

## Postprint: Correlation Between Systemic Immune-Inflammation Index and Unplanned Readmission in Patients with Stage - Lung Cancer

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### Abstract

**Background** Lung cancer is the malignant tumor with the highest global incidence and mortality. Short-term unplanned readmission (UPR) significantly impacts healthcare quality, nursing efficiency, and patient prognosis. The Systemic Immune-Inflammation Index (SII) reflects the body's inflammatory-immune status and demonstrates predictive value in lung cancer progression and treatment. Investigating the correlation between SII and short-term UPR in lung cancer patients treated with immune checkpoint inhibitors (ICIs) can provide a reference basis for clinical risk stratification.

**Objective** To investigate the correlation between SII levels and the risk of short-term UPR in advanced-stage lung cancer patients receiving ICIs therapy.

**Methods** A retrospective analysis included 247 stage III-IV lung cancer patients who received ICIs therapy between January 2023 and May 2024. Among them, 164 cases were in the UPR group and 83 in the non-UPR group. Demographic characteristics, clinical treatment parameters, routine biochemical indicators, and tumor-related markers were collected. Multivariate Logistic regression and subgroup analysis were employed to screen independent risk factors for UPR in lung cancer patients receiving ICIs therapy. The pROC package was used to plot Receiver Operating Characteristic (ROC) curves to evaluate the accuracy, sensitivity, and specificity of the regression model and SII alone in predicting unplanned readmission in lung cancer patients. Restricted cubic spline (RCS) regression combined with SHapley Additive exPlanations (SHAP) analysis was utilized to explore the dose-response relationship between SII and the risk of unplanned readmission, determine the SII threshold, and conduct subgroup analysis based on this threshold.

**Results** The incidence of UPR within 31 days was 33.60% (83/247).

Multivariate Logistic regression analysis revealed that length of hospital stay (OR=1.073, 95%CI=1.015~1.134, P=0.013), NRS2002 score  $\geq 3$  (OR=4.457, 95%CI=1.774~11.198, P<0.001), CA50>25 U/mL (OR=2.667, 95%CI=1.044~6.816, P=0.040), AFP >7 g/L (OR=5.355, 95%CI=1.845~15.539, P<0.001), and SII (OR=3.204, 95%CI=1.079~9.512, P=0.036) were independent risk factors for UPR in lung cancer patients. After controlling for length of hospital stay, NRS2002, CA50, AFP, and other factors, further multivariate Logistic regression analysis showed that compared with the Q1 group (SII  $\leq 406.42$ ), the risk of UPR increased in the Q3 group (SII  $\geq 1018.26$ ) (OR=2.262, 95%CI=1.026~4.987, P=0.042). ROC curve analysis demonstrated that the AUC of the regression model for predicting lung cancer UPR was 0.826 (95%CI=0.769~0.882), with an accuracy of 0.802, sensitivity of 0.700, and specificity of 0.854; the AUC of SII alone for predicting lung cancer UPR was 0.660 (95%CI=0.585~0.735), with an accuracy of 0.668, sensitivity of 0.590, and specificity of 0.707. Restricted cubic spline analysis revealed a non-linear positive correlation between SII and unplanned readmission, with a curve inflection point at 1363.78; when SII  $\geq 1363.78$ , the risk of UPR increased 6.37-fold (95%CI=1.93~14.90). Further subgroup analysis showed that when NRS 2002 score <3 points, AFP<7 g/L, and CA50<25 U/mL, the risk of UPR in the SII  $\geq 1363.78$  subgroup was 2.55, 3.23, and 3.67 times that of the SII<1363.78 subgroup, respectively. In the stratified analysis of length of hospital stay, no statistically significant difference was observed between the two groups (P>0.05).

**Conclusion** This study confirms that SII  $\geq 1363.78$  is an independent predictor of short-term unplanned readmission in lung cancer patients receiving ICIs therapy. Based on the good discriminatory performance of the model, dynamic monitoring of SII is recommended to be incorporated into the readmission risk management of such patients, and preventive interventions may be considered when SII exceeds the threshold to reduce the risk of readmission.

