

Relationship Between Novel Inflammatory Indices and the Incidence of Postoperative Pneumonia After Endovascular Embolization for Aneurysmal Subarachnoid Hemorrhage

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Background: Accurate identification of the risk of postoperative pneumonia (POP) in aneurysmal subarachnoid hemorrhage (aSAH) is essential for the implementation of stratified treatment. This study evaluated the relevance and utility of the Systemic Immuno-inflammatory Index (SII) and the Systemic Inflammatory Response Index (SIRI) in predicting pneumonia after aSAH.

Methods: Two hundred and forty patients undergoing aSAH intervention were included. Differences in SII and SIRI between patient groups were analyzed by propensity score matching (PSM). Receiver Operating Characteristic curves (ROC) were used to evaluate the predictive validity of SII and SIRI and to determine their predictive thresholds. The association of these indices with POP risk was assessed by multivariate logistic regression and restricted cubic spline (RCS), and subgroup analyses were performed.

Results: The overall POP prevalence was 60%, with 37.5% males and 62.5% females. PSM analyses showed statistically significant differences between the two groups for SII ($P=0.032$) and SIRI ($P=0.02$). They had a high predictive accuracy for predicting POP, with AUC values of 0.643 and 0.644, respectively. SII and SIRI were positively associated with the POP risk, independent of other confounders. Moreover, further sensitivity analysis and RCS supported the stability of this finding. Subgroup analyses showed that the relationship was stable across subgroups.

Conclusion: This study reveals the potential role of SII and SIRI in predicting the risk of postoperative pneumonia in patients with aSAH, and provides a strong basis for early identification and stratification of patients who are at high risk of postoperative pneumonia in aSAH.

Keywords: aneurysmal subarachnoid hemorrhage, interventional embolization, postoperative pneumonia, novel inflammatory index, correlation analysis

Introduction

Subarachnoid hemorrhage (SAH) is a severe form of stroke, primarily caused by the rupture of an intracranial aneurysm, which accounts for approximately 85% of all spontaneous SAH cases.¹ Aneurysmal subarachnoid hemorrhage (aSAH) is associated with an acute onset, high risk of disability, and mortality.² aSAH has a varying global incidence, typically ranging from 6 to 20 per 100,000 people per year, and accounts for approximately 5% of all stroke types.^{3,4} When treating cerebral aneurysms, endovascular treatment (especially coil spring embolization) has become a mainstream procedure, especially in developed countries.⁵ Physicians and patients increasingly favor this minimally invasive approach because it is less invasive. Although many patients have successfully managed their aneurysms surgically, postoperative complications continue to affect the patient's prognosis and increase the financial burden. Postoperative pneumonia (POP) is one of the most common postoperative complications in patients with aSAH.⁶ Studies have shown

that approximately 13% to 37% of patients with aSAH may develop POP after undergoing surgical treatment.^{7,8} A large retrospective study showed that postoperative pneumonia in these cases was directly associated with poor outcomes at the time of patient discharge and 90 days after discharge.⁶ Therefore, accurate and rapid prediction of POP is critical for the management of patients with aSAH.

Systemic inflammation after aSAH not only leads to secondary injury but is strongly associated with the development of POP. This association may be mediated through a complex neuro-immune interaction known as the brain-lung axis.⁹ Therefore, estimates of inflammatory status can help predict the development of pneumonia in patients after aSAH. The Systemic Immune Inflammation Index (SII) and the Systemic Inflammatory Response Index (SIRI) are innovative composite markers that capture both local immune activity and systemic inflammatory responses.¹⁰ These indices are comprehensive metrics that integrate four types of inflammatory cells, including platelets, neutrophils, monocytes, and lymphocytes. SII was first developed by Hu et al in 2014 who reported that SII was an independent predictor of overall survival and recurrence-free survival in patients with hepatocellular carcinoma.¹¹ It has since been extensively studied and applied in various disease areas of medicine. Previous studies have shown that in stroke patients, immunosuppression and inflammatory responses lead to a reduction in lymphocytes and platelets while increasing neutrophil counts, significantly correlating with an elevated risk of stroke.¹⁰ Recent studies have shown that the SII and SIRI are more predictive of stroke-associated pneumonia (SAP) in patients with acute ischemic stroke than traditional inflammatory biomarkers. These indices are effective in quantifying the immune response and help in the early detection of SAP.¹² However, the application of SII and SIRI in assessing the risk of pneumonia complications in patients with aSAH has received little attention. Consequently, this study investigated the validity of these markers in predicting postoperative pneumonia (POP) in patients with aneurysmal subarachnoid hemorrhage undergoing interventional embolization, which is a key factor in improving patient prognosis.

Methods

Study Design and Patients

This retrospective study was conducted at the Second Hospital of Fujian Medical University. From December 2017 to December 2023, a total of 240 patients with aneurysmal subarachnoid hemorrhage who underwent aneurysmal interventional embolization were enrolled in the study. The study protocol was approved by the Ethics Committee of the Second Hospital of Fujian Medical University (2022–35). In addition, the study was reported by following the STROBE guidelines and based on the Declaration of Helsinki.

Inclusion criteria included (1) age 18 years and older, (2) diagnosis of subarachnoid hemorrhage confirmed by computed tomography angiography or digital subtraction angiography, (3) confirmed the presence of a single aneurysm, and (4) endovascular embolization performed within 72 hours of symptom onset. Exclusion criteria included (1) death within 24 hours of admission; (2) diagnosis of pneumonia before admission; (3) history of subarachnoid hemorrhage; (4) diagnosis of other cerebrovascular diseases such as Moya-Moya disease, cerebral arteriovenous malformations, or intracranial arteriovenous fistulae; (5) history of connective tissue or autoimmune diseases, uremia, hematologic disorders, malignancies, cirrhosis of the liver, chronic lung disease, and other infectious diseases; (6) Antibiotics, systemic glucocorticoids, and immunosuppressants had been used in the month prior to admission.; (7) missing of clinically relevant data.

