10 (8.26%)	10 (3.80%)		
No	111 (91.74%)	253 (96.20%)		
Unplanned 30-day hospital readmission			χ^2 = 4.236	0.040
Yes	13 (10.74%)	12 (4.56%)		
No	108 (89.26%)	251 (95.44%)		
Overall PPC occurrence			χ^2 = 143.105	<0.001
Present	74 (61.16%)	14 (5.32%)		
Absent	47 (38.84%)	249 (94.68%)		
PPC types				
Pneumonia	27 (36.49%)	7 (50.00%)		
Atelectasis	18 (24.32%)	4 (28.57%)		
Pleural effusion (requiring intervention)	13 (17.57%)	1 (7.14%)		
Bronchospasm	10 (13.51%)	2 (14.29%)		
Respiratory failure	4 (5.41%)	0 (0.00%)		
ARDS	2 (2.70%)	0 (0.00%)		

Note: ICU, intense care unit; PPCs, postoperational pulmonary complications; ARDS, acute respiratory distress syndrome. Continuous variables are presented as mean ± SD for those passing the Shapiro-Wilk normality test and as median [IQR] for non-normally distributed variables.

higher than the "treat all" and "treat none" reference lines when the threshold probability was within the clinical reasonable range; it indicates that this model, when applied clinically to guide decision-making, can bring substantial net gains to patients with good clinical practicability (**Figure 5C** and **5D**).

Clinical outcome comparison based on the nomogram model risk stratification

The training cohort (n = 384) was divided into high- (n = 121) and low-risk groups (n = 263) according to the nomogram's best cut-off value (0.23) for comparative analysis of clinical outcome-associated indices. In terms of perioperative outcomes, we found extended postoperative hospital stay (P<0.001), chest tube indwelling time (P<0.001), time to initial postoperative ambulation (P<0.001), and antibiotic use duration (P<0.001), as well as higher total hospitalization expenses (P<0.001) in the high-risk group compared with the low-risk group. The high-risk group also showed higher rates of ICU admissions (P = 0.020) and unplanned 30-day hospital readmissions (P = 0.040). The reoperation rate was equivalent (P = 0.114). Concerning PPCs, a 61.16% incidence was determined in the high-risk group, compared to 5.32% in the low-risk group (P<0.001), suggesting the nomogram's good recognition ability for high-risk patients. Among patients who experienced PPCs, pneumonia was the most common type in both groups, followed by atelectasis. Severe complications (RF/ARDS) occurred in a greater number of patients in the high-risk group, versus none in the low-risk group (**Table 6**).