## Full Text

### Correlation Between Systemic Immune-Inflammation Index and Unplanned Readmission in Stage III-IV Lung Cancer Patients

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## Abstract

### Background

Lung cancer remains the foremost cause of cancer-related morbidity and mortality worldwide. Short-term unplanned readmissions (UPR) place a significant burden on healthcare systems, compromising care quality, nursing efficiency, and patient outcomes. The systemic immune-inflammation index (SII) serves as a composite marker of systemic inflammation and immune status and has demonstrated prognostic potential in lung cancer progression and therapeutic response. Elucidating its association with UPR in patients treated with immune checkpoint inhibitors (ICIs) may assist in refining clinical risk stratification strategies.

### Objective

This study aimed to evaluate whether SII levels are associated with the likelihood of UPR within 31 days among patients with advanced-stage lung cancer receiving ICIs therapy.

### Methods

This retrospective study included 247 patients with stage III-IV lung cancer who received immune checkpoint inhibitors (ICIs) between January 2023 and May 2024. Patients were categorized into the unplanned readmission (UPR) group (n=164) and the non-UPR group (n=83). Demographic data, clinical treatment information, routine biochemical parameters, and tumor-related markers were collected. Independent risk factors for UPR were identified using multivariate logistic regression and subgroup analyses. Receiver operating characteristic (ROC) curves were generated with the pROC package to evaluate the predictive accuracy, sensitivity, and specificity of both the regression model and SII. Restricted cubic spline (RCS) regression combined with Shapley additive explanations (SHAP) was employed to examine the dose-response relationship between SII and UPR risk, to determine the SII threshold, and to perform subgroup analyses based on this threshold.

### Results

The 31-day incidence of UPR was 33.6% (83/247). Multivariate logistic regression identified length of hospital stay (OR=1.073, 95%CI=1.015-1.134, P=0.013), NRS2002 score  $\geq 3$  (OR=4.457, 95%CI=1.774-11.198, P<0.001), CA50 >25 U/mL (OR=2.667, 95%CI=1.044-6.816, P=0.040), AFP >7 g/L (OR=5.355, 95%CI=1.845-15.539, P<0.001), and SII (OR=3.204, 95%CI=1.079-9.512, P=0.036) as independent predictors of UPR. After adjusting for hospital stay, NRS2002, CA50, and AFP, patients in the highest SII tertile (Q3: SII  $\geq 1,018.26$ ) had a significantly increased risk of UPR compared with those in the lowest tertile (Q1: SII  $\leq 406.42$ ) (OR=2.262, 95%CI=1.026-4.987, P=0.042). ROC curve analysis showed that the regression model had strong discriminatory ability, with an AUC of 0.826 (95%CI=0.769-0.882), accuracy of 0.802, sensitivity of 0.700, and specificity of 0.854. By contrast, SII alone yielded an AUC of 0.660 (95%CI=0.585-0.735), accuracy

of 0.668, sensitivity of 0.590, and specificity of 0.707. RCS analysis revealed a nonlinear positive association between SII and UPR risk, with an inflection point at 1,363.78. When SII was  $\geq 1,363.78$ , the risk of UPR increased 6.37-fold (95%CI=1.93-14.90). Subgroup analyses demonstrated that among patients with NRS2002 $\leq 3$ , AFP $\leq 7$  g/L, and CA50 $\leq 25$  U/mL, those with SII  $\geq 1,363.78$  had 2.55-, 3.23-, and 3.67-fold higher risks of UPR, respectively, compared with patients with lower SII values. Stratified analyses by hospital stay showed no statistically significant differences ( $P>0.05$ ).

### Conclusion

An elevated SII ( $\geq 1,363.78$ ) independently predicts 31-day UPR in patients with advanced lung cancer undergoing ICIs treatment. Given the robust discriminative capacity of the predictive model, incorporation of regular SII monitoring into clinical practice is recommended for early identification of high-risk individuals. Preventive interventions should be considered when SII surpasses the identified threshold to reduce the likelihood of readmission.

