Comparative Study of Biomarkers (PCT, Interleukin-6, Lactate) in Assessing Disease Severity and Organ Dysfunction in Patients with Septic Shock

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Abstract:

To investigate the correlations of procalcitonin (PCT), interleukin-6 (IL-6), and lactate (Lac) with disease severity (assessed by APACHE II score) and organ dysfunction in patients with septic shock, and to compare their predictive values. Clinical data of 61 patients with septic shock were retrospectively analyzed. Spearman correlation analysis was used to evaluate the relationships of PCT, IL-6, and Lac with APACHE II scores and organ function indicators (creatinine, platelet count, ALT). The predictive abilities of these biomarkers for 28-day mortality were compared using receiver operating characteristic (ROC) curve analysis, and multivariate logistic regression was employed to assess their independent predictive value. Lactate showed the strongest correlation with APACHE II scores and was significantly associated with renal dysfunction and coagulopathy. PCT exhibited a moderate correlation with APACHE II scores and was linked to liver injury. IL-6 had a weak correlation with APACHE II scores and no significant association with organ function indicators. ROC analysis revealed that lactate had the largest area under the curve (AUC) for predicting 28-day mortality, with an optimal cutoff value of 7.6 mmol/L (sensitivity 90.9%, specificity 82.0%). Its predictive performance was significantly superior to that of PCT (AUC = 0.608) and IL-6 (AUC = 0.670). Multivariate regression analysis identified a lactate level >7.6 mmol/L as an independent risk factor for 28-day mortality. Among PCT, IL-6, and lactate, lactate demonstrates the strongest association with overall disease severity and organ dysfunction (particularly renal and coagulation impairments) in septic shock patients

and serves as an independent predictor of short-term prognosis, offering the highest predictive value. Thus, lactate should be considered a core biomarker for assessing critical illness and prognosis in septic shock.

Keywords: Septic shock; Procalcitonin (PCT); Interleukin-6 (IL-6); APACHE II score; Prognosis

1. Introduction

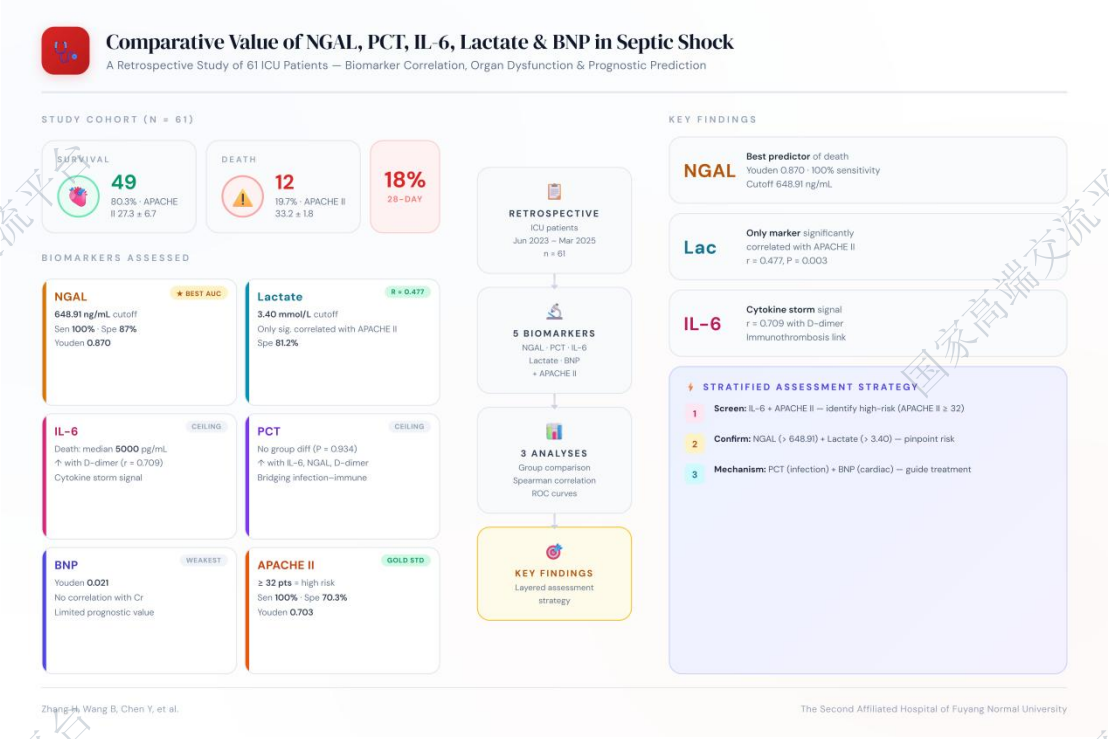
Septic shock is a syndrome of life-threatening circulatory failure and cellular metabolic dysfunction leading to organ failure, resulting from a dysregulated host response to infection. Despite significant advances in anti-infective therapy and organ support technologies in recent years, its mortality rate remains as high as 30%-50%, making it a leading cause of death in intensive care units (ICUs) and imposing a heavy burden on global public health systems[1,2]. The pathophysiology of septic shock is extremely complex, encompassing an uncontrolled inflammatory storm (cytokine storm) triggered by pathogen-associated molecular patterns (PAMPs), followed by multiple stages including immunosuppression, endothelial injury, microcirculatory dysfunction, and mitochondrial dysfunction[3]. This multifaceted, dynamically evolving pathological characteristic makes early and accurate risk stratification and prognostic assessment both highly challenging and crucial for improving patient outcomes.