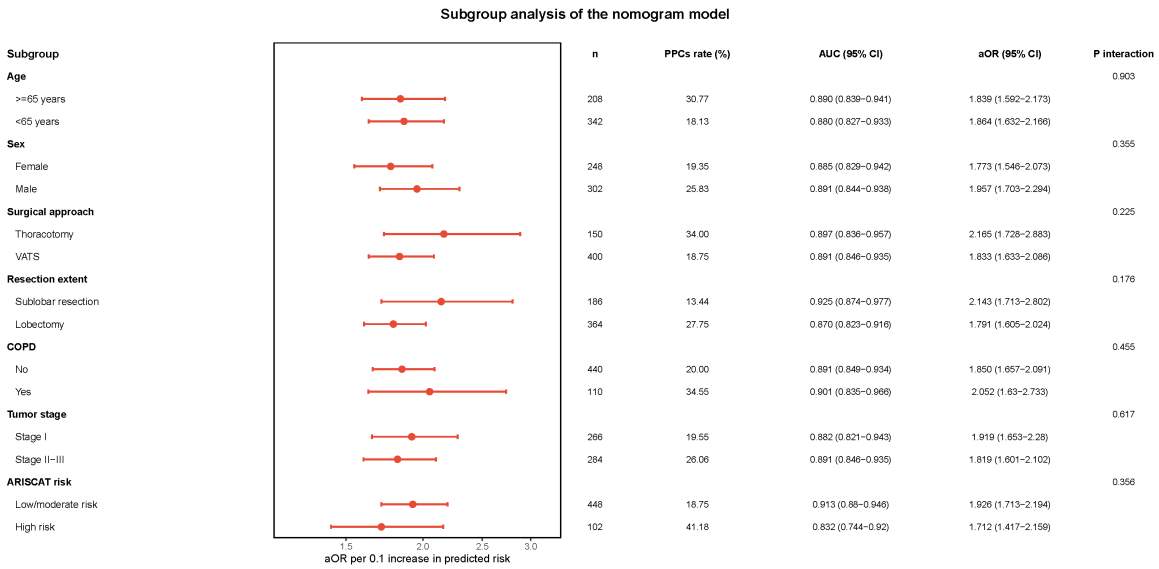

Figure 6. Forest plot of the nomogram's predictive stability across different clinical subgroups. The forest plot shows AUCs, aORs and 95% CIs of the nomogram model in subgroups of age, sex, surgical approach, resection extent, COPD, tumor stage, and ARISCAT risk score. The dots represent the point estimates of aORs, the horizontal lines represent 95% CIs, the dashed line on the vertical axis is the reference line (aOR = 1), and the horizontal axis is the logarithmic scale; P interaction tests the *P* values for the interaction terms of risk prediction between each subgroup and the nomogram. Note: PPCs, postoperative pulmonary complications; AUC, area under the curve; CI, confidence interval; aOR, adjusted odds ratio; COPD, chronic obstructive pulmonary disease; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; VATS, video-assisted thoracoscopic surgery.

Subgroup analysis of the nomogram model

Based on the merged data of training and validation sets (n = 550), the nomogram's predictive stability in different clinical subgroups was analyzed. Using each 0.1 increment in the nomogram-predicted risk as the effect unit, we calculated the adjusted odds ratio (aOR) and AUC for each subgroup, and the consistency of effects across subgroups was evaluated using the interaction test. In the whole sample, the AUC of the nomogram was 0.889 (95% CI: 0.853-0.925), the aOR was 1.864 (95% CI: 1.689-2.078), and the overall PPC incidence was 22.91%. The analysis results showed that among age (interaction *P*-value = 0.903), sex (interaction *P*-value = 0.355), surgical approach (interaction *P*-value = 0.225), resection extent (interaction *P*-value = 0.176), COPD (interaction *P*-value = 0.455), tumor stage (interaction *P*-value = 0.617) and ARISCAT risk score (interaction *P*-value = 0.356) subgroups, the nomogram demonstrated sound predictive performance (AUC range: 0.832-0.925, aOR range: 1.712-2.165), with the *P*-value for interaction greater than 0.05 for all subgroups. It is suggested that there is no significant difference in the model effect among the subgroups, and the model's predictive performance has good cross-subgroup stability (**Figure 6**).

Sensitivity analysis to verify the robustness of the nomogram model

This study carried out multi-dimensional, systematic sensitivity analysis (model construction strategy, risk stratification threshold, and internal validation approach) to further verify the robustness of the predictive nomogram. Using variables (OD, OLV time, lymph nodes dissected, and ΔNLR) screened by lambda.1se in LASSO regression, we reconstructed a conservative LR model. The predictive efficiency-associated parameters of this model were as follows: training set: AUC = 0.879 (95% CI: 0.831-0.927), Brier score = 0.096; validation set: AUC = 0.907 (95% CI: 0.856-0.959), Brier score = 0.094, and aOR = 2.213 (95% CI: 1.767-2.913) for every 0.1 increase in predicted risk. The above results were in high agreement with the main model (training set AUC = 0.888, validation set AUC = 0.887), suggesting that model performance was insensitive to variable selection strategies and demonstrat-