### Keywords

Lung cancer; Unplanned readmission; Immune checkpoint inhibitors; Systemic immune-inflammation index

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## Introduction

Lung cancer is the malignant tumor with the highest incidence and mortality worldwide. In 2022, there were approximately 2.48 million new cases and 1.8 million deaths, with about 70% of patients presenting at intermediate or advanced stages [1]. Patients with stage III-IV lung cancer, whose disease has progressed to locally advanced or metastatic stages, have limited treatment options and poor prognosis, and the phenomenon of short-term unplanned readmission is particularly prominent [2,3]. Unplanned patient readmission (UPR) not only significantly increases patients' economic and psychological burden but also leads to excessive consumption of medical resources and seriously impacts medium- and long-term prognosis [4]. Studies have shown that each additional readmission increases the risk of death within 12 months by 1.22-fold and increases medical costs within 6 months by \$2,818 in cancer patients [5]. In lung cancer patients receiving immune checkpoint inhibitors (ICIs), immune-related adverse events such as immune pneumonitis, skin toxicity, and diarrhea may lead to short-term readmission factors that differ from traditional chemotherapy and radiotherapy [6,7]. Early identification of relevant risk factors can optimize clinical intervention strategies.

The systemic immune-inflammation index (SII), as a simple and economical inflammatory marker, comprehensively reflects the body's inflammatory, immune, and platelet activation status [8] and has demonstrated unique value in disease assessment, medium- and long-term prognosis judgment, and efficacy prediction in diseases such as colorectal cancer [9], liver cancer [10,11], and diabetes [12,13].

Research indicates that SII plays an important role in tumor occurrence and development by regulating the tumor microenvironment and promoting tumor cell proliferation, invasion, and metastasis [14,15]. Studies have found that SII is closely related to clinical stage, treatment efficacy, and long-term survival in lung cancer patients [16,17]. However, research on the correlation between SII and short-term unplanned readmission in lung cancer patients remains relatively scarce.

Currently, related studies primarily focus on readmission at 90 days or longer after discharge, aiming to explore the relationship between various physiological and biochemical indicators and patients' medium- to long-term health status and medical needs [18–20]. In contrast, short-term UPR (within 31 days of discharge), as a direct manifestation of early treatment risks, can more promptly reflect patients' health changes and potential risks in the immediate post-discharge period [21]. During this phase, patients' bodies are still in recovery and adaptation, making them highly susceptible to disease progression induced by anti-tumor treatment, which may trigger readmission [22,23]. Accurately identifying risk factors affecting short-term UPR can not only help formulate targeted early intervention measures and optimize clinical treatment strategies but also complement existing long-term prognosis studies, providing evidence for whole-course management of these patients from different time dimensions, thereby reducing readmission rates. Therefore, this study retrospectively analyzed 247 stage III–IV lung cancer patients receiving ICIs treatment to explore the correlation between SII and short-term UPR in this patient population, aiming to provide an important reference for early identification of high-risk patients and formulation of personalized intervention measures to improve patient prognosis and optimize medical resource allocation.

## Methods

**1.1 Study Subjects** We retrospectively included stage III–IV lung cancer patients who visited the Department of Oncology at Chongqing Hospital of Traditional Chinese Medicine between January 2023 and May 2024. Inclusion criteria were: (1) age  $\geq 18$  years; (2) pathologically confirmed malignant lung tumor (stage III–IV); (3) complete examination data; and (4) all included patients received ICIs monotherapy (such as tislelizumab, sintilimab, toripalimab, etc.), and had not received other anti-tumor treatments including chemotherapy, radiotherapy, or targeted therapy within 3 months. Exclusion criteria were: (1) patients discharged before meeting discharge criteria after their first treatment; and (2) patients readmitted within 31 days due to periodic anti-tumor treatment needs.