Covariates

Based on clinical experience and previous studies in the literature, information about patients with subarachnoid hemorrhage was retrieved from the hospital's electronic health record system. This information included demographic characteristics, hospital admission, past medical history, laboratory results, and imaging findings. Specifically, it involved aspects such as age, gender, temperature on admission, blood pressure before any intervention, GCS, and Hunt-Hess scores. Past medical history was mainly related to hypertension, diabetes mellitus, coronary artery disease, other cerebrovascular accidents, and long-term use of anticoagulants and antiplatelet drugs. Imaging was used to assess the location of individual aneurysms and the specific occurrence of pneumonia. Laboratory tests performed within 6 hours of hospitalization included monocytes, neutrophils, lymphocytes, platelets, hemoglobin, glucose, creatinine, uric acid, triglycerides, cholesterol, and albumin.

Assessment of Exposure Variables

Novel inflammatory indices, the SII and the SIRI, were used to comprehensively assess a patient's immune function and inflammatory status. Meanwhile, elevated SII and SIRI usually indicated impaired immune function and progression of inflammation. Based on existing studies, we recalculated SII and SIRI using the following formulas: $SII = (\text{neutrophil count} \times \text{platelet count}) / \text{lymphocyte count}$; $SIRI = (\text{neutrophil count} \times \text{monocyte count}) / \text{lymphocyte count}$.

Diagnosis of Ending Variables

POP in this study is defined as any lower respiratory tract infection occurring within 30 days post-surgery, adhering to the modified Centers for Disease Control and Prevention (CDC) guidelines. The criteria stipulate that: (1) a probable case of POP cannot solely rely on initial or follow-up chest X-rays for diagnosis, nor can it be ascribed to another existing condition; (2) a proven case of POP is established when subsequent chest X-rays document a discernible diagnostic change.¹³ In this study, POP was the outcome variable.

Statistical Analysis

Continuous variables were characterized by their standard deviations and assessed using *t*-tests or Wilcoxon rank-sum tests, as appropriate. Categorical variables were presented in terms of frequencies and percentages and analyzed via chi-square tests or Fisher's exact test when necessary. To deal with the imbalance of covariates across groups and to validate the correlation results, this study implemented a 1:1 propensity score matching according to the nearest-neighbor matching method for both groups. The ability of the SII and SIRI to predict POP was determined by the area under the curve (AUC) of the subjects' work characteristics, where the optimal threshold corresponded to the point that maximized the Youden index. Multivariate logistic regression models were employed to assess the relationship between the variables. An unadjusted model 1 was first applied, followed by models progressively adjusted for covariates: model 2 adjusted for age, sex, hypertension, diabetes mellitus, coronary artery disease, and use of anticoagulant and antiplatelet medications; and model 3 included adjustments for all baseline data. In addition, to further assess the correlation between novel inflammatory indices (SII and SIRI) and POP, SII and SIRI were categorized into two groups based on predefined optimal thresholds and a trend test was performed. Based on the three models constructed, restricted cubic spline curve (RCS) regression model analysis was applied to explore the possible linear relationships between SII and SIRI with POP, respectively. To further explore the heterogeneity of the relationship between the novel inflammatory index and the prevalence of POP, some covariates with possible effects were included in the subgroup analyses, and interaction tests were done. The study was statistically analyzed using Python version 3.12.0 and R version 4.2.0.

Results

Patient Characteristics

In this investigation, 275 individuals diagnosed with SAH were initially screened. Of these, 240 fulfilled the necessary inclusion criteria and were thus included in the study (Figure 1). Among them, 62.92% were females and 37.08% were males, and their mean age was 56.37 years (standard deviation of 12.10). The mean value of the SII was 2375.01 (with a standard deviation of 1659.67) and the mean value of the SIRI was 7.74 (with a standard deviation of 8.27). Spearman correlation analysis revealed that all covariates exhibited virtually no correlation with SII and SIRI (Supplementary Figure 1). Table 1 demonstrates the detailed baseline characteristics of all participants, categorized according to whether they had POP or not. In this study, 144 individuals were diagnosed with POP, representing 60% of the total sample. The research findings showed that patients with POP were more inclined to exhibit higher Hunt-Hess score, glucose, SII, and SIRI levels, and lower Glasgow Coma Scale (GCS), albumin, and hemoglobin levels.

Relationship Between SII and SIRI With POP After Propensity Score Matching

Propensity score matching (PSM) at a 1:1 ratio was utilized to delineate the baseline characteristics of the POP and non-POP groups, yielding 74 pairs of matched patients. However, important factors that directly affect POP, such as SII and SIRI, were not considered as variables in the matching process. As shown in Table 1, the post-PSM analysis revealed that the characteristics of the two cohorts were well-balanced ($p > 0.05$). The validity of the matching process was assessed by evaluating the standardized mean difference (SMD) before and after PSM, as shown in Figure 2. The results showed

