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Predictive Value of the Systemic Immune-Inflammation Index in the 28-Day Mortality for Patients with Sepsis-Associated Acute Kidney Injury and Construction of a Prediction Model

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Purpose: The predictive value of the Systemic Immune-Inflammation Index (SII) on mortality in patients with sepsis-associated acute kidney injury (S-AKI) remains unclear. This study aims to investigate the predictive value of SII levels at the Intensive Care Unit (ICU) on the 28-day mortality of S-AKI patients.

Patients and Methods: S-AKI patients admitted to the ICU of Henan Provincial People's Hospital from January 1, 2023, to December 31, 2023. Patients who were diagnosed with S-AKI were divided into survival and death groups based on their 28-day outcome after ICU admission. Using receiver operating characteristic (ROC) curves to determine the best cut-off values and prognostic abilities of various parameters. Kaplan-Meier survival curves describe the 28-day survival of patients after ICU admission. Cox regression analysis identified the main risk factors associated with mortality in S-AKI patients, constructing a predictive nomogram. The concordance index (C-index) and decision curve analysis were used to validate the predictive ability of this model.

Results: A total of 216 patients with S-AKI were included. ROC analysis showed that SII had the highest predictive value for mortality risk in S-AKI patients after ICU admission. Compared with the low-SII group, the high-SII group had higher 28-day (86.7% vs 32.4%, respectively, P <0.001) mortality rate. Based on Cox regression analysis, a nomogram predictive model was constructed, including age, respiratory failure, SII levels, number of organ dysfunctions at ICU admission, sequential organ failure assessment (SOFA), and acute physiology and chronic health evaluation II (APACHEII). The C-index for predicting the 28-day survival rate was 0.682. Decision curve analysis indicated a high level of clinical predictive efficacy.

Conclusion: SII serves as a potential biomarker for predicting the prognosis of S-AKI patients. The constructed nomogram prognostic model can aid in assessing the prognosis of S-AKI patients.

Keywords: systemic immune-inflammation index, sepsis-associated acute kidney injury, prognosis, mortality, prediction model

Introduction

Acute kidney injury (AKI) is a common and severe complication in critically ill patients, with high incidence and mortality rates.[1] Particularly among patients with sepsis, over 60% develop AKI.[2–4] The pathogenesis of sepsis-associated acute kidney injury (S-AKI) is not yet fully understood, but evidence indicates that the inflammatory cascade

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triggered by sepsis increases the likelihood of AKI in critically ill patients.[5] A retrospective study found that the mortality rate of S-AKI patients is significantly higher than that of non-sepsis AKI patients (71.7% vs 21.3%).[6] Additionally, patients with critical S-AKI are closely associated with prolonged hospital stays and a great financial burden.[7] Therefore, early identification of S-AKI is crucial for preventing complications, reducing mortality, and improving patient outcomes.

Inflammation plays a significant role in the occurrence and progression of S-AKI.[8,9] Many biomarkers have limitations in predicting the prognosis of S-AKI. For example, the sensitivity of tissue inhibitor metalloproteinase 2 (TIMP-2), neutrophil gelatinase-associated lipocalin (NGAL), and insulin-like growth factor-binding protein-7 (IGFBP-7) in prognostic evaluation has not been validated in large-scale studies, and their high detection costs and long processing times limit their clinical application.[3] Routine blood tests that reflect inflammatory markers are simple, rapid, cost-effective, and highly reproducible and have been used for prognostic evaluation in various diseases. Parameters from complete blood counts, such as platelet count, red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), have all been reported for disease prognosis evaluation.[10–13]

The SII, calculated from neutrophil, lymphocyte, and platelet counts, is a novel inflammatory marker that reflects the balance of inflammation, immunity, and thrombosis pathways in the body.[14] As a simple, economical, and convenient indicator, SII has been proven valuable in diagnosing and evaluating the prognosis of various diseases, including tumors, infections, and cardiovascular diseases.[14–17] Studies have shown that high-SII levels are associated with poor prognosis in acute pancreatitis and severe outcomes in viral infections like COVID-19.[18,19] Therefore, SII helps assess the severity and predict the prognosis of infectious diseases. However, there are limited studies on the prognostic value of SII in patients with critical S-AKI.This study aims to explore the relationship between SII and the prognosis of critically ill S-AKI patients and to construct a prediction model for the prognosis within 28-day after ICU admission.

Material and Methods

Study Population

This study utilized a retrospective cross-sectional design. A total of 2096 ICU patients at first admission were recorded at Henan Provincial People's Hospital between January 1, 2023, and December 31, 2023. The flowchart of this study and the number of patients are presented in Figure 1. The inclusion criteria were as follows: (1) diagnosed as S-AKI; (2) aged ≥18 years; (3) first admission ICU. The exclusion criteria were as follows: (1) history of chronic kidney disease; (2) hematologic disorders; (3) recent use of immunosuppressants or steroids within 3 months; (4) ICU length of stay ≤24 hours; (5) incomplete variables. This study was approved by the Ethics Committee of Henan Provincial People's Hospital on October 2, 2023 [approval number: (2023) No. (145)]. All study procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional) and with the Helsinki Declaration of 1975. Written informed consent was obtained from all patients prior to study enrolment.

