

Predictive Value of Neutrophil-To-Lymphocyte Ratio and Systemic Immune-Inflammation Index in the Prognosis of Sepsis-Related Acute Respiratory Distress Syndrome

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Abstract

Aims/Background The neutrophil-to-lymphocyte ratio (NLR) was an independent influence factor for mortality in acute respiratory distress syndrome (ARDS). The systemic immune-inflammation index (SII) is a predictive indicator for sepsis. This study was designed to evaluate the predictive value of combined NLR and SII in sepsis-related ARDS.

Methods Patients with sepsis-related ARDS ($n = 112$), admitted to Pingyang Hospital of Wenzhou Medical University from January 2022 to January 2025, were obtained for retrospective analysis. A survivor group ($n = 62$) and a non-survivor group ($n = 50$) were formed based on 28-day survival status. Neutrophil, lymphocyte, and platelet counts were detected, and NLR and SII were subsequently calculated. Logistic regression analysis and receiver operating characteristic (ROC) curves were performed to analyze the influences of NLR and SII in the prognosis of sepsis-related ARDS.

Results Non-survivor group has longer intensive care unit (ICU) length of stay, higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score and white blood cell (WBC) count, and lower lymphocyte count than those of survivor group ($p = 0.001, 0.032, 0.028, 0.004$, respectively). Both NLR and SII values were elevated in the non-survivor group ($p < 0.001$). Furthermore, APACHE II score (odds ratio (OR): 1.150, 95% confidence interval (CI): 1.004–1.317, $p = 0.044$), ICU length of stay (OR: 1.147, 95% CI: 1.017–1.294, $p = 0.026$), NLR (OR: 1.158, 95% CI: 1.068–1.255, $p < 0.001$), and SII > 2090.37 (OR: 5.207, 95% CI: 1.800–15.064, $p = 0.002$) as independent prognostic risk factors. The combined NLR and SII had a superior predictive value (area under the curve (AUC): 0.808, 95% CI: 0.730–0.887, $p < 0.001$) compared to APACHE II score (AUC: 0.618, 95% CI: 0.503–0.733, $p = 0.045$), ICU length of stay (AUC: 0.679, 95% CI: 0.573–0.784, $p = 0.001$), NLR alone (AUC: 0.788, 95% CI: 0.701–0.875, $p < 0.001$), or SII alone (AUC: 0.748, 95% CI: 0.657–0.840, $p < 0.001$). The optimal cut-off values for APACHE II score, ICU length of stay, NLR, and SII were 19.5, 15.5, 26.13, and 2090.37, respectively.

Conclusion The combination of NLR and SII provides a strong predictive value for the prognosis of sepsis-related ARDS.

Key words: acute respiratory distress syndrome; prognosis; sepsis; neutrophil; lymphocyte; platelet

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Introduction

Sepsis is an excessive inflammatory response to an infectious agent, which can lead to organ dysfunction and circulatory failure (Qiao et al., 2024). Among the organs affected by sepsis, the lungs are the most commonly involved (Qiao et

al., 2024; Zhang et al., 2024; Chen et al., 2025). Therefore, patients with sepsis are prone to developing acute respiratory distress syndrome (ARDS). ARDS is a clinical syndrome featuring persistent hypoxemia and respiratory distress, and involves acute, diffuse inflammatory injury of alveolar epithelial cells and pulmonary vascular endothelial cells (Fujishima, 2023). Approximately 3 million patients suffer from ARDS worldwide annually. Meanwhile, the mortality rate of ARDS ranges from 35% to 45% (Fujishima, 2023; Grasselli et al., 2023). Compared with patients having non-sepsis-induced ARDS or sepsis alone, sepsis-induced ARDS has greater disease severity, lower extubation success rates, and higher mortality (Wang et al., 2021; Bardají-Carrillo et al., 2024; Shi et al., 2022). At present, there are no remarkably effective treatments for sepsis-related ARDS. In clinical practice, mechanical ventilation, oxygen therapy, and corticosteroids are primarily used for managing sepsis-related ARDS (Chaudhuri et al., 2024; Hu et al., 2020). These treatments primarily aim to control inflammation and improve oxygenation. However, their contribution to reducing mortality remains limited (Hu et al., 2020). Furthermore, there is a lack of reliable biomarkers or indicators to predict the progression of sepsis-related ARDS in clinical practice. Therefore, accurate evaluation and prediction of the condition and prognosis in patients with sepsis-induced ARDS are urgently needed.

The neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) are systemic inflammatory markers derived from neutrophil, lymphocyte, and platelet counts. Several studies have revealed the relationship between NLR and various diseases, including cancer, sepsis, and ARDS (Platini et al., 2022; Huang et al., 2020; Ma et al., 2020). An increase in NLR levels is related to the increased risk and prolonged duration of invasive mechanical ventilation in ARDS patients (Yang et al., 2022) and served as an independent risk factor for 28-day mortality in ARDS (Nie et al., 2022). Moreover, higher SII has been reported as a predictor of ARDS in premature infants with gestational age ≤ 32 weeks (Cakir et al., 2024), as well as a predictor of sepsis for patients with acute dental infections (Pricop et al., 2022). Platelet-to-lymphocyte ratio (PLR), SII and NLR were found to be the independent predictors in sepsis mortality (Mangalesh et al., 2023).