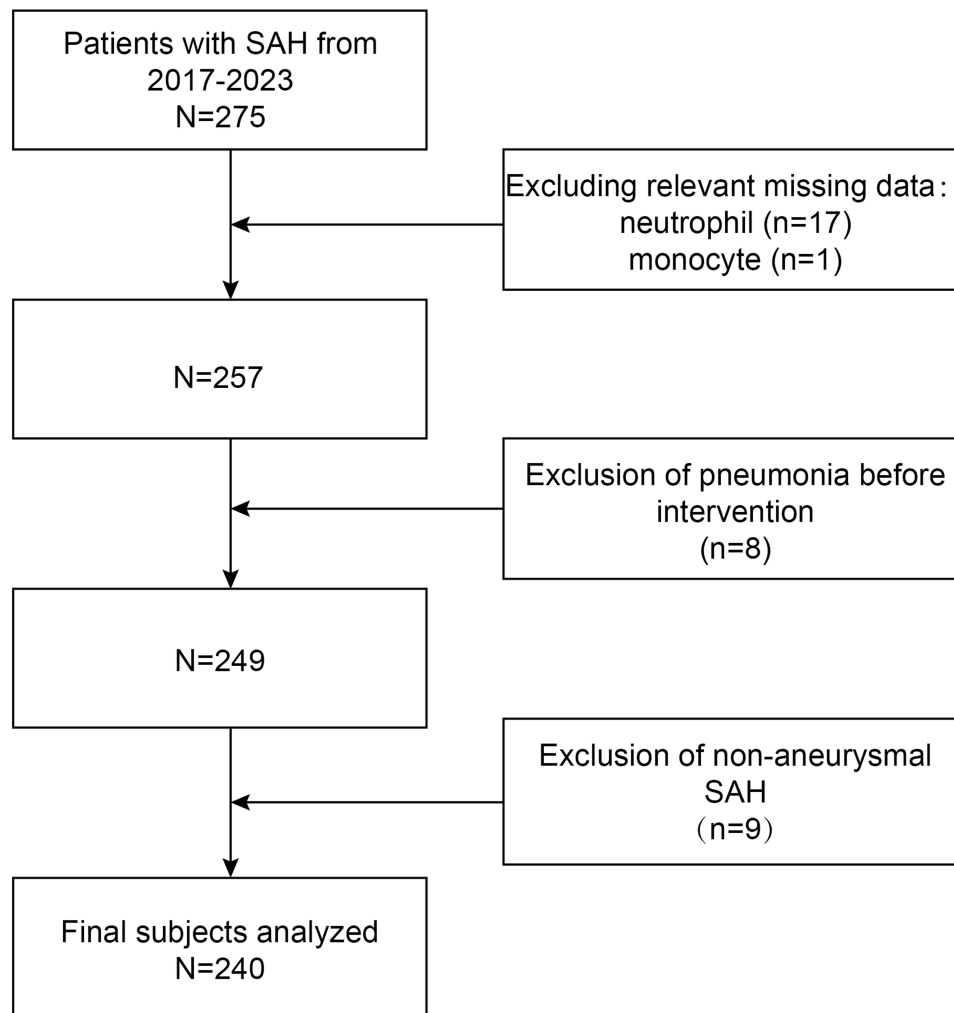


Figure 1 Participant selection flowchart.

a satisfactory balance of covariates between the two cohorts after PSM. Notably, SII and SIRI exhibited significant differences even in comparable groups ($P < 0.05$).

SII and SIRI Were Used to Predict the POP

ROC curves were used to determine the predictive efficacy of SII, SIRI, and POP prevalence (Figure 3). Study outcomes revealed that the area under the SII curve for predicting POP occurrence was 0.643 ($P < 0.001$). The established optimal cutoff value for SII in predicting POP was 2184.24, with a sensitivity of 51.39% and a specificity of 73.96%. Meanwhile, the SIRI curve's AUC for predicting POP was 0.644 ($P < 0.001$). The most optimal cutoff value for SIRI in forecasting POP occurrence was identified as 7.85, with a sensitivity of 43.75% and a specificity of 81.25%. This suggests that both SII and SIRI have a significant predictive ability for POP.

Positive Correlation Between SII and SIRI With POP

To further demonstrate the relationship between SII and SIRI with POP, multivariate logistic regression analysis was performed in this study (Table 2). The research findings revealed that in model 1 without covariate adjustment, SII (OR: 1.0003; 95% CI: 1.0001, 1.0005) and SIRI (OR: 1.101; 95% CI: 1.041, 1.164) exhibited a positive correlation with the prevalence of POP. In Model 2 with partially adjusted covariates, SII (OR: 1.0003; 95% CI: 1.0001, 1.0005) and SIRI (OR: 1.108; 95% CI: 1.046, 1.174) remained positively associated with the prevalence of POP. In the model fully adjusted for

Table 1 Comparison of Patients' Clinical Data Before and After Propensity Matching Analysis