This study calculated sample size based on the events per variable (EPV) indicator, a method widely applied in regression and risk prediction statistical analysis [24,25]. Based on literature review, the incidence of UPR in cancer patients within 31 days is approximately 30%. This study included a total of 23 variables, with the final number of variables entering regression controlled

within 6, and EPV set at 23. The required sample size was calculated using the formula: Sample size = (Variables entering regression  $\times$  EPV) / (1 - Event incidence rate) =  $6 \times 23 / (1 - 0.3)$ , resulting in 197. Setting the proportion of cases with missing data at 20%, the required sample size was 237. The final analysis included 247 cases, with 164 in the UPR group and 83 in the non-UPR group.

**1.2 Data Collection** We used a self-designed form to collect basic patient information and clinical data, obtaining basic information through the hospital HIS system and collecting biochemical indicators from patients' most recent discharge. Reference ranges for biochemical indicators were based on the laboratory instrument reference values. Data collected included gender, age, smoking status (smoking defined as not having quit and smoking at least 1 cigarette daily; non-smoking defined as never smoking or having quit after cancer diagnosis), alcohol consumption (drinking defined as not having quit and drinking at least once daily; non-drinking defined as never drinking or having quit after cancer diagnosis), diabetes history, Karnofsky Performance Status (KPS) score, NRS2002 score (Nutrition Risk Screening 2002), ADL score (Activity of Daily Living Scale), SII (SII = Platelet count  $\times$  Neutrophil count / Lymphocyte count), length of hospital stay, white blood cell (WBC), lymphocyte (LYM), neutrophil (NEUT), hemoglobin (Hb), platelet (PLT), albumin (ALB), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 50 (CA50), carbohydrate antigen 19-9 (CA19-9), and comorbidities (including diabetes, hypertension, coronary heart disease).

**1.3 Statistical Analysis** Data were analyzed using SPSS 27.0 software. Normally distributed continuous data were expressed as mean  $\pm$  standard deviation, with inter-group comparisons performed using t-tests. Categorical data were expressed as constituent ratios, with inter-group comparisons performed using  $\chi^2$  tests. Two-sided tests were used with  $\alpha$  set at 0.05, and  $P < 0.05$  was considered statistically significant. Multivariate logistic regression was used to screen influencing factors for UPR in lung cancer patients receiving ICIs. Based on SII levels and sample size, patients were divided into three groups using tertiles: Q1 group (SII  $< 406.42$ ), Q2 group (SII =  $406.43 - 1,018.25$ ), and Q3 group (SII  $> 1,018.26$ ). Binary logistic regression analysis was used to study the correlation between SII grouping and UPR, with the first group as reference, reporting odds ratios (OR) and 95% confidence intervals (CI). The pROC package was used to plot receiver operating characteristic (ROC) curves to evaluate the accuracy, sensitivity, and specificity of both the regression model and SII in predicting UPR in lung cancer patients. Trend tests were used to explore the dose-response relationship between SII grouping and UPR risk. Using Python 3.12 with the BSplines library and based on SHAP (SHapley Additive exPlanations) trend changes, restricted cubic spline (RCS) analysis was performed on SII data to determine the SII threshold and conduct stratified analysis based on this threshold.

## Results

**2.1 Comparison of Baseline Characteristics Between Groups** This study included 247 stage III-IV lung cancer patients receiving ICIs treatment, of which 164 did not experience readmission within 31 days (non-UPR group) and 83 experienced UPR (UPR group), yielding a readmission incidence of 33.60% (83/247). Significant differences between groups were observed in KPS score, NRS2002 score, ADL, WBC, LYM, NEUT, Hb, CRP, AFP, CEA, CA19-9, CA50, length of hospital stay, and SII ( $P < 0.05$ ). No significant differences were found in gender, smoking history, alcohol consumption history, TNM stage, diabetes history, hypertension history, coronary heart disease history, PLT, or ALB ( $P > 0.05$ ) (Table 1).