Subgroups and Outcome

Patients were divided into survival and death groups based on their 28-day outcome after ICU admission. Survival was defined as stabilization and discharge after 28 days in the ICU, while death was defined as mortality during the 28-day ICU treatment period or confirmed death during 28-day follow-up if ICU treatment period was less than 28 days or was abandoned. The outcome was mortality within 28-day of admission to ICU.

Definitions

S-AKI is generally defined as AKI in the presence of sepsis that cannot be explained by other important causes or meets both Sepsis 3.0 and Kidney Disease: Improving Global Outcomes (KDIGO) criteria.[9] In accordance with the Sepsis 3.0 criterion,[20] sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, which can be represented by an increase in the sequential organ failure assessment (SOFA) score of 2 points or more. According to the KDIGO criterion,[21] AKI was defined as an increase in creatinine level of at least 0.3 mg/dL (26.5 μmol/L) within the first 48 hours after sepsis diagnosis, an increase in creatinine level of at least 1.5 times baseline within the

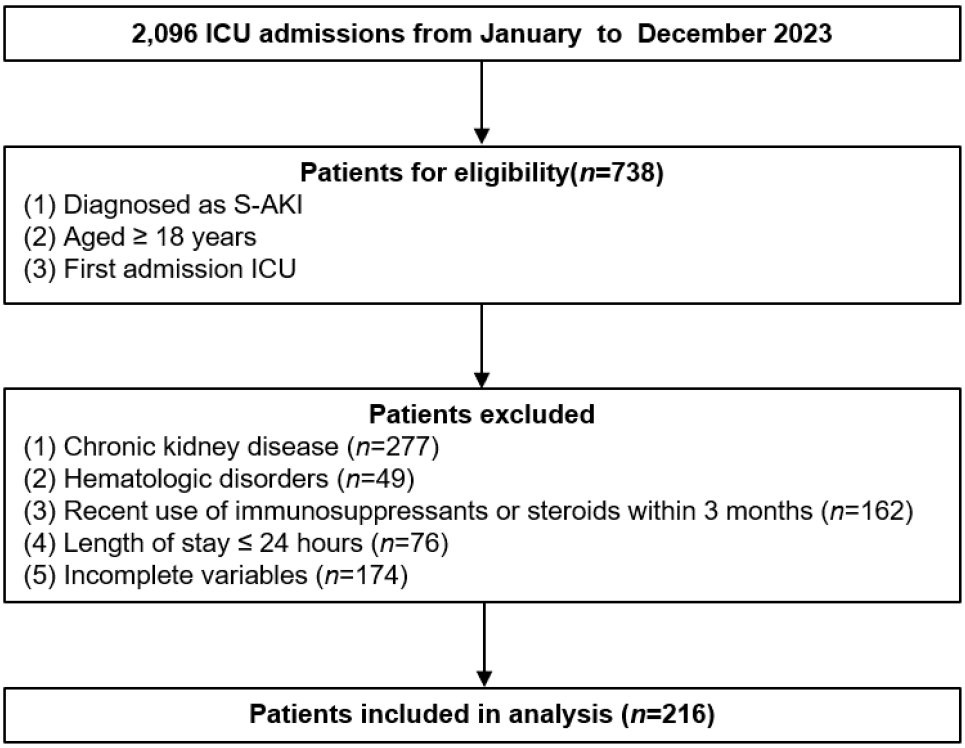

Figure 1 Flowchart of patient selection.

previous 7 days after sepsis diagnosis, or urine output ≤ 0.5 mL/kg/h for at least 6 hours. AKI is classified into 3 stages according to KDIGO guidelines.[21]

Data Collection

Patient data within the first 24 hours after ICU admission was collected as follows: 1) The basic information (gender, age, body mass index), mean arterial pressure (MAP), number of organ dysfunctions at ICU admission, length of stay in ICU, length of hospitalization, and AKI stage were extracted; 2) Comorbidities: hypertension, diabetes, coronary heart disease, stroke, respiratory failure, congestive heart failure, hepatic failure, malignant tumor); 3) Laboratory parameters: hemoglobin, white blood cell count, platelet count, neutrophil, lymphocyte, monocyte, albumin, glutamic pyruvic transaminase (ALT), glutamic oxaloacetic transaminase (AST), albumin, creatinine, serum bicarbonate, serum sodium, serum potassium, C-reactive protein, procalcitonin, and arterial blood gas analysis; 4) Scoring systems of severity-of-illness: SOFA score, Acute Physiology and Chronic Health Evaluation II (APACHEII); 5) Medical interventions: mechanical ventilation, use of vasopressors and renal replacement therapy. Clinical data were recorded as the worst value of the indicator within the first 24 hours of ICU admission. APACHE II and SOFA scores were calculated using the worst values recorded. Inflammatory markers were calculated as follows: NLR = neutrophil / lymphocyte; PLR = platelet count / lymphocyte; MLR = monocyte / lymphocyte; SII = platelet count × neutrophil / lymphocyte.[22]

