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ORIGINAL RESEARCH

Bidirectional Relationship Between Systemic Immune-Inflammation Index and Postoperative Pneumonia in Elderly Patients Undergoing Colorectal Cancer Surgery: A Retrospective Cohort Study

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Objective: To explore the bidirectional relationship between the systemic immune-inflammation index (SII) and postoperative pneumonia (POP) in elderly patients with colorectal cancer (CRC), as well as its impact on clinical prognosis, in order to provide evidence for perioperative evidence-based management.

Methods: Clinical data of 2500 patients aged ≥60 years who underwent CRC resection at two hospitals from August 2017 to August 2023 were retrospectively analyzed. Demographic characteristics, preoperative/postoperative SII ((platelet × neutrophil)/lymphocyte counts), laboratory indicators, intraoperative variables, and prognosis were collected. Univariate and multivariate logistic regression analyses were used to determine the bidirectional association between SII and POP. Propensity score matching (PSM) with a 1:3 ratio was performed to balance confounding factors and verify result robustness, and the variance inflation factor (VIF) was used to assess multicollinearity.

Results: The incidence of POP was 6.8% (171/2500), and 25.0% (625/2500) of patients had a postoperative SII increase of ≥30%. Multivariate analysis showed that the highest quartile of preoperative SII (SII_Q4) was an independent risk factor for POP (OR=6.017, 95% CI: 3.377–10.72, P<0.001), and POP was independently associated with a postoperative SII increase of ≥30% (OR=9.063, 95% CI: 4.933–18.696, P<0.001). After PSM, the risks of complications such as respiratory failure, septic shock, and anastomotic leakage, as well as the 2-year mortality rate (76.6% vs 26.5%; OR=9.078), were significantly higher in the POP group than in the non-POP group (all P<0.05). The maximum VIF was 1.30, indicating no significant multicollinearity.

Conclusion: Elevated preoperative SII has a bidirectional association with POP in elderly CRC patients—high preoperative SII increases POP risk, while POP exacerbates postoperative SII elevation, both leading to poor prognosis. Integrating routine perioperative SII screening and dynamic monitoring into clinical practice can facilitate early risk stratification and targeted interventions, thereby optimizing perioperative care quality and improving patient outcomes.

Keywords: colon cancer, immune index, pneumonia, elderly, bidirectional relationship, cohort study

Introduction

Globally, colorectal cancer (CRC) is the third most common malignant tumor and the second most common cause of cancer-related mortality.[1] According to the World Health Organization, approximately 1.93 million new CRC cases were recorded worldwide in 2020 (1.15 million colon cancer cases, 700,000 rectal cancer cases, and 50,000 anal cancer cases), resulting in 940,000 deaths.[2] Approximately 555,000 new CRC cases were diagnosed in China in 2020, accounting for

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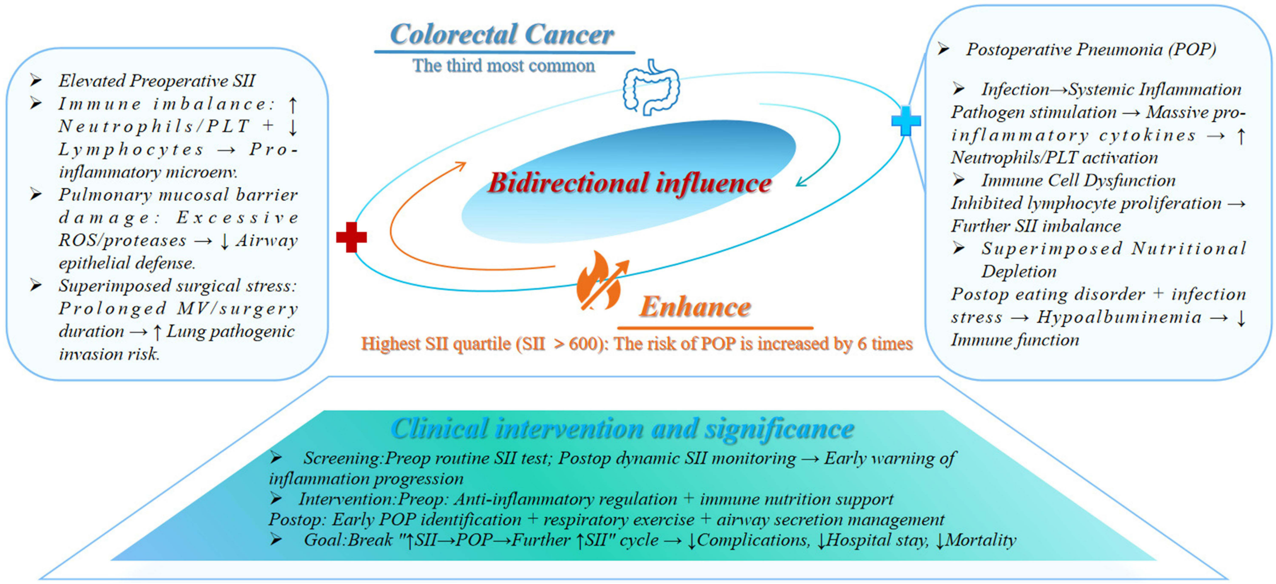
Graphical Abstract



28.8% of the global CRC cases. Among these 555,000 cases, approximately 286,000 deaths were recorded, accounting for 30.6% of the global CRC-related mortality cases.[3] Postoperative pneumonia (POP; also called postoperative pulmonary infection) is a common complication following radical resection of malignant tumors, accounting for 50% of hospital-acquired infectious pneumonias.[4] The incidence rate of POP is in the range of 1.5–15.8%[5] and can be as high as 3–30% after abdominal surgery.[6] Surgical departments, disease types, and surgical procedures contribute to the differential incidence rates of POP. Previous studies have reported the following POP incidence rates in different patients: surgical patients receiving general/local anesthesia: 2.4%;[7] patients undergoing five types of surgeries (breast cancer, CRC, hepatocellular carcinoma, lung cancer, and gastric cancer surgeries): 2%;[8] surgical patients: 1.8%;[9] non-cardiac surgical patients: 1.5%;[10] elderly patients undergoing femoral neck fracture surgery: 7.5%;[11] elderly patients undergoing hip fracture surgery: 4.1%.[12]

The occurrence of POP may prolong extubation time, lead to ventilator dependence, complicate the condition, adversely affect long-term prognosis, and increase healthcare costs. A retrospective study revealed that patients with POP exhibited significantly higher long-term mortality rates and longer hospital stays than those without POP.[13] Several large-sample surveys have revealed that the incidence of POP ranges from 0.9% to 1.6%[14–16] and that the POP incidence increases with age.[17]

An inflammatory tumor microenvironment is associated with long-term chronic inflammation, progression of precancerous lesions, and tumor progression stages. This inflammatory microenvironment comprises a complex network of tumor cells, immune-inflammatory cells around the tumor, stromal cells, extracellular matrix, and microvessels. In the peripheral blood, inflammatory responses lead to alterations in white blood cells, neutrophils, monocytes, lymphocytes, platelets, C-reactive protein (CRP), and albumin. The systemic immune-inflammation index (SII) was first proposed by Hu et al[18] as a comprehensive indicator integrating neutrophil, lymphocyte, and platelet counts, which can accurately reflect the immune status and inflammation level. Previous studies have examined the potential of SII to predict long-term prognosis in patients with malignant tumors.[19,20] SII is also reported to be a useful indicator for predicting postoperative complications (including POP).[21] However, these studies have only evaluated unidirectional associations and examined the predictive effect of preoperative SII on POP. The mechanism through which POP may conversely aggravate immune-inflammatory imbalance and further increase SII has not been elucidated.

Notably, elderly patients undergoing CRC surgery are inherently prone to systemic inflammation and immune dysfunction due to age-related physiological decline: thymic involution reduces T lymphocyte production and function, impairing adaptive immunity;[22] basal inflammatory status is elevated with increased pro-inflammatory cytokines (eg, TNF-α, IL-6) and decreased anti-inflammatory mediators, forming a "chronic low-grade inflammation" state;[23] surgical trauma further amplifies inflammatory responses by activating the NF-κB pathway, promoting neutrophil infiltration and platelet aggregation while inhibiting lymphocyte activity.[24] Such immune-inflammatory perturbations not only increase susceptibility to POP but may also be exacerbated by POP-induced infection, creating a vicious cycle—whereby infection-driven inflammation further impairs immune cell function and elevates SII.[25]

This retrospective cohort study aimed to elucidate the bidirectional relationship between SII and POP in elderly patients with CRC. In particular, the impact of preoperative SII on the risk of POP and the dynamic change in SII after POP occurrence were examined. The findings of this study can potentially elucidate the mechanism underlying the interaction between SII and POP, providing a theoretical basis for optimizing perioperative management, formulating targeted intervention strategies, and improving the clinical outcomes of elderly patients with CRC.