**2.2 Multivariate Logistic Regression Analysis of UPR Influencing Factors in Lung Cancer Patients** Using UPR occurrence as the dependent variable (assignment: yes=1, no=0) and KPS score (assignment:  $< 70 = 1$ ,  $70 = 2$ ), NRS2002 score (assignment:  $< 3 = 1$ ,  $3 = 2$ ), ADL (assignment:  $60-100 = 1$ ,  $40-60 = 2$ ,  $40 = 3$ ), WBC (assignment:  $< 3.5 \times 10^9 / L = 1$ ,  $3.5-9.5 \times 10^9 / L = 2$ ,  $9.5 \times 10^9 / L = 3$ ), LYM (assignment:  $< 1.1 \times 10^9 / L = 1$ ,  $1.1-3.2 \times 10^9 / L = 2$ ), NEUT (assignment:  $< 1.8 \times 10^9 / L = 1$ ,  $1.8-6.3 \times 10^9 / L = 2$ ,  $6.3 \times 10^9 / L = 3$ ), CRP (assignment:  $0-10 \text{ mg/L} = 1$ ,  $> 10 \text{ mg/L} = 2$ ), AFP (assignment:  $0-7 \text{ g/L} = 1$ ,  $> 7 \text{ g/L} = 2$ ), CEA (assignment:  $0-5 \text{ g/L} = 1$ ,  $> 5 \text{ g/L} = 2$ ), CA19-9 (assignment:  $0-37 \text{ U/mL} = 1$ ,  $> 37 \text{ U/mL} = 2$ ), CA50 (assignment:  $0-25 \text{ U/mL} = 1$ ,  $> 25 \text{ U/mL} = 2$ ), length of hospital stay (assigned as actual value), and SII (assigned as actual value) as independent variables, multivariate logistic regression showed that length of hospital stay (OR=1.073, 95%CI=1.015-1.134,  $P=0.013$ ), NRS2002 3 (OR=4.457, 95%CI=1.774-11.198,  $P < 0.001$ ), CA50  $> 25 \text{ U/mL}$  (OR=2.667, 95%CI=1.044-6.816,  $P=0.040$ ), AFP  $> 7 \text{ g/L}$  (OR=5.355, 95%CI=1.845-15.539,  $P < 0.001$ ), and SII (OR=3.204, 95%CI=1.079-9.512,  $P=0.036$ ) were independent risk factors for UPR (Table 2).

Further multivariate logistic regression analysis using UPR occurrence as the dependent variable and SII tertile grouping as the independent variable showed: Model 1 (unadjusted) revealed that compared with Q1 group, Q3 group had increased UPR risk (OR=3.229, 95%CI=1.660-6.281,  $P < 0.001$ ); Model 2 adjusted for length of hospital stay, NRS2002, CA50, and AFP based on Model 1, showing that compared with Q1 group, Q3 group still had increased UPR risk (OR=2.262, 95%CI=1.026-4.987,  $P=0.042$ ) (Table 3).

### 2.3 ROC Curve of SII for Predicting UPR in Lung Cancer Patients

ROC curve analysis showed that the regression model predicted lung cancer UPR with an AUC of 0.826 (95%CI=0.769-0.882), accuracy of 0.802, sensitivity of 0.700, and specificity of 0.854. SII alone predicted lung cancer UPR with an AUC of 0.660 (95%CI=0.585-0.735), accuracy of 0.668, sensitivity of 0.590, and specificity of 0.707 (Figure 1 [Figure 1: see original paper]).