Statistical Analysis

Statistical analysis were performed using SPSS software, version 26.0 and R software (version 4.3.3). Normally distributed and skewed continuous variables are presented as the mean ± standard deviation and medians (25th and 75th quartiles), respectively. Categorical variables are shown as frequency (%). Student's *t*-test, Wilcoxon rank-sum test, and chi-squared test were used, as appropriate, to compare the two groups. Receiver operating characteristic (ROC) curves were used to determine the best cut-off values and prognostic ability of parameters. Patients were divided into high- and low-SII groups based on the best SII cut-off value. Kaplan-Meier curves describe the 28-day survival status of patients with different SII levels. Using stepwise backward regression analysis, we investigated the association between

SII and 28-day mortality in the multivariate Cox proportional hazards regression model. A clinical prognostic prediction model was constructed, evaluated using the concordance index (C-index), and internally validated with the Bootstrap method. Decision curve analysis assessed the model's predictive efficacy. $P < 0.05$ was considered statistically significant.

Results

Patient Characteristics and ICU Admission Status of Patients

A total of 216 ICU patients with S-AKI were included (Figure 1), among whom 128 (59.3%) patients died. The median age was 66 years (range 18–91 years), of which 143 (66.2%) were males. Compared to the survival group, the death group had higher age, APACHE II scores, SOFA scores, the number of organ dysfunctions at ICU admission, and a higher proportion of mechanical ventilation within 24 hours of ICU admission (all $P < 0.05$). The death group also had higher proportions of comorbid coronary heart disease, respiratory failure, and malignant tumors (all $P < 0.05$). Baseline laboratory results showed higher white blood cell counts, NLR, PLR, MLR, and SII in the death group, while creatinine and procalcitonin levels were lower compared to the survival group (all $P < 0.05$) (Table 1).

Predictive Value of Inflammatory Markers, APACHE II, and SOFA Scores

ROC analysis indicated that SII had the highest predictive value for the 28-day mortality in S-AKI patients; the best cut-off value of SII was 3910; the sensitivity was 71.9%; the specificity was 85.2%; and the area under the ROC curve (AUC) was 0.867 (95% confidence interval [95% CI]: 0.821–0.914). Other parameters' AUC values, sensitivities, and specificities are detailed in Table 2 and Figure 2.

According to the best SII cut-off value, patients were divided into high-SII (105 cases) and low-SII (111 cases) groups. Compared with the low-SII group, the high-SII group had a higher 28-day mortality rate (86.7% vs 32.4%, respectively, $P <0.001$). (Figure 3).

Risk Factors Associated with 28-Day Mortality

Univariate Cox regression analysis showed that age, coronary heart disease, respiratory failure, malignant tumor, APACHE II scores, SOFA scores, number of organ dysfunctions, mechanical ventilation, white blood cell count, creatinine, blood urea nitrogen, NLR, PLR, MLR, and SII levels were associated with 28-day mortality in S-AKI patients (Table 3).

Since SII is composed of white blood cells, platelets, and other components, in order to avoid the influence of collinearity on the stability of the regression model, Spearman correlation analysis was used to exclude factors significantly associated with SII. The results showed that SII was strongly correlated with leukocytes, platelets, NLR, PLR, and MLR ($r = 0.378, 0.412, 0.729, 0.847, 0.362$; $P < 0.05$) (Supplementary Table 1). Additionally, serum creatinine was excluded from the multivariate analysis due to its influence by various factors such as renal function and nutritional status.

The results of the Cox proportional hazards regression model are shown in Table 4. We constructed model I, which showed a positive correlation with short-term mortality (HR 2.603, 95% CI 1.705–3.937, $P<0.001$) after adjusting for age, coronary heart disease, respiratory failure, and malignancy. Further based on model 1, we constructed model II and adjusted SOFA scores, APACHE II scores, number of organ dysfunctions, mechanical ventilation use, and urea nitrogen. In a fully adjusted model, 28-day mortality was 2.505 times higher in the high-SII group compared to the low-SII group (95% CI 1.609–3.898, $P<0.001$). The relationship was consistent when adjusting for confounding factors in different models. Multivariate Cox regression analysis showed that age, respiratory failure, SII, number of organ dysfunction, SOFA scores, and APACHE II scores were independent risk factors for short-term poor prognosis in S-AKI patients. The detailed results of univariate and multivariate analysis are presented in Table 3.

