International Journal of General Medicine

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

Predictive Significance of Admission-Day Blood Routine-Derived Indices for 30-Day Mortality Risk in Elderly Patients with Bacterial Pneumonia

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Objective: To investigate the prognostic value of hematological indices derived from routine blood tests in assessing 30-day mortality risk among elderly patients with bacterial pneumonia at the time of admission.

Methods: This study was conducted in the Second Affiliated Hospital of Kunming Medical University. A total of 292 elderly patients with bacterial pneumonia were enrolled. A total of 292 elderly patients diagnosed with bacterial pneumonia were classified into two groups: the survival group (n= 256) and the mortality group (n=36). Following a Propensity Score Matching at a 1:1 ratio, differences in clinical data between the two groups were analyzed using the chi-square test and Mann–Whitney *U*-test. Furthermore, Spearman correlation analysis was employed to explore the relationships among the variables. The Receiver Operating Characteristic (ROC) curve was used to evaluate the predictive value of each index for 30-day mortality in elderly patients with bacterial pneumonia. Subsequently, pivotal risk indices were identified through multivariate logistic regression and Kaplan-Meier survival curves were constructed to illustrate the survival outcomes.

Results: NLR, SII, SIRI and NMLR in the death group were significantly higher than those in the survival group (14.64 vs 5.47, 2621.05 vs 1308.01, 5.58 vs 2.36, 15.05 vs 5.75) (all P<0.05). And it was positively correlated with IL-6, PCT and hsCRP (all P<0.05). The ROC curve showed that the AUC of NLR, SII, SIRI and NMLR were 0.777,0.705,0.673 and 0.775 respectively. Multivariate Logistic regression analysis showed that NLR and PCT were the main risk indicators. When NLR≥15.46 (OR 18.44), SII≥2295.02 (OR 6.25), SIRI≥2.49 (OR 4.38) and NMLR≥15.72 (OR 17.00), the 30-day mortality of elderly patients with bacterial pneumonia was significantly increased.

Conclusion: In elderly patients with community-acquired bacterial pneumonia, increased NLR, SII, SIRI and NMLR can predict 30-day mortality to a certain extent, but further multicenter studies are needed to verify.

Keywords: elderly patients, community-acquired pneumonia, 30-day mortality, NLR, SII, SIRI, NMLR

Introduction

Community-acquired pneumonia (CAP) is an inflammation of the lung parenchyma that occurs outside the hospital and is one of the major infectious diseases leading to hospitalization and death. CAP can be caused by a variety of pathogens, including bacteria, fungi and viruses. In some cases, viruses may also be the cause of community-acquired pneumonia, but in general, bacteria are still the most important pathogenic factors. According to statistics, the annual incidence of

Received: 15 November 2024
Accepted: 28 February 2025
Published: 5 March 2025

pneumonia is 24.8/10,000, and the incidence of pneumonia in the elderly is higher, reaching 63.0/10,000, especially in the elderly aged 80 years and over.[1] The incidence and mortality of CAP in the elderly are significantly higher than those in the young, and the mortality within 30 days can be as high as 10% and 30%.[2]

This may be related to the following points:[3,4] (1) the immune system of the elderly gradually declines with age, and the response and recovery ability to infection decreases; (2) it is often complicated with a variety of chronic diseases such as diabetes and coronary heart disease, this further increases the risk of infection. (3) Elderly patients with pneumonia usually present with non-specific symptoms such as fatigue, loss of appetite or cognitive impairment. Early diagnosis is difficult, which is easy to cause misdiagnosis and missed diagnosis, leading to gradual aggravation of the disease and even death in severe cases. Therefore, early identification of high-risk individuals is essential to improve prognosis.

Numerous investigations have unequivocally revealed the pivotal role of the immune-mediated inflammatory response at the cellular level in the pathogenesis of pneumonia. The delicate equilibrium between the anti-inflammatory and pro-inflammatory mechanisms profoundly determines the dynamic fluctuations in the patient's state and ultimately governs the clinical prognosis.[5–7] Routine blood testing provides a variety of hematological parameters, such as neutrophils, lymphocytes and platelets, which is an important indicator in the assessment of infection and can directly reflect the immune response and inflammatory status. In acute infection, where neutrophils directly fight infection by phagocytosis of pathogens, releasing antimicrobial substances, and producing inflammatory mediators, the increased numbers are usually associated with bacterial infection, the reduction of lymphocytes may suggest increased immunosuppression or apoptosis,[8] While platelets are involved in hemostasis and regulation of the inflammatory response and promote tissue repair.[9] The changes in the number and function of blood cells also provide an important basis for evaluating the severity of the disease and making treatment plans. However, a single blood routine parameter is not ideal for evaluating the prognosis of patients with pneumonia, which may be related to the use of antibiotics before hospitalization, decreased immune function of elderly patients, low leukocyte reaction and other factors.

In order to solve the problem of poor sensitivity and specificity of a single index, in recent years, new inflammatory indexes such as NLR, MLR, PLR, SII, SIRI, AISI and NMLR have been derived from blood routine. NLR is an important indicator to evaluate the inflammatory response and immune status of the body. In the case of bacterial infection, an elevated NLR usually reflects an increase in neutrophils and a decrease in lymphocytes, suggesting the presence of a severe inflammatory response. Studies have shown that NLR is closely related to the prognosis and mortality of patients with bacterial pneumonia. SII and SIRI are indicators obtained by counting neutrophils, lymphocytes, platelets or monocytes, which can comprehensively reflect the inflammatory state and immune response of the body. The elevation of these indicators is usually related to the aggravation of inflammation and the severity of the disease. At the same time, NMLR can also be used as a marker of inflammatory response in bacterial infection, reflecting the body's immune response to infection.[10–12] Compared with the traditional single blood routine parameter, these new derived blood routine indicators can reflect the inflammatory state more dynamically, and are less affected by age, gender and other factors. Compared with IL-6, PCT, hsCRP and other biological indicators, it has the advantages of cheap, rapid and easy to obtain, which is more suitable for primary hospitals and has higher research value.[13,14] Therefore, the aim of this study was to evaluate the predictive ability of routine blood cell-derived indicators on the day of admission for 30-day mortality in elderly patients with bacterial pneumonia, in order to provide a simple, cost-effective and effective prognostic assessment tool.