Compared with either sepsis or ARDS alone, sepsis-related ARDS has a more complex pathogenesis, with more pronounced inflammatory changes and significantly higher mortality (Xu et al., 2023). Thus, accurately assessing the prognosis remains a major clinical challenge in sepsis-related ARDS. It is difficult for a single marker to reflect the full severity and prognostic trajectory of the disease. Due to inflammation is an important pathological mechanism of sepsis-related ARDS, we hypothesized that the combined use of NLR and SII, both comprehensive indicators of inflammation, may provide greater prognostic value and help identify high-risk patients. To date, no study has explored the combined effects of SII and NLR on the prognosis of sepsis-related ARDS. Therefore, this study was designed to investigate the prognostic value of NLR and SII in patients with sepsis-related ARDS. These findings may offer guidance for both clinical treatment and prognostic evaluation in these patients.

Methods

Patients

Patients with sepsis-related ARDS ($n = 112$) who were visited Pingyang Hospital of Wenzhou Medical University from January 2022 to January 2025 were collected for retrospective analysis. The inclusion criteria were: (1) diagnosis consistent with sepsis-related ARDS (Qian et al., 2024; Singer et al., 2016); (2) age >18 years. The exclusion criteria were: (1) comorbid with heart, liver, and kidney dysfunction; (2) admission time <24 hours; (3) chronic obstructive pulmonary disease, pulmonary vascular disease, asthma, interstitial lung disease, or other pulmonary conditions; (4) regular use of hormones or immunosuppressants; (5) history of lung surgery or organ transplantation; (6) inability or refusal of the patients or family to cooperate, or continuation of treatment was abandoned; (7) survival status on day 28 could not be obtained due to loss to follow-up; (8) incomplete clinical data.

Collection of Clinical Data

Medical records and electronic health databases were used for extraction of clinical data, including sex, age, body mass index (BMI), alcohol consumption, smoking, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, partial pressure of arterial oxygen/fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) ratio, comorbidities (e.g., diabetes, hypertension, hyperlipidemia and coronary heart disease), intensive care unit (ICU) length of stay, mechanical ventilation time, and laboratory parameters (white blood cell (WBC) count, C-reactive protein (CRP), neutrophil count, lymphocyte count, procalcitonin (PCT), and platelet count). All laboratory measurements were recorded within 24 hours of diagnosis. In addition, survival status at 28 days was obtained through telephone interviews or face-to-face follow-up. Patients were classified into a survivor group ($n = 62$) and a non-survivor group ($n = 50$) based on their 28-day survival status. The flowchart of the patient selection process is presented in Fig. 1.

NLR and SII

Venous blood samples were collected from the antecubital vein in the morning within 24 hours after diagnosis. An automatic blood cell analyzer (XS-500i, Sysmex Corporation, Kobe, Japan) was used to measure the counts of neutrophil, lymphocyte, and platelet. $\text{SII} = \text{platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$, $\text{NLR} = \text{neutrophil count} / \text{lymphocyte count}$.

Statistical Analysis

SPSS version 27.0 software (IBM, Armonk, NY, USA) was used for data processing and statistical analysis. The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were expressed as mean \pm standard deviation, and differences between the two groups were compared using the independent t -test. Non-normally distributed data were presented as median (25th and 75th percentiles), and intergroup differences were measured by the Mann-Whitney U test. Categorized data were expressed as frequencies and percentages [n

