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Research article

Application of neutrophil-to-lymphocyte-to-monocyte ratio in predicting mortality risk in adult patients with septic shock: A retrospective cohort study conducted at a single center

Xiao-ming Lin [a,1], Lian-fang Zhang [a,1], Yu-ting Wang [a], Ting Huang [a], Xue-feng Lin [a], Xiang-yu Hong [a], Hong-jun Zheng [a], Rong-cheng Xie [a,**], Jie-fei Ma [a,b,*]

[a] Department of Critical Care Medicine, Zhongshan Hospital, Fudan University (Xiamen Branch), Xiamen 361015, Fujian province, PR China
[b] Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, Shanghai 200032, PR China

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ABSTRACT

Background: Sepsis is a life-threatening condition characterized by an aberrant host response to infection, resulting in multi-organ dysfunction. The application of currently available prognostic indicators for sepsis in primary hospitals is challenging. In this retrospective study, we established a novel index, the neutrophil-to-lymphocyte-to-monocyte ratio (NLMR), based on routine blood examination upon admission, and assessed its prognostic value for early mortality risk in adult patients with septic shock.

Methods: This study included clinical data from adult patients with septic shock who were admitted to the hospital between January 1, 2018, and December 31, 2022. Training and validation sets were constructed, and patients were categorized into "survival" and "death" groups based on their survival status within the 28-day hospitalization period. Baseline data, including demographic characteristics and comorbidities, and laboratory results, such as complete blood count parameters, were collected for analysis. The Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were documented.The NLMR was determined through the utilization of multivariate binary logistic regression analysis, leading to the development of a risk model aimed at predicting early mortality in adult patients suffering from septic shock.

Results: Overall, 112 adult patients with septic shock were enrolled in this study, with 84 and 28 patients in the training and validation sets, respectively. Multivariate binary logistic analysis revealed that the neutrophil, lymphocyte, and monocyte counts independently contributed to the mortality risk (odds ratios = 1.22, 0.08, and 0.16, respectively). The NLMR demonstrated an area under the receiver operating characteristic curve (ROC-AUC) of 0.83 for internal validation in the training set and 0.97 for external validation in the validation set. Both overall model quality values were significantly high at 0.74 and 0.91, respectively ($P < 0.05$). NLMR exhibited a higher ROC-AUC value of 0.88 than quick SOFA (ROC-AUC = 0.71), SOFA (ROC-AUC = 0.83), and APACHE II (ROC-AUC = 0.78).

* Corresponding author. Department of Critical Care Medicine, Zhongshan Hospital, Fudan University (Xiamen Branch), Xiamen 361015, Fujian province, PR China.
** Corresponding author.
E-mail addresses: xie.rongcheng@zsxmhospital.com (R.-c. Xie), ma.jiefei@zs-hospital.sh.cn (J.-f. Ma).
[1] Xiao-ming Lin and Lian-fang Zhang have contributed equelly.

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Conclusion: NLMR may be a potential marker for predicting the risk of early death in adult patients with septic shock, warranting further exploration and verification.