This study recruited patients with CRC aged ≥ 60 years who underwent open radical resection. SII was measured before and after surgery by analyzing the peripheral blood. Several covariates (such as age, gender, American Society of Anesthesiologists (ASA) grade, comorbidities, and intraoperative factors) were adjusted. Multivariate logistic regression and propensity score matching (PSM) were used to evaluate the independent effect of preoperative SII on POP risk.

Methods

Study Design

This study was designed as a single-center retrospective cohort study. Patients who underwent CRC resection under general anesthesia at the Affiliated Wuxi People's Hospital of Nanjing Medical University and Affiliated Hospital of Jiangnan University from August 2017 to August 2023, were screened through the electronic medical record system.

The inclusion criteria were as follows: (1) patients aged ≥ 60 years; (2) patients undergoing laparoscopic sigmoidectomy, laparoscopic left colectomy, and extended radical resection of rectal cancer; (3) Patients with preoperative abdominal computed tomography (CT) results obtained within ≤ 3 months and pathologically diagnosed with malignant tumor; (4) patients with complete and traceable clinical and laboratory data.

The exclusion criteria were as follows: (1) Patients who underwent emergency surgery; (2) patients who received combined spinal-epidural anesthesia during surgery; (3) patients with incomplete laboratory data or unevaluable abdominal CT images; (4) patients with a history of previous malignant tumors; (5) patients with acute or chronic infectious diseases (such as pulmonary infection) before surgery; (6) patients who received anti-tumor treatment (such as radiotherapy and chemotherapy) before surgery; (7) patients who used antibiotics, glucocorticoids, or immunosuppressants within 1 week before surgery; (8) patients with lung metastasis; (9) patients with autoimmune diseases or congenital immunodeficiency.

All patients were followed up for at least 2 years after surgery to assess long-term prognosis, including postoperative complications and mortality.

Data Collection, Outcomes, Definitions, and Follow-Up

To minimize confounding bias, multiple dimensions of covariates were systematically included based on the latest literature and clinical experience. All data, including demographic characteristics, laboratory indicators, intraoperative variables, and perioperative clinical records, were extracted from the electronic medical record system of the Affiliated Wuxi People's Hospital of Nanjing Medical University and Affiliated Hospital of Jiangnan University.

The primary outcome was the incidence of pneumonia within 30 days of surgery. Patients were considered to have pneumonia if they met any two of the following four US Centers for Disease Control and Prevention (CDC) criteria for hospital-acquired pneumonia: (1) Body temperature ≥ 38.3 °C; (2) New-onset cough, expectoration, or dyspnea; (3) New infiltrates on chest X-ray or CT; (4) Positive sputum or blood culture. The date of POP onset was defined as the first day when the patient met the CDC diagnostic criteria. For patients diagnosed with POP, postoperative SII was measured on the 3rd day after POP onset; for patients without POP, postoperative SII was measured on the 7th day after surgery (the routine postoperative follow-up time point for inflammatory indicators in our institutions). This standardized timing ensured consistent assessment of SII changes relative to POP occurrence.

Patients were divided into the following two groups based on age: 60–70 years and > 70 years. Body mass index (BMI) was categorized as physiological (< 24 kg/m²), overweight (24–27.9 kg/m²), and obese (≥ 28 kg/m²). Tumor TNM stage and histological type were obtained from pathological reports. Comorbidities of patients included diabetes mellitus (previous history or admission fasting blood glucose ≥ 7.0 mmol/L), history of cerebral infarction, chronic obstructive pulmonary disease (COPD), and other chronic lung diseases. Additionally, the patients were classified based on preoperative hemoglobin levels (< 110 g/L or ≥ 110 g/L), preoperative albumin levels (< 35 g/L or ≥ 35 g/L), surgical duration (< 180 min or ≥ 180 min), anesthesia duration (< 200 min or ≥ 200 min), high-sensitivity CRP levels (≤ 8 mg/L or > 8 mg/L), and procalcitonin levels (≤ 0.3 ng/mL or > 0.3 ng/mL).

The SII was calculated as follows: SII = (platelet counts × neutrophil counts)/lymphocyte counts (/μL). Based on the distribution, the SII was divided into four quartile groups (Q1–Q4). Intraoperative variables included surgical approach (open or minimally invasive).

The increase in postoperative SII by > 30% was used for reverse analysis. This threshold was determined based on previous studies indicating that a ≥30% change in inflammatory biomarkers (including SII) postoperatively reflects clinically significant immune-inflammatory perturbation, which is associated with adverse outcomes in surgical patients.[26,27] Additionally, preliminary analysis of our cohort data showed that a 30% increase in postoperative SII best discriminated between patients with and without POP-related complications, consistent with the minimal clinically important difference (MCID) for inflammatory indices in elderly oncology populations.[28]

The patients were followed up from the date of surgery until 2 years after surgery or death (whichever occurred first). In-hospital events were extracted in real time from medical records. Post-discharge follow-up was verified via telecommunication.

This study was approved by the Ethics Committee of The Affiliated Wuxi People's Hospital of Nanjing Medical University (Approval No.: KY25172) and complied with the 2013 version of the Declaration of Helsinki. All data were anonymized. Informed consent was waived due to the retrospective nature of the study.

Statistical Analysis

Sample size adequacy was confirmed using power analysis with NCSS PASS V11.0.7 software during the study design phase. The analysis was based on the primary outcome "pneumonia within 30 days after surgery" (estimated incidence: 8%) with preoperative SII as the main exposure factor. The criteria for sample size determination were as follows: significance level: 5% (two-tailed test); power: 80%. Based on the pre-estimated effect size (odds ratio [OR] = 1.8 for the association between high preoperative SII and POP), a sample size of 2000 cases was determined to stably detect the statistical association and support multivariate model analysis with 15–20 key covariates (meeting the requirement of at least 10 outcome events per independent variable). Meanwhile, this sample size also provided sufficient power for reverse analysis (the impact of POP on postoperative SII changes), maintaining a power of over 80% to identify intergroup differences after adjusting for confounders, such as age and ASA grade. Therefore, the final sample size of 2500 cases in this study was statistically reasonable at a 5% significance level and 80% power.

The normal distribution of continuous variables was examined using the Kolmogorov–Smirnov test. Normally distributed variables are expressed as mean ± standard deviation, while skewed distributed variables are expressed as median (interquartile range) [M (P_{25}, P_{75})]. Categorical variables are described as frequency (percentage) [n (%)]. Continuous variables were compared using the independent samples *t*-test or Mann–Whitney *U*-test, while categorical variables were compared using the χ^2-test or Fisher's exact test.

For bidirectional association analysis, variables were selected (screening potential confounders with P < 0.10) using univariate logistic regression, Lasso regression, and the Boruta algorithm. Next, multivariate logistic regression was used to analyze the independent association between SII and POP. The OR and 95% confidence interval (CI) values were calculated. Furthermore, to minimize baseline differences between the POP and non-POP groups and to verify the robustness of the results, propensity score matching was performed using a 1:3 nearest-neighbor algorithm with a caliper of 0.2. PSM was implemented using the MatchIt package (version 4.5.0) in R, with the nearest method for matching and caliper setting; baseline balance after matching was assessed using the cobalt package (version 4.6.1) to generate standardized mean differences (SMD), where SMD < 0.1 was considered adequate balance.

The variance inflation factor (VIF) was used to assess multicollinearity among independent variables. VIF < 10 indicates no severe multicollinearity. All statistical analyses were performed using R software (R Foundation for Statistical Computing, version 4.5.1). Differences were considered significant at P < 0.05.

Results

Impact of Preoperative SII on POP

This study analyzed the data of 2500 patients. The incidence of POP in the study cohort was 6.8% (171/2500). The maximum VIF value for POP (Figure 1) was 1.30, indicating no significant multicollinearity among variables.