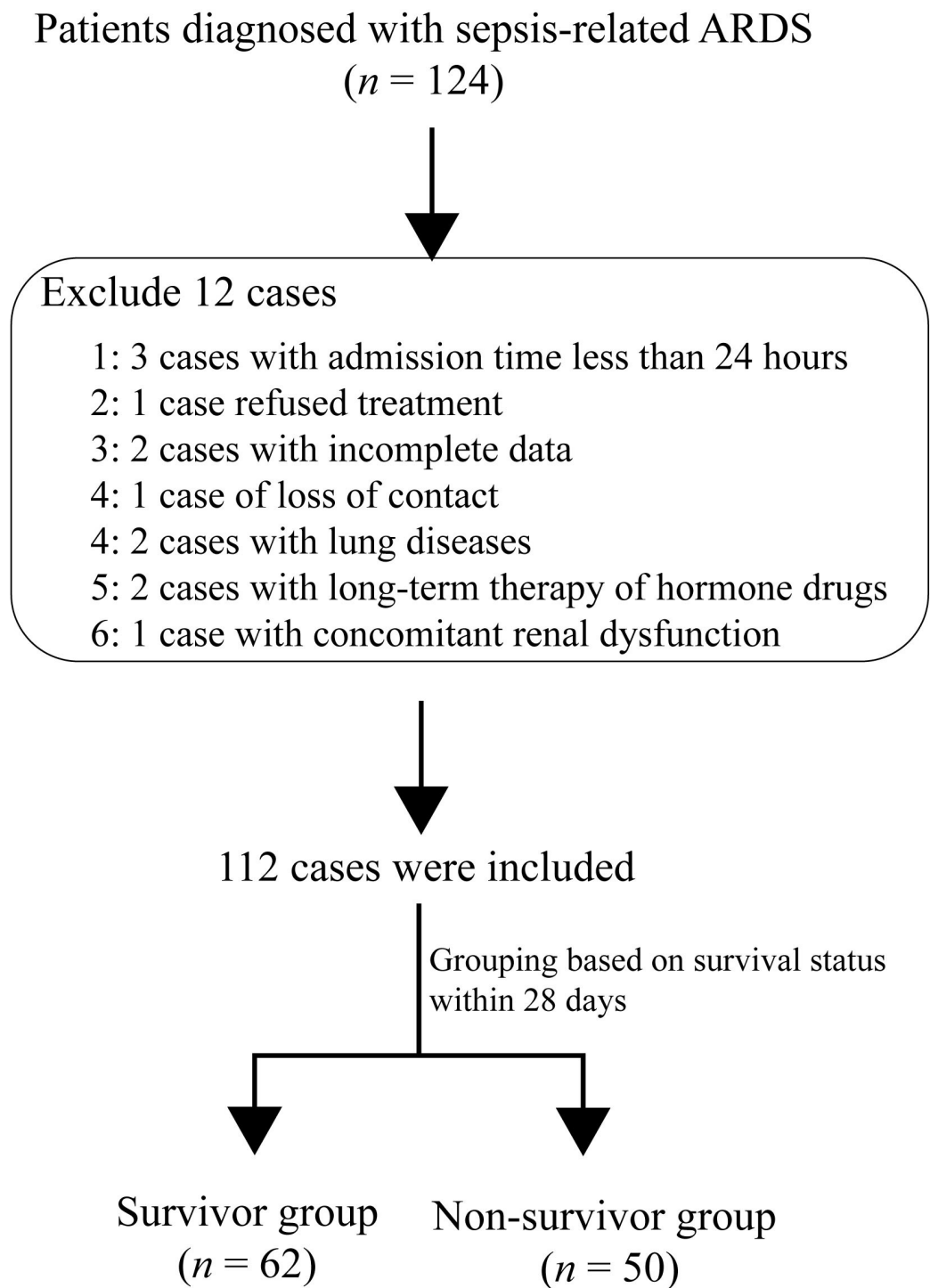


Fig. 1. Flowchart of patient inclusion and grouping. Abbreviation: ARDS, acute respiratory distress syndrome.

(%)], and intergroup differences were evaluated using the chi-square test or Yates' continuity correction (when expected count <5). Binary logistic regression was used to analyze factors associated with patient survival. A variance inflation factor (VIF) <5 indicated no multicollinearity among variables. Receiver operating characteristic (ROC) curves were drawn to assess the prognostic value of influencing

Table 1. Baseline characteristics of patients in the survivor and non-survivor groups.

Characteristic	Survivor group (n = 62)	Non-survivor group (n = 50)	<i>t</i> / <i>Z</i> / χ^2	<i>p</i> -value
Sex (n, %)			0.663	0.416
Male	37 (59.7%)	26 (52.0%)		
Female	25 (40.3%)	24 (48.0%)		
Age (years)	55.26 \pm 8.69	57.94 \pm 9.45	1.572	0.119
BMI (kg/m ²)	23.6 (21.7, 27.1)	23.9 (21.6, 26.5)	0.044	0.965
Alcohol consumption (n, %)			1.211	0.271
Yes	35 (56.5%)	23 (46.0%)		
No	27 (43.5%)	27 (54.0%)		
Smoking status (n, %)			0.455	0.500
Yes	32 (51.6%)	29 (58.0%)		
No	30 (48.4%)	21 (42.0%)		
APACHE II score	17 (15, 19)	20 (14, 22)	2.146	0.032
PaO ₂ /FiO ₂ ratio	152.16 \pm 47.32	137.67 \pm 40.79	1.719	0.090
Hypertension (n, %)	16 (25.8%)	12 (24.0%)	0.048	0.826
Diabetes (n, %)	12 (19.4%)	12 (24.0%)	0.355	0.551
Coronary heart disease (n, %)	5 (8.1%)	3 (6.0%)	0.003	0.958
Hyperlipidemia (n, %)	5 (8.1%)	6 (12.0%)	0.484	0.487
Mechanical ventilation time (days)	11 (8, 13)	13 (10, 14)	1.430	0.153
ICU length of stay (days)	12 (10, 14)	16 (12, 18)	3.248	0.001

Note: BMI, body mass index; APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; PaO₂/FiO₂, partial pressure of arterial oxygen/fraction of inspired oxygen.

factors in patients with sepsis-related ARDS. The threshold for significant differences is *p*-value < 0.05.

Results

General Information of Patients

Table 1 presents the general information of patients. There were no significant differences between two groups in sex, age, BMI, alcohol consumption, smoking status, PaO₂/FiO₂ ratio, comorbidities, or mechanical ventilation duration (*p* > 0.05). Non-survivor group has higher APACHE II score and longer ICU length of stay than those of survivor group (*p* = 0.032 and 0.001, respectively) (Table 1).

Laboratory Data of Patients

The WBC count, NLR and SII in non-survivor group were higher (*p* = 0.028, <0.001, <0.001, respectively), but lymphocyte count was lower (*p* = 0.004) than those of survivor group. There were no significant differences between the two groups in CRP, PCT, neutrophil count, or platelet count (*p* > 0.05) (Table 2).