Variable	Before-PSM				After-PSM			
	Overall	Non-POP	POP	P-value	Overall	Non-POP	POP	P-value
	N = 240	N = 96	N = 144		N = 148	N = 74	N = 74	
Age	56.37 (12.10)	55.68 (10.44)	56.83 (13.11)	0.449	55.76 (11.97)	55.07 (9.96)	56.45 (13.73)	0.486
Temperature (°C)	36.61 (0.29)	36.57 (0.26)	36.63 (0.32)	0.155	36.61 (0.28)	36.61 (0.27)	36.61 (0.28)	0.929
Systolic blood pressure (mmHg)	150.86 (25.97)	152.28 (23.59)	149.92 (27.48)	0.477	151.97 (26.61)	152.51 (24.33)	151.42 (28.86)	0.803
Diastolic blood pressure (mmHg)	87.28 (13.09)	86.63 (11.18)	87.72 (14.24)	0.506	87.04 (13.77)	87.05 (10.86)	87.03 (16.24)	0.991
GCS	12.45 (3.46)	13.57 (2.55)	11.71 (3.79)	<0.001	13.03 (3.05)	13.28 (2.80)	12.78 (3.28)	0.32
Hunt-Hess	2.30 (1.08)	1.92 (0.84)	2.55 (1.15)	<0.001	2.14 (0.95)	2.07 (0.85)	2.22 (1.04)	0.342
Glucose (mmol/L)	9.08 (2.46)	8.39 (2.21)	9.54 (2.52)	<0.001	8.64 (2.06)	8.62 (2.24)	8.67 (1.87)	0.884
Creatinine (umol/L)	64.68 (45.72)	59.47 (13.18)	68.16 (57.86)	0.084	60.98 (21.22)	60.53 (13.59)	61.42 (26.86)	0.8
Uric acid (umol/L)	318.31 (108.02)	311.15 (104.40)	323.09 (110.47)	0.397	319.85 (114.19)	315.16 (108.20)	324.54 (120.44)	0.619
Albumin (mg/L)	40.06 (4.17)	40.78 (3.71)	39.59 (4.40)	0.024	40.19 (3.90)	40.49 (3.40)	39.89 (4.34)	0.35
Cholesterol (mmol/L)	4.62 (0.97)	4.71 (1.01)	4.57 (0.95)	0.289	4.68 (0.99)	4.71 (0.94)	4.66 (1.04)	0.714
Triglyceride (mmol/L)	1.25 (0.61)	1.29 (0.67)	1.22 (0.58)	0.426	1.23 (0.64)	1.25 (0.68)	1.21 (0.60)	0.751
Hemoglobin (g/L)	122.44 (20.82)	126.09 (16.39)	120.00 (23.04)	0.017	123.97 (17.88)	124.99 (16.52)	122.96 (19.21)	0.492
SII	2,375.01 (1,659.67)	1,952.99 (1,439.07)	2,656.36 (1,740.29)	<0.001	2,227.94 (1,563.09)	1,953.74 (1,510.50)	2,502.14 (1,576.69)	0.032
SIRI	7.74 (8.27)	5.58 (4.55)	9.17 (9.77)	<0.001	6.55 (5.31)	5.53 (4.86)	7.56 (5.58)	0.02
Gender (%)				0.978				>0.999
Female	151.00 (62.92%)	61.00 (63.54%)	90.00 (62.50%)		87.00 (58.78%)	44.00 (59.46%)	43.00 (58.11%)	
Male	89.00 (37.08%)	35.00 (36.46%)	54.00 (37.50%)		61.00 (41.22%)	30.00 (40.54%)	31.00 (41.89%)	
Aneurysm Location (%)				0.126				0.89
Internal carotid artery	17.00 (7.08%)	5.00 (5.21%)	12.00 (8.33%)		10.00 (6.76%)	5.00 (6.76%)	5.00 (6.76%)	
Anterior communicating artery	82.00 (34.17%)	40.00 (41.67%)	42.00 (29.17%)		53.00 (35.81%)	29.00 (39.19%)	24.00 (32.43%)	
Posterior communicating artery	58.00 (24.17%)	25.00 (26.04%)	33.00 (22.92%)		34.00 (22.97%)	16.00 (21.62%)	18.00 (24.32%)	
Middle cerebral artery	23.00 (9.58%)	6.00 (6.25%)	17.00 (11.81%)		13.00 (8.78%)	6.00 (8.11%)	7.00 (9.46%)	
Anterior cerebral artery	4.00 (1.67%)	0.00 (0.00%)	4.00 (2.78%)		1.00 (0.68%)	0.00 (0.00%)	1.00 (1.35%)	
Others	56.00 (23.33%)	20.00 (20.83%)	36.00 (25.00%)		37.00 (25.00%)	18.00 (24.32%)	19.00 (25.68%)	
History of hypertension (%)				0.853				>0.999
No	128.00 (53.33%)	50.00 (52.08%)	78.00 (54.17%)		83.00 (56.08%)	42.00 (56.76%)	41.00 (55.41%)	
Yes	112.00 (46.67%)	46.00 (47.92%)	66.00 (45.83%)		65.00 (43.92%)	32.00 (43.24%)	33.00 (44.59%)	
History of diabetes (%)				0.323				>0.999
No	230.00 (95.83%)	94.00 (97.92%)	136.00 (94.44%)		147.00 (99.32%)	73.00 (98.65%)	74.00 (100.00%)	
Yes	10.00 (4.17%)	2.00 (2.08%)	8.00 (5.56%)		1.00 (0.68%)	1.00 (1.35%)	0.00 (0.00%)	
History of coronary heart disease (%)				>0.999				>0.999

(Continued)

Table I (Continued).

Variable	Before-PSM				After-PSM			
	Overall	Non-POP	POP	P-value	Overall	Non-POP	POP	P-value
	N = 240	N = 96	N = 144		N = 148	N = 74	N = 74	
No	231.00 (96.25%)	92.00 (95.83%)	139.00 (96.53%)	0.607	146.00 (98.65%)	73.00 (98.65%)	73.00 (98.65%)	>0.999
Yes	9.00 (3.75%)	4.00 (4.17%)	5.00 (3.47%)		2.00 (1.35%)	1.00 (1.35%)	1.00 (1.35%)	
History of other cerebrovascular accidents (%)								
No	232.00 (96.67%)	94.00 (97.92%)	138.00 (95.83%)	0.584	146.00 (98.65%)	73.00 (98.65%)	73.00 (98.65%)	>0.999
Yes	8.00 (3.33%)	2.00 (2.08%)	6.00 (4.17%)		2.00 (1.35%)	1.00 (1.35%)	1.00 (1.35%)	
History of anticoagulant and antiplatelet medication use (%)								
No	233.00 (97.08%)	92.00 (95.83%)	141.00 (97.92%)	0.584	147.00 (99.32%)	74.00 (100.00%)	73.00 (98.65%)	>0.999
Yes	7.00 (2.92%)	4.00 (4.17%)	3.00 (2.08%)		1.00 (0.68%)	0.00 (0.00%)	1.00 (1.35%)	

