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ORIGINAL RESEARCH

A novel model for predicting the short-term prognosis of acute pulmonary embolism: immuno-inflammatory age-specific shock index model (LogSII-SIA)

Lingwei Huang[1,2], Juan Liao[2,3], Meimei Yang[4], Ruixue Liu[5], Dan Lv[1,2], Ying Li[1,2], Fei He[1,2,*]

[1]Department of Geriatrics, The Affiliated Yongchuan Hospital of Chongqing Medical University, 402160 Chongqing, China
[2]Chongqing Municipality Clinical Research Center for Geriatric Diseases (Yongchuan Hospital, Chongqing Medical University), 402160 Chongqing, China
[3]Central Laboratory, The Affiliated Yongchuan Hospital of Chongqing Medical University, 402160 Chongqing, China
[4]Department of Clinical Pharmacy, West China Hospital of Sichuan University, 610041 Chengdu, Sichuan, China
[5]Department of Neurology, Chongqing Changshou People's Hospital, 401220 Chongqing, China

***Correspondence**
700416@hospital.cqmu.edu.cn
(Fei He)

Abstract

Background: To evaluate the forecasting reliability of the systemic immuno-inflammatory index (SII) in combination with the age-specific shock index (SIA) for the near-term prognosis of acute pulmonary embolism (APE) individuals. **Methods**: The base-10 logarithm was applied to SII, denoted as LogSII. Models were constructed using univariate analysis, Least Absolute Shrinkage and Selection Operator (LASSO) regression for variable selection, and binary logistic regression with 5-fold cross-validation, followed by efficacy analysis. Receiver operator characteristic (ROC) curves and area under the curves (AUC) were plotted, and the forecasting reliability of each indicator was assessed using DeLong's test. **Results**: In the original binary logistic regression model (4 variables), LogSII (Odds Ratio (OR) = 6.969, 95% confidence interval (CI): 2.676–18.150, $p < 0.001$) and SIA (OR = 1.040, 95% CI: 1.013–1.068, $p = 0.004$) were significant predictors. A simplified model, referred to collectively as Immuno-Inflammatory Age-Specific Shock Index (LogSII-SIA), was subsequently derived: logit (p) = $-10.071 + 1.732 \times$ LogSII $+ 0.052 \times$ SIA. The Hosmer-Lemeshow test indicated a good fit ($p = 0.241$). The model demonstrated good predictive performance (mean AUC: 0.835 ± 0.080, AUC range: 0.726–0.923), accurate probabilistic prediction (mean Brier score: 0.103) and a low risk of overfitting. The AUC of the simplified pulmonary embolism severity index (sPESI) score was 0.742 (95% CI: 0.687–0.792, $p < 0.001$). DeLong's test analysis indicated that the difference between the AUCs of the sPESI score and LogSII-SIA was statistically significant ($Z = 1.991$, $p = 0.0464$). **Conclusions**: LogSII and SIA served as standalone risk factors for the near-term prognosis of APE cases. LogSII-SIA has a higher predictive value for the short-term prognosis of APE than sPESI, and its generalizability needs to be further verified.

Keywords

Systemic inflammation; Shock index; Simplified pulmonary embolism severity index (sPESI); Acute pulmonary embolism (APE); Prognosis

1. Introduction

Acute pulmonary embolism (APE) involves a blockage of the pulmonary arteries caused by various emboli, with thrombus emboli being the most common [1]. Classified as the third most frequent cardiovascular disorder, it carries high morbidity and fatality rates [2]. The adverse outcomes of APE vary widely among at-risk patients, ranging from asymptomatic cases to severe presentations, including shock [3]. Current management of pulmonary embolism emphasizes the benefits of early-stage diagnosis, particularly the prompt assessment of disease severity and patient prognosis [4]. Klok *et al.* [5] concluded that the early development of targeted therapeutic strategies and return-to-activity programs can minimize the likelihood of severe issues in APE individuals, which depends on effective risk stratification and prognostic evaluation.

Risk stratification and prognostic assessment of patients with APE are predominantly conducted using clinical parameters such as hemodynamics, right ventricular echocardiography, computed tomography pulmonary angiography, cardiac injury markers, and the pulmonary embolism severity index (PESI) or simplified pulmonary embolism severity index (sPESI) [6, 7]. These risk assessment models are often criticized for their complexity and high cost. Clinically, it is often impossible to apply these models without delay, in light of the patient's condition, medical constraints and other circumstances [8]. The extensive crosstalk between inflammation, coagulation and immunity holds a major position in the pathophysiology of pulmonary embolism [9]. The systemic immuno-inflammatory index (SII) provides comprehensive in-

formation on neutrophil, lymphocyte, and platelet counts and is readily derived from routine blood tests [10]. The shock index (SI), which reflects the hemodynamic stability of the patient, is a simple, valid, and widely utilized tool for the assessment of acute and critical conditions [11] and has given rise to the age-specific shock index (SIA) [12].

Although a small number of studies have found that SII [13] and SIA [14] may help to project the prognosis for APE individuals, no studies have combined SII and SIA to evaluate the short-range forecast for APE patients. To further simplify the assessment process and explore a more effective prognostic model, we aim to examine the clinical effectiveness of combining SII with SIA in assessing the short-term prognosis of APE patients. This approach seeks to offer clinicians a theoretical foundation and a novel method to accurately evaluate pulmonary embolism severity and develop personalized treatment plans early in the clinical course.

2. Methods

2.1 Study population

Patients admitted to The Affiliated Yongchuan Hospital of Chongqing Medical University from January 2018 to June 2024 and diagnosed with APE were consecutively enrolled. Inclusion criteria: ① Computed Tomography Pulmonary Angiography (CTPA)-confirmed pulmonary embolism; ② Over the age of 18; ③ Symptom onset within less than two weeks. Exclusion criteria: ① Relapsed pulmonary embolism; ② Patients lacking complete clinical information; ③ Patients treated with anticoagulation or thrombolysis prior to hospital admission; ④ Patients with chronic thromboembolic pulmonary hypertension. The patient inclusion process is shown in Fig. 1.