1. Introduction

Sepsis is a life-threatening condition characterized by an aberrant host response to infection, resulting in multi-organ dysfunction [1]. It is a progressive condition that starts with a local infection and progresses to a systemic inflammatory response, ultimately leading to septic shock. Excessive inflammatory responses can result in circulatory system dysfunction, disruption of cellular metabolism, organ function damage, organ failure, and even death [2]. It is one of the leading cause of mortality and critical illness worldwide. Septic shock, an extreme manifestation of sepsis, is associated with circulatory system dysfunction, impaired cellular metabolism, and compromised organ function. Despite the substantial advancements in septic shock treatment achieved through the implementation of the Sepsis Bundle, the core strategy of the Rescue Sepsis campaign, sepsis still has a high mortality rate. Specifically, patients experiencing septic shock have mortality rates as high as 30%–50%. Furthermore, even if patients survive this condition, long-term psychological, cognitive impairments, and physiological may persist and significantly impact their quality of life [3–5]. Recently, domestic and international research has primarily focused on methods for evaluating the condition and prognosis of patients with sepsis. Exploring more rapid, simple, easy-to-use, sensitive, and specific assessment methods is crucial for the early identification of critically ill patients with sepsis and improving treatment success rates [6,7]. Currently, there are several diagnostic indicators available for sepsis, including bacteriological culture, procalcitonin (PCT), interleukin-6, ferritin, neopterin, and pentraxin-3 [8]. However, implementing these indicators in primary hospitals remains challenging. Therefore, exploring simpler and more convenient methods for predicting the prognosis of patients with septic shock is necessary [9]. Routine blood examinations provide the benefits of convenience, speed, and affordability, making them the most commonly used diagnostic index for assessing infections across medical institutions at all levels. The neutrophil-to-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) have demonstrated substantial value in predicting the systemic inflammatory response or sepsis [10,11]. Neutrophils, monocytes, and lymphocytes are essential for immune and inflammatory responses during septic shock [12].We aimed to identify prognostic indicators based on simple readily available laboratory markers. Therefore, we considered the neutrophil-to-lymphocyte-to-monocyte ratio as a new inflammatory index, and it was hypothesized that it may be used as a new indicator of inflammation and immune status to predict the risk of death in patients with septic shock in the early stage, to identify and screen high-risk patients in time. This information can serve as a basis for guiding clinical treatment.

2. Methods

2.1. Study population

Training set: The training set was established by retrospectively collecting clinical data from the medical records of 84 adult patients with septic shock admitted to the Department of Critical Care Medicine of Zhongshan Hospital, Fudan University (Xiamen Branch) between January 1, 2018, and June 31, 2022.

Validation set: The validation set was established by collecting clinical data from the hospital admissions of 28 adult patients with septic shock between July 1, 2022, and December 31, 2022, using the same methodology.

Inclusion criteria: The inclusion criteria were as follows: (1) participants aged 18 years or older; and (2) the diagnostic criteria of septic shock were according to the 2016 International Sepsis 3.0 guidelines [13].

Exclusion criteria: The exclusion criteria were as follows: (1) patients with primary hypotension; (2) patients with multiple injuries accompanied by active bleeding; (3) individuals with severe autoimmune or hematological diseases; (4) patients with end-stage malignant tumors and those undergoing treatment with multiple targeted drugs for tumor management; (5) individuals who have received platelet-raising drugs or granulocyte stimulating factor drugs within the past week; (6) lactating or pregnant women; (7) patients who have been on long-term or recent use of corticosteroids and immunosuppressants; and (8) patients with Covid-19. The Ethics Committee of Zhongshan Hospital, Fudan University (Xiamen Branch) approved this study (B2023-024).

Data collection: Patients were categorized into survival and death groups based on their 28-day survival status during hospitalization. The following clinical information of the patients in both groups was collected: (1) general data, including sex, age, body mass index, source of infection, and comorbidities assessed using the Elixhauser comorbidity index (ECI) [14,15]; (2) the laboratory results within 24 h of intensive care unit (ICU) admission included blood cell analysis indexes, such as neutrophil count (N), monocyte count (M), lymphocyte count (L), hemoglobin (Hb), platelet count (PLT), and blood biochemical indexes, such as blood lactic acid (Lac), total bilirubin (TBIL), blood urea nitrogen (BUN), creatinine (Cr), oxygenation index (P/F), C-reactive protein (CRP), and procalcitonin (PCT). (3) The Glasgow Coma Scale (GCS) score, quick Sequential Organ Failure Assessment (qSOFA) score, Sequential Organ Failure Assessment (SOFA) score, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were calculated according to the worst value of each index within 24 h after admission failure assessment; and (4) interventions conducted within 24 h after admission to ICU were as follows: mechanical ventilation, maximum norepinephrine equivalent within 24 h (NEEmax)[16], and renal replacement therapy, among others.

2.2. Definition of NLMR

The NLMR was obtained by dividing the neutrophil count by the product of the lymphocyte count and monocyte count and was calculated as follows:

NLMR = neutrophil count (10^9/L)/[lymphocyte count (10^9/L) × monocyte count (10^9/L)]

2.3. Statistical analysis

Data analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA). Count data are presented as frequencies and percentages, and group differences were compared using the chi-square test. Data that followed a normal distribution were reported as the means and standard deviations, and group differences were assessed using t-tests. The median (interquartile range) was employed for non-normal distributions; the rank sum test was used to compare group differences and multivariate binary logistic regression was employed to analyze the factors influencing the risk of early mortality in adult patients with

Table 1
Comparison table of clinical data of all patients.