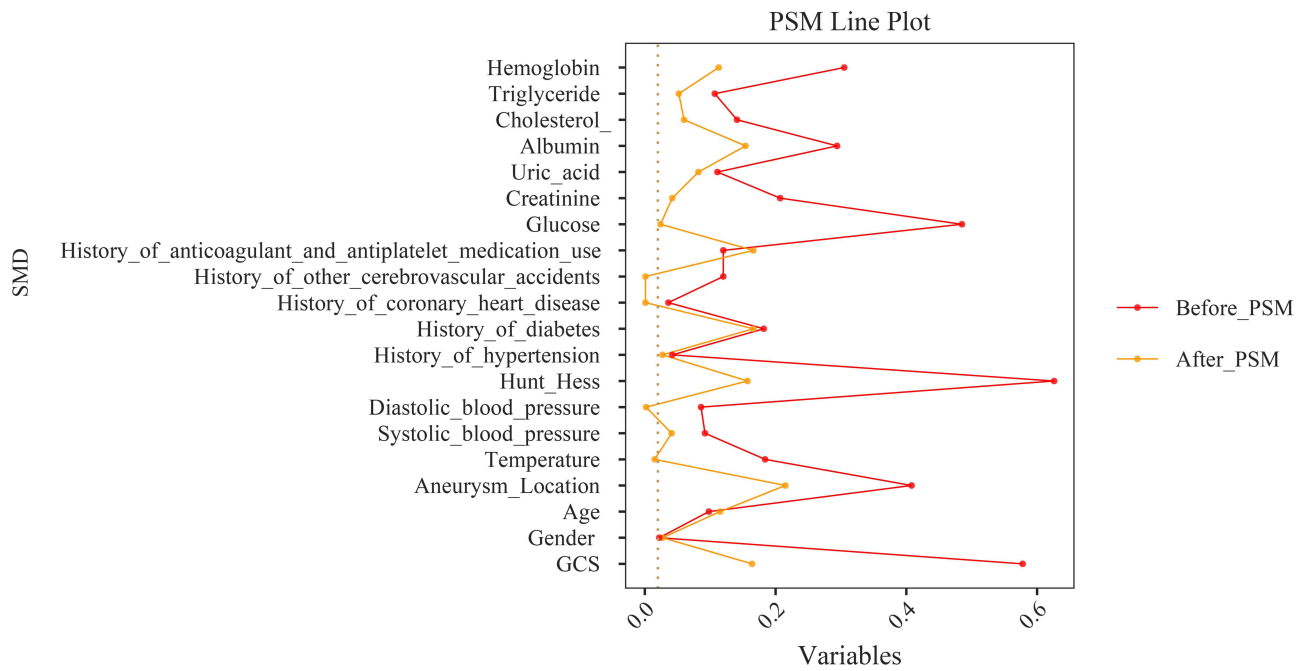


Figure 2 Standardized Mean Differences (SMD) in Covariates Before and After PSM.

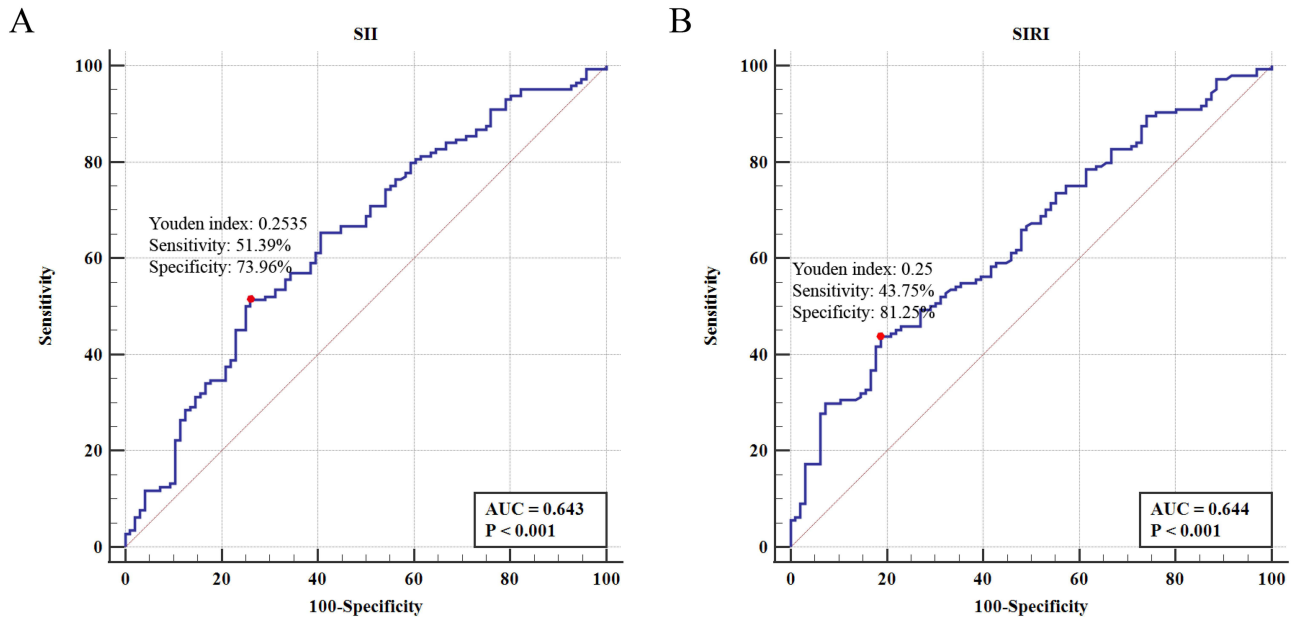


Figure 3 Predictive value of SII and SIRI for the prevalence of POP (A). SII (B). SIRI.