2.2 Data collection

Patients' clinical data comprising gender, age, cerebrovascular disease, chronic lung disease, diabetes, malignancy, surgery, heart failure, lower extremity venous thrombosis, sPESI score, sPESI risk classification, and 30-day prognosis of confirmed pulmonary embolism were collected through a review of medical records. Laboratory markers obtained within 24 hours of APE diagnosis included serum creatinine, troponin, N-terminal pro-brain natriuretic peptide (NT-proBNP), lymphocyte count, leukocyte count, erythrocyte count, platelet count, neutrophil count, hemoglobin, hematocrit, D-dimer, and fibrinogen. Vital signs recorded at the onset of APE diagnosis comprising arterial oxygen saturation (SpO_2), heart rate, respiratory rate, and systolic blood pressure. All test samples from patients were collected and measured at room temperature (25 °C). Calculations were performed to determine SII (platelet count × neutrophil count/lymphocyte count), SI (heart rate/systolic blood pressure) and SIA (age × SI). The sPESI scoring and grading criteria [15] are shown in Table 1.

TABLE 1. sPESI scoring and grading criteria.

Relevant factor	Score
Age >80 yr	1 point
Systolic blood pressure <100 mmHg	1 point
Combined chronic heart failure or chronic lung disease	1 point
Heart rate >110 beats/min	1 point
SpO_2 <90%	1 point
Malignant tumor	1 point

Note: sPESI: simplified pulmonary embolism severity index; SpO_2: arterial oxygen saturation. Patients with a score of 0 were labeled as low risk, and those with a score of 1 or higher were labeled as high risk.

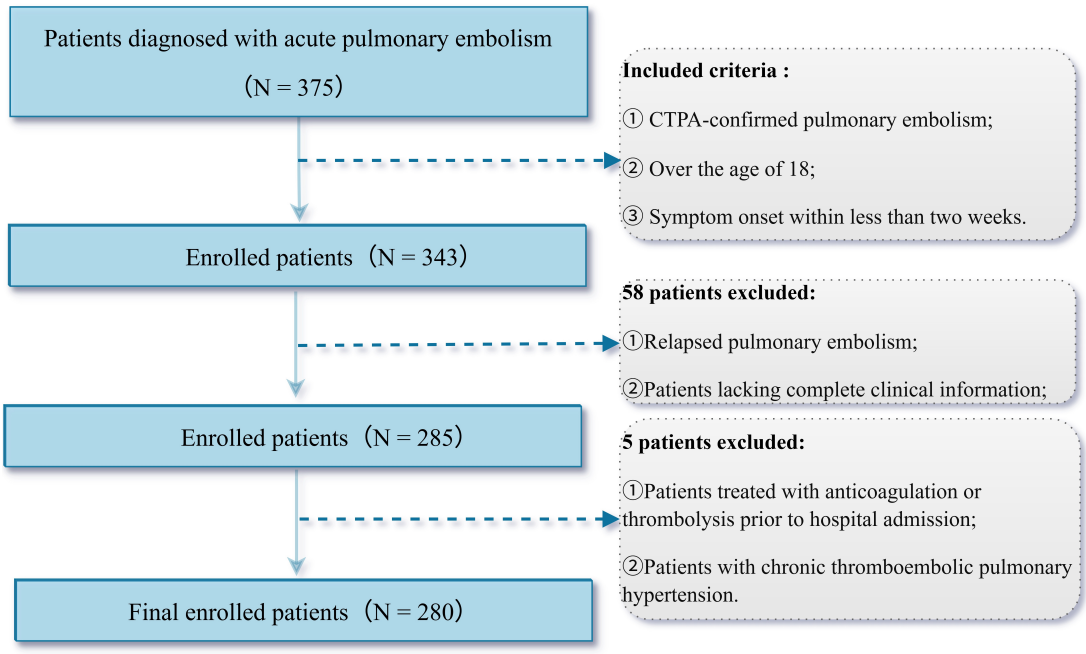

FIGURE 1. Patient inclusion flowchart. CTPA: Computed Tomography Pulmonary Angiography.

2.3 Statistical assessment

All continuous variables were evaluated for normality using the Kolmogorov-Smirnov test. Normally distributed variables were presented as the mean ± standard deviation, though data deviating from normality were expressed as the median (interquartile range (IQR)). Unpaired *t*-tests and Mann-Whitney U-tests were employed to compare normally and non-normally distributed variables between the two groups, respectively. The chi-square test was utilized to examine categorical variables across the study groups. Variables showing statistically significant differences ($p < 0.05$) in the univariate analysis were subsequently analyzed using Least Absolute Shrinkage and Selection Operator (LASSO) regression to identify key predictors [16]. Continuous variables (SII and NT-proBNP) with right-skewed distributions and large differences (in the thousands) between their maximum and minimum values were log-transformed using base 10 to compress the range and mitigate the impact of extreme values, denoted as LogSII and LogNT-proBNP, respectively [17]. Binary logistic regression was used to construct the original model (Model 1) and a simplified version (Model 2). The variance inflation factor (VIF) was used to assess multicollinearity, using a threshold of 5. A 5-fold cross-validation was performed to verify model stability and assess the risk of overfitting [18]. The joint LogSII-SIA score was defined as a weighted formula. The efficacy of the study sample was assessed. ROC curves were plotted for LogSII, SIA, sPESI and LogSII-SIA. A comparison of the ROC curve AUCs was conducted using DeLong's test. Statistical analyses and visualizations were conducted using SPSS 26.0 (IBM Corp., Armonk, NY, USA), MedCalc 22.0 (MedCalc Software Ltd., Ostend, Belgium) and RStudio 4.4.2. *p*-values of < 0.05 were judged to be statistically significant.