Univariate analysis revealed that POP was significantly associated with age, BMI, ASA grade, smoking history, COPD, other chronic lung diseases, TNM stage, histological type, intraoperative blood transfusion, postoperative nasogastric tube placement, hemoglobin, albumin, CRP, procalcitonin, surgical duration, and SII_Q4 (all P < 0.05). Multivariate analysis revealed that the independent risk factors for POP were age > 70 years (OR =1.490), ASA grade III/IV (OR = 2.433), smoking history (OR = 3.431), COPD (OR = 1.861), other chronic lung diseases (OR = 1.950), TNM stage (OR = 1.328), intraoperative blood transfusion (OR = 1.903), postoperative nasogastric tube placement (OR = 1.996), hemoglobin < 110 g/L (OR = 2.553), albumin < 35 g/L (OR = 4.200), CRP > 8 mg/L (OR = 3.279), procalcitonin > 0.3 ng/mL (OR = 4.185), surgical duration ≥ 180 min (OR = 1.590), and SII_Q4 (OR = 6.017) (all P < 0.05) (Table 1).

Impact of POP on Postoperative SII Elevation

The maximum VIF for postoperative SII elevation (Figure 2) was 1.20, indicating no significant multicollinearity among variables. In this study, the postoperative SII increased by ≥ 30% in 625 patients (25.0%) but not in 1875 patients (75.0%).

In patients with POP, the significant elevation of SII (≥30%) was observed at 3 days after the onset of POP symptoms (per CDC diagnostic criteria), which represented the peak of inflammatory response induced by postoperative pulmonary infection. In contrast, the SII levels of non-POP patients were measured at the routine 7-day postoperative time point, with no obvious abnormal elevation observed in the majority (75.0%).

Univariate analysis revealed that the factors associated with a postoperative SII increase of ≥ 30% were age, ASA grade, COPD, postoperative nasogastric tube placement, hemoglobin, albumin, CRP, procalcitonin, and POP (all P < 0.05). Multivariate analysis revealed that the independent risk factors for a postoperative SII increase of ≥ 30% were age > 70 years (OR = 2.976, 95% CI: 2.128–4.149, P < 0.001), ASA grade III/IV (OR = 4.878, 95% CI: 3.390–6.993, P < 0.001), postoperative nasogastric tube placement (OR = 1.629, 95% CI: 1.119–2.375, P = 0.011), hemoglobin < 110 g/L (OR = 3.620, 95% CI: 2.090–6.268, P < 0.001), albumin < 35 g/L (OR = 4.882, 95% CI: 2.802–8.506, P < 0.001), CRP > 8 mg/L (OR = 7.774, 95% CI: 5.070–11.922, P < 0.001), and POP (OR = 9.603, 95% CI: 4.933–18.696, P < 0.001) (Table 2).

Impact of POP on Patient Prognosis

After propensity score weighting, the standardized mean differences (SMDs) decreased significantly. The SMDs of all relevant covariates were < 0.15, indicating that the potential impact of confounding factors was eliminated. This enabled a reliable comparison of treatment effects (Table 3 and Figure 3). Post-matching analysis demonstrated that the incidence and risk of respiratory failure (7.6% vs 2.1%, OR = 3.752), multiple organ dysfunction (5.8% vs 1.4%, OR = 4.488), anastomotic leakage (8.8% vs 3.9%, OR = 2.371), and septic shock (8.2% vs 2.1%, OR=4.065) in the POP group were significantly higher than those in the non-POP group (all P < 0.05). In contrast, the incidence of myocardial infarction (2.3% vs 1.2%, P = 0.29) was not significantly different between the POP and non-POP groups. The total mortality (25.1% vs 8.4%, OR = 3.667), 30-day mortality (5.8% vs 1.6%, OR = 3.919), 6-month mortality (19.3% vs 7.4%, OR = 2.978), 1-year mortality (29.2% vs 12.5%, OR = 2.897), and 2-year mortality (76.6% vs 26.5%, OR = 9.078) rates in the POP group were significantly higher than those in the non-POP group (all P < 0.05) (Table 4).

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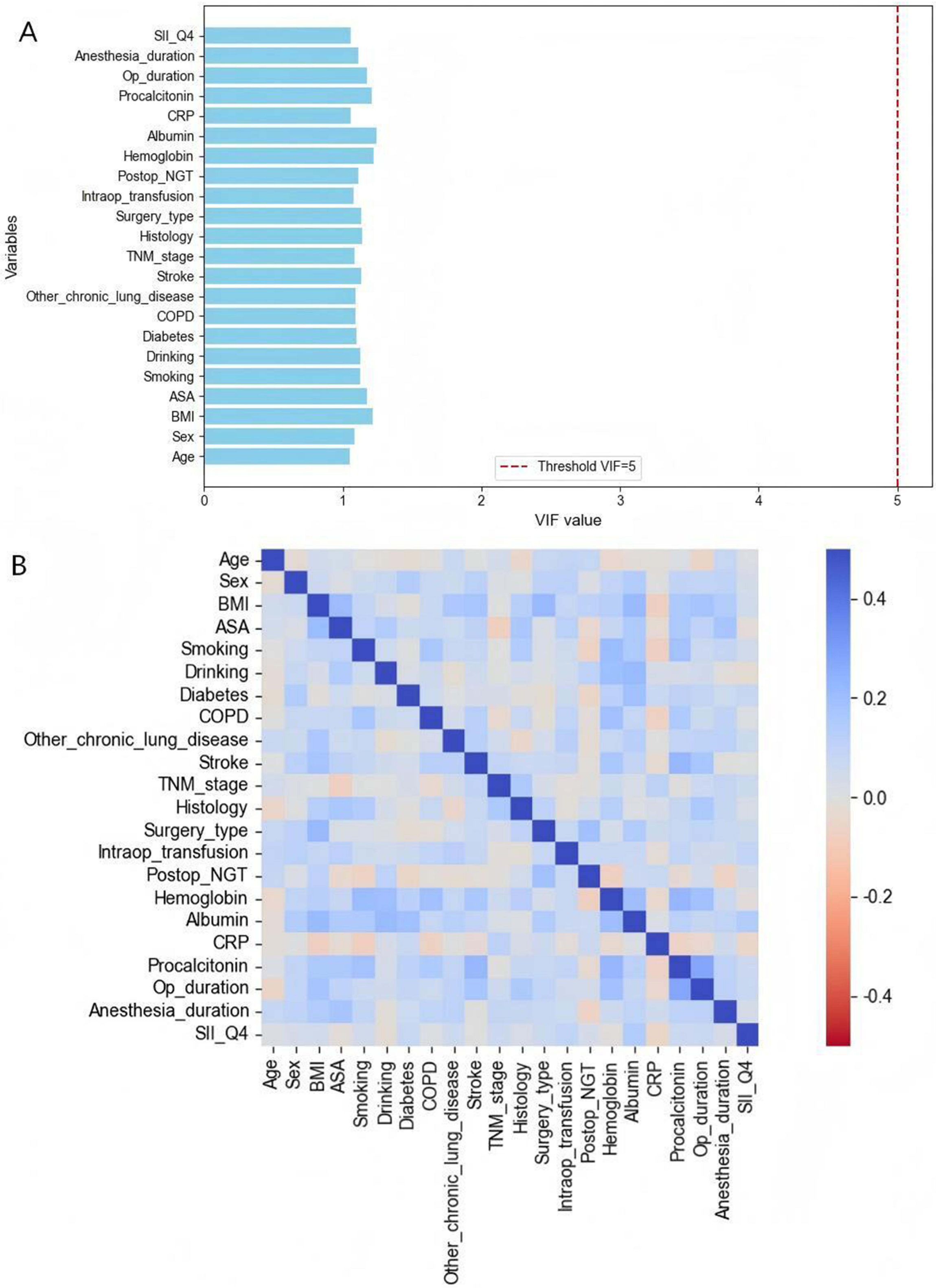

Figure 1 (**A**) Variance inflation factor (VIF) plot for predictors of postoperative pneumonia. (**B**) Correlation heatmap of predictors (Pneumonia model).