Logistic Multivariate Regression Analysis

In logistic regression analysis, due to the wide range of SII values (722.72 to 11,941.70), SII was transformed into a categorical variable according to the opti-

Table 2. Comparison of laboratory parameters between survivor and non-survivor groups.

Index	Survivor group (n = 62)	Non-survivor group (n = 50)	Z/t	p-value
WBC count (10 ⁹ /L)	13.2 (10.4, 18.3)	16.1 (13.0, 18.8)	2.198	0.028
CRP (mg/L)	128.25 ± 36.58	138.22 ± 26.99	1.606	0.111
PCT (ng/mL)	4.13 ± 1.11	4.49 ± 1.21	1.639	0.104
Neutrophil count (10 ⁹ /L)	10.6 (8.4, 13.4)	11.9 (10.3, 14.0)	1.835	0.066
Lymphocyte count (10 ⁹ /L)	0.5 (0.4, 0.6)	0.4 (0.3, 0.5)	2.893	0.004
Platelet count (10 ⁹ /L)	87.1 (43.2, 146.7)	101.9 (77.1, 146.6)	1.773	0.076
NLR	22.5 (19.4, 27.7)	31.2 (27.3, 33.8)	5.227	<0.001
SII	1879.4 (932.6, 2939.0)	3260.9 (2234.5, 4511.4)	4.507	<0.001

Note: WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index.

mal cut-off value determined by ROC analysis (2090.37). Univariate analysis revealed that APACHE II score, ICU length of stay, WBC count, lymphocyte count, NLR and SII >2090.37 were significantly related to the prognosis of sepsis-related ARDS.

These variables with statistical significance were further entered into a multivariate logistic regression. To avoid multicollinearity, the lymphocyte count was excluded. The results indicated that APACHE II score (odds ratio (OR): 1.150, 95% confidence interval (CI): 1.004–1.317, $p = 0.044$), ICU length of stay (OR: 1.147, 95% CI: 1.017–1.294, $p = 0.026$), NLR (OR: 1.158, 95% CI: 1.068–1.255, $p < 0.001$), and SII >2090.37 (OR: 5.207, 95% CI: 1.800–15.064, $p = 0.002$) were independent risk factors influencing the prognosis of sepsis-related ARDS (Table 3).

ROC Curve Analysis

The ROC analysis showed that the combination of NLR and SII had the highest predictive value for prognosis (area under the curve (AUC): 0.808, 95% CI: 0.730–0.887, $p < 0.001$), which was superior to that of APACHE II score (AUC: 0.618, 95% CI: 0.503–0.733, $p = 0.045$), ICU length of stay (AUC: 0.679, 95% CI: 0.573–0.784, $p = 0.001$), NLR (AUC: 0.788, 95% CI: 0.701–0.875, $p < 0.001$), and SII alone (AUC: 0.748, 95% CI: 0.657–0.840, $p < 0.001$). The cut-off values for APACHE II score, ICU length of stay, NLR, and SII were 19.5, 15.5, 26.13, and 2090.37, respectively (Table 4 and Fig. 2).

Discussion

Sepsis is a systemic inflammatory response associated with high mortality. According to statistics, between 2017 and 2019, sepsis-related deaths accounted for 13.1% of total mortality in China, and this proportion continues to rise (Weng et al., 2023). ARDS is often considered a fatal consequence of severe sepsis. Clinically, ARDS is characterized by severe diffuse alveolar damage, typically driven by endothelial dysfunction and localized inflammation. Its high incidence and mortality not only threaten patient health but also pose a serious public health burden (Fujishima, 2023; Grasselli et al., 2023). Compared to ARDS or sepsis alone, sepsis-

Table 3. Logistic regression analysis of factors influencing the prognosis of sepsis-related ARDS.

Variable	Univariate analysis					Multivariate analysis				
	β	SE	Wald	OR (95% CI)	<i>p</i> -value	β	SE	Wald	OR (95% CI)	<i>p</i> -value
Sex (Female)	−0.312	0.384	0.662	0.732 (0.345–1.552)	0.416					
Age	0.033	0.022	2.379	1.034 (0.991–1.079)	0.123					
BMI	−0.017	0.055	0.093	0.983 (0.883–1.095)	0.760					
Alcohol consumption	−0.420	0.382	1.206	0.657 (0.311–1.390)	0.272					
Smoking status	0.258	0.383	0.455	1.295 (0.611–2.743)	0.500					
APACHE II score	0.119	0.051	5.482	1.260 (1.020–1.244)	0.019	0.140	0.069	4.058	1.150 (1.004–1.317)	0.044
PaO ₂ /FiO ₂ ratio	−0.008	0.004	2.828	0.992 (0.984–1.001)	0.093					
Hypertension	−0.097	0.440	0.048	0.908 (0.383–2.152)	0.826					
Diabetes	0.274	0.462	0.354	1.316 (0.533–3.251)	0.552					
Coronary heart disease	−0.318	0.756	0.177	0.728 (0.165–3.205)	0.674					
Hyperlipidemia	0.441	0.638	0.478	1.555 (0.445–5.427)	0.489					
Mechanical ventilation time	0.070	0.052	1.776	1.072 (0.968–1.187)	0.183					
ICU length of stay	0.138	0.049	7.834	1.148 (1.042–1.264)	0.005	0.137	0.062	4.967	1.147 (1.017–1.294)	0.026
WBC count	0.066	0.034	3.894	1.069 (1.000–1.142)	0.048	0.089	0.051	3.128	1.094 (0.990–1.208)	0.077
CRP	0.009	0.006	2.237	1.009 (0.997–1.021)	0.135					
PCT	0.265	0.170	2.427	1.304 (0.934–1.820)	0.119					
Neutrophil count	0.104	0.057	3.312	1.109 (0.992–1.240)	0.069					
Lymphocyte count	−2.631	0.997	6.971	0.072 (0.010–0.508)	0.008					
Platelet count	0.003	0.003	1.180	1.003 (0.998–1.008)	0.277					
NLR	0.156	0.035	19.960	1.169 (1.091–1.251)	<0.001	0.147	0.041	12.754	1.158 (1.068–1.255)	<0.001
SII >2090.37	1.984	0.442	20.142	7.273 (3.058–17.299)	<0.001	1.650	0.542	9.265	5.207 (1.800–15.064)	0.002