3. Results

3.1 General data

Among the 280 patients, 52% were admitted through emergency admission, 37% were admitted to the Intensive Care Unit (ICU) and 27% had massive pulmonary embolism. A total of 237 patients (84.6%) survived, including 140 males (59.1%) and 97 females (40.9%), with a mean age of 65.03 ± 13.09 years, while 43 patients (15.4%) died, comprising 31 males (72.1%) and 12 females (27.9%), with a mean age of 71.67 ± 14.99 years, during the 30-day follow-up period. The age, leukocyte count, neutrophil count, NT-proBNP, troponin, creatinine, heart rate, respiratory rate, D-dimer, SII, SI and SIA in the deceased group were notably greater than those in the survival group. Conversely, the lymphocyte count, erythrocyte count, hemoglobin, hematocrit, systolic blood pressure, and arterial oxygen saturation were notably reduced in the deceased group. These differences were statistically significant ($p < 0.05$). The incidence of malignant tumors, cerebrovascular disease, heart failure, chronic lung disease, sPESI scores and sPESI risk classifications were greater in the deceased group versus the survival group, demonstrating notable statistical disparities ($p < 0.05$). The remaining metrics did not exhibit statistically significant variations ($p > 0.05$). A comparison of general data is shown in Table 2.

3.2 Multifactorial logistic regression analysis

The LASSO regression identified twelve key variables: Leucocyte, SpO_2, Respiratory, Systolic blood pressure, Chronic lung disease, SII, SIA, hemoglobin, D-dimer, creatinine, NT-proBNP and malignant tumor (**Supplementary material 1**). Due to the limited number of deaths (n = 43), four core predictors with minimal cross-validation errors SIA (reflecting circulatory failure), LogSII (reflecting inflammation), Hemoglobin (associated with oxygen delivery) and LogNT-proBNP (a marker predictive of heart failure)—were retained to construct the original multivariate logistic regression model: logit (p) = −13.585 − 0.023 × Hemoglobin + 1.942 × LogSII + 1.999 × LogNT-proBNP + 0.039 × SIA (Table 3). VIF values for all included variables were below 5 (LogSII: 1.065; SIA: 1.161; LogNT-proBNP: 1.129; Hemoglobin: 1.040), suggesting the absence of significant multicollinearity. The Hosmer-Lemeshow test indicated good calibration ($p = 0.982$). The five-fold cross-validation demonstrated excellent predictive performance (mean AUC: 0.896 ± 0.057, AUC range: 0.833–0.987) and high accuracy in probability estimation (mean Brier score: 0.088), with a controlled risk of overfitting (**Supplementary material 2**). LogSII was a strong predictor of risk (OR = 6.969, 95% CI: 2.676–18.150, $p < 0.001$), while SIA also showed a significant association (OR = 1.040, 95% CI: 1.013–1.068, $p = 0.004$). Both LogSII and SIA were independent risk factors in the multivariate model, and their significance was held after controlling for other variables (*e.g.*, NT-proBNP, Hemoglobin). The prediction model was further simplified by incorporating only two variables, LogSII and SIA, to construct a simplified model (Model 2), referred to as LogSII-SIA: logit (p) = −10.071 + 1.732 × LogSII + 0.052 × SIA (Table 4). The Hosmer-Lemeshow test showed good calibration ($p = 0.241$). The results of the five-fold cross-validation demonstrated good predictive performance (mean AUC: 0.835 ± 0.080, AUC range: 0.726–0.923) and good probabilistic accuracy (mean Brier score: 0.103), with a low risk of overfitting (**Supplementary material 3**). Compared with the original model, the simplified model exhibited a 6.1% reduction in AUC and a 17% increase in Brier score but required 50% fewer variables and offered improved clinical applicability (Table 5). The formula for calculating the weights of the joint LogSII-SIA score, derived from our study sample, was LogSII-SIA Score = 0.444 × (LogSII − 3.0)/0.4 + 0.556 × (SIA − 50.3)/16.7 (see **Supplementary material 4** for a detailed explanation of the calculation steps). Based on post hoc efficacy analysis ($\alpha = 0.05$, effect size $f^2 = 0.35$), the statistical power of the current sample size (n = 280) was 92%, indicating that the model was sufficiently powered to detect a significant effect of the predictor variables on the outcome. This analysis reinforces the study's methodological robustness, eliminating the need for an expanded sample size.

3.3 ROC curve

The ROC curve showed that the AUC of the sPESI score, LogSII, SIA and LogSII-SIA were 0.742, 0.755, 0.777 and 0.832, and all demonstrated predictive value for the immediate

TABLE 2. Basic data on patients with acute pulmonary embolism in the survival and death groups.