covariates (Model 3), the relationship between SII (OR: 1.0003; 95% CI: 1.0001, 1.0005) and SIRI (OR: 1.100; 95% CI: 1.024, 1.181) and POP remained significant. Further analyses were performed after categorizing SII and SIRI according to their respective optimal cutoff values. The results showed that in the fully adjusted model, compared with the low SII group (SII < 2184.24), patients in the high SII group (SII ≥ 2184.24) had an 185% increase in risk of POP (OR: 2.85; 95% CI: 1.63, 4.96) for each unit rise in SII. Similarly, compared with the low SIRI group (SIRI < 7.85), the high SIRI group (SIRI ≥ 7.85) had a 2.374-fold increase in risk. Both of these trends were statistically significant (P for trend < 0.01).

Table 2 Relationship Between SII and SIRI With POP

SII	Model 1		Model 2		Model 3	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Continuous	1.0003 (1.0001, 1.0005)	0.001848	1.0003 (1.0001, 1.0005)	0.000891	1.0003 (1.0001, 1.0005)	0.011585
Categories						
<2184.24	Reference		Reference		Reference	
≥2184.24	2.85 (1.63, 4.96)	0.0002	2.97 (1.68, 5.25)	0.0002	2.74 (1.34, 5.62)	0.0058
P for trend	0.00023		0.00018		0.00581	
SIRI						
Continuous	1.101 (1.041, 1.164)	0.00076	1.108 (1.046, 1.174)	0.00049	1.100 (1.024, 1.181)	0.00924
Categories						
<7.85	Reference		Reference		Reference	
≥7.85	3.152 (1.729, 5.746)	0.00018	3.531 (1.891, 6.591)	0.00007	3.374 (1.589, 7.168)	0.00156
P for trend	0.00018		0.00007		0.00156	

Note: Model 1: variables were not adjusted. Model 2: gender, age, hypertension, diabetes, coronary heart disease, other cerebrovascular accidents, anticoagulant and antiplatelet medication use adjusted. Model 3: adjusted for gender, age, aneurysm location, body temperature, systolic blood pressure, diastolic blood pressure, GCS, Hunt-Hess score, hypertension, diabetes, coronary heart disease, other cerebrovascular accidents, anticoagulant and antiplatelet medication use, glucose, creatinine, uric acid, albumin, cholesterol, triglycerides, hemoglobin.

Linear Relationships Between SII and SIRI With POP

RCS was applied to analyze the dose-response relationship between SII, SIRI, and POP prevalence. As shown in Figure 4, in the three models constructed based on multivariate logistic regression, a possible linear relationship was shown between SII (Figure 4A-C) and SIRI (Figure 4D-F) and POP prevalence (P for nonlinear > 0.05).