Table 1 Comparison of the Variables Between the Survival Group and Death Group

Variable	Survival group (*n*=88)	Death group (*n*=128)	$Z/\chi^2/t$	p-value
Age, years	55 (39,67%)	71 (62,81%)	7.368	<0.001
Sex, male	62 (70.45%)	81 (63.28%)	1.199	0.273
Body mass index, (kg/m^2)	26.27 (±4.98)	24.89 (±4.21)	−1.588	0.115
MAP (mmHg)	88.70 (±17.89)	87.82 (±15.88)	−0.381	0.704
APACHE II	18.80 (±5.66)	24.87 (±5.70)	7.718	<0.001
SOFA	9.65 (±3.49)	11.92 (±3.05)	5.072	<0.001
Mechanical ventilation use	45 (51.14%)	93 (72.66%)	10.468	0.001
Vasopressors use	59 (67.05%)	90 (70.31%)	0.260	0.610
Renal replacement therapy	10 (11.4%)	26 (20.3%)	3.007	0.083
Number of organ dysfunction	1 (0,2)	2 (1,3)	−4.305	<0.001
Length of stay in ICU (days)	26 (±14)	11 (±7)	−9.209	<0.001
Length of hospitalization (days)	33 (±16)	14 (±9)	−10.072	<0.001
Comorbidity				
Hypertension	42 (47.70%)	56 (43.80%)	0.333	0.564
Diabetes	25 (28.40%)	46 (35.90%)	1.339	0.247
Coronary heart disease	18 (20.50%)	46 (35.90%)	5.996	0.014
Stroke	10 (11.40%)	11 (8.60%)	0.456	0.500
Respiratory failure	20 (22.72%)	97 (75.78%)	84.500	<0.001
Congestive heart failure	32(36.40%)	54 (42.20%)	0.738	0.390
Hepatic failure	32 (36.40%)	32 (25.00%)	3.23	0.072
Malignant tumor	6 (6.80%)	23 (18.00%)	5.578	0.018
Blood test				
White blood cell count ($10^9/L$)	13.66 (10.38,18.72)	15.66 (12.42,20.32)	−2.313	0.021
Hemoglobin (g/L)	113.17 (±25.61)	108.60 (±23.54)	−1.353	0.178
Platelet count ($10^9/L$)	161.80 (±86.99)	179.65 (±93.06)	1.422	0.156
ALT (U/L)	34.70 (21.60,62.0)	35.50 (16.43,86.85)	−0.218	0.828
AST (U/L)	60.05(32.80,104.00)	38.30 (27.30,107.80)	−0.738	0.461
Albumin (g/L)	30.06 (±4.84)	29.99 (±5.40)	−0.104	0.917
Creatinine (μmol/L)	116.50 (70.00,211.75)	85.50 (62.00,129.95)	−3.504	<0.001
Blood urea nitrogen (μmol/L)	11.48 (6.64,17.43)	11.65 (7.95,18.42)	−0.413	0.679
Sodium (mmol/L)	139.00 (136.00,143.75)	140.00 (135.00,144.30)	−0.199	0.843
Potassium (mmol/L)	4.50 (±0.88)	4.33 (±0.78)	−1.468	0.144
C-reactive protein (mg/L)	100.24 (28.47,233.11)	98.34 (29.71,180.56)	−0.685	0.494

(*Continued*)

Table 1 (Continued).

Variable	Survival group (*n*=88)	Death group (*n*=128)	$Z/\chi^2/t$	p-value
Procalcitonin (μg/L)	3.16 (0.66,16.81)	2.20 (0.33,5.21)	−2.122	0.034
Arterial blood gas analysis				
Ph	7.39 (7.30,7.43)	7.39 (7.29,7.46)	−1.405	0.16
$PaCO_2$ (mmHg)	35.55 (29.83,43.18)	37.55 (30.48,49.80)	−1.441	0.149
PaO_2 (mmHg)	97.80 (78.13,128.93)	85.65 (67.50,117.65)	−1.924	0.054
Lactic acid (mmol/L)	2.27 (1.53,3.37)	2.53 (1.79,3.85)	−1.387	0.165
AKI stage			1.727	0.422
StageI	38 (43.20%)	44 (34.40%)		
StageII	21 (23.90%)	36 (28.10%)		
StageIII	29 (33.00%)	48 (37.50%)		
NLR	12.93 (8.41,26.62)	35.17 (25.16,53.81)	−8.214	<0.001
PLR	172.22 (112.84,252.07)	406.03 (251.62,575.32)	−8.133	<0.001
MLR	0.60 (0.39,1.00)	0.93 (0.48,1.66)	−3.058	<0.001
SII	2167.39 (1062.52,3341.30)	5176.09 (3600.46,8364.21)	−9.045	<0.001

Notes: Data are expressed as mean ± SD, median with interquartile range or n (%).

Abbreviations: MAP, Mean arterial pressure; APACHEII, Acute physiology and chronic health evaluationII; SOFA, Sequential organ failure assessment; ICU, Intensive care unit; ALT, Glutamic pyruvic transaminase; AST, Glutamic oxaloacetic transaminase; Ph, Potential of hydrogen; PaCO2, Partial pressure of carbon dioxide in arterial blood; PaO2, Partial pressure of oxygen in arterial blood; AKI, Acute kidney injury; NLR, Neutrophil-to-lymphocyte ratio; PLR, Platelet-to-lymphocyte ratio; MLR, Monocyte-to-lymphocyte ratio; SII, Systemic immune-inflammation index; n, number.