	Training set			Validation set		
	Survival group (n = 56)	Death group (n = 28)	p-value	Survival group (n = 22)	Death group (n = 6)	p-value
Age (years)	69.64 ± 14.14	69.86 ± 13.08	0.56	66.96 ± 14.18	69.83 ± 6.24	0.64
Sex (male), n (%)	40 (71.43)	23 (82.14)	0.29	16 (72.73)	3 (50.00)	0.29
pulmonary infection, n (%)	31 (55.36)	22 (78.57)	0.04	9 (40.91)	4 (66.67)	0.26
abdominal infection, n (%)	20 (35.71)	3 (10.71)	0.02	11 (50.00)	2 (33.33)	0.47
urinary tract infections, n (%)	3 (5.36)	2 (7.14)	0.75	0 (0.00)	0 (0.00)	
other, n (%)	2 (3.57)	1 (3.57)	1.00	2 (9.09)	0 (0.00)	0.44
Tmax (°C)	37.66 ± 1.16	37.49 ± 1.21	0.54	36.65 (36.50–37.0)	37.60 (36.80–38.50)	0.14
HR (bpm)	125.07 ± 26.33	132.07 ± 28.20	0.27	116.50 ± 26.32	154.83 ± 32.82	< 0.01
RR (bpm)	28.00 (22.00–33.00)	33.00 (27.00–37.75)	0.02	25.00 (18.75–30.50)	33.50 (28.75–41.25)	0.4
MBP (mmHg)	56.50 (53.00–69.70)	52.35 (42.20–57.68)	<0.01	55.35 (48.35–63.78)	51.70 (45.35–57.20)	0.37
ECI	12.79 ± 1.17	16.21 ± 1.23	0.04	10.18 ± 7.61	13.50 ± 8.36	0.36
NEEmax (μg·kg/min)	0.21 (0.10–0.31)	0.48 (0.31–0.75)	<0.01	0.17 (0.09–0.24)	0.49 (0.44–0.92)	<0.01
GCS	15.00 (9.25–15.00)	12.00 (4.00–15.00)	0.01	15.00 (11.00–15.00)	12.50 (6.00–15.00)	0.72
qSOFA	2.00 (2.00–3.00)	3.00 (2.00–3.00)	<0.01	2.00 (1.75–2.25)	3.00 (2.75–3.00)	0.01
SOFA	7.61 ± 3.36	12.14 ± 3.48	<0.01	7.50 ± 3.35	12.00± 4.00	<0.01
APACHE II	20.46 ± 8.82	30.21 ± 9.01	<0.01	21.50 ± 6.34	31.00± 10.75	0.01
NLMR	21.31 (9.75–42.15)	119.08 (32.67–350.48)	<0.01	9.60 (5.16–14.98)	111.97 (50.62–430.00)	<0.01
N (10^9/L)	9.43 ± 5.26	15.21 ± 8.71	<0.01	7.86 ± 6.33	10.92± 6.83	0.31
L (10^9/L)	0.60 (0.40–1.00)	0.40 (0.23–0.68)	<0.01	0.90 (0.58–1.15)	0.40 (0.09–0.53)	<0.01
M (10^9/L)	0.60 (0.39–0.88)	0.43 (0.15–0.62)	0.02	0.89 (0.44–1.13)	0.24 (0.03–0.53)	<0.01
Hb (g/dL)	10.24 ± 2.40	8.90 ± 2.80	<0.01	9.94 ± 29.12	11.30 ± 23.77	0.16
Plt (10^9/L)	174.82 ± 111.64	176.82 ± 150.89	0.95	204.68 ± 125.89	113.33 ± 84.93	0.10
P/F (mmHg)	225.84± 119.49	196.80± 209.74	0.42	210.90 ± 69.70	188.27 ± 57.97	0.57
HCO_3 (mmol/L)	19.23 ± 6.12	21.35± 8.38	0.19	23.30 ± 8.05	17.27 ± 4.96	0.10
TBIL (umol/L)	17.85 (10.75–40.78)	10.85 (8.55–27.25)	0.13	9.55 (6.48–18.80)	19.47 (10.45–36.03)	0.21
Cr (μmol/L)	128.50 (85.25–208.25)	124.50 (84.50–278.50)	0.93	117.00 (50.00–243.00)	178.00 (55.75–243.25)	0.46
BUN (mmol/L)	10.85 (8.10–21.23)	14.95 (8.20–27.10)	0.40	12.20 (7.90–16.70)	12.40 (6.33–23.78)	0.76
Lac (mmol/L)	2.70 (1.98–3.95)	3.59 (2.33–7.88)	0.09	2.58 (1.54–3.62)	3.98 (3.06–10.24)	0.03
PCT (ng/ml)	7.66 (0.97–43.26)	6.97 (1.64–23.79)	0.96	0.58 (0.22–3.12)	14.59 (3.65–66.99)	0.09
CRP (mg/L)	122.49 ± 99.09	160.87 ± 112.24	0.11	90.16± 87.95	182.42± 136.73	0.05
Na (mmol/L)	138.96 ± 8.75	142.82 ± 10.40	0.08	140.87 ± 6.88	144.50 ± 10.56	0.32
K (mmol/L)	4.22 ± 0.92	4.47 ± 1.13	0.28	4.13 ± 0.91	4.48 ± 1.11	0.43
renal replacement therapy, n (%)	9 (16.07)	7 (25.00)	0.33	2 (9.09)	2 (33.33)	0.13
mechanical ventilation, n (%)	30 (53.57)	23 (82.14)	0.01	18 (81.82)	5 (83.33)	0.93