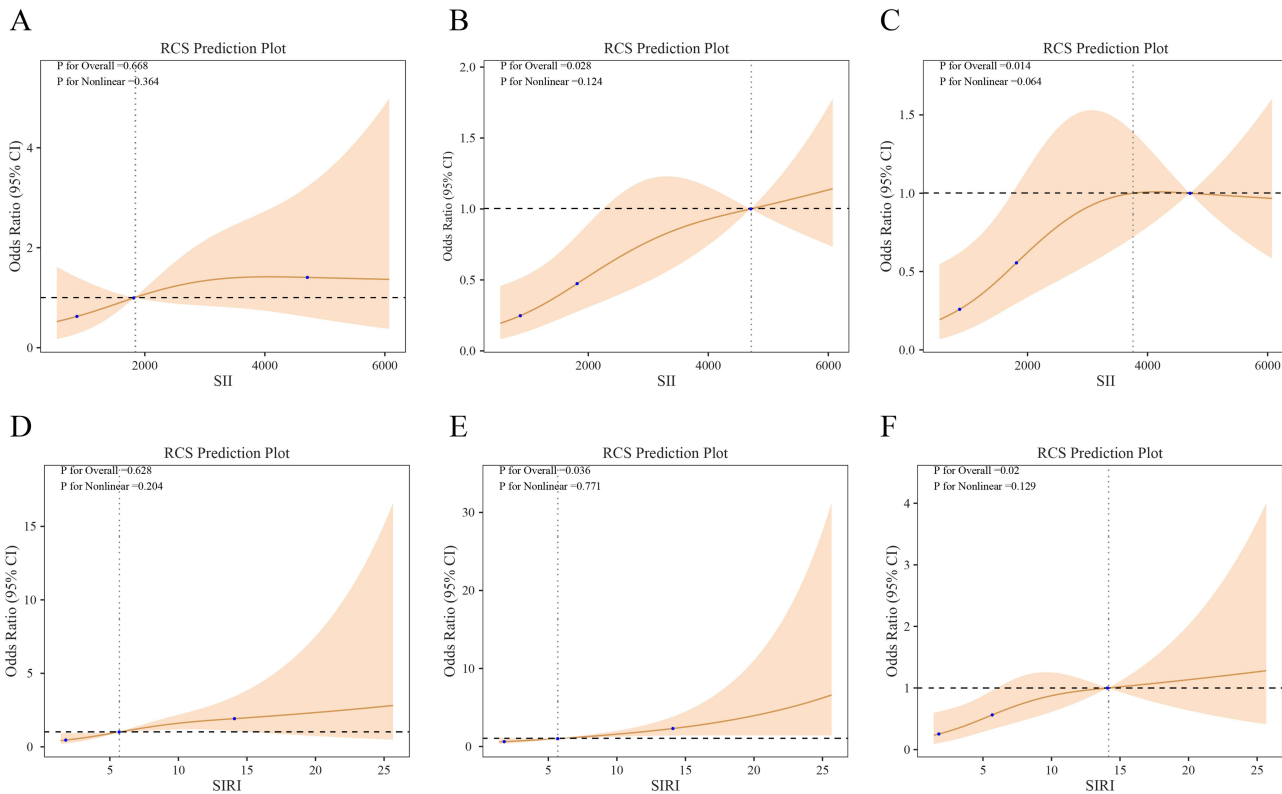


Figure 4 Dose-response relationship between SII and SIRI with POP prevalence in the 3 models (A). Relationship between SII and POP in the unadjusted model (B). Relationship between SII and POP in the partially adjusted model (C). Relationship between SII and POP in the fully adjusted model (D). Relationship between SIRI and POP in an unadjusted model (E). Relationship between SIRI and POP in a partially adjusted model (F). Relationship between SIRI and POP in a fully adjusted model.

Table 3 Subgroup Analysis of the Relationship Between SII and SIRI With POP

Subgroup	SII			SIRI		
	OR	95% CI	P for interaction	OR	95% CI	P for interaction
Age			0.2917			0.7442
<60	1.0002	(1.0000, 1.0005)		1.0905	(1.0007, 1.1883)	
≥60	1.0005	(1.0000, 1.0009)		1.119	(0.9844, 1.2720)	
Gender			0.2858			0.4537
Female	1.0002	(0.9999, 1.0005)		1.127	(1.0211, 1.2439)	
Male	1.0005	(1.0001, 1.0009)		1.0646	(0.9558, 1.1858)	
GCS			0.7765			0.7486
Severe	1.0002	(0.9994, 1.0009)		1.1927	(0.8358, 1.7020)	
Moderately	1.0002	(0.9998, 1.0006)		1.1307	(0.9733, 1.3136)	
Mildly	1.0003	(1.0001, 1.0006)		1.0789	(0.9925, 1.1729)	
History of hypertension			0.6625			0.2076
No	1.0003	(1.0000, 1.0005)		1.062	(0.9745, 1.1575)	
Yes	1.0004	(1.0000, 1.0007)		1.167	(1.0293, 1.3232)	
History of diabetes			0.0468			0.0134
No	1.0003	(1.0000, 1.0005)		1.0955	(1.0200, 1.1766)	
Yes	1.0065	(0.9982, 1.0149)		1.1732	(0.9320, 1.1938)	

Subgroup Analysis

The association of SII and SIRI with POP was found to be consistent in all subgroups except the diabetic group ($P=0.0134$) and no significant interaction ($P>0.05$) was observed in Table 3. The results suggest that patients with subarachnoid hemorrhage and higher levels of SII and SIRI usually face a higher risk of POP. Moreover, the correlation between higher SII and the incidence of POP was stronger in specific subgroups, such as the elderly, men with mild impairment of consciousness (GCS: 13–15), and those with hypertension or diabetes. Similarly, the correlation between higher SIRI and the incidence of POP was stronger in subgroups such as older adults, women with severely impaired consciousness (GCS: 3–8), and those with diabetes or hypertension.

Discussion

In the present study, we found that there were significant positive correlations between SII and SIRI and the prevalence of POP. Through multiple logistic regression analyses and propensity score matching (PSM), the robustness of our results was further confirmed, indicating that these results were reliable and less likely to be significantly affected by potential confounders. This association remained stable in most subgroups but may differ in diabetic patients ($P=0.0134$).

Two novel inflammatory markers were used in this study: the SII and the SIRI. Recent studies have shown that SII and SIRI have significant advantages in predicting the prognosis of a wide range of diseases. A meta-analysis of acute ischemic stroke showed that SII and SIRI outperformed traditional inflammatory markers in predicting stroke-associated pneumonia (SAP).^{14,15} Hu et al (2014) conducted a study on the survival prognosis of patients with hepatocellular carcinoma. In their study, they found that the Systemic Immune-Inflammation Index (SII) served as a significant independent predictor, which could play an important role in predicting the survival outcome of these patients. These findings are consistent with the findings of the present study and further confirm the utility of SII and SIRI in assessing inflammation-related complications. In addition, this study used multiple logistic regression analysis, which considered and adjusted for several possible confounders, such as age, gender, hypertension, and diabetes mellitus. This comprehensive approach to statistical analysis allowed us to assess the relationship between SII and SIRI and the prevalence of POP as accurately as possible. In a study on SIRI and prognosis in acute coronary syndrome patients, Han et al used multivariate COX regression to control for confounders. They found a significant association between SIRI and major adverse cardiovascular events (HR: 1.127; 95% CI: 1.034–1.229 and the results were consistent in multiple sensitivity analyses.¹⁶ Also, this study ensured comparability between the POP and non-POP groups by PSM to reduce the