Table 1 Univariate and Multivariate Analyses of Factors Associated with Postoperative Pneumonia

Variables	**Univariate Analysis**				**Multivariate Analysis**	
	Total (n=2500)	**Pneumonia [171 (6.8%)]**	**No Pneumonia [2329 (93.2%)]**	**P**	**OR (95% CI)**	**P**
Age (years)						
60-70	1486 (59.4%)	82 (48.0%)	1404 (60.3%)	0.041*	1.490(1.029,2.155)	0.035*
>70	1014 (40.6%)	89 (52.0%)	925 (39.7%)			
Gender						
Female	1121 (44.8%)	73 (42.7%)	1048 (45.0%)	0.558		
Male	1379 (55.2%)	98 (57.3%)	1281 (55.0%)			
BMI		24.25±2.66	23.86±3.03	0.070*	1.051(0.987,1.12)	0.123
ASA						
I/II	1659 (66.4%)	82 (48.0%)	1577 (67.7%)	0.000*	2.433(1.681, 3.521)	0.000*
III/IV	841 (33.6%)	89 (52.0%)	752 (32.3%)			
Smoking history						
No	1747 (69.9%)	84 (49.1%)	1663 (71.4%)	0.000*	3.431(2.352,5.004)	0.000*
Yes	753 (30.1%)	87 (50.9%)	666 (28.6%)			
Alcohol history						
No	1851 (74.0%)	126 (73.7%)	1725 (74.1%)	0.912		
Yes	649 (26.0%)	45 (26.3%)	604 (25.9%)			
Diabetes mellitus						
No	1729 (69.2%)	111 (64.9%)	1618 (69.5%)	0.213		
Yes	771 (30.8%)	60 (35.1%)	711 (30.5%)			
COPD						
No	2108 (84.3%)	132 (77.2%)	1976 (84.8%)	0.008*	1.861(1.163,2.857)	0.003*
Yes	392 (15.7%)	39 (22.8%)	353 (15.2%)			
Other chronic lung diseases						
No	1968 (78.7%)	119 (69.6%)	1849 (79.4%)	0.003*	1.950(1.293,2.942)	0.001*
Yes	532 (21.3%)	52 (30.4%)	480 (20.6%)			
History of cerebral infarction						
No	2242 (89.7%)	148 (86.5%)	2094 (89.9%)	0.163		
Yes	258 (10.3%)	23 (13.5%)	235 (10.1%)			

(*Continued*)

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Table 1 (Continued).

Variables	Univariate Analysis				Multivariate Analysis	
	Total (n=2500)	**Pneumonia [171 (6.8%)]**	**No Pneumonia [2329 (93.2%)]**	**P**	**OR (95% CI)**	**P**
TNM stage						
I	513 (20.5%)	28 (16.4%)	485 (20.8%)	0.007*	1.328(1.082,1.631)	0.007*
II	757 (30.3%)	38 (22.2%)	719 (30.9%)			
III	1002 (40.1%)	89 (52.0%)	913 (39.2%)			
IV	228 (9.1%)	16 (9.4%)	212 (9.1%)			
Histological type						
Others	57 (2.3%)	5 (2.9%)	52 (2.2%)	0.388		
Adenocarcinoma	2138 (85.5%)	144 (84.2%)	1994 (85.6%)			
Mucinous adenocarcinoma	278 (11.1%)	19 (11.1%)	259 (11.1%)			
Signet ring cell carcinoma	27 (1.1%)	3 (1.8%)	24 (1.0%)			
Surgical approach						
Minimally invasive	1501 (60.0%)	96 (56.1%)	1405 (60.3%)	0.281		
Open	999 (40.0%)	75 (43.9%)	924 (39.7%)			
Intraoperative blood transfusion						
No	2155 (86.2%)	133 (77.8%)	2022 (86.8%)	0.001*	1.903(1.194,3.034)	0.007*
Yes	345 (13.8%)	38 (22.2%)	307 (13.2%)			
Postoperative nasogastric tube placement						
No	1753 (70.1%)	102 (59.6%)	1651 (70.9%)	0.002*	1.996(1.364,2.919)	0.000*
Yes	747 (29.9%)	69 (40.4%)	678 (29.1%)			
Hemoglobin (g/L)						
≥110	1496 (59.8%)	74 (43.3%)	1422 (61.1%)	0.000*	2.553(1.365,4.777)	0.003*
<110	1004 (40.2%)	97 (56.7%)	907 (38.9%)			
Albumin (g/L)						
≥35	1392 (55.7%)	57 (33.3%)	1335 (57.3%)	0.000*	4.2(2.255,7.822)	0.000*
<35	1108 (44.3%)	114 (66.7%)	994 (42.7%)			
CRP (mg/L)						
≤8	1573 (62.9%)	79 (46.2%)	1494 (64.1%)	0.000*	3.279(2.025,5.311)	0.000*
>8	927 (37.1%)	92 (53.8%)	835 (35.9%)			
Procalcitonin (ng/mL)						
≤0.3	746 (29.8%)	24 (14.0%)	722 (31.0%)	0.000*	4.185(2.407,7.277)	0.000*
>0.3	1754 (70.2%)	147 (86.0%)	1607 (69.0%)			

(*Continued*)

Table 1 (Continued).

Variables	Univariate Analysis				Multivariate Analysis	
	Total (n=2500)	**Pneumonia [171 (6.8%)]**	**No Pneumonia [2329 (93.2%)]**	**P**	**OR (95% CI)**	**P**
Surgical duration (min)						
<180	1732 (69.3%)	106 (62.0%)	1626 (69.8%)	0.032*	1.590(1.084,2.331)	0.018
≥180	768 (30.7%)	65 (38.0%)	703 (30.2%)			
Anesthesia duration (min)						
<200	1474 (59.0%)	98 (57.3%)	1376 (59.1%)	0.207		
≥200	1026 (41.0%)	73 (42.7%)	953 (40.9%)			
SII_Q4						
No	1875 (75.0%)	58 (33.9%)	1817 (78.0%)	0.000*	6.017(3.377,10.72)	0.000*
Yes	625 (25.0%)	113 (66.1%)	512 (22.0%)			

Note: *P<0.05.

Discussion

This study demonstrated that the incidence of POP in patients undergoing CRC resection was 6.84%, which is consistent with the previously reported range (3–30%).[6] Advanced age was identified as an independent risk factor for POP. One study reported that the incidence rates of POP in patients aged 60–70 years and > 70 years were 5.5% and 8.8%, respectively, indicating the correlation between POP and age.[17] The functions of the respiratory system decline with age. Additionally, elderly patients exhibited multiple comorbidities. Thus, elderly patients are at risk of developing post-surgical severe pulmonary complications.

Laporta et al demonstrated that the functional reserve of various systems, especially cardiopulmonary function, declines with age. The aging of respiratory muscles and the diaphragm decreases the elastic recoil of alveoli, vital capacity, and maximum ventilation volume and increases the residual volume and functional residual capacity. These age-related changes lead to gradual enlargement of distal respiratory bronchioles and alveolar ducts, increasing the anatomical dead space of the lungs. Pulmonary capillaries undergo contraction, increasing pulmonary vascular resistance, which may lead to pulmonary hypertension in severe cases. This series of changes significantly increases the incidence of pulmonary complications in patients.[29]

The lungs of long-term smokers comprise toxic and harmful substances, such as tar and nicotine, which can enhance inflammatory responses,[30] increase mucus secretion in the airways, and decrease airway purification capacity, enhancing the risk of pathogen invasion and proliferation.[31] Chronic lung diseases (such as chronic bronchitis and COPD), which are common in the elderly population, are characterized by airway damage with airflow limitation. Patients with chronic lung diseases exhibit impaired respiratory function and decreased ability to resist pathogens, which enhance the risk of pulmonary infection.[32,33] Therefore, clinicians must focus on airway clearing after radical resection in patients with CRC with a history of smoking or chronic lung diseases to avoid the accumulation of secretions in the lungs, ensure unobstructed breathing, and reduce the incidence of postoperative pulmonary infection.