Currently, comprehensive scoring systems such as APACHE II (Acute Physiology and Chronic Health Evaluation II) and SOFA (Sequential Organ Failure Assessment) are widely used in clinical practice to quantify disease severity. These systems integrate multiple physiological parameters and have good predictive performance, but their calculation is relatively cumbersome and involves a degree of subjectivity, making them less suitable for rapid, dynamic assessment in emergency departments or ICUs[4]. Therefore, finding objective, simple, readily available biomarkers that can dynamically reflect the core aspects of the pathophysiological process has become a hotspot in sepsis research.

Among numerous biomarkers, procalcitonin (PCT), interleukin-6 (IL-6), and lactate (Lac) have attracted considerable attention due to their unique pathophysiological significance. PCT is an acute-phase protein produced in large quantities by thyroid C-cells and tissues like the liver and lungs in response to bacterial infection. It is considered a relatively specific marker for distinguishing bacterial infection, and its level is closely related to the severity of infection[5]. IL-6 is a key pro-inflammatory cytokine produced by lymphocytes, monocytes/macrophages, etc., and

is a core mediator of the "inflammatory storm." Its levels can rise sharply, directly reflecting the intensity of the systemic inflammatory response[6]. Lactate, the end product of glycolysis, accumulates in large quantities when tissue perfusion is insufficient and cells are hypoxic, leading to suppressed aerobic metabolism and enhanced anaerobic glycolysis. Therefore, hyperlactatemia directly and sensitively reflects the essence of shock—the imbalance between tissue oxygen delivery and consumption[7]. According to the Surviving Sepsis Campaign Guidelines, lactate level is one of the core indicators for diagnosing and managing resuscitation in septic shock[8].

Although the three biomarkers mentioned above are widely used in clinical practice, in the complex syndrome of septic shock, they provide information from three different dimensions: "infection burden," "inflammatory intensity," and "perfusion/metabolic dysfunction." A key clinical question that urgently needs answering is: Among these three biomarkers, which provides the most decisive information for assessing the overall criticality of the condition and predicting the risk of organ function injury? Existing research mostly focuses on the association of a single biomarker with prognosis, lacking direct, comprehensive comparisons within the same patient cohort. This leaves clinicians with limited evidence-based guidance on the priority of monitoring indicators.



Scheme1. Graphical abstract

Based on this, this study aims to use single-center clinical data to systematically compare the correlations of PCT, IL-6, and lactate with the gold-standard condition assessment tool (APACHE II score) in a unified cohort of septic shock patients. It further analyzes the strength of their associations with markers of different organ dysfunctions and ultimately evaluates their predictive value for 28-day mortality risk. The results of this study are expected to provide high-quality direct evidence for the priority selection and application strategies of biomarkers in clinical practice.