Variables	All patients (n = 280)	Death group (n = 43)	Survival group (n = 237)	Statistic	*p* value
Age (IQR, yr)	68 (56, 76)	73 (65, 85)	67 (56, 75)	$Z = -2.936$	0.003*
Gender (Male (n (%)))	171 (61.1)	31 (72.1)	140 (59.1)	$\chi^2 = 2.596$	0.107
Cerebrovascular disease (n (%))	92 (32.9)	21 (48.8)	71 (30.0)	$\chi^2 = 5.880$	0.015*
Surgery (n (%))	34 (12.1)	4 (9.3)	30 (12.7)	$\chi^2 = 0.134$	0.714
Chronic lung disease (n (%))	95 (33.9)	23 (53.5)	72 (30.4)	$\chi^2 = 8.670$	0.003*
Congestive heart failure (n (%))	78 (27.9)	24 (55.8)	54 (22.8)	$\chi^2 = 19.757$	<0.001*
Lower extremity venous thrombosis (n (%))	151 (53.9)	27 (62.8)	124 (52.3)	$\chi^2 = 1.606$	0.205
Diabetes (n (%))	51 (18.2)	8 (18.6)	43 (18.1)	$\chi^2 = 0.005$	0.943
Malignant tumor (n (%))	53 (18.9)	13 (30.2)	40 (16.9)	$\chi^2 = 4.230$	0.040*
Heart rate (IQR, Times/min)	89 (80, 105)	102 (90, 108)	88 (79, 103)	$Z = -3.665$	<0.001*
Respiratory (IQR, Times/min)	23 (20, 28)	29 (25, 31)	22 (20, 26)	$Z = -5.588$	<0.001*
Systolic blood pressure ($\bar{x} \pm s$, mmHg)	125.26 ± 21.397	113.19 ± 22.727	127.45 ± 20.443	$T = -4.137$	<0.001*
SpO_2 (IQR, %)	96 (93, 98)	93 (86, 95)	97 (94, 98)	$Z = -5.436$	<0.001*
Creatinine (IQR, μmoL/L)	70.00 (57.00, 89.75)	91.00 (64.00, 110.00)	69.00 (56.00, 85.00)	$Z = -3.803$	<0.001*
Troponin (IQR, ng/mL)	0.013 (0.011, 0.048)	0.069 (0.028, 0.223)	0.012 (0.010, 0.033)	$Z = -6.097$	<0.001*
NT-proBNP (IQR, pg/mL)	558.50 (205.25, 2107.50)	2810.00 (1150.00, 7790.00)	444.00 (158.00, 1325.50)	$Z = -6.595$	<0.001*
Lymphocyte count (IQR, $\times 10^9$/L)	1.14 (0.79, 1.60)	0.84 (0.50, 1.45)	1.19 (0.84, 1.63)	$Z = -3.137$	0.002*
Leucocyte count (IQR, $\times 10^9$/L)	8.70 (6.33, 11.83)	14.40 (10.10, 19.30)	8.00 (6.15,10.30)	$Z = -6.314$	<0.001*
Erythrocyte count (IQR, $\times 10^{12}$/L)	4.19 (3.55, 4.59)	3.71 (2.98, 4.45)	4.20 (3.68, 4.60)	$Z = -2.587$	0.010*
Neutrophil count (IQR, $\times 10^9$/L)	6.28 (4.37, 9.77)	12.03 (8.22, 15.60)	5.75 (4.17, 8.21)	$Z = -6.377$	<0.001*
Platelet count (IQR, $\times 10^9$/L)	187.50 (141.25, 252.50)	204.00 (125.00, 300.00)	184.00 (142.00, 242.00)	$Z = -1.191$	0.233
Hemoglobin (IQR, g/L)	125.50 (108.00, 140.75)	113.00 (88.00, 134.00)	127.00 (112.00, 143.00)	$Z = -3.266$	0.001*
Hematocrit (IQR, %)	0.38 (0.33, 0.42)	0.36 (0.30, 0.41)	0.39 (0.33, 0.43)	$Z = -2.420$	0.016*
D-dimer (IQR, mg/L)	7.94 (3.52, 12.95)	12.84 (5.40, 21.48)	7.49 (3.13, 12.18)	$Z = -3.790$	<0.001*
Fibrinogen (IQR, g/L)	3.30 (2.50, 4.50)	3.90 (2.80, 4.80)	3.20 (2.40, 4.45)	$Z = -1.508$	0.132
SII (IQR)	906.41 (568.81, 1927.39)	2934.77 (1465.89, 6708.91)	844.88 (560.98, 1423.83)	$Z = -5.325$	<0.001*
SI (IQR)	0.719 (0.609, 0.883)	0.907 (0.726, 1.083)	0.699 (0.602, 0.833)	$Z = -4.985$	<0.001*
SIA (IQR)	45.88 (38.56, 59.86)	62.78 (53.18, 76.08)	44.03 (37.10, 57.31)	$Z = -5.789$	<0.001*
sPESI score (IQR, point)	1 (0, 2)	2 (2, 3)	1 (0, 2)	$Z = -5.243$	<0.001*
sPESI risk classification (n (%))				$\chi^2 = 15.761$	<0.001*
Low risk	97 (34.6)	3 (7.0)	94 (39.7)		
High risk	183 (65.4)	40 (93.0)	143 (60.3)		

*Note: SpO_2: arterial oxygen saturation; NT-proBNP: N-terminal pro-brain natriuretic peptide; SII: systemic immune-inflammatory index; SI: shock index; SIA: age-specific shock index; sPESI: simplified pulmonary embolism severity index; IQR: interquartile range. *$p < 0.05$.*

TABLE 3. Original model 1.

Variables	β	SE	Wald	OR (95% CI)	p
Hemoglobin	−0.023	0.009	6.643	0.977 (0.961–0.995)	0.010*
LogSII[#]	1.942	0.488	15.806	6.969 (2.676–18.150)	<0.001*
LogNT-proBNP[#]	1.999	0.408	23.959	7.379 (3.315–16.426)	<0.001*
SIA	0.039	0.014	8.454	1.040 (1.013–1.068)	0.004*

*Note: SII: systemic immuno-inflammatory index; NT-proBNP: N-terminal pro-brain natriuretic peptide; SIA: age-specific shock index; CI: confidence interval; SE: Standard Error; OR: Odds Ratio. [#]: SII and NT-proBNP were logarithmized with a base of 10; *: $p < 0.05$.*

TABLE 4. Simplified model 2.