Hemoglobin, albumin, and surgical duration were among the factors influencing POP. Low hemoglobin is associated with poor prognosis after non-cardiac surgery, including an increased risk of postoperative pulmonary complications.[34] Meanwhile, low albumin is associated with poor postoperative prognosis, such as postoperative infection and pulmonary complications.[29,35] Prolonged surgical duration increases the risk of postoperative complications.[36] Albumin is one of the objective indicators of the overall nutritional status. Early postoperative hypoalbuminemia is associated with post-operative infection. Wierdak et al revealed that a decrease in early postoperative serum albumin level is a risk factor

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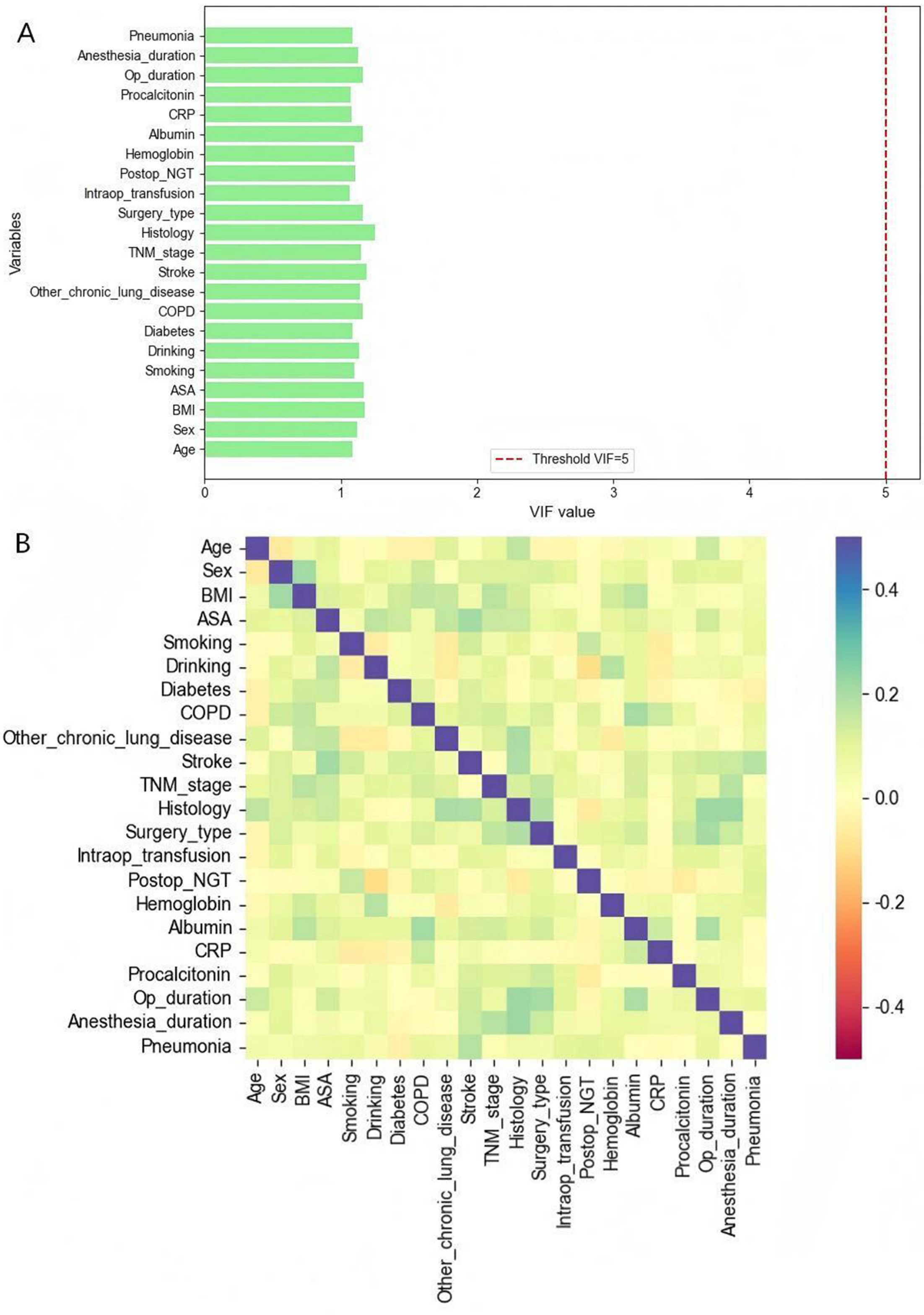

Figure 2 (**A**) Variance inflation factor (VIF) plot for predictors of postoperative SII elevation ≥30%. (**B**) Correlation heatmap of predictors (Postop SII elevation model).

Table 2 Univariate and Multivariate Analyses of Factors Associated with Postoperative SII Elevation ≥30%

Variables	**Univariate Analysis**				**Multivariate Analysis**	
	Total (n=2500)	**Postop SII Elevation ≥30% [625 (25.0%)]**	**Postop SII no Elevation ≥30% [1875 (75.0%)]**	**P**	**OR (95% CI)**	**P**
Age (years)						
60-70	1486 (59.4%)	145 (39.5%)	1341 (62.9%)	0.000*	2.976(2.128,4.149)	0.000*
>70	1014 (40.6%)	222 (60.5%)	792 (37.1%)			
Gender						
Female	1121 (44.8%)	171 (46.6%)	950 (44.5%)	0.464		
Male	1379 (55.2%)	196 (53.4%)	1183 (55.5%)			
BMI		23.96±2.88	23.87±3.03	0.606		
ASA						
I/II	1659 (66.4%)	126 (34.3%)	1533 (71.9%)	0.000*	4.878(3.390,6.993)	0.000*
III/IV	841 (33.6%)	241 (65.7%)	600 (28.1%)			
Smoking history						
No	1747 (69.9%)	247 (67.3%)	1500 (70.3%)	0.244		
Yes	753 (30.1%)	120 (32.7%)	633 (29.7%)			
Alcohol history						
No	1851 (74.0%)	281 (76.6%)	1570 (73.6%)	0.232		
Yes	649 (26.0%)	86 (23.4%)	563 (26.4%)			
Diabetes mellitus						
No	1729 (69.2%)	245 (66.8%)	1484 (69.6%)	0.281		
Yes	771 (30.8%)	122 (33.2%)	649 (30.4%)			
COPD						
No	2108 (84.3%)	297 (80.9%)	1811 (84.9%)	0.053*	1.385(0.910,2.105)	0.129
Yes	392 (15.7%)	70 (19.1%)	322 (15.1%)			
Other chronic lung diseases						
No	1968 (78.7%)	278 (75.7%)	1690 (79.2%)	0.132		
Yes	532 (21.3%)	89 (24.3%)	443 (20.8%)			
History of cerebral infarction						
No	2242 (89.7%)	332 (90.5%)	1910 (89.5%)	0.593		
Yes	258 (10.3%)	35 (9.5%)	223 (10.5%)			

(*Continued*)

Table 2 (Continued).

Variables	Univariate Analysis				Multivariate Analysis	
	Total (n=2500)	**Postop SII Elevation ≥30% [625 (25.0%)]**	**Postop SII no Elevation ≥30% [1875 (75.0%)]**	**P**	**OR (95% CI)**	**P**
TNM stage						
I	513 (20.5%)	58 (15.8%)	455 (21.3%)	0.102		
II	757 (30.3%)	122 (33.2%)	635 (29.8%)			
III	1002 (40.1%)	153 (41.7%)	849 (39.8%)			
IV	228 (9.1%)	34 (9.3%)	194 (9.1%)			
Histological type						
Others	57 (2.3%)	10 (1.6%)	47 (2.5%)	0.719		
Adenocarcinoma	2138 (85.5%)	532 (85.1%)	1606 (85.7%)			
Mucinous adenocarcinoma	278 (11.1%)	74 (11.8%)	204 (10.9%)			
Signet ring cell carcinoma	27 (1.1%)	9 (1.4%)	18 (1.0%)			
Surgical approach						
Minimally invasive	1501 (60.0%)	218 (59.4%)	1283 (60.2%)	0.787		
Open	999 (40.0%)	149 (40.6%)	850 (39.8%)			
Intraoperative blood transfusion						
No	2155 (86.2%)	315 (85.8%)	1840 (86.3%)	0.824		
Yes	345 (13.8%)	52 (14.2%)	293 (13.7%)			
Postoperative nasogastric tube placement						
No	1753 (70.1%)	243 (66.2%)	1510 (70.8%)	0.077*	1.629(1.119,2.375)	0.011
Yes	747 (29.9%)	124 (33.8%)	623 (29.2%)			
Hemoglobin (g/L)						
≥110	1496 (59.8%)	151 (41.1%)	1345 (63.1%)	0.000*	3.620(2.09,6.268)	0.000*
<110	1004 (40.2%)	216 (58.9%)	788 (36.9%)			
Albumin (g/L)						
≥35	1392 (55.7%)	101 (27.5%)	1291 (60.5%)	0.000*	4.882(2.802,8.506)	0.000*
<35	1108 (44.3%)	266 (72.5%)	842 (39.5%)			
CRP (mg/L)						
≤8	1573 (62.9%)	116 (31.6%)	1457 (68.3%)	0.000*	7.774(5.07,11.922)	0.000*
>8	927 (37.1%)	251 (68.4%)	676 (31.7%)			

(*Continued*)

Table 2 (Continued).