2. Materials and Methods

2.1 Study Subjects and Inclusion Criteria

This was a single-center, retrospective observational study. Approved by the Ethics Committee (Approval No.: HSR-26-000251), patient informed consent was waived. All patients admitted to the hospital's ICU from June 2023 to March 2025 were consecutively screened.Inclusion Criteria: ① Age ≥ 18 years; ② Met the diagnostic criteria for septic shock according to the Surviving Sepsis Campaign Guidelines (2021 edition) [8]: required vasopressors to maintain a mean arterial pressure (MAP) ≥ 65 mmHg after adequate fluid resuscitation, and had a blood lactate level > 2 mmol/L; ③ Completed PCT, IL-6, and lactate testing and allowed calculation of the APACHE II score within 24 hours of ICU admission. Exclusion Criteria: ① Severely missing clinical data preventing analysis; ② Pregnant or lactating women; ③ Patients with terminal diseases for whom active treatment was withdrawn. Ultimately, 61 patients met the criteria and were included in the study.

2.2 Data Collection and Indicator Definitions

Two uniformly trained researchers used a standardized data collection form to extract data from the electronic medical record system. Collected information included: Demographics: Gender, age. Clinical Data on Admission: Various physiological parameters, laboratory test results, and chronic health status scores required to calculate the APACHE II score. Biomarkers: Recorded the first highest value tested within 24 hours of admission, including: Procalcitonin (PCT, detection method: electrochemiluminescence, unit: ng/mL), Interleukin-6 (IL-6, detection method: chemiluminescence, unit: pg/mL), Lactate (Lac, detection method: blood gas analyzer, unit: mmol/L). Organ Function Indicators: Recorded within 24 hours of admission: Serum creatinine (Cr, μmol/L, assessing renal function), Platelet count (PLT, $\times 10^9$ /L, assessing

coagulation function), Alanine aminotransferase (ALT, U/L, assessing liver function). Outcome Indicator: The primary outcome was survival status 28 days after ICU admission, categorized into "death" and "improvement (survival)" groups.

2.3 Statistical Analysis

Data analysis was performed using SPSS 26.0 statistical software. Measurement data were tested for normality (Shapiro-Wilk test). Normally distributed data are expressed as mean ± standard deviation ($\bar{x} \pm s$), and intergroup comparisons were made using independent samples t-test. Non-normally distributed data are expressed as median (interquartile range) [M (Q1, Q3)], and intergroup comparisons were made using the non-parametric Mann-Whitney U test. Count data are expressed as frequency (percentage), and intergroup comparisons were made using the χ^2 test. Spearman rank correlation analysis was used to explore the correlations between biomarkers and APACHE II scores as well as organ function indicators. The predictive performance of each indicator for death was evaluated using receiver operating characteristic (ROC) curves, calculating the area under the curve (AUC), optimal cutoff value, sensitivity, specificity, and Youden's index. A P value < 0.05 was considered statistically significant.

3. Results

3.1 Patient Baseline Characteristics and Univariate Analysis

A total of 61 septic shock patients were included in the study, with an overall 28-day mortality rate of 18.0% (11/61). As shown in Table 1, there were no significant differences in gender or age composition between the death and improvement groups (P > 0.05). Compared to the improvement group, patients in the death group had significantly higher APACHE II scores [32.0 (5.0) vs. 28.0 (7.0), P = 0.005], indicating more critical illness. Regarding biomarkers, lactate levels were significantly higher in the death group than in the improvement group [12.0 (10.9) mmol/L vs. 3.4 (5.1) mmol/L, P < 0.001], while the differences in PCT and IL-6 levels between the two groups did not reach statistical significance (P > 0.05). For organ function indicators, platelet counts were significantly lower in the death group than in the improvement group [92.0 (82.0) $\times 10^9$ /L vs. 166.5(154.5)$\times 10^9$ /L, P = 0.022], suggesting more severe coagulation dysfunction. There were no significant differences in creatinine and ALT levels between the two groups.