Variables	β	SE	Wald	OR (95% CI)	p
LogSII[#]	1.732	0.412	17.650	5.653 (2.520–12.684)	<0.001*
SIA	0.052	0.011	22.134	1.053 (1.031–1.076)	<0.001*

*Note: SII: systemic immuno-inflammatory index; SIA: age-specific shock index; CI: confidence interval; SE: standard error; OR: odds ratio. [#]: SII was logarithmized with a base of 10; *: $p < 0.05$.*

TABLE 5. Comparison of original model 1 and simplified model 2.

Model	AUC	Brier scores	Hosmer-Lemeshow test, p-value	Number of variables	Clinical operability
Original model 1 (4 variables)	0.896 ± 0.057	0.088	0.982	4	Higher (more variables required)
Simplified model 2 (LogSII-SIA)	0.835 ± 0.080	0.103	0.241	2	Better (bedside fast)

LogSII-SIA: Immuno-Inflammatory Age-Specific Shock Index; AUC: area under the curves.

prognosis of individuals suffering from acute pulmonary embolism ($p < 0.05$). DeLong's test analysis suggested that the difference in AUC between the sPESI score and LogSII-SIA was statistically significant ($Z = 1.991$, $p < 0.05$), indicating that LogSII combined with SIA had a greater ability to predict 30-day all-cause mortality in patients with APE compared to the sPESI score. ROC curve and analysis are shown in Tables 6,7 and Fig. 2. AUC values derived from RStudio 4.4.2 (5-fold cross-validation) and MedCalc 22.0 (ROC curve analysis) may exhibit minor numerical variations due to platform-specific computational algorithms.

4. Discussion

Due to the complexity of APE, clinicians must assess the severity and progression of pulmonary embolism through multiple complex steps, which are difficult to perform quickly and may delay effective treatments such as thrombolysis or intervention for high-risk patients. Such delays can ultimately result in patient mortality [19]. Studies have shown [19] that mortality due to pulmonary embolism is higher within 30 days of diagnosis compared to longer follow-up periods, with half of patients succumbing to causes other than pulmonary embolism by 90 days. The main advantage of PESI and sPESI is the ability to reliably identify patients with a low 30-d mortality rate. It is therefore the current mainstream method for predicting death occurring within a 30-day period in APE patients and is recommended by international guidelines [20, 21]. However, several limitations of sPESI have been noted. First, sPESI has high sensitivity but low specificity [7]. Second, the fact that sPESI is based only on the subjective personal history of illness and does not take into account objective imaging examination, laboratory indices, and other parameters may be a serious limitation [20, 21]. In addition, the score has limitations in terms of the authenticity of the medical history and difficulty in data collection. In this study, an attempt was made to find a simple and easy, more objective, and accurate method to predict the short-term prognosis of patients with APE. Therefore, we constructed a combined SII and SIA model the Immuno-Inflammatory Age-Specific Shock Index (LogSII-SIA) which demonstrated superior predictive performance for short-term prognosis in acute pulmonary embolism compared with the sPESI score. While its performance was slightly lower than that of the original model, it offered substantial clinical convenience, particularly in resource-limited settings.

Studies have shown [14] that SI can be used to determine the prognosis of patients with APE. As people age, their blood pressure increases, and their heart rate slows down [22]. Catecholamine levels and the application of vasoactive substances considerably influence heart rate and systolic blood pressure [23]. When peripheral perfusion is inadequate, catecholamine secretion increases, leading to arterial vasoconstriction and an elevated heart rate to sustain basic tissue metabolism [23]. This physiological phenomenon may reduce the accuracy of SI as a prognostic indicator. Age is a stable indicator that is not

TABLE 6. LogSII, SIA, sPESI score, LogSII-SIA predictors of 30-day all-cause mortality in patients with APE.

Variables	AUC Value	95% CI	Youden Index	Optimal cut-off value	Sensitivity (%)	Specificity (%)	*Z* value	*p* value
LogSII	0.755	0.701–0.804	0.5354	3.16	76.74	76.79	5.103	<0.001*
SIA	0.777	0.724–0.825	0.5165	51.10	83.72	67.93	7.922	<0.001*
sPESI score	0.742	0.687–0.792	0.4299	1.00	76.74	66.24	6.707	<0.001*
LogSII-SIA	0.832	0.782–0.873	0.5968	0.12	88.37	71.31	10.534	<0.001*

*Note: APE: acute pulmonary embolism; SII: systemic immuno-inflammatory index; SIA: age-specific shock index; sPESI: simplified pulmonary embolism severity index; LogSII: SII was logarithmized with a base of 10; CI: confidence interval; AUC: area under the curves. *: $p < 0.001$.*

TABLE 7. DeLong's test analyzing the AUC of LogSII, SIA, sPESI score and LogSII-SIA.

Verify by comparing two cases	Statistic	*p* value
LogSII *vs.* SIA	$Z = 0.388$	0.6982
LogSII *vs.* sPESI score	$Z = 0.197$	0.8436
LogSII *vs.* LogSII-SIA	$Z = 1.868$	0.0617
SIA *vs.* sPESI score	$Z = 0.840$	0.4012
SIA *vs.* LogSII-SIA	$Z = 2.503$	0.0123*
sPESI score *vs.* LogSII-SIA	$Z = 1.991$	0.0464*

*Note: SII: systemic immuno-inflammatory index; SIA: age-specific shock index; sPESI: simplified pulmonary embolism severity index; LogSII: SII was logarithmized with a base of 10; *: $p < 0.05$.*