ing model robustness. Sensitivity analysis of alternative risk threshold validation: Based on the prediction probability of the main model, the training set (n = 384) was stratified for risk with 0.20, 0.25, and 0.30 as alternative cutoff values, respectively. When the threshold was 0.20, the PPC incidence was 58.27% in the high-risk group (n = 127) and 5.45% in the low-risk group (n = 257). Using a threshold of 0.25, the PPC prevalence was 62.83% and 6.27% in the high- (n = 113) and low-risk (n = 271) groups, respectively, and the corresponding incidence was 65.38% (high-risk group, n = 104) and 7.14% (low-risk group, n = 280) when a threshold of 0.30 was applied. There was a significant difference in PPC incidence between the high- and low-risk groups under the three thresholds (all P<0.001); PPCs occurred in the high-risk group showed an increasing trend with the increase in thresholds, which indicates the model's stable risk stratification effect under different cutoffs and thus supports its strong clinical applicability. Sensitivity analysis of Bootstrap internal validation: Internal validation with 1000 bootstrap iterations was carried out on the main model, and all iterations (1,000) converged. The average AUC of Bootstrap validation was 0.886 (median AUC = 0.886, 2.5%-97.5% percentile: 0.879-0.889), which is highly consistent with the measured AUC (0.888) in the training set, suggesting that the model has not been obviously over-fitted with good internal validation validity.

Discussion

Taking 550 NSCLC patients undergoing surgical treatment as the research participants, this study systematically examined the association between dynamic changes in perioperative inflammatory markers and PPCs, and built a predictive nomogram based on age, lobectomy, lymph nodes dissected, ΔNLR, and ΔPNI that was further verified. The model had excellent discrimination, satisfactory calibration performance, and significant clinical net benefits in both training and validation sets, with robust predictive performance across several clinical subgroups, which provides an effective tool for early identification and accurate perioperative management of PPCs in NSCLC patients.

Analysis of the incidence and clinical characteristics of PPCs

In this study, the total PPC incidence after NSCLC surgery was 22.91%, which was basically consistent with the 15%-30% reported in previous literature. Pneumonia occurred most frequently among various PPCs observed (36.51%), followed by atelectasis (26.98%) and intervention-requiring PE (20.63%). Severe complications (RF and ARDS), though happened at a low incidence, exerted a significant impact on patient prognosis. The literature shows that PPCs not only prolong hospital stays but also significantly delay patient recovery, seriously affecting their short-term quality of life [17]. The above characteristics are closely related to local inflammation, airway secretion retention, and PE induced by OLV, lung tissue traction, and lymph node dissection during NSCLC surgery.

In terms of traditional risk factors, PPC patients were older, with greater proportions of smoking history, COPD comorbidity, worse ASA classification, thoracotomy, and lobectomy, extended durations of operation, anesthesia, and OLV, and a higher IFV than their non-PPC counterparts, which is highly consistent with previous research conclusions. Saetang et al. [18] confirmed in a study on elderly patients undergoing LC surgery that old age, concurrent COPD, and smoking history are independent predictors for Clavien-Dindo ≥II postoperative complications. Besides, Huang et al. [19] employed propensity score matching analysis to demonstrate the role of high ASA classification and thoracotomy as important predictors of PPCs in elderly patients. Chang et al.'s research [20] further revealed that in addition to traditional clinical factors, high preoperative NLR was also related to postoperative adverse events and survival, suggesting that inflammatory status may predate clinical outcomes. The combined effects of these factors - decreased PF reserve in elderly patients, airway hyperresponsiveness and mucus clearance disorders caused by smoking and COPD, as well as greater trauma due to thoracotomy and OLV-induced oxidative stress - constitute the pathophysiological basis of PPCs. The notably higher proportion of the ARISCAT high-risk category in the PPCs group (33.33% vs. 14.15%) confirmed

the score's predictive value in NSCLC patients. Ülger et al. [21] found that the ARISCAT score, with limited independent predictive ability, had predictive value for PPCs after thoracic surgery when integrated with ASA grading and preoperative ALB level. It indicates that the ARISCAT score needs to be supplemented by other dynamic indicators for prediction, which is mutually confirmed by an AUC of only 0.598 in this study.