Note: ARDS, acute respiratory distress syndrome; BMI, body mass index; APACHE II, Acute Physiology and Chronic Health Evaluation II; PaO₂/FiO₂, partial pressure of arterial oxygen/fraction of inspired oxygen; ICU, intensive care unit; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; OR, odds ratio; CI, confidence interval; SE, standard error.

Table 4. ROC curve analysis for predicting the prognosis of sepsis-related ARDS.

Variable	AUC	<i>p</i> -value	95% CI	Sensitivity	Specificity	Cut-off value
APACHE II score	0.618	0.045	0.503–0.733	0.500	0.839	19.50
ICU length of stay	0.679	0.001	0.573–0.784	0.520	0.839	15.50
NLR	0.788	<0.001	0.701–0.875	0.840	0.710	26.13
SII	0.748	<0.001	0.657–0.840	0.800	0.645	2090.37
NLR and SII combination	0.808	<0.001	0.730–0.887	0.920	0.597	/

Note: ARDS, acute respiratory distress syndrome; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic.

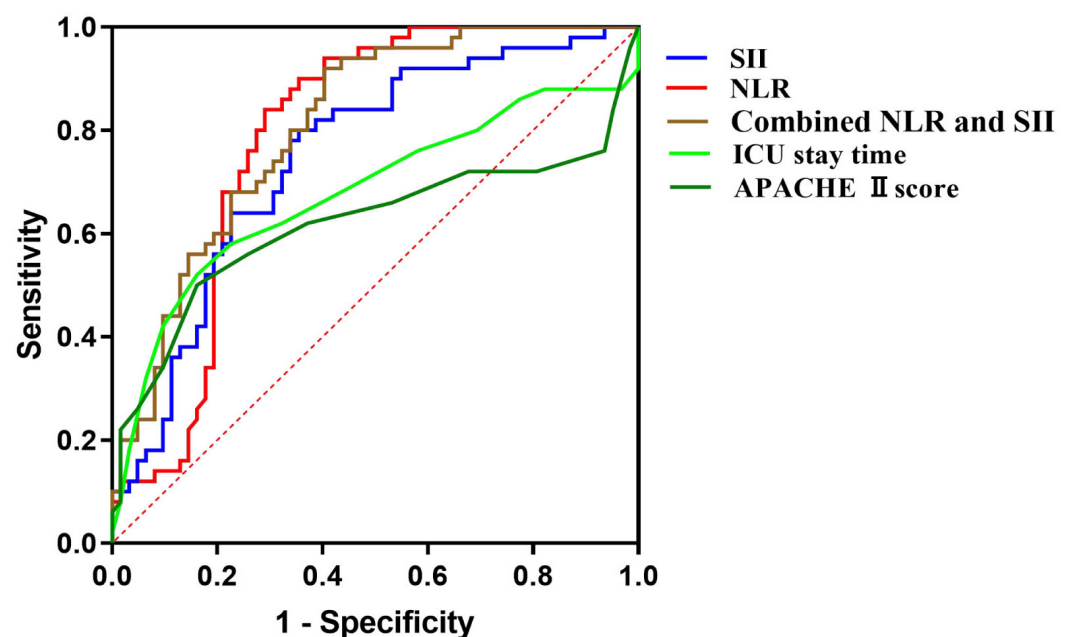


Fig. 2. ROC curves for the prognosis of sepsis-related ARDS. The red dashed line is the reference line. Abbreviations: ARDS, acute respiratory distress syndrome; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II.

related ARDS presents with greater severity and a higher mortality rate (Wang et al., 2021; Bardají-Carrillo et al., 2024; Shi et al., 2022).

In this study, 112 patients with sepsis-related ARDS were included, with a 28-day mortality rate of 44.6% (50/112), which aligns with previously published data (Shi et al., 2022). The non-survivor group exhibited higher WBC count and lower lymphocyte count than those of survivor group. Neutrophil and platelet counts were also higher in the non-survivor group, although the differences were not statistically significant. However, WBC and lymphocyte counts were not independent prognostic factors for sepsis-related ARDS. Sun et al. (2024) similarly reported no significant differences in WBC, neutrophil, or platelet counts between the survivor and non-survivor groups. Their findings differ slightly from ours, possibly due to variations in follow-up duration. Their study only monitored patient outcomes

during ICU hospitalization. These findings collectively suggest the difficulty of predicting prognosis in patients with sepsis-related ARDS based solely on routine blood parameters.