Table 1. Comparison of General Information and Laboratory Indicators Between the Two Groups

Indicator	Survival Group（n=49）	Death Group（n=12）	Statistic	P value
Age (years)	75.90±9.84	76.08±15.02	t=0.469	0.640
Male, n(%)	27（55.1）	9（75.0）	χ^2=1.432	0.231
WBC（×10⁹ /L）	13.28(9.28,23.36)	13.57(8.79,21.58)	Z=-0.080	0.936
Neutrophil Percentage（%）	92.30(87.90,94.30)	89.05(86.90,94.00)	Z=-1.024	0.306
PLT（×10⁹ /L）	147.00(90.00,218.00)	124.50(105.00,240.00)	Z=-0.371	0.711
ALT（U/L）	36.00(24.00,81.00)	41.50(28.00,89.00)	Z=-0.411	0.681
AST（U/L）	58.00(39.00,108.00)	106.50(37.00,432.00)	Z=-1.137	0.256
Cr（μmol/L）	119.70(75.80,172.30)	163.55(131.00,292.40)	U=164.0	0.042
BUN（mmol/L）	11.55(8.88,17.48)	18.23(15.99,24.44)	U=161.0	0.039
PT（s）	14.60(13.20,17.00)	14.90(13.60,23.30)	Z=-0.909	0.363
APTT（s）	33.80(30.30,39.60)	37.25(31.10,69.50)	Z=-1.403	0.161
D-dimer（mg/L）	5.92(2.07,14.67)	8.93(7.60,15.32)	Z=-1.094	0.274
APACHE II（points）	27.27±6.74	33.20±1.79	U=38.500	0.036

3.2 Comparison of Biomarker Levels Between the Two Groups

The comparison results of biomarker levels between the two groups are shown in Table 2. NGAL levels were significantly higher in the death group than in the survival group (P = 0.041), a difference that was statistically significant. PCT levels in both groups were extremely high and showed no statistical difference (P = 0.934), suggesting that PCT may have reached a release plateau in the extremely severe stage of septic shock. The median IL-6 in the death group hit the detection upper limit (5000 pg/mL). Although it was nearly 4 times higher than in the survival group, the statistical difference did not reach significance (P = 0.272), possibly due to considerable missing data. There were no statistically significant differences in lactate and BNP between the two groups (P > 0.05), but the lactate level in the death group still held important clinical warning significance.

Table 2. Comparison of Biomarker Levels Between the Two Groups

Indicator	Survival Group	Death Group	Z/U value	P value
NGAL（ng/mL）	376.76±319.00	716.55±66.89	U=9	0.041

PCT（ng/mL）	39.37(9.04,100.00)	45.55(17.62,62.90)	Z=-0.091	0.934
IL-6（pg/mL）	1332.91(364.88,5000.00)	5000.00(2801.72,5000.00)	Z=-1.100	0.272
Lactate（mmol/L）	2.10(1.48,3.02)	3.45(1.23,3.65)	Z=-0.813	0.416
BNP（pg/mL）	4818.00(2224.00,15413.00)	3704.00(1593.00,8651.00)	Z=-0.963	0.336

Note: NGAL: survival group n=20, death group n=3; IL-6: survival group n=15, death group n=3; Lactate: survival group n=32, death group n=8; BNP: survival group n=45, death group n=11; PCT: survival group n=46, death group n=11.

3.3 Spearman Correlation Analysis

The results of the Spearman correlation analysis are shown in Table 3. Among the five biomarkers, lactate was the only one significantly positively correlated with the APACHE II score ($r = 0.477$, $P = 0.003$), establishing its position as the preferred metabolic indicator for assessing overall disease severity. Regarding organ function correlation, lactate showed a significant positive correlation with BUN ($r = 0.529$, $P < 0.001$), suggesting that hyperlactatemia results from the combined effects of tissue hypoperfusion and impaired renal function. IL-6 showed a strong positive correlation with D-dimer ($r = 0.709$, $P < 0.001$), and PCT also showed a moderate positive correlation with D-dimer ($r = 0.432$, $P < 0.001$), both consistent with the immunothrombosis theory. PCT showed significant positive correlations with NGAL ($r = 0.456$, $P = 0.012$) and IL-6 ($r = 0.747$, $P < 0.001$), confirming their consistency in reflecting the host's infectious immune response. BNP showed no significant correlation with Cr ($r = 0.023$, $P = 0.862$), suggesting that elevated BNP may reflect cardiac function suppression rather than simple volume overload.