Methods

The Objects of Study and Grouping

Clinical data of 292 elderly patients with pneumonia who were hospitalized in the Second Affiliated Hospital of Kunming Medical University from January 2018 to January 2022 were retrospectively analyzed. All patients met the diagnostic criteria of "Chinese Guidelines for the diagnosis and treatment of adult Community-acquired pneumonia (2016 edition)". Exclusion criteria included: (1) incomplete clinical information; (2) hospital-acquired pneumonia, novel coronavirus pneumonia or aspiration pneumonia; (3) hematological diseases; (4) acute myocardial infarction; (5) immunosuppression; (6) chronic obstructive pulmonary disease or combined with non-infectious interstitial lung disease, such as atelectasis, pulmonary edema, pulmonary embolism and tuberculosis (Figure 1). Viral and bacterial pneumonia can be

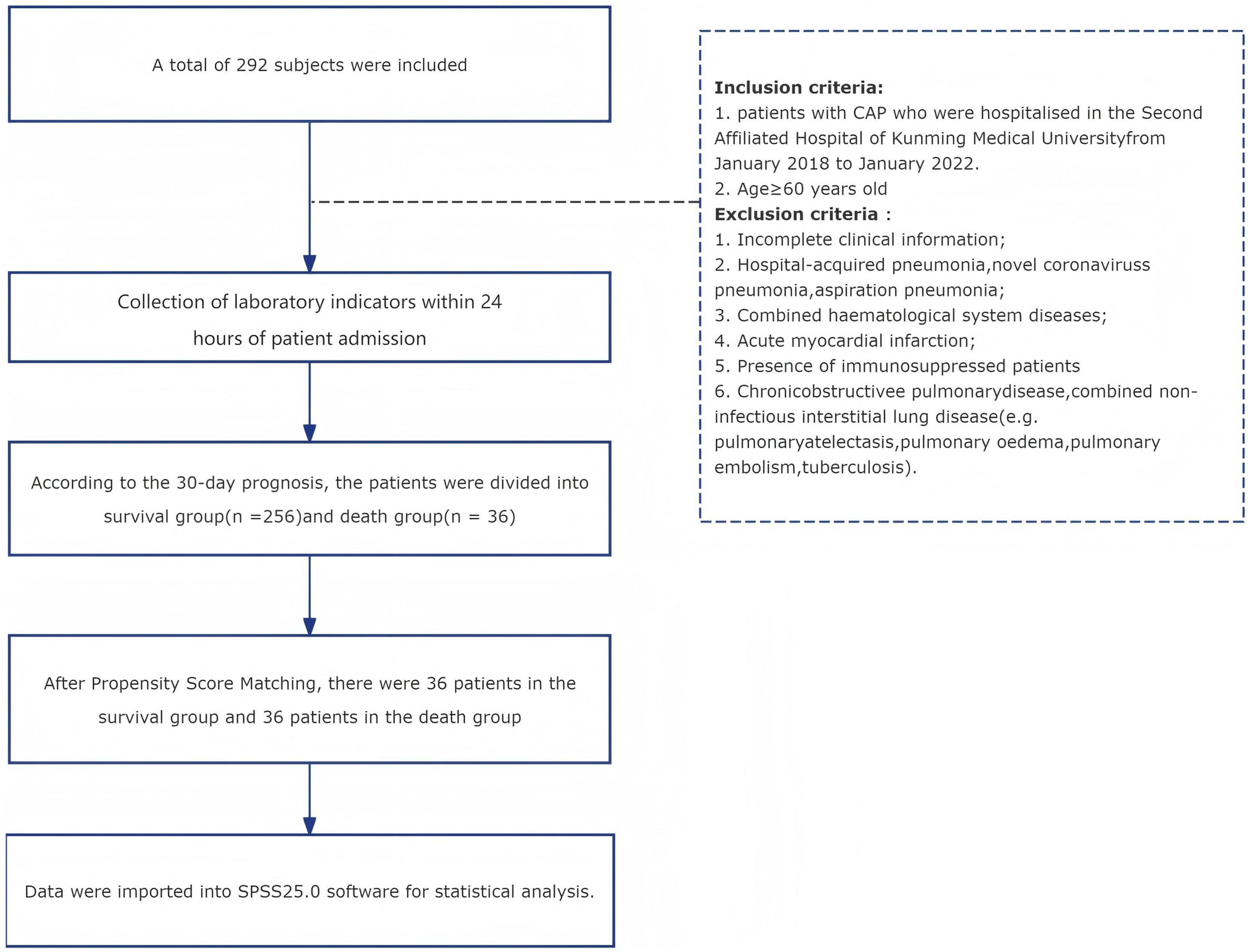

Figure 1 Flow chart of the study.

effectively distinguished by the detection of viral nucleic acid in respiratory specimens by polymerase chain reaction (PCR) combined with the results of sputum culture. At the same time, we also reviewed the medical records at the time of admission and excluded other types of pneumonia such as aspiration pneumonia and ventilator-associated pneumonia. According to the 30-day follow-up, the patients were divided into survival group (n=256) and death group (n=36).

Clinical Data Collection

The comprehensive baseline data of both patient groups were meticulously collected through the utilization of the sophisticated Hospital Information System (HIS), which encompasses vital information including age, gender, smoking history, and underlying diseases such as hypertension, diabetes, and coronary heart disease. Furthermore, the laboratory parameters obtained on the day of admission were methodically documented. Subsequently, several key indices were calculated to provide a more comprehensive understanding of the patients' condition. These indices encompassed the Neutrophil-Lymphocyte Ratio (NLR), Monocyte-Lymphocyte Ratio (MLR), Platelet-Lymphocyte Ratio (PLR), Systemic Immune-Inflammation Index (SII), Systemic Immune-Response Index (SIRI), Acute Inflammation Severity Index (AISI), and Neutrophil-Monocyte-Lymphocyte Ratio (NMLR). Youden index = sensitivity + specificity − 1, when the Youden index was the largest, the corresponding index value was the best critical value.