The NLR reflects two aspects of the immune response, including innate immunity (primarily neutrophils) and adaptive immunity (primarily lymphocytes) (Zahorec, 2021). Inflammatory responses promote neutrophil production while accelerating lymphocyte apoptosis, resulting in immune cell dysregulation (Nedeva, 2021). NLR can, to some extent, represent the equilibrium state of two types of cells. An elevated NLR indicates an increase in neutrophil levels and/or reduced lymphocyte counts (Zahorec, 2021; Song et al., 2021). NLR is closely linked to the progression and prognosis of various diseases (Huang et al., 2020; Erre et al., 2019; Li et al., 2021). In our study, NLR was significantly higher in the non-surviving group than that in the survivor group. And NLR is a prognostic risk factor and has good predictive value in sepsis-related ARDS. A retrospective study examining ARDS patients reported similar findings, where survivors had lower NLR than non-survivors, and $\text{NLR} > 14$ was associated with poorer overall survival (Wang et al., 2018). A meta-analysis also revealed that high NLR was related to poor prognosis in sepsis patients (Huang et al., 2020), which is consistent with our results.

SII was originally defined by Hu et al. (2014) and its concept involves neutrophils, lymphocytes, and platelets. These three cell types are critical in the progression of inflammatory conditions. As key mediators of inflammatory response, activated platelets facilitate the release of anti-/pro-inflammatory factors, such as interleukin- 1β (IL- 1β), regulated on activation, normal T-cell expressed and secreted (RANTES), and cluster of differentiation (CD)154, and can directly activate immune cells (polymorphonuclear neutrophils (PMNs) and dendritic cells) via the CD 40 ligand (CD40L)/CD40 pathway (Cognasse et al., 2022). The role of SII in ARDS and sepsis has been validated. Mangalesh et al. (2023) observed that SII, NLR, and PLR could serve as independent predictors for the mortality of sepsis. Additionally, sepsis with elevated SII and altered T cell subsets (Th1/Th2) exhibited lower survival rates (Zhou, 2024). Pan et al. (2024) identified $\text{SII} \geq 1694$ as an independent and significant risk factor in ARDS mortality. In our study, SII was markedly lower in the survivor group than in the non-survivor group. Furthermore, SII emerged as an independent prognostic risk factor for sepsis-related ARDS, consistent with previous research (Mangalesh et al., 2023; Pan et al., 2024).

Notably, we also found that combining SII and NLR improved the prognostic predictive accuracy for sepsis-related ARDS compared to using either index alone. However, it is worth noting that the specificity of the combined index was relatively low, potentially resulting in a high false-positive rate. This limitation may be related to the small sample size. Therefore, validation in larger clinical cohorts is warranted.

Our study also found that the ICU length of stay and APACHE II score were influencing factors for the prognosis of sepsis-related ARDS, which is similar to another study's findings (Xu et al., 2025). They noted that the APACHE III score was an important risk factor for in-hospital mortality in sepsis-related ARDS. It reflects the physiological status of the patient and the severity of the condition (Xu

[et al., 2025](#)). A previous study reported that the ICU length of stay for survivors was shorter than that for non-survivors among ARDS patients ([Li et al., 2019](#)), which was consistent with our research findings. However, the ROC curves for the ICU length of stay and APACHE II score crossed the reference (diagonal) line. When a curve dips below the diagonal, it indicates poor predictive performance. This may be due to the high heterogeneity of sepsis-related ARDS ([Xu et al., 2023](#)). The APACHE II score is a comprehensive index that encompasses multiple clinical dimensions. A prolonged ICU stay may reflect either a higher severity of illness or a delayed therapeutic response. Additionally, the small sample size in our study may have contributed to the instability of the predictive model, resulting in fluctuations of these two indicators around the reference line. These observations suggest that the ICU length of stay and APACHE II score may lack consistent predictive power for the prognosis of sepsis-related ARDS.

There are several limitations to this study. Firstly, the sample size was relatively small, and it was conducted as a single-center retrospective study. Therefore, multi-center prospective studies are needed to enhance the reliability of these findings. Moreover, this study did not assess the long-term prognosis of patients. Future research could include long-term follow-up. Finally, we did not grade the severity of ARDS due to the limited sample size. In future studies, ARDS patients could be stratified based on the severity, and then assess the prognostic value of SII and NLR across different subgroups.

Conclusion

The SII and NLR levels in patients from the non-survival group were significantly higher than those in the survival group. APACHE II score, ICU length of stay, SII, and NLR are identified as risk factors influencing the prognosis of sepsis-related ARDS. Both SII and NLR demonstrate good predictive value for the prognosis of sepsis-related ARDS, and their combined use is more effective than either indicator alone.

Key Points

- A total of 112 patients with sepsis-related acute respiratory distress syndrome (ARDS) were enrolled, with a 28-day mortality rate of 44.6% (50/112).
- Non-survival patients have higher SII and NLR values than those in the survival group.
- Intensive care unit (ICU) length of stay, Acute Physiology and Chronic Health Evaluation II (APACHE) II score, neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) >2090.37 were independent risk factors affecting the prognosis of sepsis-related ARDS.
- The combination of NLR and SII showed superior predictive value than ICU length of stay, APACHE II score, NLR, or SII alone for the prognosis of sepsis-related ARDS.