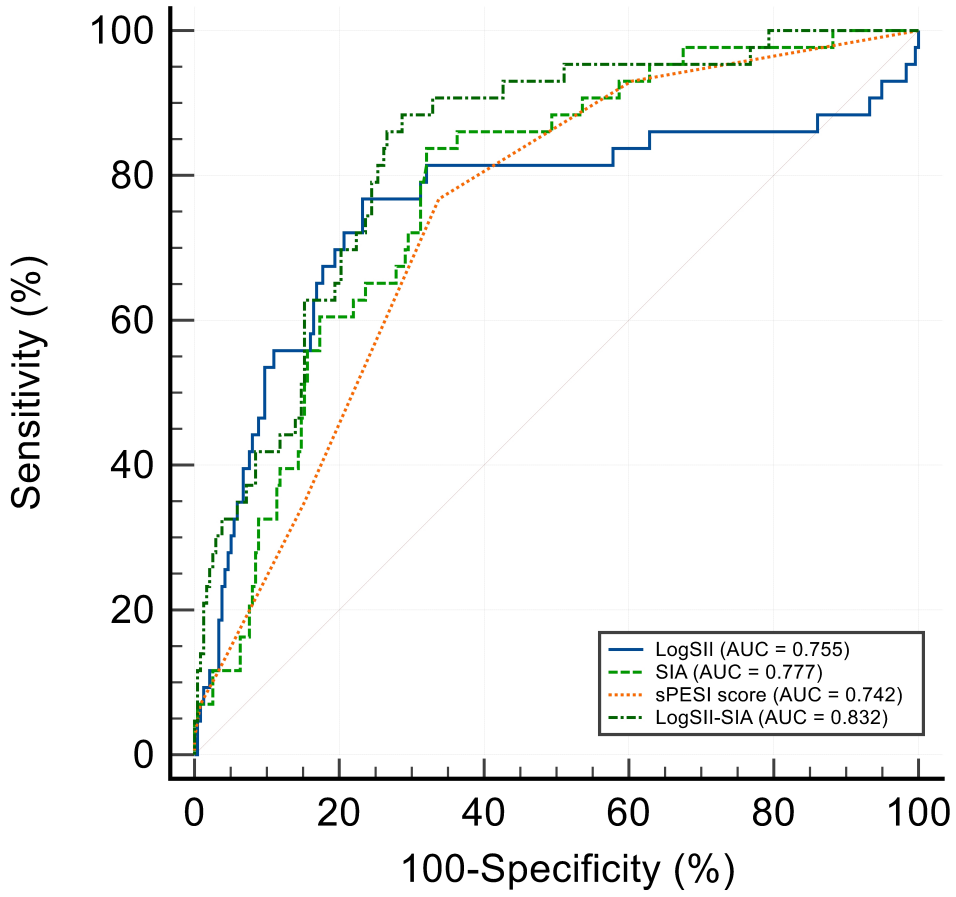

FIGURE 2. ROC Curves of LogSII, SIA, sPESI Score and LogSII-SIA. Note: SII: systemic immuno-inflammatory index; SIA: age-specific shock index; sPESI: simplified pulmonary embolism severity index; LogSII: SII was logarithmized with a base of 10; AUC: area under the curves.

disturbed by other factors. Therefore, age, a risk factor, was included in addition to heart rate and blood pressure to enhance the accuracy of patient prognosis evaluation [24]. We find that SIA effectively forecasts adverse outcomes in APE patients. For each one-unit increase in SIA, the risk of death increased by 5.3% (OR = 1.053, 95% CI: 1.031–1.076). Although the effect size is relatively modest, its status as a continuous variable enables meaningful risk stratification around critical thresholds (*e.g.*, SIA >50 *vs.* ≤50). When combined with LogSII (OR = 5.653), the joint model demonstrates a multiplicative effect on risk. Moreover, the simple, non-invasive, rapidly obtainable, and accurate nature of SIA as a risk index for circulatory failure is one of its key strengths, making it a practical tool.

Our findings identified SII as an independent predictor of APE severity. Each one-unit increase in LogSII was associated with a 5.653-fold increase in the risk of death (OR = 5.653, 95% CI: 2.520–12.684), indicating strong predictive performance. Additionally, SII is derived from budget-friendly and routine complete blood counts, making it a practical tool. The mechanism is considered as follows: Serum levels of procoagulant and proinflammatory cells such as leukocytes, platelets, and endothelial cells are elevated following the occurrence of APE [9]. The release of procoagulant and proinflammatory particles triggers increased platelet activation and neutrophil recruitment. This process disrupts the vascular wall's anticoagulant and anti-inflammatory phenotypes, fosters thrombus formation, and generates oxygen radicals, leading to tissue damage [9, 25, 26]. This is tied to an adverse prognosis and a greater recent mortality risk in patients diagnosed with pulmonary embolism. In addition, neutrophils and macrophages in APE patients can infiltrate the walls of the pulmonary arteries and the right ventricle, leading to right ventricular dysfunction, myocardial inflammation, and necrosis [9, 27]. Lymphocytes are immune cells, and infection and immunity play critical roles in pulmonary embolism [28]. The secretion of epinephrine and glucocorticoids during the sympathetic nervous system activation elicited by APE may lead to a decrease in lymphocyte counts [29]. Lymphopenia leads to a weakened immune response, contributing to a poor prognosis [29].

However, elevated LogSII is limited in specificity and can be influenced by various factors such as trauma, infections, acute coronary syndromes, malignancies, renal insufficiency, and chronic cardiopulmonary disease [30]. Comorbidities were adjusted for the fact that LogSII remained an independent predictor of 30-day mortality. Furthermore, the combination of LogSII and SIA for predicting the prognosis of pulmonary embolism enhances prognostic accuracy and reduces false-positive rates, making it an important research focus. However, no relevant studies have been conducted to date. In this study, we found that LogSII, SIA and LogSII-SIA demonstrated strong forecasting potential for the near-term prognosis of APE patients. In comparison, LogSII-SIA increased sensitivity and demonstrated significantly greater predictive efficacy compared to the sPESI score. This suggests that in clinical practice, it is necessary to make full use of all important clinical data and adopt a multi-indicator (subjective and objective) joint prediction model to enhance prognostic efficacy and provide a reliable basis for early risk stratification and individualized treatment of APE.