Statistical Analysis

For statistical analysis, SPSS 25.0 software was utilized. Non-normally distributed measurement data were presented as median (quartile) [M(P25~P75)], and the comparison between groups was assessed using the Mann–Whitney *U*-test. Categorical data were expressed as frequency and percentage [n(%)] and group comparisons were conducted using the X2 test. We performed a 1:1 propensity score match for the five variables: age, sex, hypertension, diabetes, and CHD. Subsequently, chi-square test and Mann–Whitney *U*-test were used to evaluate the differences in clinical data between the death group and the survival group, and Spearman correlation analysis was used to explore the relationship between each variable. Receiver Operating Characteristic Curve (ROC) was used to analyze the predictive value of each variable for 30-day mortality in elderly patients with bacterial pneumonia, and multivariate logistic regression was used to explore the main risk factors. Kaplan-Meier survival analysis was used to compare the effects of different blood routine derived indicators on 30-day mortality in elderly patients with bacterial pneumonia and log-rank method was used to compare the differences in survival curves. $P<0.05$ was considered statistically significant. In the graphs of this study: * denotes $P<0.05$, ** denotes $P<0.01$ and *** denotes $P<0.001$.

Results

Comparative Analysis of Clinical Data Between the Group of Survivors and the Group of Deceased Individuals

Prior to PSM matching, notable disparities were observed in age, gender, and the prevalence of diabetes mellitus between the survival group and the death group, as evidenced by a statistically significant difference ($P<0.05$). However, after the meticulous implementation of PSM matching, a remarkable equilibrium was achieved, as there were no substantial discrepancies in age, gender, and the prevalence of diabetes mellitus between the two groups ($P>0.05$). Moreover, it is noteworthy that before PSM matching, there were statistically significant variations in IL-6, PCT, hsCRP, WBC, NEUT, LYMPH, NLR, PLR, SII, SIRI, AISI, NMLR, RBC, HGB, and PLT levels between the survival group and the death group. However, even after the PSM matching, several key parameters, including IL-6, PCT, hsCRP, WBC, NEUT, LYMPH, NLR, SII, SIRI, NMLR, RBC, HGB, retained their statistical significance ($P<0.05$) (Tables 1, 2 and Figures 2, 3).

Table 1 Comparison of Clinical Data Between the Survival Group and the Death Group

	Survival (n = 256)	Death (n = 36)	x^2/Z	P value
Demographics				
Age	74.00 (66.00, 81.00)	79.50 (66.75, 85.00)	−2.19	0.028
Male sex (n,%)	136 (53.12)	26 (72.22)	4.66	0.031
Smoke (yes,%)	85 (33.20)	10 (27.78)	0.42	0.515
Underlying disease				
Hypertension (yes,%)	141 (55.08)	23 (63.89)	1.00	0.318
Diabetes mellitus (yes,%)	55 (21.48)	15 (41.67)	7.05	0.008
Coronary heart disease (yes,%)	42 (16.41)	9 (25.00)	1.62	0.204
Laboratory indices				
IL-6 (pg/mL)	19.87 (5.99, 84.04)	275.10 (79.06, 305.45)	−6.16	<0.001
PCT (ng/mL)	0.13 (0.06, 0.76)	1.56 (0.28, 5.91)	−5.53	<0.001

(*Continued*)

Table 1 (Continued).

	Survival (n = 256)	Death (n = 36)	x^2/Z	P value
HsCRP (mg/L)	42.45 (5.18, 117.22)	114.73 (65.92, 155.32)	−4.27	<0.001
WBC (×10^9/L)	8.27 (5.92, 11.57)	11.84 (8.18, 15.90)	−3.57	<0.001
NEUT (×10^9/L)	6.29 (3.85, 9.83)	10.37 (6.60, 12.50)	−4.26	<0.001
LYMPH (×10^9/L)	1.19 (0.86, 1.70)	0.76 (0.46, 1.21)	−3.48	<0.001
MONO (×10^9/L)	0.45 (0.32, 0.65)	0.42 (0.19, 0.78)	−0.69	0.489
NLR	5.47 (2.62, 10.39)	14.64 (7.23, 22.42)	−5.14	<0.001
MLR	0.38 (0.24, 0.62)	0.48 (0.30, 0.95)	−1.84	0.065
PLR	180.08 (128.83,265.00)	240.20 (145.41, 461.04)	−1.97	0.048
SII	1106.17 (583.08,2224.55)	2621.05 (1007.99,5151.87)	−3.72	<0.001
SIRI	2.51 (0.99, 5.64)	5.58 (2.65, 9.59)	−3.32	<0.001
AISI	539.65 (226.41,1097.43)	1001.94 (342.82,2279.12)	−2.41	0.016
NMLR	5.75 (2.92, 11.16)	15.05 (7.91, 22.96)	−5.10	<0.001
RBC (×10^{12}/L)	4.41 (3.98, 4.86)	4.01 (3.77, 4.60)	−2.05	0.040
HGB (g/L)	135.00 (124.00,146.00)	126.50 (109.75, 139.00)	−2.19	0.029
RDWSD (fL)	44.75 (42.40, 47.23)	46.25 (43.35, 50.20)	−1.86	0.063
PLT (×10^9/L)	215.00 (167.75,272.25)	182.00 (142.50, 227.75)	−2.19	0.028
PDW (%)	13.30 (11.10, 16.10)	13.20 (11.85, 16.02)	−0.35	0.723
MPV (fL)	10.10 (9.30, 10.80)	10.40 (9.88, 10.90)	−1.37	0.170

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

Table 2 Comparison of Clinical Data Between the Survival Group and the Death Group After Propensity Score Matching

	Survival (n = 36)	Death (n = 36)	x^2/Z	*P value*
Demographics				
Age	75.00 (71.50, 83.25)	79.50 (66.75, 85.00)	−0.38	0.702
Male sex (n,%)	21 (58.33)	26 (72.22)	1.53	0.216
Smoke (yes,%)	8 (22.22)	10 (27.78)	0.30	0.586
Underlying disease				
Hypertension (yes,%)	23 (63.89)	23 (63.89)	0.00	<0.999
Diabetes mellitus (yes,%)	16 (44.44)	15 (41.67)	0.06	0.812
Coronary heart disease (yes,%)	9 (25.00)	9 (25.00)	0.00	<0.999

(*Continued*)

Table 2 (Continued).