Table 2 ROC Curves of Different Variables for Predicting S-AKI Prognosis

Variable	Cut-off	Sensitivity	Specificity	AUC	95% CI	p-value
SII	3910.0	0.719	0.852	0.867	0.821–0.914	<0.001
NLR	22.9	0.813	0.750	0.848	0.794–0.902	<0.001
PLR	250.3	0.758	0.761	0.832	0.777–0.887	<0.001
MLR	1.075	0.438	0.784	0.624	0.550–0.699	0.002
APACHEII	22.5	0.641	0.739	0.769	0.706–0.832	<0.001
SOFA	9.5	0.813	0.489	0.688	0.615–0.761	<0.001

Abbreviations: ROC, Receiver operating curve; AUC, Area under the ROC; CI, Confidence interval; SII, Systemic immune-inflammation index; NLR, Neutrophil-lymphocyte ratio; PLR, Platelet-lymphocyte ratio; MLR, Monocyte-lymphocyte ratio; APACHEII, Acute physiology and chronic health evaluationII; SOFA, Sequential organ failure assessment.

Construction of the Nomogram Model

Based on the abovementioned variables, the nomogram was constructed for the prediction of 28-day mortality rates with S-AKI patients. For the nomogram, each predictive indicator's scale value corresponded to a score, with the total score representing the predicted 28-day prognosis for S-AKI patients after ICU admission. A higher total score indicated a poorer prognosis and a higher mortality risk (Figure 4). Using the Bootstrap method (1000 samples) to assess the

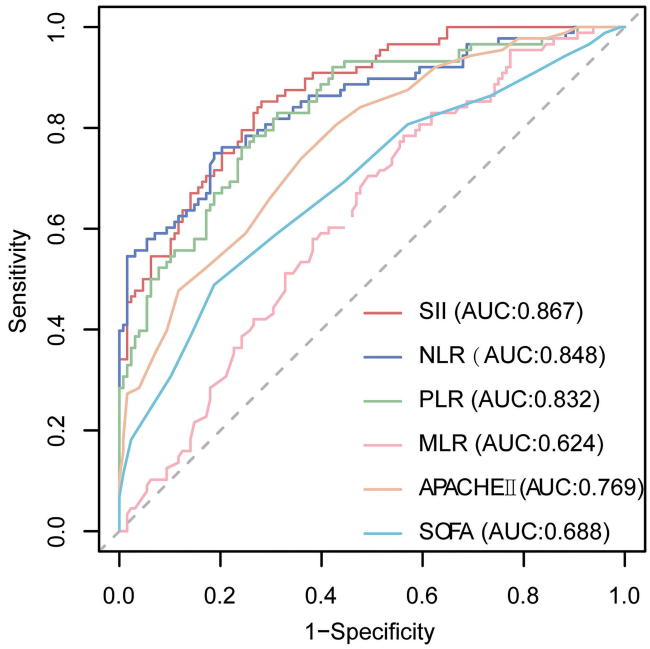

Figure 2 ROC analysis of different variables for the prediction of 28-day mortality.

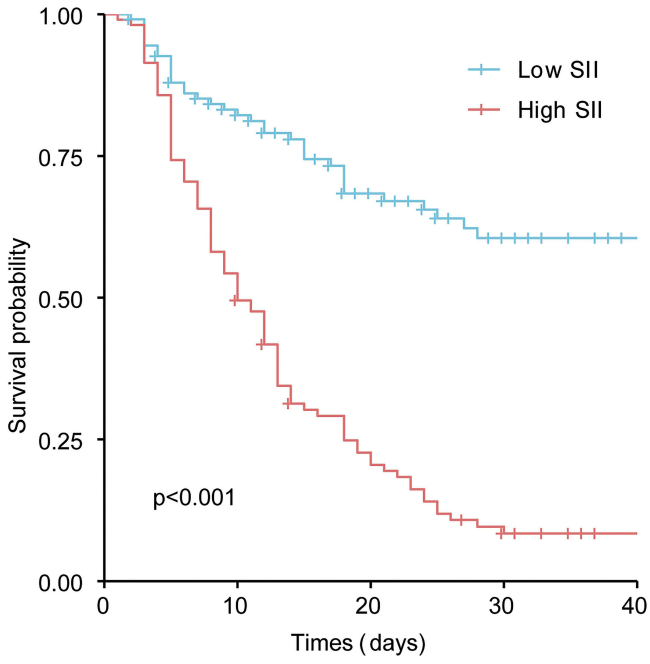

Figure 3 Kaplan-Meier curves for the description of survival between groups with different SII values (cut-off value: 3910) during the follow-up.

performance of the model, the C-index was 0.682 (95% CI 0.616–0.748). The calibration curve shows good agreement between the predicted and observed values in the nomogram model (Figure 5A). The day 28 ROC curve for the evaluation model showed an AUC of 0.916 (95% CI 0.892–0.938) (Figure 5B). Decision curve analysis demonstrated the model's high clinical predictive efficacy (Figure 5C).