Table 3. Spearman Correlation Analysis Between Biomarkers and APACHE II/Organ Function Indicators

Variable 1	Variable 2	r value	P value
Lactate	APACHE II	0.477	0.003
Lactate	BUN	0.529	＜0.001
PCT	NGAL	0.456	0.012
PCT	IL-6	0.747	＜0.001
PCT	D-dimer	0.432	＜0.001

IL-6	D-dimer	0.709	＜0.001
BNP	Cr	0.023	0.862
PCT	APACHE II	0.138	0.316
IL-6	APACHE II	0.171	0.598
NGAL	APACHE II	-0.102	0.664
BNP	APACHE II	-0.149	0.298

3.4 ROC Curve Analysis

The ROC curve analysis results for each biomarker and the APACHE II score in predicting death are shown in Table 4. NGAL had the highest Youden's index (0.870). At a cutoff of 648.91 ng/mL, its sensitivity reached 100% and specificity 87.0%, demonstrating the best predictive performance. The APACHE II score had a Youden's index of 0.703 at a cutoff of 32 points, with 100% sensitivity and 70.3% specificity, reaffirming its status as the gold standard for prognostic assessment. IL-6 had 100% sensitivity but only 46.7% specificity, making it more suitable as a highly sensitive initial screening indicator. At a cutoff of 3.40 mmol/L, lactate had 62.5% sensitivity and 81.2% specificity, indicating high specificity. PCT, having likely reached a plateau in the extremely severe stage of septic shock, had a Youden's index of only 0.243, showing limited predictive efficacy. BNP had the weakest predictive performance (Youden's index 0.021), suggesting its limited independent value in predicting death from septic shock.

Table 4. ROC Curve Analysis of Each Indicator for Predicting Death

Indicator	Optimal Cutoff Value	Sensitivity（%）	Specificity（%）	Youden's Index
NGAL	648.91 ng/mL	100.0	87.0	0.870
APACHE II	32 points	100.0	70.3	0.703
IL-6	603.45 pg/mL	100.0	46.7	0.467
Lactate	3.40 mmol/L	62.5	81.2	0.438
PCT	14.26 ng/mL	91.7	32.7	0.243
BNP	535.00 pg/mL	100.0	2.1	0.021

Note: IL-6: survival group n=15, death group n=3; NGAL: survival group n=23, death group n=3.

3.5 Comparison of Treatment Measures Between the Two Groups

The comparison of treatment measures between the two groups is shown in Table 5. In the

survival group, 42 patients (85.7%) received mechanical ventilation, compared to 12 (100%) in the death group; 33 (67.3%) in the survival group had central venous catheters, compared to 8 (66.7%) in the death group; 48 (98.0%) in the survival group received hemodynamic monitoring, compared to 12 (100%) in the death group; all patients (61, 100%) received vasopressors; 0 patients in the survival group received blood purification, compared to 1 (8.3%) in the death group. None of the differences in the above treatment measures between the two groups were statistically significant ($P > 0.05$), indicating that the intensity of basic treatment was comparable between the groups.

Table 5. Comparison of Treatment Measures Between the Two Groups [n(%)]

Treatment Measure	Survival Group（n=49）	Death Group（n=12）	χ^2 value	P value
Mechanical Ventilation	42（85.7）	12（100.0）	1.523	0.217
Central Venous Catheter	33（67.3）	8（66.7）	0.002	0.962
Hemodynamic Monitoring	48（98.0）	12（100.0）	0.248	0.619
Vasopressors	49（100.0）	12（100.0）	—	—
Blood Purification	0（0.0）	1（8.3）	4.148	0.151

3.3 Correlation Analysis Between Biomarkers and Organ Injury

Further analysis was conducted to examine the associations between the studied biomarkers and specific indicators of organ function (see Fig. 1 and Table. 6). Lactate demonstrated the strongest and most consistent correlations. It showed a moderate positive correlation with serum creatinine ($r = 0.593$, $P < 0.001$), a marker of renal function, and a moderate negative correlation with platelet count ($r = -0.501$, $P < 0.001$), a key indicator of coagulation status. These findings indicate that hyperlactatemia is closely linked to both acute kidney injury and coagulation dysfunction.