imbalance of baseline characteristics. In recent years, the PSM method has been widely used in medical research to reduce selection bias in retrospective studies.¹⁷⁻¹⁹ Zhou et al adopted the PSM method in their study on the effect of SII on the prognosis of patients undergoing cardiac surgery. The results showed that cardiovascular surgery involving CPB had a poorer prognosis than that of non-corporeal circulation surgery. Therefore, they further suggested that the novel inflammatory index may become a reliable prognostic indicator.²⁰ PSM provides comparability for the study of intergroup variables. The selection of inflammatory markers was limited in earlier years, focusing on traditional markers such as C-reactive protein (CRP) and leukocytes, and failing to fully explore the value of multiple composite indices such as novel inflammatory indices.^{21,22} Zhang et al showed that CRP combined with albumin was significantly associated with WFNS classification and was strongly correlated with poor prognosis in aSAH (AUC=0.862).²³ A recent study confirmed the systemic inflammation composite index (AISI) as the most effective predictor of inflammation severity by comparing several inflammation composite indices with the predictive ability of CRP in infectious diseases. The AISI demonstrated the highest sensitivity (SE = 82.93) and specificity (SP=81.63) among all analyzed indices. In addition, these composite inflammation indices showed greater accuracy than CRP in predicting severe infections, especially odontogenic abscesses, with AUC values of 0.90 compared with CRP of 0.74. Furthermore, it was suggested that these composite inflammation indices were also significantly correlated with the duration of hospitalization and the development of systemic inflammatory response syndrome.²⁴ In the field of neurology, a similar phenomenon has been validated. In a retrospective study involving 1543 stroke patients, it was found that composite inflammatory indices such as NLR, PLR, MLR, PNI, SII, SIRI, GPS, mGPS, and PI were significantly elevated in SAP patients. These indicators have been shown to be effective in predicting the occurrence of SAP.¹² Therefore, the reliability of the theoretical framework of this study could be further reinforced by the significant correlation between composite inflammatory indicators and post-stroke pulmonary changes.

Subarachnoid hemorrhage caused by ruptured aneurysm and intracerebral hemorrhage can lead to local tissue injury and trigger a local neuroinflammatory response. This response involves vascular endothelial damage, disruption of the blood-brain barrier, and activation of platelets.²⁵ After cerebral hemorrhage, erythrocytes, leukocytes, and platelets in the blood release a variety of inflammatory mediators, such as interleukin, interleukin-6, and tumor necrosis factor- α .²⁶ These factors not only enhanced the permeability of the blood-brain barrier but also further attracted neutrophils to the site of injury, triggering a severe local inflammatory response.²⁷ As the inflammatory response progressed, the levels of pro-inflammatory factors such as IL-6 and TNF- α increased significantly, promoting the development of systemic inflammatory response syndrome. This process suppressed patients' immune function and increased their susceptibility to bacteria, especially respiratory pathogens.²⁸ In addition, endocrine disruption caused by the neuroinflammatory response following cerebral hemorrhage can lead to endocrine disruption, further increasing the risk of lung infection.^{29,30} As a result of the strong inflammatory response triggered by aSAH, patients often enter a state of immunosuppression, which is known as compensatory anti-inflammatory response syndrome (CARS). Compensatory anti-inflammatory response syndrome manifests itself as a situation where there is a decrease in peripheral blood lymphocytes and a decrease in the functioning of immune cells. This results in a weakened body's defenses against infections and increases the likelihood that patients will develop postoperative pneumonia.^{31,32} SII and SIRI, as new systemic inflammatory indices, combine the interrelationships between neutrophils, monocytes, lymphocytes, and platelets. Compared with other traditional indices, they can better reflect the level of systemic immune-inflammatory response in aSAH.

However, the present study has the following limitations. First, as a retrospective single-center study, this study may have suffered from selection bias and the extrapolation of the results may have been limited. Although we included 240 patients, the sample size was relatively limited, especially when subgroup analyses were performed, so this may lead to insufficient statistical efficacy. Therefore, future studies should incorporate larger sample sizes and be conducted in multiple centers to validate our findings. Second, this study only assessed SII and SIRI levels at admission but failed to dynamically monitor how these markers changed in the postoperative period. It has been shown that dynamic changes in inflammatory markers may have more predictive value than measurements at a single point in time.³³ Thus, future studies should consider dynamic monitoring of changes in SII and SIRI to better assess their predictive ability for POP. In addition, although we adjusted for multiple covariates, the limitations of the retrospective design did not allow us to

completely exclude other potential confounders that were not included, such as the nutritional status of the patients and other immunosuppressive factors. For instance, poor nutritional status might lead to weakened immune function, thereby altering the body's inflammatory response and ultimately influencing the results we obtained. Similarly, other immunosuppressive factors could interfere with the normal immune-inflammatory processes and have an impact on the measured outcomes.

Conclusion

This study systematically evaluated the SII and the SIRI and confirmed their validity as independent factors in predicting postoperative pneumonia in aneurysmal subarachnoid hemorrhage. This finding provides clinicians with new strategies for identifying high-risk patients during the postoperative period and implementing targeted stratified management aimed at optimizing patient prognosis. Nevertheless, multicenter and large-scale prospective studies are essential for further confirmation to ensure the broad applicability of these findings.

Data Availability Statement for this Work

Research data are not available at this time.

Ethical Approval and Consent to Participate

The study protocol was approved by the ethics committees of the Second Affiliated Hospital of Fujian Medical University (2022-35). This study was conducted in accordance with the Declaration of Helsinki. The need for written informed consent was waived by the Ethics Committee due to the non-interventional design of the study. Additionally, this research exclusively utilized previously collected medical record information from which all personally identifiable information had been removed, ensuring no risk to the subjects and no adverse effects on their rights and health.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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