Advantages and biological basis of difference analysis of perioperative inflammatory markers

The core innovation of this study is to introduce the perioperative differences (Δ) in inflammatory markers as predictive indices. Preoperative baseline analysis indicated statistically different AGR and PNI between the study cohorts, suggesting a somewhat weaker preoperative nutritional and immune status in patients who developed PPCs. The non-significant intergroup disparities in preoperative WBC, NLR, PLR, CAR, and LCR indicate that relying solely on preoperative inflammatory state is inadequate to effectively distinguish high-risk populations of PPCs. Ginesu et al. [7] also observed a similar trend, reporting the association of NLR and MLR measured on the 4th postoperative day, but not their preoperative levels, with complications, which supported the view that postoperative dynamic indices were superior to preoperative single baseline measurements. On day 1 post-operation, all inflammatory markers in the two groups changed significantly, especially in the PPCs group: WBC, NLR, PLR, and CAR increased significantly, while LCR, AGR, and PNI decreased sharply, suggesting more intense inflammation and more obvious loss of nutritional and immune functions in PPC-affected individuals.

The theoretical strength of Δ is that it contains both preoperative baseline status and postoperative stress response, which can more directly quantify the intensity of the body's inflammatory response to surgical trauma on the premise of correcting individual baseline differences. Using a methodology similar to ours, He et al. [3] confirmed that the difference in inflammatory markers such as postoperative SII, ΔSII, ΔPLR, and ΔAISI can effectively predict cardiopulmonary complications after NSCLC surgery. What differs is that the preceding research focused on the combination of postoperative static values and difference indices, while our study constructs a more comprehensive prediction system by further integrating dynamic indexes such as ΔNLR and ΔPNI with traditional clinical factors. Compared with single-time point measurements, the difference analysis is more sensitive to the prediction signals of PPC risk, which is also verified in this study: all Δ indices exhibited significant between-group differences (P<0.001), while only part of the corresponding preoperative baseline indices were different.

Interpretation of independent predictors

Multivariate LR screened out five independent predictors of PPCs. Age, as an independent risk factor (P = 0.018), reflects the decline in PF reserve, immunosenescence, and the increased comorbidity burden in elderly patients. Zhang et al. [12] also unveiled that age is an independent predictor for PPCs in non-adenocarcinoma NSCLC patients following NAT, indicating that the effect of age is not interfered by pathological types or a NAT background. Compared with sublobectomy, lobectomy has the largest OR among all factors, suggesting that resection extent is the most important surgical factor affecting PPCs. Gómez Hernández et al. [22] reported a higher PPC incidence in patients who underwent lobectomy after neoadjuvant chemoradiotherapy, which confirmed the exact relationship between the scope of surgical resection and PPCs. Besides a large loss of functional lung tissue, lobectomy also involves longer OD, greater anatomical operation complexity, and more extensive treatment of the bronchial stump. The combination of multiple factors significantly increases the risk of postoperative airway complications. It is worth noting that the number of lymph nodes dissected entered the model as an independent predictor (P = 0.006). Its biological significance lies in that it is a substitute index for procedural complexity and tissue trauma scope: the more lymph nodes are dissected, the wider the anatomical scope of the mediastinum, the higher the risk of damage to the vagus nerve and thoracic duct, and the stronger the activation degree of local inflammation, thus increasing the probability of PPCs.