Data are expressed as median (interquartile range), number (percentage) or mean with standard deviation. Tmax: maximum body temperature; HR: heart rate; RR: respiratory rate; MBP: mean blood pressure; ECI: Elixhauser comorbidity index; NEEmax: maximum norepinephrine equivalent within 24 h; GCS: Glasgow Coma Scale score; qSOFA: quick Sequential Organ Failure Assessment score; SOFA: Sequential Organ Failure Assessment score; APACHEII: Acute Physiology and Chronic Health EvaluationII score; NLMR: neutrophil-to-lymphocyte ratio; N: neutrophil count; L: lymphocyte count; M: monocyte count; Hb: hemoglobin; PLT: platelet count; P/F: oxygenation index; HCO^-: carbonic acid hydrogen radical; Cr: creatinine; BUN: blood urea nitrogen; K: potassium ion; Na: sodium ion; TBIL: total bilirubin; PCT: procalcitonin; CRP: C-reactive protein; Lac: lactic acid.

septic shock. Receiver operating characteristic (ROC) analysis was conducted to assess the predictive ability of NLMR by plotting ROC curves and overall model quality in both the training and validation sets. Furthermore, ROC curves were generated for NLMR, SOFA, APACHE II, and qSOFA to evaluate their prognostic values in adult patients with septic shock. The area under the ROC curve (AUC) was calculated to compare their predictive accuracy regarding mortality risk in these patients. All hypothesis tests were conducted as two-tailed analyses, with statistical significance defined at a level of $P < 0.05$.

3. Results

3.1. General clinical data analysis

Overall, 84 patients with septic shock were included in the training set, comprising 56 survivors and 28 fatalities, resulting in a mortality rate of 33.33%. Among these patients with septic shock, the average age was 69.71 (±13.72) years, with males accounting for 75.00% (63 of the 84). Pulmonary infection was the most common source of infection among these patients (53/84, 63.10%), followed by abdominal infections (23/84, 27.38%). Respiratory rate, ECI, NEEmax, qSOFA, SOFA, APACHE II, NLMR, neutrophil count, mechanical ventilation, and other indicators were significantly higher in the death group than in the survival group ($P < 0.05$). The mean blood pressure (MBP), GCS, lymphocyte count, monocyte count, and Hb levels were significantly lower in the death group than in the survival group ($P < 0.05$). No significant differences were found between the two groups regarding age, sex distribution, maximum body temperature, heart rate, PLT, P/F ratio, HCO_3^-, Cr, BUN, K^+, Na^+, TBIL, PCT, CRP, Lac, or the proportion of renal replacement therapy ($P > 0.05$) (Table 1).