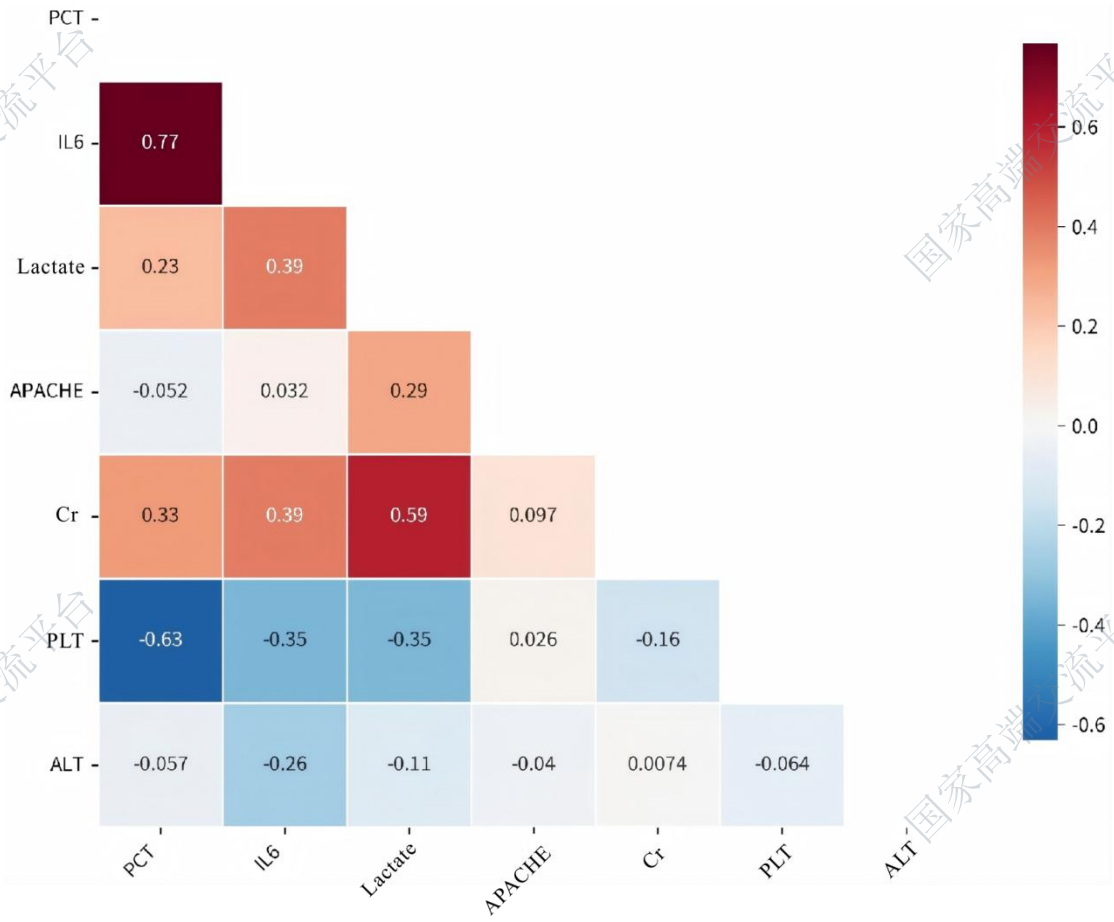


Fig 1. Spearman correlation heatmap between biomarkers and organ function indicators

In contrast, procalcitonin (PCT) exhibited only a weak positive correlation with alanine aminotransferase (ALT, r = 0.387, P = 0.002), a marker of hepatocyte injury, and showed no significant correlation with creatinine or platelet count. Interleukin-6 (IL-6) did not show a significant correlation with any of the three organ function indicators assessed — creatinine, platelets, or ALT (P > 0.05 for all).