ΔNLR (P<0.001) was the inflammation index with the highest contribution to model predictions. NLR elevation reflects the coexistence of neutrophil-dominated hyperinflammatory reaction and lymphocyte-mediated adaptive immunosuppression. The acute phase reaction induced by surgical trauma leads to a large number of neutrophils mobilized into the blood, and stress hormones (glucocorticoids and catecholamine) promote lymphocyte apoptosis and redistribution, which greatly increases NLR. Literature shows that short-term preoperative exercise training can significantly reduce NLR and complications after LC surgery, which proves the effectiveness of NLR as a marker of inflammatory stress from an intervention perspective [23]. A greater increase in ΔNLR indicates more severe postoperative inflammatory reactions and a more obviously imbalanced immune system, and thus a higher likelihood of infectious and non-infectious pulmonary complications. For each unit increase in ΔPNI (OR = 0.95, 95% CI: 0.91-1.00, P = 0.047), the risk of PPCs was significantly reduced, indicating that a smaller perioperative decline in PNI - reflecting better preservation of nutritional and immune reserves - is protective against postoperative pulmonary complications. The decrease in ALB indicates damaged anabolism and increased capillary permeability, and the reduction in the lymphocyte absolute value suggests weakened cellular immune defense ability, which together weakens the post-injury repair ability of lung tissues. In contrast, ΔLCR and ΔAGR lost their significance in the multivariate model, which may be related to their overlapping information with ΔNLR and ΔPNI; in the model that already included these latter two variables, their independent contribution was limited.

Prediction performance evaluation of nomogram model

The model shows excellent discrimination ability (training set AUC = 0.888, validation set AUC = 0.887). Chen et al. [24] reported a stacked ensemble machine learning model for predicting PPCs after lung cancer surgery with an external validation AUC of 0.790, and Li et al. [13] constructed a CPET parameter-based nomogram with a C-index of 0.790. While direct cross-study comparison is inherently limited by differences in PPC definitions, study populations, and variable availability, the present nomogram's discriminative performance (training AUC 0.888; validation AUC 0.887) compares favorably with these recently reported models. This suggests that integrating perioperative dynamic inflammatory difference indices may enhance predictive efficiency, although definitive comparative conclusions require head-to-head validation within the same prospective cohort. Compared with individual indexes, the nomogram had a superior AUC during training than ΔNLR (0.848, P = 0.008), ΔPNI (0.695, P<0.001) and ARISCAT score (0.598, P<0.001); in the validation set, the model showed an AUC equivalent to ΔNLR (0.900; P = 0.544), but was significantly better than ΔPNI (P<0.001) and the ARISCAT score (P = 0.001). The literature has identified perioperative inflammatory burden, diabetes, hypertension, and smoking history as key predictors of PPCs in SHAP analysis based on machine learning [25]. This study further integrates the above factors into the nomogram, highlighting the incremental value of difference indicators. The C-index of the nomogram constructed by Kim et al. [26] in the surgical population after neoadjuvant chemoradiotherapy for NSCLC is 0.756, which further highlights the advantage of incorporating perioperative dynamic inflammatory markers in predictive performance. The studies by Sha et al. [25] and Qiu et al. [27] also explored the application of a machine learning model in PPCs prediction after VATS, but both focused on algorithm optimization and did not include difference analysis in the core variable strategy. This supports the superior overall prediction performance of the nomogram model, which integrates multi-dimensional clinical and inflammatory information, over any single index, and that ΔNLR, as the most sensitive dynamic inflammatory marker with an AUC of 0.900 in the validation set, also has important independent prediction value.

From a calibration performance perspective, the model showed an HL test *P*-value of 0.897 upon validation, with high consistency between the calibration curve and the ideal diagonal, which indicates that the model is accurate and reliable in estimating PPC probabilities in external populations. An HL test P = 0.018 in the training set suggests a certain fitting bias, possibly due to the relatively limited sample size of the training set and the uneven distribution