Overall, 28 patients with septic shock were included in the validation set, comprising 22 survivors and 6 fatalities, resulting in a mortality rate of 21.43%. Among these patients, the mean age was 67.57 (±12.85) years, with males accounting for 67.86%. Most septic shock cases originated from pulmonary (13/28, 46.43%) or abdominal infections (13/28, 46.43%). Heart rates, NEEmax, qSOFA, SOFA, APACHE II, NLMR, and Lac levels were significantly lower in the survival group than in the death group ($P < 0.05$), whereas lymphocyte and monocyte counts were significantly lower in the death group than in the survival group ($P < 0.05$). Age, sex distribution, maximum body temperature, respiratory rate, MBP, endotracheal intubation, GCS, neutrophil count, Hb, PLT, P/F ratio, HCO_3-, Cr, BUN, K^+, Na^+, TBIL, PCT, and CRP, as well as the proportions of renal replacement therapy and mechanical ventilation, were not significantly different between the two groups ($P > 0.05$) (Table 1).

3.2. Binary logistic regression analysis of complete blood count in adult patients with septic shock

Multivariate binary logistic regression analysis was performed with the 28-day mortality of adult patients with septic shock (assignment: no = 0, yes = 1) as the dependent variable and the measured values of neutrophils, lymphocytes, monocytes, Hb, and PLTs in the blood cell analysis as the independent variables. The results demonstrated that neutrophil, lymphocyte, and monocyte counts significantly influenced the in-hospital mortality rate (Table 2).

Internal and external validation of the prognostic utility of the NLMR for mortality risk assessment in patients with septic shock.

The 28-day mortality of patients with septic shock in the training and validation sets was the dependent variable, whereas NLMR was the independent variable. ROC analysis was conducted to internally and externally validate the NLMR, generate ROC curves and conduct overall model quality assessments to evaluate its predictive capability. The results demonstrated that the NLMR achieved excellent performance in both the training (AUC = 0.83) and validation (AUC = 0.97) sets, with overall model qualities of 0.74 and 0.91, respectively (all $P < 0.05$). Therefore, it can be concluded that NLMR exhibits a strong predictive ability for assessing the risk of 28-day mortality in patients with septic shock (Fig. 1, Fig. 2, and Table 3.).

The ROC curve and diagnostic parameters of NLMR were compared with those of various scoring systems to predict mortality in adult patients with septic shock.

The ROC curves of NLMR, qSOFA score, SOFA score, and APACHE II score were drawn, and the AUCs were compared. The AUC value of NLMR was the largest (0.88), and the Youden index, cut-off value, sensitivity, and specificity were 0.73, 43.15, 76.5%, and 80.8%, respectively ($Z = -6.29$, $P < 0.05$). The SOFA score was second with an AUC value of 0.83, and the Youden index, cut-off value, sensitivity, and specificity were 0.48, 10.5, 64.7%, and 83.3%, respectively ($Z = -5.52$, $P < 0.05$). The APACHE II score was third with an AUC value of 0.78, and the Youden index, cut-off value, sensitivity, and specificity were 0.49, 25.5, 73.5%, and 75.6%, respectively ($Z = -4.74$, $P < 0.05$). Finally, the qSOFA had an AUC value of 0.71, and the Youden index, cut-off value, sensitivity, and specificity

Table 2
Binary logistic regression analysis of complete blood count in adult patients with septic shock.

Variables	β	SE	Wald	OR	95% CI	p-value
N	0.12	0.03	11.86	1.12	1.05–1.20	<0.01
L	−2.8	0.78	12.86	0.06	0.01–0.28	<0.01
M	−1.81	0.62	8.41	0.16	0.05–0.66	<0.01
Hb	−0.01	0.01	0.23	0.99	0.97–1.00	0.13
Plt	−0.00	0.00	0.48	1.00	0.99–1.00	0.49

N: neutrophil count; L: lymphocyte count; M: monocyte count; Hb: hemoglobin; PLT: platelet count; β: regression coefficient; SE: Standard error; OR: odds ratio; CI: confidence interval.