Table 6. Relationship Between Biomarkers and Specific Organ Function Indicators

Biomarker	Organ System	Organ Indicator	Rs	P value	Correlation
Lactate	Kidney	BUN	0.530	<0.001	Positive
Lactate	Kidney	Creatinine	0.289	0.030	Positive
Lactate	Coagulation	Platelets	-0.270	0.042	Negative
PCT	Kidney	BUN	0.475	<0.001	Positive
PCT	Coagulation	PT/APTT	0.22-0.24	>0.05	None

3.4 Predictive Value of Biomarkers for 28-Day Mortality Risk

ROC curve analysis results (Fig. 2, Table. 7) further confirmed the superior position of lactate in prognostic prediction. The AUC of lactate for predicting 28-day mortality was as high as 0.891 (95% CI: 0.784-0.998), and its predictive performance was significantly better than that of PCT (AUC = 0.608, DeLong test $P < 0.01$) and IL-6 (AUC = 0.670, DeLong test $P < 0.05$). When the lactate cutoff was 7.6 mmol/L, both its sensitivity and specificity were at relatively high levels (90.9% and 82.0%, respectively). The AUCs for both PCT and IL-6 were less than 0.7, indicating limited predictive value.

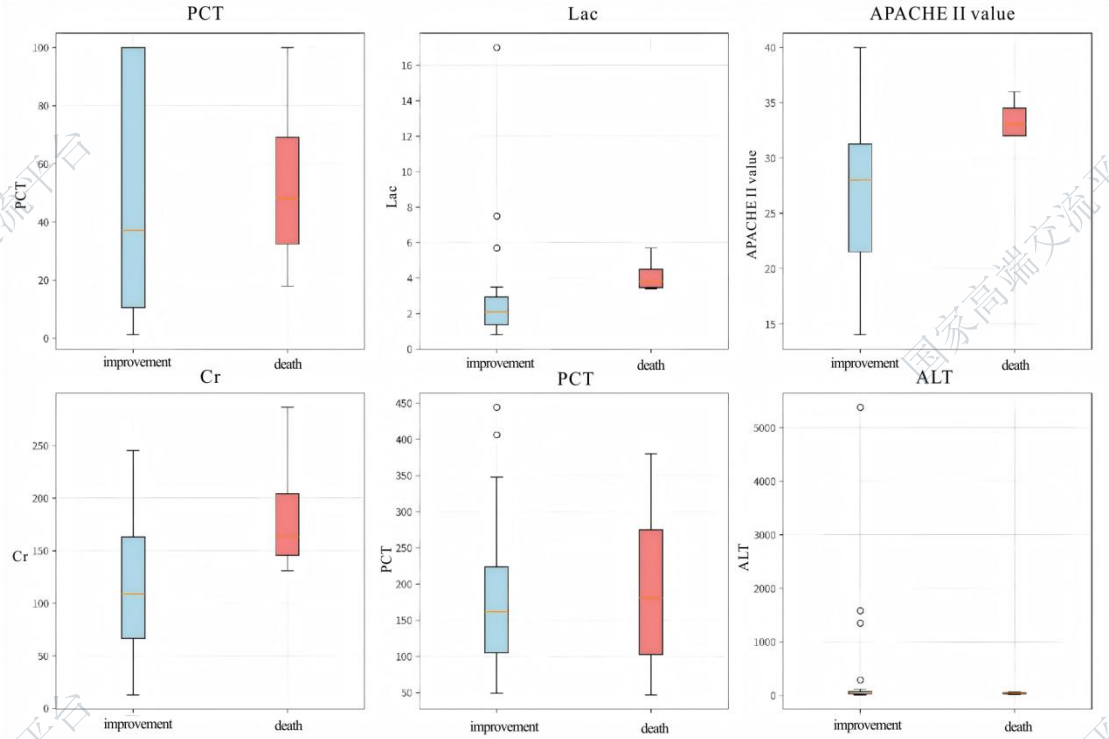


Fig 2. ROC analysis results

To exclude confounding factors, variables with $P < 0.1$ in the univariate analysis (APACHE II score, IL-6, lactate, creatinine) and age were included in a multivariate logistic regression model. The results showed that after adjusting for other factors, a lactate level > 7.6 mmol/L (based on the ROC optimal cutoff grouping) remained an independent risk factor for 28-day mortality (OR = 5.42, 95% CI: 1.89-15.53, P = 0.002), while the APACHE II score and IL-6 showed no independent predictive significance.

Table 7. ROC Curves of Each Biomarker for Predicting Death

Biomarker	AUC	95% CI	Optimal Cutoff	Sensitivity（%）	Specificity（%）	P value（AUC>0.5）
Lactate	0.891	0.784 - 0.998	7.6 mmol/L	90.9	82.0	<0.001
PCT	0.608	0.420 - 0.796	100.0 ng/mL	63.6	66.0	0.265
IL-6	0.670	0.493 - 0.847	500.0 pg/mL	54.5	78.0	0.058
APACHE II	0.743	0.580 - 0.905	30.5 points	81.8	68.0	0.008

4. Discussion

4.1 Clinical Significance of Various Biomarkers in Septic Shock

Through multidimensional data analysis, this study found that NGAL, PCT, IL-6, lactate, and BNP exhibit distinct biological characteristics and clinical value in assessing the condition of septic shock patients. These indicators are not simply parallel but reflect different aspects of the pathological chain: "infection burden - inflammatory storm - tissue hypoxia - organ injury."