Table 3 Univariate and Multivariate Cox Proportional Hazards Regression Analysis for Risk Factors of 28-Day Mortality

Variable	Univariate analysis			Multivariate analysis		
	p-value	HR	95% CI	p-value	HR	95% CI
Age, years	<0.001	1.035	1.023–1.047	0.001	1.023	1.010–1.038
Sex, male	0.332	1.195	0.834–1.712			
Body mass index, (kg/m^2)	0.159	0.965	0.915–1.1015			
MAP (mmHg)	0.456	0.996	0.986–1.007			
APACHEII	<0.001	1.111	1.079–1.143	0.002	1.112	1.039–1.190
SOFA	<0.001	1.154	1.092–1.219	0.004	1.051	1.016–1.087
Mechanical ventilation use	0.015	1.623	1.100–2.395	0.720	0.925	0.606–1.414
Vasopressors use	0.222	1.267	0.867–1.852			
Renal replacement therapy	0.188	1.335	0.868–2.054			
Number of organ dysfunction	<0.001	1.641	1.359–1.981	0.006	1.362	1.094–1.696
Hypertension	0.296	0.830	0.585–1.117			
Diabetes	0.104	1.350	0.941–1.939			
Coronary heart disease	0.028	1.499	1.043–2.152	0.159	0.746	0.497–1.121
Stroke	0.616	0.854	0.460–1.584			
Respiratory failure	<0.001	3.574	2.377–5.374	0.019	1.708	1.091–2.674
Heart failure	0.190	1.264	0.890–1.796			
Liver failure	0.334	0.821	0.549–1.226			
Malignancy	0.001	2.122	1.348–3.340	0.308	1.284	0.795–2.074
White blood cell count (10^9/L)	<0.001	1.048	1.023–1.073			
Hemoglobin (g/L)	0.308	0.996	0.989–1.003			
Platelet count (10^9/L)	0.112	1.002	1.000–1.003			
ALT (U/L)	0.234	1.000	1.000–1.001			
AST (U/L)	0.430	1.000	1.000–1.001			
Albumin (g/L)	0.753	0.994	0.959–1.031			
Creatinine (μmol/L)	0.013	0.997	0.994–0.999			
Blood urea nitrogen (μmol/L)	0.013	1.009	1.002–1.015	0.510	1.003	0.994–1.011
Sodium (mmol/L)	0.872	0.998	0.975–1.022			
Potassium (mmol/L)	0.450	0.919	0.739–1.144			
C-reactive protein (mg/L)	0.720	1.000	0.998–1.001			
Procalcitonin (μg/L)	0.139	0.995	0.989–1.002			
Lactic acid (mmol/L)	0.058	1.053	0.998–1.111			
High NLR group	<0.001	4.280	2.738–6.689			

(*Continued*)

Table 3 (Continued).

Variable	Univariate analysis			Multivariate analysis		
	p-value	HR	95% CI	p-value	HR	95% CI
High PLR group	<0.001	3.740	2.481–5.638			
High MLR group	0.001	1.767	1.244–2.509			
High SII group	<0.001	4.118	2.784–6.091	<0.001	2.505	1.609–3.898

Abbreviations: HR, Hazard ratio; CI, Confidence interval; MAP, Mean arterial pressure; APACHEII, Acute physiology and chronic health evaluationII; SOFA, Sequential organ failure assessment; ALT, Glutamic pyruvic transaminase; AST, Glutamic oxaloacetic transaminase; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; SII: Systemic immune-inflammation index.

Table 4 The Relationship Between SII and the Mortality of S-AKI Patients in a Cox Regression Model

	β	SE	HR (95% CI)	p-value
Non-adjusted model	1.415	0.200	4.118 (2.784–6.091)	<0.001
Adjust model I	0.957	0.216	2.603 (1.705–3.937)	<0.001
Adjust model II	0.918	0.226	2.505 (1.609–3.898)	<0.001

Notes: Non-adjusted model adjust for: none; Adjust I model adjust for: age, coronary heart disease, respiratory failure, malignancy; Adjust II model adjust for: age, coronary heart disease, respiratory failure, malignancy, SOFA scores, APACHE II scores, number of organ dysfunction, mechanical ventilation use, urea nitrogen.
Abbreviations: β, Regression coefficient; SE, Standard error; HR, Hazard ratio; CI, Confidence interval.

Discussion

S-AKI has high incidence, mortality, and poor prognosis.[8] Early identification and intervention are crucial for improving patient outcomes. This study compared the predictive power conventional risk factors and inflammatory markers for prognosis, revealing that the SII exhibited superior prognostic value for short-term outcomes in patients with S-AKI.