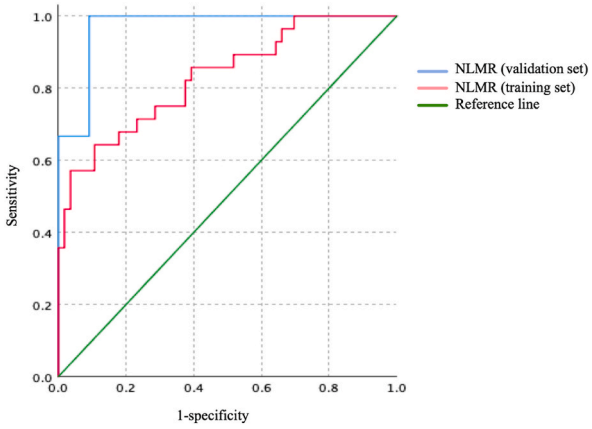

Fig. 1. The ROC curves of the training set and validation set.

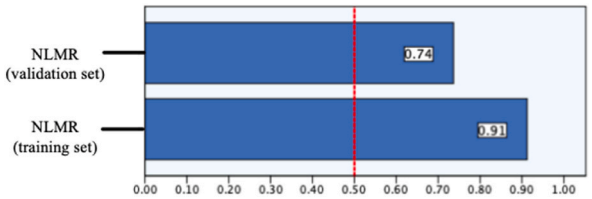

Fig. 2. Overall model quality.

Table 3
Internal and external validation results of NLMR in the training set and validation set.

Variables	AUC	SE	OR	95%CI	p-value
Training set	0.83	0.05	1.02	1.01–1.04	< 0.01
Validation set	0.97	0.03	1.06	1.01–1.10	< 0.01

AUC, area under the curve; SE: Standard error; OR: odds ratio; CI: confidence interval.

were 0.411, 2.5, 70.6%, and 70.5%, respectively, ($Z = -3.96$, $P < 0.05$) (Fig. 3 and Table 4.)

4. Discussion

In the current study, we constructed, for the first time, a potential inflammatory marker, NLMR, that combines the levels of neutrophils, monocytes, and lymphocytes derived from the analysis of peripheral blood cells on admission and is calculated as

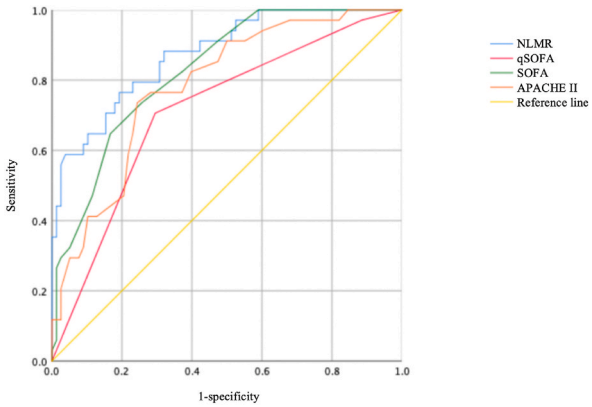

Fig. 3. The ROC curves of NLMR and various scoring systems.

Table 4
Results of diagnostic parameters of NLMR and different scoring systems.

Variables	AUC	SE	95% CI	Sensitivity (%)	specificity (%)	Youden index	Cut-off value	Z	p-value
NLMR	0.88	0.04	0.81–0.94	76.5	80.8	0.73	43.15	−6.29	<0.01
qSOFA	0.71	0.05	0.61–0.82	70.6	70.5	0.41	2.5	−3.96	<0.01
SOFA	0.83	0.04	0.75–0.90	64.7	83.3	0.48	10.5	−5.52	<0.01
APACHE II	0.78	0.05	0.79–0.87	73.5	75.6	0.49	25.5	−4.74	<0.01

NLMR: neutrophil-to-lymphocyte-to-monocyte ratio; qSOFA: quick Sequential Organ Failure Assessment score; SOFA: Sequential Organ Failure Assessment score; APACHEII: Acute Physiology and Chronic Health EvaluationII score; AUC, area under the curve; SE: Standard error; CI, confidence interval.

neutrophil count (10^9/L)/[lymphocyte count (10^9/L) × monocyte count (10^9/L)]. We found that elevated levels of NLMR on ICU admission were associated with an increased risk of 28-day mortality in adult patients with septic shock. It may be a good predictor of early death risk in adult patients with septic shock, and its predictive value is not weaker than those of APACHE II, SOFA, qSOFA, and other traditional scoring systems.