**2.4 SHAP-RCS Fitting Curve of SII and Lung Cancer UPR** SHAP-RCS curve fitting analysis revealed a significant dose-response relationship between SII and lung cancer UPR ( $P=0.003$ ). The black solid line represents the smoothed curve fitting between variables, and the light blue band represents the 95% confidence interval. After adjusting for platelet, WBC, and LYM counts, results showed a significant nonlinear relationship between SII and lung cancer UPR ( $P=0.029$ ). The risk of UPR increased linearly with SII level. Based on the SHAP zero-crossing point, the SII inflection point was determined to be 1,363.78. When  $SII < 1,363.78$ , the risk of unplanned readmission could be reduced, while  $SII > 1,363.78$  increased readmission risk. Piecewise logistic regression analysis based on the SII inflection point showed that when  $SII > 1,363.78$ , patients' UPR risk increased 6.37-fold (95%CI=1.93-14.90) (Figure 2 [Figure 2: see original paper]).

**2.5 Subgroup Analysis Results** To further clarify the association between SII and UPR in lung cancer patients receiving ICIs, subgroup analysis was performed using an SII threshold of 1,363.78 for grouping, with length of hospital stay, NRS2002 score, AFP, and CA50 included as stratification factors. After adjusting for these subgroup factors, SII remained significantly associated with UPR in lung cancer patients: compared with the  $SII < 1,363.78$  subgroup, the  $SII > 1,363.78$  subgroup showed significantly elevated UPR risk (OR=3.03, 95%CI=1.73-5.29,  $P < 0.001$ ). Further stratified analysis showed: when NRS2002 score  $< 3$ , the  $SII > 1,363.78$  subgroup had higher UPR risk than the  $SII < 1,363.78$  subgroup (OR=2.55, 95%CI=1.32-4.91,  $P=0.005$ ). When  $AFP < 7$  g/L, the  $SII > 1,363.78$  subgroup had higher UPR risk (OR=3.23, 95%CI=1.74-5.99,  $P < 0.001$ ). When  $CA50 < 25$  U/mL, the  $SII > 1,363.78$  group had higher UPR risk (OR=3.67, 95%CI=1.85-7.30,  $P < 0.001$ ). Stratified analysis by length of hospital stay showed no statistically significant difference between groups ( $P > 0.05$ ) (Figure 3 [Figure 3: see original paper]).

## Discussion

In recent years, with the widespread application of ICIs in stage III-IV lung cancer treatment, the prognosis of some patients has significantly improved. However, the associated UPR problem has become increasingly prominent, affecting not only treatment efficacy and quality of life but also increasing medical burden [4]. Existing research has focused on the incidence and predictive indicators (such as ALB, Hb, PLT, etc.) of medium- to long-term UPR in patients receiving ICIs, but results vary across studies, and simple, easily accessible sensitive markers are lacking [9,10]. Moreover, insufficient attention to predictive factors for short-term UPR hinders the early development of targeted intervention strategies. SII is a simple and economical inflammatory marker that has shown good predictive efficacy in other systemic diseases and is closely related to tumor occurrence and development [14]. Therefore, this study investigated the incidence of short-term UPR in stage III-IV lung cancer patients after ICIs treatment, analyzed the correlation between SII and other clinical indicators

with short-term UPR, and constructed an effective short-term UPR prediction model to provide basis for clinical prevention and intervention.

This study found that the short-term UPR incidence in stage III-IV lung cancer patients receiving ICIs treatment reached 33.60%, higher than reported by Lennes et al. [26] and Shah et al. [27]. This difference may be attributed to the higher proportion of advanced-stage patients, longer anti-tumor treatment cycles, and most patients having a history of chemotherapy or radiotherapy in our study population, which collectively increased UPR risk. The study showed that the short-term readmission prediction model incorporating SII had good performance ( $AUC > 0.8$ ). When SII reached 1,363.78, it showed a positive dose-response relationship with UPR risk, with the positive impact peaking at 26,778.11. Although SII alone had limited predictive efficacy (accuracy=0.668, specificity=0.707), model performance improved significantly when combined with clinical indicators including length of hospital stay,  $CA50 > 25$  U/mL,  $AFP > 7$  g/L, and  $NRS2002 > 3$ .