	Survival (n = 36)	Death (n = 36)	x^2/Z	P value
Laboratory indices				
IL-6 (pg/mL)	22.84 (5.51, 67.47)	275.10 (79.06, 305.45)	−4.43	<0.001
PCT (ng/mL)	0.08 (0.06, 0.35)	1.56 (0.28, 5.91)	−4.78	<0.001
HsCRP (mg/L)	32.59 (3.25, 74.65)	114.73 (65.92, 155.32)	−4.15	<0.001
WBC (×10^9/L)	8.32 (5.96, 11.54)	11.84 (8.18, 15.90)	−2.90	0.004
NEUT (×10^9/L)	6.17 (4.19, 9.95)	10.37 (6.60, 12.50)	−3.42	<0.001
LYMPH (×10^9/L)	1.12 (0.93, 1.42)	0.76 (0.46, 1.21)	−2.52	0.012
MONO(×10^9/L)	0.47 (0.34, 0.66)	0.42 (0.19, 0.78)	−0.61	0.539
NLR	5.47 (2.63, 10.81)	14.64 (7.23, 22.42)	−4.04	<0.001
MLR	0.39 (0.29, 0.59)	0.48 (0.30, 0.95)	−1.31	0.191
PLR	183.32 (131.70, 251.29)	240.20 (145.41, 461.04)	−1.50	0.133
SII	1308.01 (616.40, 1710.86)	2621.05 (1007.99, 5151.87)	−3.03	0.002
SIRI	2.36 (1.08, 6.31)	5.58 (2.65, 9.59)	−2.54	0.011
AISI	550.05 (237.54, 1217.93)	1001.94 (342.82, 2279.12)	−1.92	0.054
NMLR	5.75 (2.94, 11.36)	15.05 (7.91, 22.96)	−4.13	<0.001
RBC (×10^{12}/L)	4.55 (4.08, 5.03)	4.01 (3.77, 4.60)	−2.24	0.025
HGB (g/L)	138.00 (131.75, 152.00)	126.50 (109.75, 139.00)	−2.72	0.007
RDWSD (fL)	45.25 (42.72, 46.42)	46.25 (43.35, 50.20)	−1.43	0.153
PLT (×10^9/L)	203.00 (173.00, 247.50)	182.00 (142.50, 227.75)	−1.40	0.163
PDW (%)	16.00 (11.85, 16.40)	13.20 (11.85, 16.02)	−1.23	0.219
MPV (fL)	9.90 (9.20, 10.70)	10.40 (9.88, 10.90)	−1.08	0.282

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

Elucidating the Correlation Between Blood Routine Derivative Indices and Classical Infection Indices

Moreover, the Spearman correlation analysis was employed to examine the intricate relationship between the derived indices of NLR (Neutrophil-Lymphocyte Ratio), SII (Systemic Immune-Inflammatory Index), SIRI (Systemic Immune-Inflammation Index), NMLR (Neutrophil-Monocyte-Lymphocyte Ratio), and the classical infection markers IL-6 (Interleukin-6), PCT (Procalcitonin), and hsCRP (high-sensitivity C-reactive protein). The findings unveiled a noteworthy positive correlation between NLR, SII, SIRI, NMLR, and the classical infection markers. Notably, NLR exhibited the most robust correlation with the classical infection markers, with correlation coefficients of 0.457, 0.606, and 0.617 for IL-6, PCT, and hsCRP, respectively (P<0.001) (Table 3 and Figure 4).

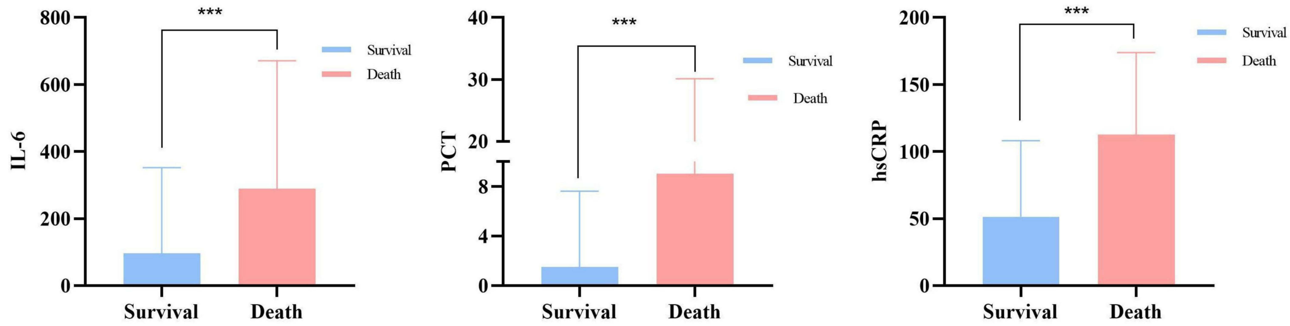

Figure 2 Difference analysis of IL-6, PCT and hsCRP between the survival group and the death group after Propensity Score Matching. ****P*<0.001.