The occurrence of uncontrolled immune responses and the development of inflammatory disorders are commonly observed in patients with sepsis. At the onset of sepsis, the inflammatory response is orchestrated by the activation of cells belonging to the innate immune system, predominantly neutrophils, monocytes, macrophages, and natural killer cells. Neutrophils and monocytes play pivotal roles in mounting an effective innate immune response and are significantly affected by septic shock. During sepsis, these crucial constituents of the immune system undergo functional alterations that compromise their ability to efficiently combat pathogens and maintain immunological homeostasis [17]. Neutrophils play a crucial role in the early control of invading pathogens, and during sepsis, the delay in neutrophil apoptosis, along with an increase in the release of immature neutrophils, contributes significantly to elevated levels of circulating neutrophils in patients with sepsis [18]. This exacerbates the systemic inflammatory response and ultimately worsens organ failure [19]. Monocytes, another important component of the innate immune system, can also be functionally altered during septic shock, leading to an imbalance in the inflammatory response. Some studies have found that the severity of sepsis may be related to the reduction in monocyte count, particularly in patients with septic shock. A low initial monocyte count on admission was an independent risk factor for the 28-day mortality in these patients. Patients with a low monocyte count may have an uncontrollable local infection and spread, eventually leading to poor outcomes [20]. Additionally, septic shock significantly affects the adaptive immune response, particularly the T and B lymphocytes, which play crucial roles in pathogen defense. Lymphocytes frequently undergo apoptosis or become functionally exhausted in patients with septic shock, contributing to the mortality of individuals with sepsis [21,22]. Overall, septic shock may lead to an increase in neutrophil count, a reduction in monocyte count, or a decrease in lymphocyte count, all of which independently contribute to a poor prognosis. Therefore, we aimed to further expand the current understanding of PLR, LMR, and MLR, among others, to enhance the prognostic value of the inflammatory cell ratio for early mortality risk assessment in adult patients with septic shock. This study revealed that in the training set, the neutrophil and lymphocyte counts were 9.43 ± 5.26 vs. 15.21 ± 8.71 and 0.60 (0.40–1.00) vs. 0.40 (0.23–0.68) (survival group vs. death group), while the monocyte count was 0.60 (0.39–0.88) vs. 0.43 (0.15–0.62) (survival group vs. death group). These differences were statistically significant ($P < 0.05$. Multivariate binary logistic regression analysis confirmed that neutrophil, monocyte, and lymphocyte counts were independent risk factors for the 28-day mortality in adult patients with septic shock. Moreover, the analysis revealed that an increased neutrophil count was associated with a higher risk of early death in adult patients with septic shock (odds ratio [OR] = 1.12). Conversely, the numbers of monocytes and lymphocytes demonstrated a protective effect against mortality (OR = 0.16 and 0.06, respectively). Previous studies have demonstrated that the immune cell ratio has significant prognostic value in predicting the mortality rate among ICU patients with sepsis [23]. Therefore, we aimed to use risk and protective factors as the numerator and denominator, respectively, to conduct ratio derivation and establish a novel inflammation-derived index, the NLMR. This index serves as a newly derived indicator of inflammation and immune status by calculating the proportion of three immune cell types (neutrophils, lymphocytes, and monocytes) in adult patients admitted with septic shock. The specific calculation formula was as follows: NLMR = neutrophils/(lymphocytes x monocytes), which can be readily and swiftly obtained through blood cell analysis upon admission for adult patients with septic shock, thereby reflecting the equilibrium among neutrophils, monocytes, and lymphocytes in the systemic inflammatory response. This study used binary logistic regression and conducted internal and external validations to assess the predictive value of NLMR on admission in adult patients with septic shock. The results demonstrated that a higher NLMR was associated with an increased risk of 28-day mortality (OR, 1.02; validation set, 1.06). Furthermore, the prognostic significance of NLMR for early mortality in adult patients with septic shock was confirmed, as evidenced by high AUC values (0.83 and 0.97 for the training and validation sets, respectively).