Variables	Univariate Analysis				Multivariate Analysis	
	Total (n=2500)	Postop SII Elevation ≥30% [625 (25.0%)]	Postop SII no Elevation ≥30% [1875 (75.0%)]	P	OR (95% CI)	P
Procalcitonin (ng/mL)						
≤0.3	746 (29.8%)	91 (24.8%)	655 (30.7%)	0.022*	1.271(0.843,1.916)	0.252
>0.3	1754 (70.2%)	276 (75.2%)	1478 (69.3%)			
Surgical duration (min)						
<180	1732 (69.3%)	245 (66.8%)	1487 (69.7%)	0.257		
≥180	768 (30.7%)	122 (33.2%)	646 (30.3%)			
Anesthesia duration (min)						
<200	1474 (59.0%)	216 (58.9%)	1258 (59.0%)	0.965		
≥200	1026 (41.0%)	151 (41.1%)	875 (41.0%)			
Postoperative pneumonia						
No	2329 (93.2%)	239 (65.1%)	2090 (98.0%)	0.000*	9.603(4.933,18.696)	0.000*
Yes	171 (6.8%)	128 (34.9%)	43 (2.0%)			

Note: *P<0.05.

Table 3 Comparison of Characteristics and Baseline Covariates Between Patients with and without Postoperative Pneumonia Before and After Matching

Variables	Before Matching				After Matching			
	Pneumonia (n=171)	No Pneumonia (n=2329)	SMD	P	Pneumonia (n=171)	No Pneumonia (n=513)	SMD	P
Age(years)								
60-70	89 (52.0%)	1397 (60.0%)	0.160	0.041*	89 (52.0%)	288 (56.1%)	0.082	0.351
>70	82 (48.0%)	932 (40.0%)			82 (48.0%)	225 (43.9%)		
Gender								
Female	73 (42.7%)	1048 (45.0%)	0.046	0.558	73 (42.7%)	255 (49.7%)	0.141	0.112
Male	98 (57.3%)	1281 (55.0%)			98 (57.3%)	258 (50.3%)		
Obesity								
No	156 (91.2%)	2139 (91.8%)	0.022	0.778	156 (91.2%)	452 (88.1%)	0.102	0.261
Yes	15 (8.8%)	190 (8.2%)			15 (8.8%)	61 (11.9%)		
ASA								
I/II	82 (48.0%)	1577 (67.7%)	0.408	0.000*	82 (48.0%)	249 (48.5%)	0.012	0.895
III/IV	89 (52.0%)	752 (32.3%)			89 (52.0%)	264 (51.5%)		

(*Continued*)

Table 3 (Continued).

Variables	**Before Matching**				**After Matching**			
	Pneumonia (n=171)	**No Pneumonia (n=2329)**	**SMD**	**P**	**Pneumonia (n=171)**	**No Pneumonia (n=513)**	**SMD**	**P**
Smoking history								
No	84 (49.1%)	1663 (71.4%)		0.000*	84 (49.1%)	260 (50.7%)	0.031	0.724
Yes	87 (50.9%)	666 (28.6%)	0.467		87 (50.9%)	253 (49.3%)		
Alcohol history								
No	126 (73.7%)	1725 (74.1%)	0.009	0.912	126 (73.7%)	371 (72.3%)	0.031	0.908
Yes	45 (26.3%)	604 (25.9%)			45 (26.3%)	142 (27.7%)		
Diabetes mellitus								
No	111 (64.9%)	1618 (69.5%)	0.097	0.213	111 (64.9%)	347 (67.6%)	0.058	0.511
Yes	60 (35.1%)	711 (30.5%)			60 (35.1%)	166 (32.4%)		
COPD								
No	132 (77.2%)	1976 (84.8%)	0.196	0.008*	119 (69.6%)	383 (74.7%)	0.000	1.000
Yes	39 (22.8%)	353 (15.2%)			52 (30.4%)	130 (25.3%)		
Other chronic lung diseases								
No	119 (69.6%)	1849 (79.4%)	0.226	0.003*	119 (69.6%)	383 (74.7%)	0.113	0.194
Yes	52 (30.4%)	480 (20.6%)			52 (30.4%)	130 (25.3%)		
History of cerebral infarction								
No	148 (86.5%)	2094 (89.9%)	0.104	0.163	148 (86.5%)	456 (88.9%)	0.071	0.410
Yes	23 (13.5%)	235 (10.1%)			23 (13.5%)	57 (11.1%)		
TNM stage								
I	28 (16.4%)	485 (20.8%)	0.114	0.007*	28 (16.4%)	100 (19.5%)	0.081	0.591
II	38 (22.2%)	719 (30.9%)	0.197		38 (22.2%)	110 (21.4%)	0.019	
III	89 (52.0%)	913 (39.2%)			89 (52.0%)	243 (47.4%)		
IV	16 (9.4%)	212 (9.1%)	0.009		16 (9.4%)	60 (11.7%)	0.076	
Histological type								
Others	5 (2.9%)	52 (2.2%)		0.2568	5 (2.9%)	12 (2.3%)		0.800
Adenocarcinoma	144 (84.2%)	1994 (85.6%)	0.045		144 (84.2%)	436 (85.0%)	0.009	
Mucinous adenocarcinoma	19 (11.1%)	259 (11.1%)	0.109		19 (11.1%)	58 (11.3%)	0.054	
Signet ring cell carcinoma	3 (1.8%)	24 (1.0%)	0.111		3 (1.8%)	7 (1.4%)	0.056	

(*Continued*)

Table 3 (Continued).

Variables	Before Matching				After Matching			
	Pneumonia (n=171)	**No Pneumonia (n=2329)**	**SMD**	**P**	**Pneumonia (n=171)**	**No Pneumonia (n=513)**	**SMD**	**P**
Surgical approach								
Minimally invasive	96 (56.1%)	1405 (60.3%)	0.085	0.281	96 (56.1%)	293 (57.1%)	0.020	0.824
Open	75 (43.9%)	924 (39.7%)			75 (43.9%)	220 (42.9%)		
Intraoperative blood transfusion								
No	133 (77.8%)	2022 (86.8%)	0.238	0.001*	133 (77.8%)	374 (72.9%)	0.113	0.208
Yes	38 (22.2%)	307 (13.2%)			38 (22.2%)	139 (27.1%)		
Postoperative nasogastric tube placement								
No	102 (59.6%)	1651 (70.9%)	0.237	0.002*	102 (59.6%)	301 (58.7%)	0.020	0.822
Yes	69 (40.4%)	678 (29.1%)			69 (40.4%)	212 (41.3%)		
Hemoglobin (g/L)								
≥110	74 (43.3%)	1422 (61.1%)	0.361	0.000*	74 (43.3%)	192 (37.4%)	0.119	0.174
<110	97 (56.7%)	907 (38.9%)			97 (56.7%)	321 (62.6%)		
Albumin (g/L)								
≥35	57 (33.3%)	1335 (57.3%)	0.496	0.000*	57 (33.3%)	151 (29.4%)	0.084	0.337
<35	114 (66.7%)	994 (42.7%)			114 (66.7%)	362 (70.6%)		
Surgical duration (min)								
<180	106 (62.0%)	1626 (69.8%)	0.165	0.032*	106 (62.0%)	320 (62.4%)	0.008	0.927
≥180	65 (38.0%)	703 (30.2%)			65 (38.0%)	193 (37.6%)		
Anesthesia duration (min)								
<200	98 (57.3%)	1376 (59.1%)	0.036	0.207	98 (57.3%)	296 (57.7%)	0.008	0.929
≥200	73 (42.7%)	953 (40.9%)			73 (42.7%)	217 (42.3%)		
CRP (mg/L)								
≤8	79 (46.2%)	1494 (64.1%)	0.366	0.000*	79 (46.2%)	258 (50.3%)	0.082	0.354
>8	92 (53.8%)	835 (35.9%)			92 (53.8%)	255 (49.7%)		
Procalcitonin (ng/mL)								
≤0.3	24 (14.0%)	722 (31.0%)	0.414	0.000*	24 (14.0%)	98 (19.1%)	0.136	0.134
>0.3	147 (86.0%)	1607 (69.0%)			147 (86.0%)	415 (80.9%)		
SII_Q4								
No	58 (33.9%)	1817 (78.0%)	0.990	0.000*	58 (33.9%)	192 (37.4%)	0.073	0.409
Yes	113 (66.1%)	512 (22.0%)			113 (66.1%)	321 (62.6%)		

Note: *P<0.05.