There are some limitations to this study: (1) This study was a single-center, retrospective analysis with a relatively small sample size drawn exclusively from our hospital. It provided preliminary evidence that LogSII-SIA outperformed sPESI in internal validation (AUC: 0.832 *vs.* 0.742), although its generalizability remains to be established. Large-scale, multicenter, prospective studies are needed to validate these findings further. (2) The possibility of selection bias and unaccounted confounders cannot be fully excluded. Elevated LogSII has limited specificity and can be influenced by factors such as malignant tumors, cerebrovascular disease, and chronic cardiopulmonary conditions. Comorbidities (cerebrovascular disease, chronic lung disease, heart failure, cancer, diabetes) were included as covariates in the logistic regression model. Even after adjustment, LogSII remained an independent predictor of 30-day mortality. (3) Blood samples were collected within 24 hours of diagnosis but not at standardized time points. Parameters such as SII may fluctuate over time due to dynamic physiological responses post-APE (*e.g.*, platelet activation, inflammatory cascades). Variability in sampling timing could introduce bias into SII measurements, potentially affecting the model's prognostic accuracy. Future studies should standardize blood collection protocols to minimize this confounder. (4) Heart rate and blood pressure values are influenced by numerous factors, some of which were not assessable or controllable within this study population. Additionally, heart rate and blood pressure measurements were limited to a short period at diagnosis and may have been affected by prehospital medications or interventions. These limitations warrant further investigation in future research.

5. Conclusions

In a study involving 280 APE patients from The Affiliated Yongchuan Hospital of Chongqing Medical University, we found that both LogSII and SIA served as standalone risk factors for the near-term prognosis of APE cases. Our findings indicated that the combination of SII and SIA, termed the Immuno-Inflammatory Age-Specific Shock Index (LogSII-SIA), outperformed sPESI in predicting the near-term prognosis of APE patients. Its generalizability requires validation through large-scale prospective studies.

ABBREVIATIONS

APE, acute pulmonary embolism; SII, systemic immuno-inflammatory index; LogSII, systemic immuno-inflammatory index (SII) was logarithmized with a base of 10; SI, shock index; SIA, age-specific shock index; PESI, pulmonary embolism severity index; sPESI, simplified pulmonary embolism severity index; ROC curve, receiver operator characteristic curve; AUC, area under the curve; CI, confidence interval; LASSO, Least Absolute Shrinkage and Selection Operator; SpO_2, arterial oxygen saturation; NT-proBNP, N-terminal pro-brain natriuretic peptide; LogSII-SIA, the systemic immuno-inflammatory index (SII) in combination with the age-specific shock index (SIA); Or Immuno-Inflammatory Age-Specific Shock Index Model;

VIF, variance inflation factor; IQR, interquartile range; OR, Odds Ratio; CTPA, Computed Tomography Pulmonary Angiography; ICU, Intensive Care Unit.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

LH and FH—designed the research study. LH, JL, MY, RL, DL, YL and FH—performed the research. LH and JL—analyzed the data. LH, JL, MY and RL—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted by the guidelines set out in the Declaration of Helsinki. The study was approved by The Medical Ethics Committee of The Affiliated Yongchuan Hospital of Chongqing Medical University (No. 2024EC0045) and was carried out in strict accordance with the requirements. This study is a retrospective study that involves only the collection of data, files and medical records that are already in existence. Therefore, the Medical Ethics Committee of The Affiliated Yongchuan Hospital of Chongqing Medical University gave a waiver of informed consent. We respect and protect the rights and privacy of the participants and ensure the confidentiality of their personal information, and the privacy and personally identifiable information of the participants has been de-informatized and does not involve destructive and sensitive research on the participants of the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1997923503871803392/attachment/Supplementary%20material.zip.

REFERENCES

[1] Freund Y, Cohen-Aubart F, Bloom B. Acute pulmonary embolism: a review. JAMA. 2022; 328: 1336–1345.

[2] Hobohm L, Keller K, Konstantinides S. Pulmonary embolism. Innere Medizin. 2023; 64: 40–49.

[3] Trott T, Bowman J. Diagnosis and management of pulmonary embolism. Emergency Medicine Clinics of North America. 2022; 40: 565–581.

[4] Millington SJ, Aissaoui N, Bowcock E, Brodie D, Burns KEA, Douflé G, *et al*. High and intermediate risk pulmonary embolism in the ICU. Intensive Care Medicine. 2024; 50: 195–208.

[5] Klok FA, Ageno W, Ay C, Bäck M, Barco S, Bertoletti L, *et al*. Optimal follow-up after acute pulmonary embolism: a position paper of the European Society of Cardiology Working Group on Pulmonary Circulation and Right Ventricular Function, in collaboration with the European Society of Cardiology Working Group on Atherosclerosis and Vascular Biology, endorsed by the European Respiratory Society. European Heart Journal. 2022; 43: 183–189.

[6] Machanahalli BA, Reddi V, Belford PM, Alvarez M, Jaber WA, Zhao DX, *et al*. Intermediate-risk pulmonary embolism: a review of contemporary diagnosis, risk stratification and management. Medicina. 2022; 58: 1186.

[7] Leidi A, Bex S, Righini M, Berner A, Grosgurin O, Marti C. Risk stratification in patients with acute pulmonary embolism: current evidence and perspectives. Journal of Clinical Medicine. 2022; 11: 2533.

[8] Wrenn JO, Kabrhel C. Emergency department diagnosis and management of acute pulmonary embolism. British Journal of Haematology. 2024; 205: 1714–1716.