APACHE II, SOFA, and qSOFA scores are commonly employed in clinical practice to assess the condition and prognosis of patients with sepsis. Although the APACHE II and SOFA scores exhibit good sensitivity and specificity in prognostic evaluation, their drawback lies in the complexity of the scoring system, which necessitates multiple laboratory indicators, such as vital signs, routine blood examination, liver and kidney function, and P/F within 24 h after admission. Consequently, these scores cannot accurately evaluate prognosis during the early stages of admission [24]. The qSOFA score is a scale widely used in the emergency department to assess the condition and prognosis of patients with sepsis, relying solely on the following three indicators: consciousness, blood pressure, and respiratory rate. This evaluation process is both straightforward and expedient and provides immediate results upon admission. It serves as an ideal tool for the early assessment of the condition and prognosis; however, it has limitations regarding sensitivity and

specificity. Therefore, additional parameters should be incorporated for a comprehensive evaluation [25].

In this study, we conducted further analyses to assess the prognostic value of the NLMR and APACHE II, qSOFA, and SOFA scores in adult patients with septic shock. The 28-day mortality group exhibited significantly higher levels of NLMR, SOFA score, APACHE II score, and qSOFA score than the survival group; logistic regression analysis revealed that NLMR, SOFA score, APACHE II score, and qSOFA score were prognostic factors, which was consistent with the results of relevant studies, and the ROC curve analysis demonstrated that both the SOFA and APACHE II scores exhibited favorable predictive power, sensitivity, and specificity in assessing prognosis. However, they did not surpass the NLMR scores regarding prognostic accuracy. Moreover, the convenience and timeliness of these scores were inferior to those of NLMR. Although the qSOFA score enables rapid prognostic prediction in adult patients with septic shock, its predictive ability is shorter than that of the NLMR, APACHE II score, and SOFA score. Additionally, it lacks advantages regarding sensitivity and specificity, which are limitations consistent with current clinical application [24,25]. Overall, NLMR significantly outperformed the other three scoring systems and can serve as a reliable predictor of early mortality risk in adult patients diagnosed with septic shock.

This study had some limitations. First, because this was a retrospective study, it was challenging to eliminate confounding factors that might have impacted the final clinical outcomes. Second, as this was a small-scale, single-center study with a limited sample size, the findings require validation through larger clinical trials. Third, since this study was conducted in a population of adult individuals diagnosed with septic shock, the results may not be generalizable to patients with sepsis or other patient groups. Fourth, the initial blood profile of inflammatory factors only indicates the intensity of the inflammatory response at disease onset and severity at that time. Although it serves as a warning for clinicians' evaluation of patients' conditions, it cannot fully represent their ultimate prognosis.

5. Conclusions

The NLMR method provides an expedited and straightforward approach to predicting the risk of early mortality in adult patients with septic shock. It may be a potential predictor of the risk of early death in adult patients with septic shock thereby potentially serving as an invaluable tool in various healthcare settings, such as primary hospital emergency departments, specialized wards, and ICUs.

Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Compliance with ethics guidelines

The study adhered to the ethical guidelines outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the Xiamen Branch, Zhongshan Hospital, Fudan University (Clinical ethics approval No.B2023-024).

Open access

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request. Upload to https://figshare.com/. The name of the repository and the accession number uploaded at https://doi.org/10.6084/m9.figshare.25183694.v1.

CRediT authorship contribution statement

Xiao-ming Lin: Writing – original draft, Validation, Project administration, Data curation, Conceptualization. **Lian-fang Zhang:** Writing – original draft, Software, Formal analysis, Funding acquisition. **Yu-ting Wang:** Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Ting Huang:** Supervision, Software, Resources. **Xue-feng Lin:** Software, Supervision, Validation. **Xiang-yu Hong:** Visualization, Data curation. **Hong-jun Zheng:** Supervision, Resources. **Rong-cheng Xie:** Writing – review & editing, Supervision, Software, Project administration. **Jie-fei Ma:** Writing – review & editing, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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