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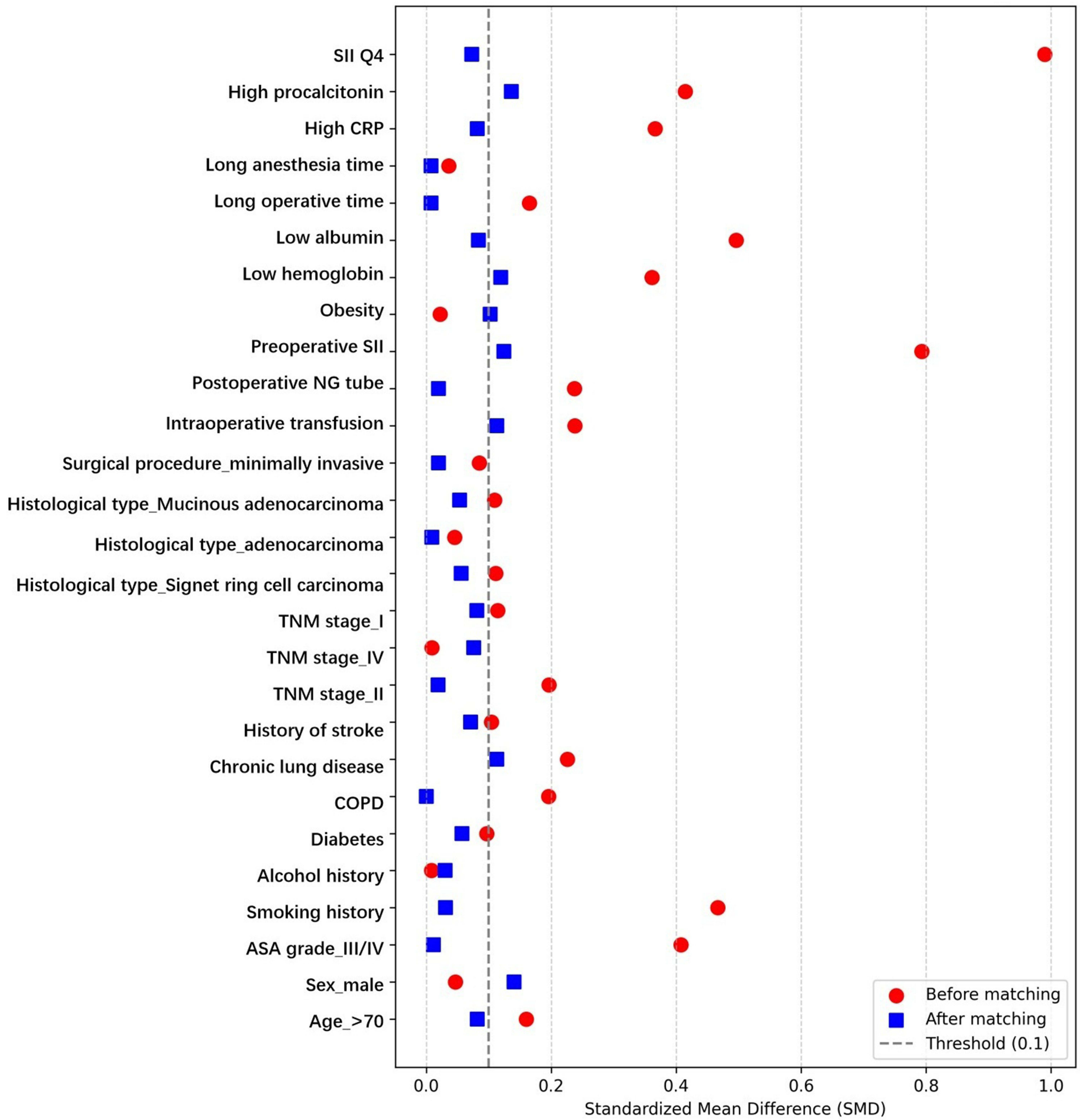

Figure 3 Love Plot: Covariate Balance Before and After Matching.

for infectious complications (including pneumonia) in patients with CRC undergoing laparoscopic surgery.[37] Preoperative hypoalbuminemia is also reported to be associated with pneumonia after hip fracture surgery,[38] which is consistent with the results of this study.

This study demonstrated that procalcitonin can aid in the early diagnosis of POP. Procalcitonin is an indicator of infection, which is beneficial for the early diagnosis of POP and sepsis, monitoring treatment response, and predicting prognosis.[39]

Prolonged surgical duration (≥ 3 hours) is reported to be an independent risk factor for POP. This risk further increases when the mechanical ventilation duration is > 3 hours,[40] which is consistent with the results of this study. Prolonged surgical duration increases the time patients receive controlled ventilation with anesthetic machines, enhancing

Table 4 Comparison of Complications and Mortality Between Patients with and without Postoperative Pneumonia After Matching

Variables	Pneumonia (n=171)	No Pneumonia (n=513)	OR (95% CI)	P
Complications				
Respiratory failure				
No	158 (92.4%)	502 (97.9%)	3.752 (1.644,8.563)	0.002*
Yes	13 (7.6%)	11 (2.1%)		
Multiple organ dysfunction				
No	161 (94.2%)	506 (98.6%)	4.488 (1.694,11.892)	0.004*
Yes	10 (5.8%)	7 (1.4%)		
Myocardial infarction				
No	167 (97.7%)	507 (98.8%)	1.985 (0.556,7.091)	0.29
Yes	4 (2.3%)	6 (1.2%)		
Anastomotic leakage				
No	156 (91.2%)	493 (96.1%)	2.371 (1.193,4.714)	0.014*
Yes	15 (8.8%)	20 (3.9%)		
Septic shock				
No	157 (91.8%)	502 (97.9%)	4.065 (1.822,9.064)	0.000*
Yes	14 (8.2%)	11 (2.1%)		
Mortality				
Total mortality				
No	128 (74.9%)	470 (91.6%)	3.667 (2.303,5.838)	0.000*
Yes	43 (25.1%)	43 (8.4%)		
30-day mortality				
No	161 (94.2%)	505 (98.4%)	3.919 (1.525,10.074)	0.006*
Yes	10 (5.8%)	8 (1.6%)		
6-month mortality				
No	138 (80.7%)	475 (92.6%)	2.978 (1.801,4.925)	0.000*
Yes	33 (19.3%)	38 (7.4%)		
1-year mortality				
No	121 (70.8%)	449 (87.5%)	2.897 (1.907,4.402)	0.000*
Yes	50 (29.2%)	64 (12.5%)		
2-year mortality				
No	40 (23.4%)	377 (73.5%)	9.078 (6.057,13.608)	0.000*
Yes	131 (76.6%)	136 (26.5%)		

Note: *P<0.05.

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their susceptibility to pathogen infection. Upper respiratory tract secretions enter the distal trachea through the gap between the cuff of the endotracheal tube and the tracheal wall, carrying pathogenic bacteria into the deep lungs and causing infection.[41] Additionally, prolonged surgery may lead to inappropriate fluid management, increasing the risk of pulmonary edema, which may lead to pneumonia and even respiratory failure.[4] Furthermore, prolonged surgery can promote enhanced blood loss. Blood loss decreases the number of immune cells and albumin, weakening the immune system function. Prolonged surgery also significantly increases the probability of intraoperative blood transfusion. Blood product transfusion may cause transfusion-related acute lung injury.[7] Therefore, timely intervention should be implemented for major surgeries with long durations.