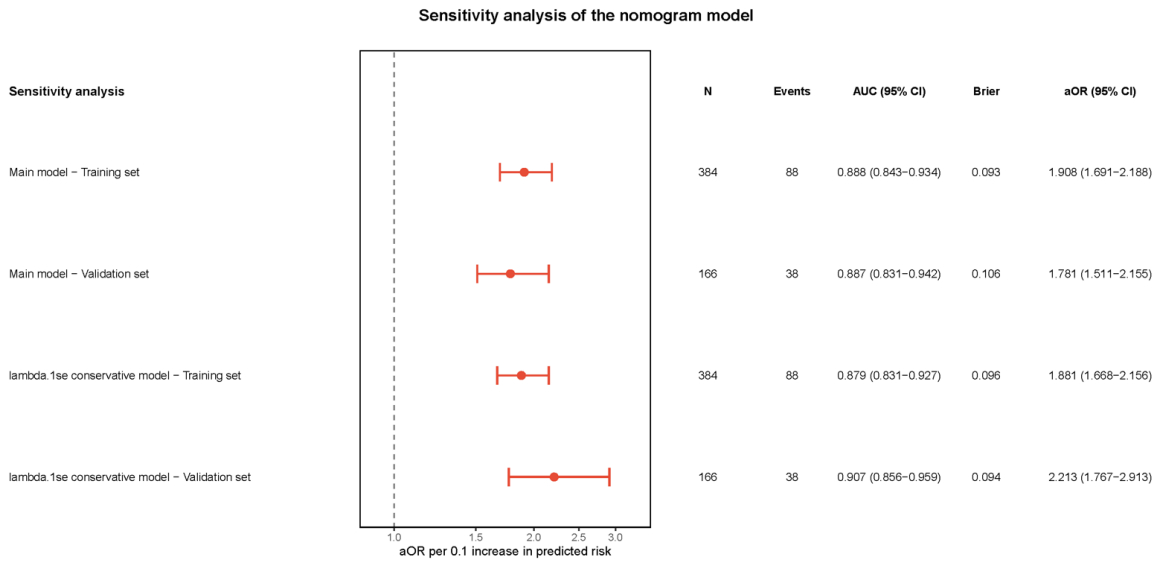

Figure 7. Forest plot of sensitivity analysis of the predictive nomogram. The plot shows the discriminant performance and effect size estimation of each model in the three sensitivity analyses. The vertical axis lists the analysis items (the main model and the lambda.1se conservative model, which are evaluated in the training and validation sets, respectively); the horizontal axis is the aOR for every 0.1 increase in predicted risk, expressed on a logarithmic scale. In the plot, the solid dots represent the point estimates of aORs, the horizontal line segments indicate 95% CIs, and the vertical dotted line marks the reference value (aOR = 1). The data column on the right presents sample size (N), Events, AUC, and 95% CI, Brier, and aOR (95% CI) in turn. In all analyses, the point estimate of aOR exceeds 1 with the lower bound of the 95% CI above 1, suggesting a significant positive correlation between the predicted risk and the actual occurrence of PPCs. Note: AUC, area under the curve; CI, confidence interval; aOR, adjusted odds ratio; Brier, Brier score.

of some low probability intervals; nonetheless, the clinical application value of the overall model was not affected. DCA further confirmed that within the clinically reasonable threshold probability range, the nomogram contributed to markedly better net benefits than the two extreme strategies, i.e., "treat all" and "treat none", supporting its ability to effectively guide the identification and intervention of high-risk patients in the early postoperative period.

Clinical significance of risk stratification

Using a prediction probability cutoff of 0.23, the PPC incidence reached up to 61.16% in the high-risk group (n = 121), which differed statistically than 5.32% in the low-risk group (n = 263). According to the perioperative outcome comparison, the high-risk group was significantly worse in postoperative hospitalization time, chest tube indwelling time, ICU admission rate, unplanned 30-day hospital readmission rate, and hospitalization expenses. Lee et al.'s research [11] found that even for mild-to-moderate COPD patients, the high-risk population of PPCs can be effectively identified by CAT score-based symptom severity evaluation, which is consistent with the core idea of risk stratification in this study, that is, stratifying and managing patients based on early and quantifiable indicators. Kim et al. [10] further confirmed that DF parameters (e.g., DLCO/VA) hold predictive significance in mild COPD patients, but DF detection is not as convenient as routine hematological indexes in clinical practice. For the model-predicted high-risk patients, clinicians can take more proactive intervention measures in the early postoperative period, including strengthening airway secretion management, optimizing respiratory function exercise, rational use of preventive antibiotics, and enhancing nutritional support, in order to reduce the actual incidence of PPCs and its negative impact on clinical outcomes.