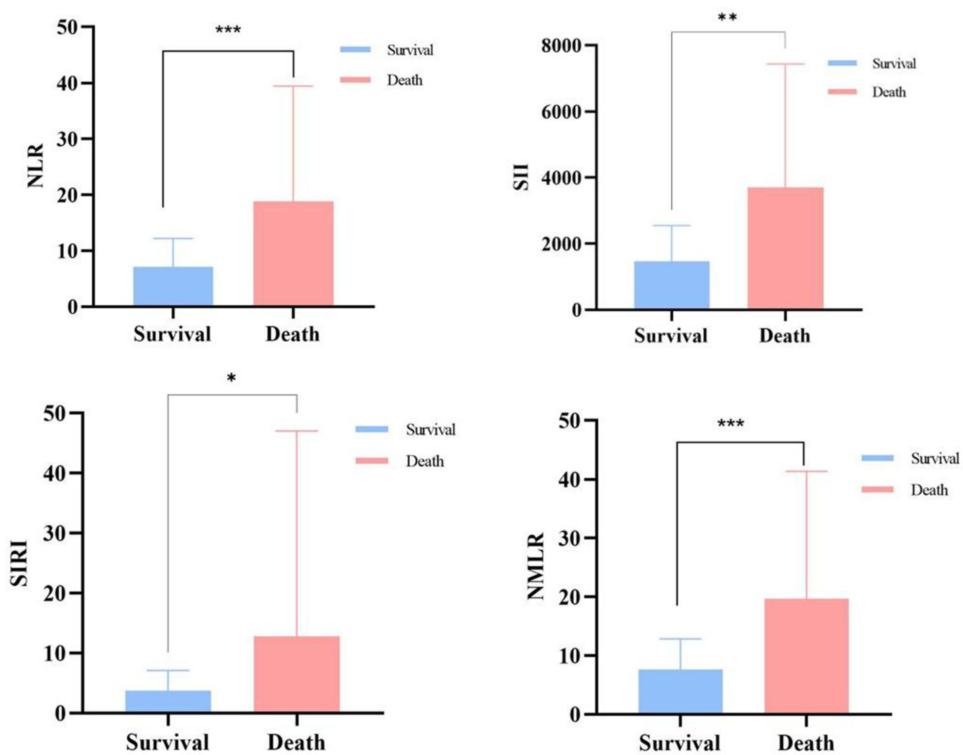

Figure 3 Difference analysis of NLR, SII, SIRI and NMLR between the survival group and the death group after Propensity Score Matching. **P*<0.05, ** *P*<0.01, ****P*<0.001.

Receiver Operating Characteristic (ROC) Curve Analysis of Blood Routine Derived Indicators and Classic Infection Indicators for 30-Day Mortality in Elderly Patients with Bacterial Pneumonia

To evaluate the performance of blood routine derived measures for predicting 30-day mortality, we performed ROC curve analysis. The outcomes of this analysis revealed the Area Under the Curve (AUC) values for IL-6, PCT, hsCRP, NLR, SII, SIRI, and NMLR to be 0.804, 0.828, 0.785, 0.777, 0.705, 0.673, and 0.775, respectively ($P<0.05$) (Table 4). Remarkably, the sensitivity of PCT was found to be the highest at 91.7%, while NLR exhibited the highest specificity at 97.2% (Table 4 and Figures 5, 6).

https://doi.org/10.2147/IJGM.S501744

Table 3 Correlation Analysis Between Blood Routine Derived Indicators and Classical Inflammatory Indicators

	IL-6		PCT		hsCRP	
	r	*P* value	*r*	*P* value	*r*	*P* value
NLR	0.457	0.000	0.606	0.000	0.617	0.000
SII	0.355	0.002	0.422	0.000	0.489	0.000
SIRI	0.394	0.001	0.346	0.003	0.415	0.000
NMLR	0.450	0.000	0.603	0.000	0.612	0.000

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

Logistic Regression Analysis was Used to Screen the Independent Risk Factors for 30-Day Mortality in Elderly Patients with Bacterial Pneumonia After PSM

Next, Logistic regression analysis was used to explore the independent risk factors for 30-day mortality in elderly patients with bacterial pneumonia. When the Youden index reaches its maximum value, the corresponding index value is regarded as the best critical value. We assigned a value to each variable based on this optimal cutoff (Table 5). Univariate

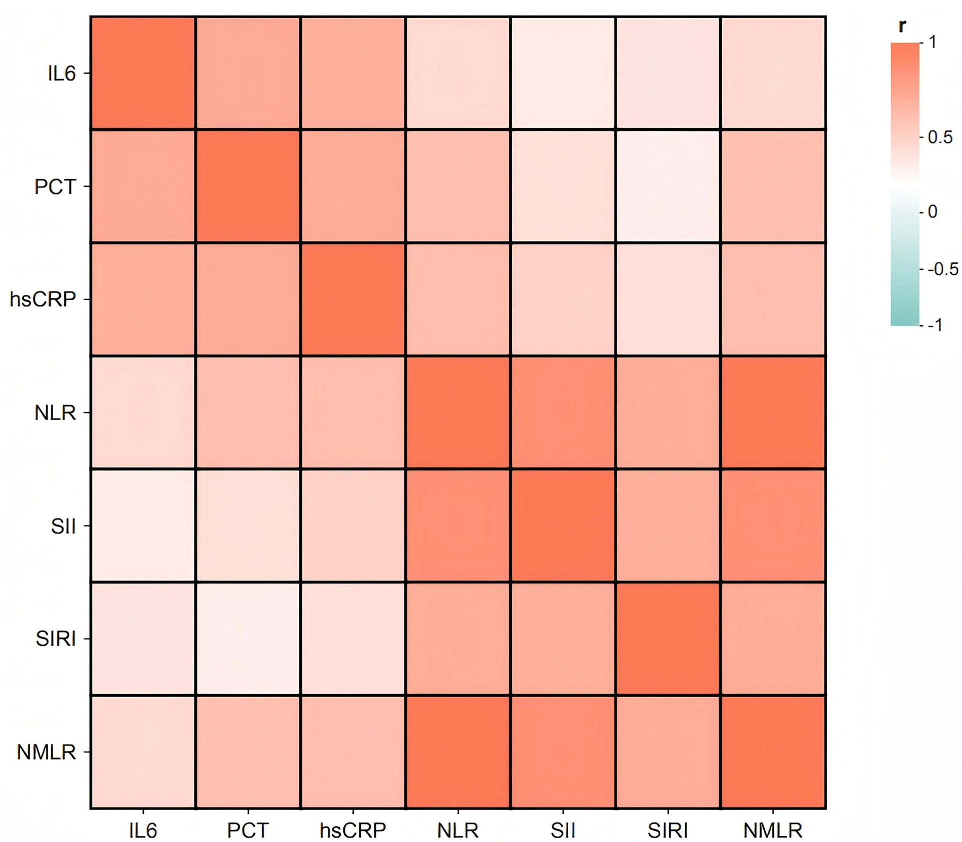

Figure 4 Correlation analysis between NLR, SII, SIRI, NMLR and IL-6, PCT, hsCRP.