Previous studies have shown that SII is positively correlated with the risk of various malignant tumors (including colorectal cancer, renal cancer, liver cancer, lung cancer, ovarian cancer, lymphoma, and myeloma), with the strongest correlations observed for rectal and lung cancer [28]. In small cell lung cancer,  $SII > 820$  indicates poor long-term prognosis and increased mortality risk [29]. Other studies have confirmed that SII can serve as an effective indicator for predicting overall survival in small cell lung cancer patients and helps achieve precision treatment and nursing when combined with other biological indicators [30,31]. Unlike these studies focusing on long-term prognosis, our study specifically examined the correlation between SII and short-term UPR in stage III-IV lung cancer patients receiving ICIs, revealing a positive dose-response relationship between SII and short-term UPR. It is speculated that high SII levels reflect excessive inflammation and low immune status, thereby promoting tumor progression and increasing the risk of poor prognosis [32]. This suggests that in the domestic stage III-IV lung cancer population receiving ICIs, SII is an important risk factor for patient readmission and could be considered a potential predictor for short-term UPR risk.

The mechanism by which SII increases short-term UPR risk remains unclear. ICIs therapy activates the immune system by blocking immune signals, thereby restoring immune cell killing function [33]. However, tumor cells can evade immune surveillance by activating inflammatory signaling pathways to alter the immune microenvironment [34]. SII comprises peripheral LYM, NEUT, and PLT counts, comprehensively reflecting systemic inflammation, thrombosis, and adaptive immunity [35]. NEUT promotes tumor angiogenesis by releasing vascular endothelial growth factor (VEGF) and other pro-angiogenic factors, and secretes interleukin-6 (IL-6) and tumor necrosis factor- (TNF- ) to inhibit anti-tumor immunity [36]. Platelet-derived transforming growth factor- (TGF- ) can activate Smad/Mad protein (Smad) and nuclear factor B (NF- B) pathways, promoting epithelial-mesenchymal transition and enhancing tumor cell activity

and invasiveness [37,38]. Meanwhile, high PLT counts induce cancer thrombus formation, increasing patients' UPR risk [39,40]. Elevated SII levels indicate relative decreases in LYM levels and reduced immunity, leading to decreased benefits from ICIs therapy, which is an important cause of UPR [41,42]. Some studies have also pointed out that high SII levels cause muscle loss and malnutrition in lung cancer patients, and sarcopenia and malnutrition have been confirmed as independent risk factors for UPR in cancer patients [43,44]. Additionally, this study found a positive correlation between SII and elevated tumor markers, suggesting that the inflammatory microenvironment may accelerate disease progression by regulating tumor marker expression, while AFP and CA50 have been confirmed as independent risk factors for UPR in lung cancer patients.

This study provides a biological indicator that can be obtained from routine blood tests, which may contribute to the future development of risk prediction tools for unplanned readmission in this patient population. However, we also found that tumor markers AFP, CA50, length of hospital stay, and NRS2002 score affect short-term UPR and SII levels. This suggests that the synergistic effects of other biological indicators should be considered in clinical practice to avoid amplifying the independent predictive effect of SII. Moreover, our study population mainly comprised domestic stage III-IV lung cancer patients receiving ICIs monotherapy; the applicability of our findings to patients receiving combination therapies (such as ICIs plus chemotherapy or radiotherapy) requires further validation.

This study reveals that in the domestic stage III-IV lung cancer population receiving ICIs, SII is an important predictor of short-term UPR. The prediction model constructed with other clinical parameters showed good performance, helping clinicians take early intervention measures to reduce readmission rates and improve patient prognosis. However, this study has several limitations. First, the small sample size from a single cancer center limits the generalizability of the results. Although we employed subgroup analysis, regression analysis, and adjusted curve fitting analysis to minimize data bias, as a retrospective study, it lacks prospective and dynamic validation. Future studies with larger sample sizes and comprehensive consideration of other confounding treatment factors are needed to further explore the correlation between SII and long-term UPR in this patient population and increase the clinical utility of this indicator for diagnosis, treatment, and nursing care.

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