Availability of Data and Materials

All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

NW and YL designed the research study. ZLC and YZY collected and analyzed the data. NW and YL wrote the initial draft. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The research was approved by the Ethics Committee of Pingyang Hospital of Wenzhou Medical University (No. LW-2025-023) and was conducted in compliance with the Declaration of Helsinki. Informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

References

- Bardaji-Carrillo M, Martín-Fernández M, López-Herrero R, Priede-Vimbela JM, Heredia-Rodríguez M, Gómez-Sánchez E, et al. Post-operative sepsis-induced acute respiratory distress syndrome: risk factors for a life-threatening complication. *Frontiers in Medicine*. 2024; 11: 1338542. <https://doi.org/10.3389/fmed.2024.1338542>
- Cakir U, Tugcu AU, Tayman C, Yildiz D. Evaluation of the Effectiveness of Systemic Inflammatory Indices in the Diagnosis of Respiratory Distress Syndrome in Preterm with Gestational Age of ≤ 32 Weeks. *American Journal of Perinatology*. 2024; 41: e1546–e1552. <https://doi.org/10.1055/a-2051-8544>
- Chaudhuri D, Nei AM, Rochweg B, Balk RA, Asehnoune K, Cadena R, et al. 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia. *Critical Care Medicine*. 2024; 52: e219–e233. <https://doi.org/10.1097/CCM.0000000000006172>
- Chen X, Chen J, Ren Y, Wang M, Yang Z, Zhang W, et al. β -Sitosterol Enhances Lung Epithelial Cell Permeability by Suppressing the NF- κ B Signaling Pathway. *Discovery Medicine*. 2023; 35: 946–955. <https://doi.org/10.24976/Descov.Med.202335179.90>. Erratum in: *Discovery Medicine*. 2025; 37: 202. <https://doi.org/10.24976/Descov.Med.202335179.90corr>.

- Cognasse F, Ducheze AC, Audoux E, Ebermeyer T, Arthaud CA, Prier A, et al. Platelets as Key Factors in Inflammation: Focus on CD40L/CD40. *Frontiers in Immunology*. 2022; 13: 825892. <https://doi.org/10.3389/fimmu.2022.825892>
- Erre GL, Paliogiannis P, Castagna F, Mangoni AA, Carru C, Passiu G, et al. Meta-analysis of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in rheumatoid arthritis. *European Journal of Clinical Investigation*. 2019; 49: e13037. <https://doi.org/10.1111/eci.13037>
- Fujishima S. Guideline-based management of acute respiratory failure and acute respiratory distress syndrome. *Journal of Intensive Care*. 2023; 11: 10. <https://doi.org/10.1186/s40560-023-00658-3>
- Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Medicine*. 2023; 49: 727–759. <https://doi.org/10.1007/s00134-023-07050-7>
- Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clinical Cancer Research*. 2014; 20: 6212–6222. <https://doi.org/10.1158/1078-0432.CCR-14-0442>
- Hu Q, Hao C, Tang S. From sepsis to acute respiratory distress syndrome (ARDS): emerging preventive strategies based on molecular and genetic researches. *Bioscience Reports*. 2020; 40: BSR20200830. <https://doi.org/10.1042/BSR20200830>
- Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. *The American Journal of Emergency Medicine*. 2020; 38: 641–647. <https://doi.org/10.1016/j.ajem.2019.10.023>
- Li W, Ai X, Ni Y, Ye Z, Liang Z. The Association Between the Neutrophil-to-Lymphocyte Ratio and Mortality in Patients With Acute Respiratory Distress Syndrome: A Retrospective Cohort Study. *Shock*. 2019; 51: 161–167. <https://doi.org/10.1097/SHK.0000000000001136>
- Li W, Hou M, Ding Z, Liu X, Shao Y, Li X. Prognostic Value of Neutrophil-to-Lymphocyte Ratio in Stroke: A Systematic Review and Meta-Analysis. *Frontiers in Neurology*. 2021; 12: 686983. <https://doi.org/10.3389/fneur.2021.686983>
- Ma A, Cheng J, Yang J, Dong M, Liao X, Kang Y. Neutrophil-to-lymphocyte ratio as a predictive biomarker for moderate-severe ARDS in severe COVID-19 patients. *Critical Care*. 2020; 24: 288. <https://doi.org/10.1186/s13054-020-03007-0>
- Mangalesh S, Dudani S, Malik A. The systemic immune-inflammation index in predicting sepsis mortality. *Postgraduate Medicine*. 2023; 135: 345–351. <https://doi.org/10.1080/00325481.2022.2140535>
- Nedeva C. Inflammation and Cell Death of the Innate and Adaptive Immune System during Sepsis. *Biomolecules*. 2021; 11: 1011. <https://doi.org/10.3390/biom11071011>
- Nie S, Wang H, Liu Q, Tang Z, Tao W, Wang N. Prognostic value of neutrophils to lymphocytes and platelets ratio for 28-day mortality in patients with acute respiratory distress syndrome: a retrospective study. *BMC Pulmonary Medicine*. 2022; 22: 314. <https://doi.org/10.1186/s12890-022-02112-w>
- Pan X, Xu J, Wu H, Wang J, Kong W. Prognostic value of the systemic immune-inflammation index in patients with acute respiratory distress syndrome: A retrospective study. *Heliyon*. 2024; 10: e26569. <https://doi.org/10.1016/j.heliyon.2024.e26569>
- Platini H, Ferdinand E, Kohar K, Prayogo SA, Amirah S, Komariah M, et al. Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Prognostic Markers for Advanced Non-Small-Cell Lung Cancer Treated with Immunotherapy: A Systematic Review and Meta-Analysis. *Medicina*. 2022; 58: 1069. <https://doi.org/10.3390/medicina58081069>
- Pricop M, Ancusa O, Talpos S, Urechescu H, Bumbu BA. The Predictive Value of Systemic Immune-Inflammation Index and Symptom Severity Score for Sepsis and Systemic Inflammatory Response Syndrome in Odontogenic Infections. *Journal of Personalized Medicine*. 2022; 12: 2026. <https://doi.org/10.3390/jpm12122026>
- Qian F, van den Boom W, See KC. The new global definition of acute respiratory distress syndrome: insights from the MIMIC-IV database. *Intensive Care Medicine*. 2024; 50: 608–609. <https://doi.org/10.1007/s00134-024-07383-x>
- Qiao X, Yin J, Zheng Z, Li L, Feng X. Endothelial cell dynamics in sepsis-induced acute lung injury and acute respiratory distress syndrome: pathogenesis and therapeutic implications. *Cell Communication and*