Subgroup and sensitivity analyses

In the subgroup analysis, the AUC range of the nomogram model was 0.832-0.925 among age, sex, surgical method, resection extent, COPD, tumor stage, and ARISCAT risk score subgroups, with the interaction *P*-value all

exceeding 0.05. It suggests that the model's predictive performance has good cross-population stability and is not affected by the characteristics of specific subgroups. Literature shows that, even after incorporating more detailed physiological parameters such as DF and CPET, the traditional multivariate regression or machine learning models still have fluctuations in prediction performance among different datasets [13, 24]. In this study, the model fluctuates slightly in various sensitivity analyses, which verifies the robustness of the difference indicators as prediction variables. Sensitivity analysis further verified model robustness from three dimensions: the AUC of the lambda.1se conservative model rose to 0.907 in the validation set, which was highly consistent with the main model; With three alternative thresholds of 0.20, 0.25, and 0.30 for risk stratification, the PPC incidence in high- and low-risk groups differed significantly and showed an increasing trend with the increase of threshold; the average AUC of internal validation using 1000 bootstrap replications was 0.886, which was highly consistent with the measured value of the training set (0.888) with no obvious over-fitting found (**Figure 7**).

Research limitations

This study has several limitations. First, this study adopts a single-center retrospective design, which may be biased by selection and information. External generalization of the research conclusions needs to be verified by multi-center prospective studies. Second, the judgment of PPCs depends on clinical diagnosis and medical records, which is subjective to some extent. Standardized imaging and physiological function evaluation can further improve the consistency of diagnosis. Third, important PF parameters such as preoperative FEV1/FVC, as well as nutritional interventions, were not systematically included in this study, which may have some influence on the prediction efficiency of the model. Fourth, the difference in inflammatory markers is only based on two time points (before operation vs. the first day after operation), warranting further exploration of the value of dynamic multi-time point monitoring in identifying the evolution trend of complications. Fifth, the ARISCAT risk score demonstrated limited discriminative performance in our cohort (training AUC 0.598; validation AUC 0.713). This is consistent with recent evidence from lung resection populations - Zorrilla-Vaca et al. [28] reported an ARISCAT c-index of 0.60 (95% CI: 0.55-0.65) in 2,104 lung resection patients, and Zhou et al. [29] reported an ARISCAT AUC of 0.689 in 1,898 older noncardiac thoracic surgery patients - reflecting the fact that ARISCAT score was originally derived from general surgical populations rather than thoracic surgery populations. This performance gap underscores the unmet need for novel, procedure-specific prediction tools; however, our nomogram also requires multi-center prospective external validation before it can be considered a mainstream clinical instrument.

Conclusion

To sum up, based on age, lobectomy, number of lymph nodes dissected, ΔNLR, and ΔPNI, this study developed a predictive nomogram with good predictive performance, stable in calibration performance, and significant in clinical net benefits for PPCs in surgically-treated NSCLC patients. The difference analysis of perioperative inflammatory markers provides a new dynamic perspective for early risk identification of PPCs, which has certain advantages over traditional single-time point indicators or scoring tools. The model uses the routine laboratory test data on the first postoperative day, which is convenient and low-cost, and is easy to be popularized and applied in clinical practice. Future research should further verify and optimize the model in a multi-center prospective cohort, and explore its practical benefits in perioperative precise intervention and decision-making.

Disclosure of conflict of interest

None.

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