Table 4 Predictive Value of Indicators for 30-Day Mortality in Elderly Patients With CAP

	AUC	95% CI	Sensitivity	Specificity	*P* value	Cut-off
IL-6	0.804	0.701–0.907	75.0%	77.8%	<0.001	80.57
PCT	0.828	0.732–0.923	91.7%	66.7%	<0.001	0.16
HsCRP	0.785	0.678–0.891	86.1%	66.7%	<0.001	49.99
NLR	0.777	0.671–0.883	50.0%	97.2%	<0.001	15.46
SII	0.705	0.584–0.826	55.6%	83.3%	0.003	2295.02
SIRI	0.673	0.548–0.798	77.8%	55.6%	0.012	2.49
NMLR	0.775	0.667–0.882	50.0%	94.4%	<0.001	15.72

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

Logistic regression analysis showed that IL-6, PCT, hsCRP, NLR, SII, SIRI and NMLR were all risk factors for poor outcomes in elderly patients with bacterial pneumonia. However, multivariate Logistic regression analysis further showed that PCT and NLR were the main risk indicators for 30-day mortality in elderly patients with bacterial pneumonia (Table 6).

Survival Curve Analysis of NLR, SII, SIRI and NMLR

Finally, we determined the cutoff values of NLR, SII, SIRI, and NMLR based on the Youden index, and performed survival analysis and plotted Kaplan-Meier survival curves. The results showed that the 30-day mortality of elderly bacterial patients with NLR≥15.46, SII≥2295.02, SIRI≥2.49 and NMLR≥15.72 was significantly higher than that of the corresponding low value group ($P<0.05$) (Figure 7).

Discussion

With the acceleration of the global aging process, the elderly are facing more and more health challenges, and bacterial pneumonia is one of the main reasons for the increase in hospitalization rate and mortality rate, especially among hospitalized patients, they tend to pay more attention to short-term prognosis, such as 30-day mortality.[4,15] Therefore, early identification of high-risk population is very important to improve the prognosis of patients. In order to solve the

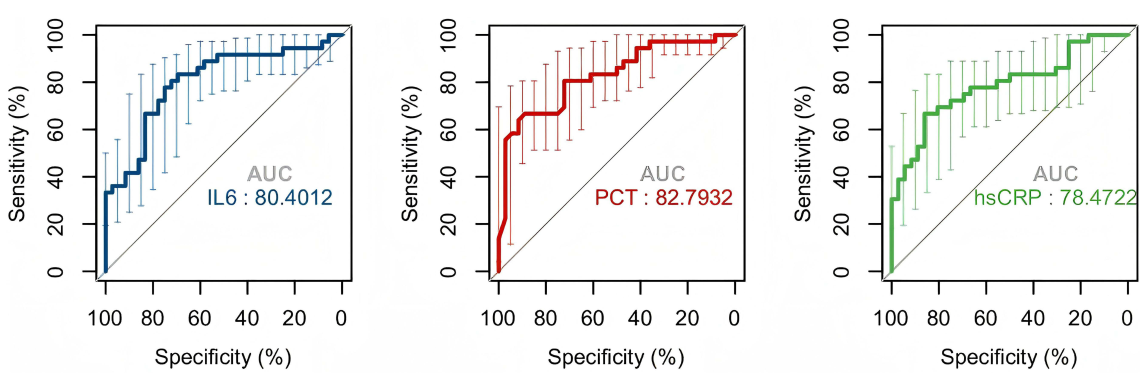

Figure 5 Receiver Operating Characteristic curve (ROC) of IL-6, PCT and hsCRP for predicting 30-day mortality in elderly patients with CAP.

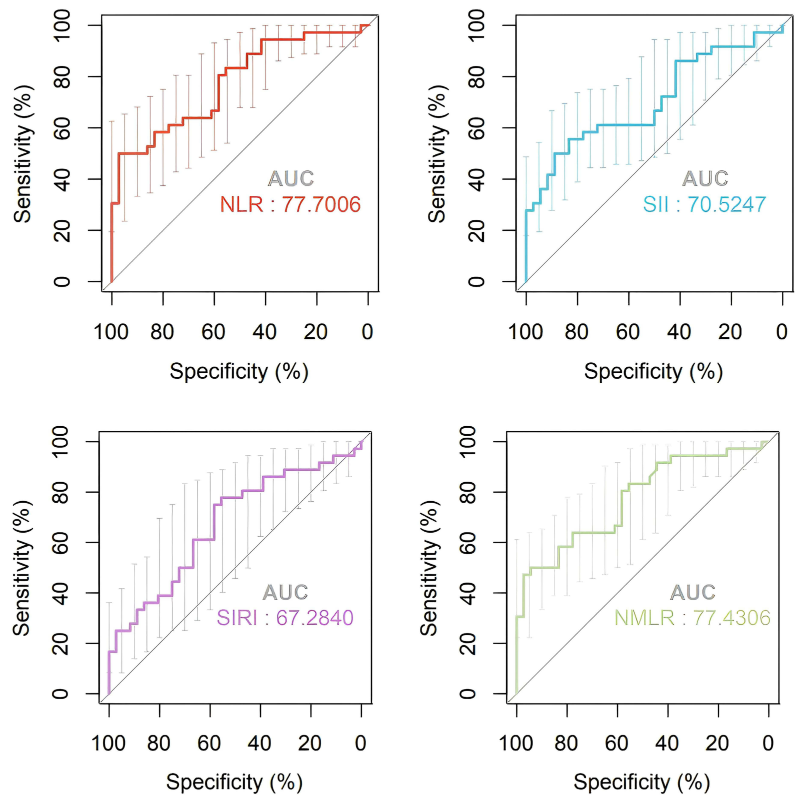

Figure 6 ROC curves of NLR, SII, SIRI and NMLR for predicting 30-day mortality in elderly patients with CAP.

above key problems, after 1:1 tendency score matching (PSM) to adjust age, sex and other clinical features, we obtained the following results: (1) the NLR, SII, SIRI and NMLR in the death group were significantly higher than those in the survival group; (2) the blood routine derivative indexes NLR, SII, SIRI and NMLR were positively correlated with the classical infection indexes IL-6, PCT and hsCRP. (3) ROC curve analysis showed that the AUC of NLR, SII, SIRI and