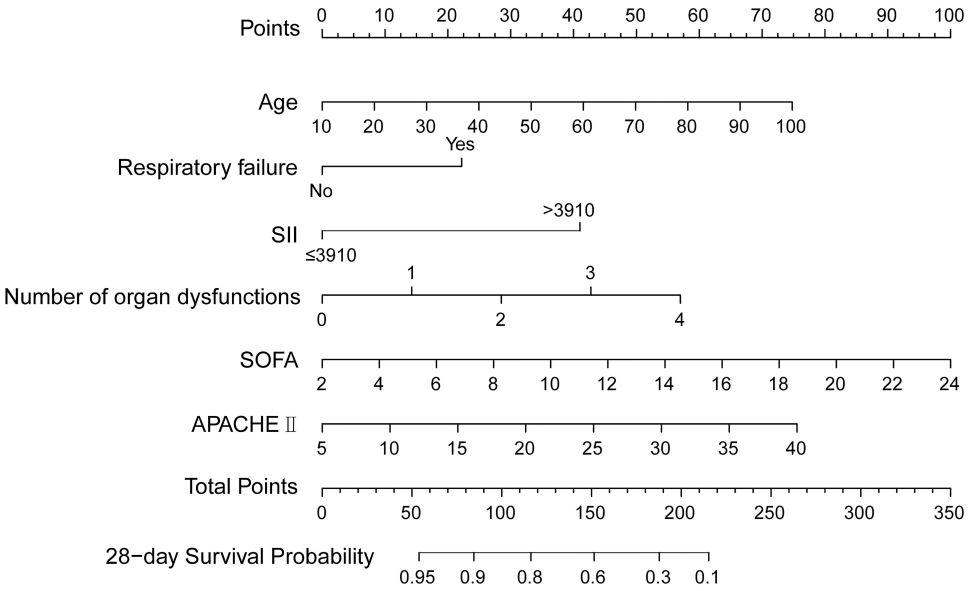

Figure 4 Nomogram model for estimating 28-day OS.

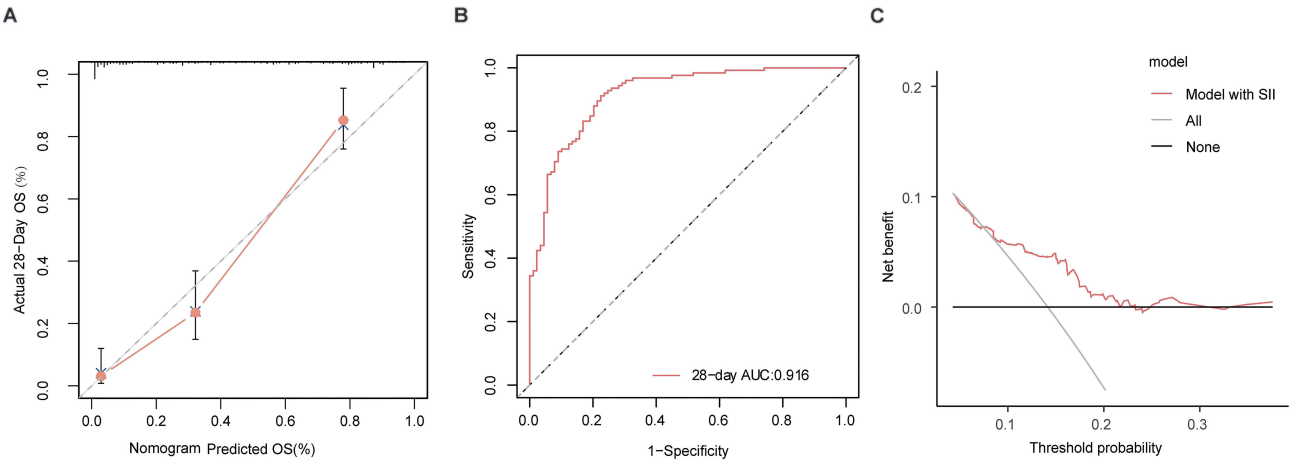

Figure 5 (**A**) Calibration curves of the predictive model for 28-day mortality. (**B**) ROC curves of prediction model for the day 28 mortality. (**C**) Decision curves of the predictive model for 28-day mortality.

A cutoff point of 3910 was established for SII to predict prognosis in S-AKI patients, with an AUC of 0.867 (sensitivity 0.719, specificity 0.852). The 28-day mortality rate in the ICU was significantly higher in the high-SII group than in the low-SII group (87.6% vs 32.4%, $P < 0.001$). Multivariate Cox regression analysis showed that SII as an independent predictor of prognosis for patients with S-AKI 28 days following their admission to ICU (HR 2.505, 95% CI 1.609–3.898, $P < 0.001$).