- Signaling. 2024; 22: 241. <https://doi.org/10.1186/s12964-024-01620-y>
- Shi Y, Wang L, Yu S, Ma X, Li X. Risk factors for acute respiratory distress syndrome in sepsis patients: a retrospective study from a tertiary hospital in China. *BMC Pulmonary Medicine*. 2022; 22: 238. <https://doi.org/10.1186/s12890-022-02015-w>
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016; 315: 801–810. <https://doi.org/10.1001/jama.2016.0287>
- Song M, Graubard BI, Rabkin CS, Engels EA. Neutrophil-to-lymphocyte ratio and mortality in the United States general population. *Scientific Reports*. 2021; 11: 464. <https://doi.org/10.1038/s41598-020-79431-7>
- Sun C, Xie Y, Zhu C, Guo L, Xu B, Qin H, et al. Prognostic value of serum Mrp 8/14 in sepsis-induced acute respiratory distress syndrome patients: a retrospective cohort study. *PeerJ*. 2024; 12: e18718. <https://doi.org/10.7717/peerj.18718>
- Wang Y, Ju M, Chen C, Yang D, Hou D, Tang X, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker in acute respiratory distress syndrome patients: a retrospective study. *Journal of Thoracic Disease*. 2018; 10: 273–282. <https://doi.org/10.21037/jtd.2017.12.131>
- Wang Y, Zhang L, Xi X, Zhou JX, China Critical Care Sepsis Trial (CCCST) Workgroup. The Association Between Etiologies and Mortality in Acute Respiratory Distress Syndrome: A Multicenter Observational Cohort Study. *Frontiers in Medicine*. 2021; 8: 739596. <https://doi.org/10.3389/fmed.2021.739596>
- Weng L, Xu Y, Yin P, Wang Y, Chen Y, Liu W, et al. National incidence and mortality of hospitalized sepsis in China. *Critical Care*. 2023; 27: 84. <https://doi.org/10.1186/s13054-023-04385-x>
- Xu H, Sheng S, Luo W, Xu X, Zhang Z. Acute respiratory distress syndrome heterogeneity and the septic ARDS subgroup. *Frontiers in Immunology*. 2023; 14: 1277161. <https://doi.org/10.3389/fimmu.2023.1277161>
- Xu Z, Zhang K, Liu D, Fang X. Predicting mortality and risk factors of sepsis related ARDS using machine learning models. *Scientific Reports*. 2025; 15: 13509. <https://doi.org/10.1038/s41598-025-96501-w>
- Yang L, Gao C, He Y, Wang X, Yang L, Guo S, et al. The Neutrophil-to-Lymphocyte Ratio is Associated with the Requirement and the Duration of Invasive Mechanical Ventilation in Acute Respiratory Distress Syndrome Patients: A Retrospective Study. *Canadian Respiratory Journal*. 2022; 2022: 1581038. <https://doi.org/10.1155/2022/1581038>
- Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. *Bratislavske Lekarske Listy*. 2021; 122: 474–488. https://doi.org/10.4149/BLL_2021_078
- Zhang J, Yan W, Dong Y, Luo X, Miao H, Maimaijuma T, et al. Early identification and diagnosis, pathophysiology, and treatment of sepsis-related acute lung injury: a narrative review. *Journal of Thoracic Disease*. 2024; 16: 5457–5476. <https://doi.org/10.21037/jtd-24-1191>
- Zhou H. The Value of Systemic Immune-Inflammation Index and T Cell Subsets in the Severity and Prognosis of Sepsis. *Critical Reviews in Immunology*. 2024; 44: 1–12. <https://doi.org/10.1615/CritRevImmunol.2024051413>