Table 5 Variable Assignment Table

Variant	Variable Type	Assignment of Values
IL-6	Dichotomous variables	<80.57=0; ≥80.57=1
PCT	Dichotomous variables	<0.16=0; ≥0.16=1
hsCRP	Dichotomous variables	<49.99=0; ≥49.99=1
NLR	Dichotomous variables	<15.46=0; ≥15.46=1
SII	Dichotomous variables	<2295.02=0; ≥2295.02=1
SIRI	Dichotomous variables	<2.49=0; ≥2.49=1
NMLR	Dichotomous variables	<15.72=0; ≥15.72=1

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

Table 6 Logistic Regression Analysis of Inflammatory Indicators in Elderly CAP Patients After Propensity Score Matching

Variables	Univariate Analysis			Multivariate Analysis		
	OR	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
IL-6	10.50	3.53 ~ 31.21	<0.001			
PCT	16.00	4.59 ~ 55.80	<0.001	9.43	2.47–35.98	0.001
hsCRP	12.40	3.84 ~ 40.01	<0.001			
NLR	35.00	4.32 ~ 283.65	0.001	18.44	2.09–162.41	0.009
SII	6.25	2.09 ~ 18.70	0.001			
SIRI	4.38	1.57 ~ 12.19	0.005			
NMLR	17.00	3.54 ~ 81.60	<0.001			

Abbreviations: IL-6, Interleukin-6; PCT, Procalcitonin; hsCRP, high-sensitivity C-Reactive Protein; WBC, White Blood Cell; NEUT, Neutrophil; LYMPH, Lymphocyte; MONO, Monocyte; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SII, Systemic Inflammatory Index; SIRI, Systemic Inflammatory Response Index; AISI, Aggregate Index of Systemic Inflammation; NMLR, (Monocyte+Neutrophil)/Lymphocyte; RBC, Red Blood Cells; HGB, Hemoglobin; RDWSD-Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet volume.

NMLR in predicting 30-day mortality were 0.777,0.705,0.673 and 0.775 respectively. (4) multivariate Logistic regression analysis showed that NLR and PCT were the main risk indexes affecting the 30-day prognosis of elderly CAP patients. (5) When NLR≥15.46, the 30-day mortality of elderly patients with bacterial pneumonia was significantly higher than that of patients with NLR<15.46.

Neutrophils usually increase rapidly in bacterial infection and inflammatory reaction, while lymphocytes may decrease due to stress reaction, resulting in the increase of NLR, the increase of NLR is usually related to the severity of infection, especially in elderly patients, the inflammatory response is often more obvious.[16,17] The increase of platelets is usually related to inflammatory response, while lymphocytes are related to the immune response of the body.[9,17] During pneumonia infection, neutrophils and platelets increase and lymphocytes decrease, which further leads to the increase of SII.[12,14] In addition, in the early stage of infection, neutrophils increased, while monocytes participated in tissue repair and pathogen clearance in the later stage.[18] NMLR reflects the balance between neutrophils and monocytes.[19] The increase of NMLR may indicate the imbalance of its response to infection, which means that the body can not effectively control the infection, and the tissue damage may be more serious.[20] To sum up, SII, SIRI and NMLR consider the interaction of neutrophils, lymphocytes, monocytes and platelets, which can reflect the inflammatory state and immune response of the body more comprehensively. It is worth noting that the above findings were confirmed in this study. At the same time, NLR, SII, SIRI, and NMLR were positively correlated with IL-6, PCT, and hsCRP, indicating that with the aggravation of inflammation, the body's immune response was also enhanced. This means that NLR, SII, SIRI and NMLR can also be used as effective tools for rapid assessment of inflammatory status. In addition, elderly patients are often accompanied by a variety of chronic diseases such as hypertension and diabetes, which may aggravate the severity of infection and enhance inflammatory response, thus affecting the changes of NLR, SII, SIRI and NMRI.[21–23] Studies have shown that the increase of NLR, SII, SIRI and NMRI may be related to chronic diseases and their systemic inflammatory response, suggesting that elderly patients need more careful management and comprehensive evaluation under the condition of infection.[24–26] In the course of treatment, we can also adjust the medication regimen according to the changes of NLR, SII, SIRI and NMLR levels. The decrease of NLR, SII, SIRI and NMLR levels indicates that the treatment is effective, otherwise, the current anti-infective treatment needs to be re-evaluated. High levels of NLR, SII, SIRI and NMLR are not only associated with the risk of death, but also provide evidence for clinicians to adjust treatment strategies and monitor patients' condition.

Further ROC curve analysis showed that NLR, SII, SIRI and NMLR all showed good performance in predicting 30-day mortality in elderly patients with bacterial pneumonia. Although the AUC of these indicators is slightly lower than