This study demonstrated that postoperative nasogastric tube placement also leads to POP in elderly patients. One study revealed that enteral nutrition in the neurosurgical intensive care unit can lead to pulmonary complications. Prolonged nasogastric tube placement can damage the tissues around the lumen, injure the nasopharyngeal mucosa, and increase secretions. This can impair spontaneous breathing function and the cough-swallow reflex, leading to massive reflux of gastric contents. Consequently, gastrointestinal bacteria move upward, increasing the incidence of pulmonary complications.[42] However, some studies have reported that nasogastric tube placement can reduce the incidence of aspiration, decreasing the occurrence of aspiration pneumonia.[43] Therefore, for patients at high risk of aspiration, preoperative gastric tube placement can effectively reduce the occurrence of reflux and aspiration during and after surgery, decreasing the risk of pulmonary complications caused by aspiration.

The incidence of chronic lung diseases, including COPD, significantly varied between the POP and non-POP groups. COPD adversely affects the quality of life of the elderly. Previous studies have confirmed that the incidence of pulmonary complications is significantly high in patients with COPD who undergo surgery.[44] Smoking is a major risk factor for COPD. Smokers are more likely to develop postoperative pulmonary complications than non-smokers.[4] In this study, patients with other comorbidities (diabetes mellitus and cerebral infarction) exhibited differential disease durations, severities, and treatment histories. However, POP did not occur in these patients. This does not indicate that these underlying diseases do not affect the occurrence of POP. The impact of these comorbidities on patients must be comprehensively evaluated to determine the condition of patients.

This retrospective cohort study aimed to explore the bidirectional relationship between SII and POP in elderly patients with CRC and analyze the impact of this interaction on clinical outcomes. Elevated preoperative SII was an independent risk factor for POP. Meanwhile, POP can increase the SII. Thus, elevated SII and POP may form a potential vicious cycle that is associated with adverse patient prognosis. SII can be calculated based on platelet, neutrophil, and lymphocyte counts, which are routinely performed in clinical settings. Patients with high SII exhibit significantly increased serum levels of inflammatory factors and chemokines.[45] Elevated SII is a marker of immune dysfunction and excessive inflammatory response. Previous studies have reported that elevated SII is correlated with postoperative complications in patients with cancer.[46] High preoperative SII is associated with an increased risk of surgical site infection and prolonged hospital stay.[20] However, most of these studies have evaluated the unidirectional predictive value of SII for complications but not the reverse impact of complications on SII. In this study, multivariate logistic regression analysis revealed that preoperative SII of $\geq$ 600 (Q4) is an independent risk factor for POP (OR = 6.017, 95% CI = 3.377–10.72, $P < 0.001$). After adjusting for confounders, such as age and ASA grade, POP was associated with an enhanced risk of a 30% increase in postoperative SII (OR = 24.366, 95% CI = 16.683–35.590, $P = 0.002$). This bidirectional association has rarely been systematically studied in elderly patients with CRC, suggesting a potential "biomarker-complication" interaction pattern in this specific elderly surgical population.

The observed bidirectional association between SII and POP in elderly patients with CRC may be explained by interconnected immune-inflammatory mechanisms and pathological processes (a hypothesis requiring further validation). Elevated preoperative SII increases the risk of POP by suppressing immune responses and inducing excessive inflammation. High SII is associated with increased pro-inflammatory cell counts (neutrophils and platelets) and decreased anti-inflammatory lymphocyte counts. Neutrophils may release excessive reactive oxygen species and proteases, damaging the airway mucosal barrier. Meanwhile, platelets undergo activation and aggregation to form microthrombi, affecting pulmonary microcirculation. A decrease in lymphocyte counts weakens the ability of the host to clear pathogens (such as *Streptococcus pneumoniae* and *Escherichia coli*, which are associated with POP in patients with CRC and intestinal flora translocation).

Conversely, POP exacerbates the increase in SII through multiple pathways, amplifying the cycle effect. Pulmonary infection may trigger a systemic inflammatory response; pathogens and their toxins may stimulate the release of pro-inflammatory cytokines (such as interleukin-6 and tumor necrosis factor-α), which could promote neutrophil proliferation and platelet activation and inhibit lymphocyte proliferation and function, potentially increasing the SII value. Additionally, elderly patients with CRC often exhibit decreased food intake and absorption disorders after surgery. POP further aggravates nutritional depletion, which impairs immune cell function (such as lymphocyte activation) and maintains excessive inflammation.

CRC-specific factors further strengthen this cycle. For example, if the primary tumor is located in the rectum, neoadjuvant radiotherapy may pre-activate the systemic inflammatory response, potentially increasing baseline SII; POP may then exacerbate this inflammatory state, possibly leading to a prolonged increase in SII. Similarly, anastomotic leakage (a common complication of CRC surgery) may occur concurrently with POP, and the resulting intra-abdominal infection may further amplify the inflammatory response (this interaction requires further verification). SII is more efficient in capturing this "multiple complication overlap" phenomenon than a single biomarker, suggesting potential clinical value of SII in elderly patients with CRC.

Therefore, there may be clinical value in developing targeted intervention measures to potentially disrupt the proposed elevated SII-POP cycle, as this interaction is associated with adverse short-term and long-term outcomes. Post-matching analysis (1:3 PSM) revealed that patients with high preoperative SII + POP exhibited higher risks of postoperative complications, longer hospital stays, and higher mortality rates at all stages than those without high preoperative SII + POP.

The results of this study provide a clear direction for clinical intervention. The following targeted strategies may be worth exploring for elevated preoperative SII ($\geq$ 600): preoperative administration of low-dose non-steroidal anti-inflammatory drugs (such as celecoxib) to potentially regulate the inflammatory response (gastrointestinal side effects must be closely monitored); supplementation of immune-nutritional agents (such as omega-3 fatty acids and arginine) to potentially improve lymphocyte function; optimization of comorbidity management (such as controlling COPD) to reduce baseline inflammation levels (the efficacy of these strategies requires prospective validation).

SII has several advantages in clinical applications. First, SII can be easily calculated based on routine blood test indicators (platelets, neutrophils, and lymphocytes) without additional costs or specimen collection. In contrast to inflammatory markers (such as procalcitonin), SII may be a convenient option for perioperative screening of elderly patients with CRC.

Limitations and Future Research Directions

This study has several limitations that should be considered when interpreting the results: ① Residual confounding may exist due to its retrospective design, as preoperative functional capacity, cognitive function, and postoperative rehabilitation intensity—factors potentially influencing immune-inflammatory recovery and POP risk—were not included. ② POP was defined based on in-hospital events, which may underestimate the incidence of late-onset pneumonia post-discharge. ③ A fixed SII threshold ($\geq$600) was used, while the optimal cutoff for elderly CRC patients may vary by tumor stage and surgical approach. ④ The findings are limited to surgically treated patients and not validated in non-surgical populations (eg, those receiving palliative chemotherapy).

Future studies should address these gaps: conduct prospective cohorts to verify the SII-POP bidirectional relationship and evaluate targeted interventions (eg, preoperative SII-lowering therapy); develop a combined predictive model with SII and other biomarkers (eg, albumin, CRP) to improve risk stratification; determine subgroup-specific optimal SII thresholds via piecewise regression; and explore underlying mechanisms (eg, gut microbiota-mediated immune-inflammatory regulation) to inform precise interventions.

Conclusions

This retrospective cohort study identified a bidirectional association between elevated preoperative systemic immune-inflammation index (SII) and postoperative pneumonia (POP) in elderly patients with colorectal cancer (CRC). Elevated preoperative SII is associated with an increased risk of POP, and the development of POP is in turn associated with a further elevation in postoperative SII, with this interaction linked to adverse short-term and long-term clinical outcomes. These results suggest that routine preoperative SII screening and dynamic postoperative SII monitoring may be integrated into the perioperative management of elderly CRC patients to facilitate risk stratification. Targeted interventions for patients with elevated preoperative SII and timely clinical management of POP to mitigate excessive postoperative SII elevation may help reduce the incidence of perioperative complications and improve clinical prognosis in this patient population. Future prospective multicenter cohort studies are needed to validate this bidirectional association and enhance the generalizability of the findings; additional research should explore subgroup-specific optimal SII thresholds (eg, by tumor stage, surgical approach) to refine risk stratification strategies, and randomized controlled trials are required to evaluate the efficacy of SII-guided targeted interventions (eg, anti-inflammatory therapy, immune modulation) for the translational application of these findings in clinical practice.

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Disclosure

The authors affirm that no conflicts of interest exist regarding this research.

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