Previous studies have demonstrated that the SII is effective in predicting both the occurrence and prognostic outcomes of AKI across various settings.[13,23,24] Jiang et al[23] assessed the predictive capacity of SII in 4381 patients who underwent coronary angiography, among whom 786 developed AKI (AUC [95% CI] 0.625 [0.602–0.647]). In a study encompassing 305 patients with spontaneous cerebral hemorrhage after craniotomy, Wang et al[24] demonstrated that SII exhibited predictive capability for AKI occurrence (AUC [95% CI] 0.669 [0.608–0.730]) and displayed favorable performance in prognosticating post-AKI outcomes (AUC: 0.888, sensitivity 0.789, specificity 0.874). Lan et al[13] observed that there was a J-shaped correlation between SII and all-cause mortality in patients with severe AKI, especially at high levels of SII, which increased the mortality of patients. However, limited research has been conducted on the prognostic value of SII for short-term outcomes in patients with S-AKI admitted to the ICU. Therefore, we conducted an evaluation of the predictive performance of SII in predicting the prognosis of S-AKI and found that SII served as a reliable marker for short-term prognosis in these patients.

It was previously thought that AKI caused by sepsis was acute tubular necrosis due to reduced renal perfusion.[25] However, in recent years, further studies have revealed a multifaceted pathogenesis of S-AKI, including inflammation, oxidative stress, microcirculatory dysfunction, metabolic reprogramming, mitochondrial metabolism disorders, and cell cycle arrest.[9] Sepsis triggers widespread activation of cytokines and chemokines, it would result in immune system dysfunction.[26] Studies found that excessive inflammation induces toll-like receptor expression in tubular epithelial cells, which initiates the downstream signaling cascade and results in the injury of glomeruli and peripheral tubular cells.[27,28] The imbalance of inflammatory cells caused by sepsis is mainly manifested as neutrophilia and lymphocytopenia. Therefore, NLR, calculated by a complete blood count, has been proposed as an indicator to reflect the body's inflammatory and immune status.[29] Xi et al[30] found that NLR can be used to predict the prognosis of S-AKI, but its sensitivity and specificity are limited. The possible mechanism is that over-activated inflammation leads to platelet activation, abnormal clotting pathways, microcirculation dysfunction, and microthrombus formation.[31] In addition, platelets can also express toll-like receptors and further aggravate tubular epithelial cell damage.[32] Therefore, considering the close relationship between coagulation and immunity, both immune cells and platelets play key roles in the development of S-AKI.

SII, which combines neutrophil, lymphocyte, and platelet counts, can reflect the relationship between systemic inflammation, immunity, and coagulation disorders comprehensively.[22] Hu et al[14] first used it as an indicator to predict

the prognosis of patients undergoing resection for hepatocellular carcinoma. Recent studies have shown that SII is associated with poor outcomes in various diseases and serve as a prognostic indicator for mortality in patients with AKI, sepsis, cardiovascular disease, and acute pancreatitis.[13,16,17,33] Thus far, there are few studies on the value of SII in the prognosis of S-AKI. Previous studies based on the MIMIC-IV database have shown that a J-shaped association between SII and short-term mortality in patients, with both low and high SII being associated with increased mortality, particularly elevated SII levels; however, statistical significance was not reached for lower SII levels.[34] In addition, Li et al[35] reported a strong correlation between elevated SII and an increased incidence of AKI following sepsis. Therefore, further investigation is needed to determine the association between SII and short-term mortality risk in patients with S-AKI.

In our study, focusing on SII, we assessed the prognostic value of six biomarkers (SII, NLR, PLR, MLR, SOFA, and APACHE II). The study found that the high SII levels were significantly associated with the short-term risk of mortality in S-AKI patients. Additionally, two adjusted models were developed to account for confounding factors and further confirmed that SII levels were independently associated with the short-term risk of mortality in patients with S-AKI. To comprehensively improve the accuracy of prognostic assessment and develop a multi-parameter prognostic model, this study included various clinical data and serological markers to construct a prediction model for 28-day mortality in S-AKI patients after ICU admission, with a C-index of 0.682. The calibration curve showed good agreement between the predicted and actual risks of poor short-term prognosis in S-AKI patients, and the decision curve showed good clinical predictive efficacy and applicability. Therefore, SII serves as a potential novel marker for predicting the prognosis of S-AKI patients.

This study has certain limitations. First, it is a single-center retrospective study with a small sample size, and the results may have selection bias. The constructed nomogram model was only internally validated and lacked external or multicenter validation. Additionally, we used a single SII value rather than continuous measurements, not considering the evolution of the inflammatory state in sepsis patients. Therefore, future studies need to expand the sample sizes and conduct more in-depth research to validate the predictive value of inflammatory markers in critically ill patients.

Conclusion

In conclusion, this study showed that SII is independently associated with mortality in S-AKI patients and has a certain predictive value for prognosis within 28-day after ICU admission. A novel nomogram predictive model based on clinical data and the serum inflammatory marker SII was constructed, which can help assess the short-term mortality risk and prognosis of S-AKI patients. Routine blood tests are cost-effective, easily accessible, and highly reproducible, and the derived SII combined with clinical data can quickly and accurately quantify patient conditions, providing important implications for prognostic judgment and clinical application.

Statement of Ethics

This study was approved by the Ethics Committee of Henan Provincial People's Hospital ((2023) No. (145) and was accordance with the principles of the Declaration of Helsinki.

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

All authors report no conflicts of interest in this work.

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