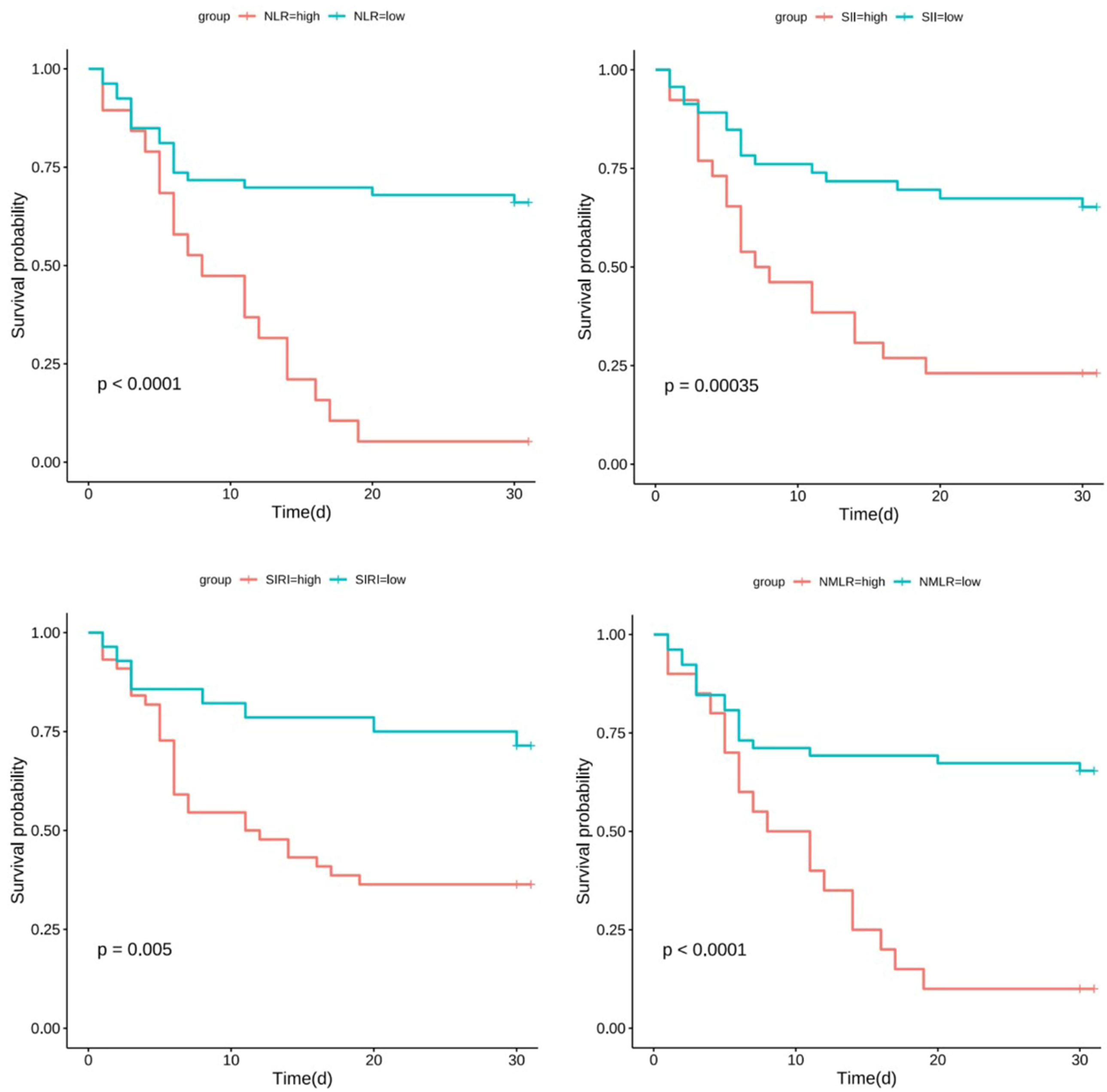

Figure 7 Comparison of survival curves of NLR, SII, SIRI, and NMLR at different levels in elderly CAP patients.

that of IL-6, PCT and hsCRP, the specificity of NLR is higher than that of PCT, indicating that NLR may have more advantages in identifying the risk of death, especially in reducing the false positive rate. Therefore, clinicians should give priority to NLR, SII, SIRI and NMLR when evaluating elderly patients with bacterial pneumonia. These indexes not only have good predictive value, but also have the advantages of simple operation and low cost, so they can be obtained quickly in routine blood tests, and are helpful for early risk assessment and clinical decision-making.

Then, multivariate Logistic regression analysis showed that NLR and PCT were the main risk indexes affecting the 30-day prognosis of elderly patients with bacterial pneumonia. The increase of PCT usually indicates the existence of bacterial infection, and NLR represents the balance of immune response. Our multivariate analysis shows that the increase of NLR and PCT can be used as an important index to predict the prognosis of elderly patients with bacterial pneumonia, especially in the elderly with decreased immune function. In the future, we can consider combining NLR with classical inflammatory indicators such as IL-6 and PCT to improve the accuracy of risk prediction, help clinicians identify high-risk patients early, and then take more active treatment measures, such as early anti-infection or admission to ICU, which will also contribute to the rational allocation of medical resources, ensure that critically ill patients receive necessary customs injection and treatment, and improve hospital efficiency and patient survival rate.

Although SII, SIRI and NMLR were not the main risk factors for 30-day prognosis of elderly patients with bacterial pneumonia, univariate analysis revealed their potential risks. Therefore, we drew survival curves of NLR, SII, SIRI and NMLR according to the cutoff value of ROC curve. The results showed that the 30-day mortality of elderly patients with bacterial pneumonia with NLR≥15.46, SII≥2295.02, SIRI ≥2.49 and NMLR≥15.72 was significantly higher than that of the corresponding low value group. The differences were statistically significant ($P < 0.05$). In clinical practice, doctors can use these thresholds to assess the need for more active treatment or monitoring measures for patients.

Different from other studies, we focus on elderly patients and match age, gender and other characteristics through propensity scores to ensure comparability between groups, thus highlighting the role of blood routine derivative indicators in prognosis assessment. In addition, this study comprehensively considered a number of blood routine derivative indexes, which provided a more comprehensive perspective for clinical practice and improved the accuracy of clinical decision-making.

Limitations

Although there are some findings in this study, this study still has some limitations: (1) this study is a single-center retrospective study with a small sample size and a single source, which may lead to selection bias. (2) the dynamic changes of blood routine derivative indexes in the whole course of disease were not further considered in the study design stage, however, the 30-day prognosis of elderly patients with bacterial pneumonia could be evaluated early by blood routine derivative indexes on the day of admission, so as to provide early guidance for clinical decision-making. (3) lack of pathogen type data, there is no way to explore its value in differential diagnosis of pneumonia infection types. In the future, a multicenter prospective study should be considered to improve the reliability of fruit, to explore the predictive model of other biomarkers or imaging examination combined with blood routine index, and to evaluate the effect of blood routine derivative index on the long-term prognosis of patients.

Conclusion

In conclusion, NLR, SII, SIRI and NMLR derived from routine blood test may be closely related to 30-day mortality in elderly patients with bacterial pneumonia. Among them, NLR is more effective in predicting mortality, but the increase of SII, SIRI and NMLR can still be used as potential warning signals. It is helpful to provide reference for clinical diagnosis and treatment.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Consent to Participate

This study conformed to the guidelines of the Helsinki Declaration. Ethics approval was obtained by the Research Ethics Committee of the Second Affiliated Hospital of Kunming Medical University. (Report-PJ-Sec-2023-158). And the Ethics Committee waived the requirement for informed consent due to the retrospective and observational nature of the investigation, as well as the anonymity of the data.

Consent for Publication

Written informed consent for publication was obtained from all participants.

Acknowledgment

The authors would like to thank all the patients who participated in this study.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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