[9] Imiela AM, Mikołajczyk TP, Guzik TJ, Pruszczyk P. Acute pulmonary embolism and immunity in animal models. Archivum Immunologiae et Therapiae Experimentalis. 2024; 72: 1–13.

[10] Ma F, Li L, Xu L, Wu J, Zhang A, Liao J, *et al*. The relationship between systemic inflammation index, systemic immune-inflammatory index, and inflammatory prognostic index and 90-day outcomes in acute ischemic stroke patients treated with intravenous thrombolysis. Journal of Neuroinflammation. 2023; 20: 220.

[11] Valiente Fernández M, Lesmes González de Aledo A, Delgado Moya FdP, Martín Badía I, Álvaro Valiente E, Blanco Otaegui N, *et al*. Shock index and physiological stress index for reestratifying patients with intermediate-high risk pulmonary embolism. Medicina Intensiva. 2024; 48: 309–316.

[12] Kara H, Degirmenci S, Bayir A, Ak A. Pulmonary embolism severity index, age-based markers and evaluation in the emergency department. Acta Clinica Belgica. 2015; 70: 259–264.

[13] Gok M, Kurtul A. A novel marker for predicting severity of acute pulmonary embolism: systemic immune-inflammation index. Scandinavian Cardiovascular Journal. 2021; 55: 91–96.

[14] Gökçek K, Gökçek A, Demir A, Yıldırım B, Acar E, Alataş ÖD. In-hospital mortality of acute pulmonary embolism: predictive value of shock index, modified shock index, and age shock index scores. Medicina Clínica. 2022; 158: 351–355.

[15] Korkut M, Yavuz A, Selvi F, Zortuk Ö, İnan EH, Güven HÇ. Prognostic performance of the Bova, sPESI, and Qanadli scores in patients with acute pulmonary embolism. Acta Radiologica. 2024; 65: 1482–1490.

[16] Ali H, Shahzad M, Sarfraz S, Sewell KB, Alqalyoobi S, Mohan Babu P. Application and impact of lasso regression in gastroenterology: a systematic review. Indian Journal of Gastroenterology. 2023; 42: 780–790.

[17] Kong Y, Lin M, Fu Y, Huang B, Jin M, Ma L. Elevated log uric acid-to-high-density lipoprotein cholesterol ratio (UHR) as a predictor of increased female infertility risk: insights from the NHANES 2013–2020. Lipids in Health and Disease. 2025; 24: 127.

[18] Gao C, Bian X, Wu L, Zhan Q, Yu F, Pan H, *et al*. A nomogram predicting the histologic activity of lupus nephritis from clinical parameters. Nephrology Dialysis Transplantation. 2024; 39: 520–530.

[19] Sifuentes AA, Goldar G, Abdul-Aziz AAA, Lee R, Shore S. Mechanical circulatory support and critical care management of high-risk acute

pulmonary embolism. Interventional Cardiology Clinics. 2023; 12: 323–338.

[20] El-Bouri WK, Sanders A, Lip GYH; BBC-VTE investigators. Predicting acute and long-term mortality in a cohort of pulmonary embolism patients using machine learning. European Journal of Internal Medicine. 2023; 118: 42–48.

[21] Li S, Huang S, Feng Y, Mao Y. Development of a nomogram model to predict 30-day mortality in ICU cancer patients with acute pulmonary embolism. Scientific Reports. 2025; 15: 9232.

[22] Tan I, Barin E, Butlin M, Avolio AP. Relationship between heart rate and central aortic blood pressure: implications for assessment and treatment of isolated systolic hypertension in the young. Minerva Medica. 2022; 113: 807–816.

[23] Baffour-Awuah B, Man M, Goessler KF, Cornelissen VA, Dieberg G, Smart NA, *et al*. Effect of exercise training on the renin-angiotensin-aldosterone system: a meta-analysis. Journal of Human Hypertension. 2024; 38: 89–101.

[24] Vakhshoori M, Bondariyan N, Sabouhi S, Shakarami M, Emami SA, Nemati S, *et al*. Impact of shock index (SI), modified SI, and age-derivative indices on acute heart failure prognosis; a systematic review and meta-analysis. PLOS ONE. 2024; 19: e0314528.

[25] Mandel J, Casari M, Stepanyan M, Martyanov A, Deppermann C. Beyond hemostasis: platelet innate immune interactions and thromboinflammation. International Journal of Molecular Sciences. 2022; 23: 3868.

[26] Viswanathan G, Kirshner HF, Nazo N, Ali S, Ganapathi A, Cumming I, *et al*. Single-cell analysis reveals distinct immune and smooth muscle cell populations that contribute to chronic thromboembolic pulmonary hypertension. American Journal of Respiratory and Critical Care Medicine. 2023; 207: 1358–1375.

[27] Luijten D, de Jong CMM, Ninaber MK, Spruit MA, Huisman MV, Klok FA. Post-pulmonary embolism syndrome and functional outcomes after acute pulmonary embolism. Seminars in Thrombosis and Hemostasis. 2023; 49: 848–860.

[28] Jiang C, Lin J, Xie B, Peng M, Dai Z, Mai S, *et al*. Causal association between circulating blood cell traits and pulmonary embolism: a mendelian randomization study. Thrombosis Journal. 2024; 22: 49.

[29] Lange T, Luebber F, Grasshoff H, Besedovsky L. The contribution of sleep to the neuroendocrine regulation of rhythms in human leukocyte traffic. Seminars in Immunopathology. 2022; 44: 239–254.

[30] Bedel C, Korkut M, Armağan H. Can NLR, PLR and LMR be used as prognostic indicators in patients with pulmonary embolism? A commentary. Bosnian Journal of Basic Medical Sciences. 2021; 21: 501.

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