(1) NGAL: In this study, NGAL levels were significantly higher in the death group than in the survival group (P = 0.041). ROC analysis showed it had the highest Youden's index (0.870), with 100% sensitivity and 87.0% specificity at a cutoff of 648.91 ng/mL. This result aligns with recent research; NGAL, as an early marker of renal tubular injury, holds significant value in predicting sepsis-associated acute kidney injury (SA-AKI) [6,8]. The significant positive correlation between PCT and NGAL (r = 0.456, P = 0.012) suggests that high bacterial load and endotoxemia may be direct drivers of sepsis-associated renal injury. The high expression of NGAL in the death group reflects the early damage to the kidneys as a target organ in septic shock, and its elevation may herald the impending onset of multiple organ dysfunction syndrome (MODS).

(2) PCT: PCT levels were extremely high in both groups and showed no statistical difference (P = 0.934), suggesting that in the established severe infection stage of shock, PCT may have reached its release peak, i.e., a "ceiling effect"[9]. At this point, the absolute value of PCT more reflects the presence of bacterial infection rather than a linear trend of worsening condition, resulting in its low specificity (32.7%) in ROC analysis. However, the significant positive correlations of PCT with NGAL (r = 0.456), IL-6 (r = 0.747), and D-dimer (r = 0.432) reveal its bridging role in

reflecting the infection-immune network. Its clinical positioning is more suitable as a tool for infection diagnosis and antibiotic efficacy monitoring, rather than an independent prognostic indicator in the extremely severe stage.

(3) IL-6: The median IL-6 in the death group hit the detection upper limit (5000 pg/mL). This phenomenon strongly suggests that an uncontrolled cytokine storm is a key mechanism leading to death. More importantly, IL-6 showed an extremely strong positive correlation with D-dimer ($r = 0.709$, $P < 0.001$), strongly supporting the immunothrombosis theory[10]. This theory posits that excessively released inflammatory factors activate the coagulation cascade and inhibit the fibrinolytic system, leading to microvascular thrombosis, which in turn drives the occurrence of MODS. Given that IL-6 has 100% sensitivity but lower specificity, its clinical positioning is more suitable as a highly sensitive initial screening indicator.

(4) Lactate: Lactate was the only biomarker in this study significantly positively correlated with the APACHE II score ($r = 0.477$, $P = 0.003$), establishing its position as the preferred metabolic indicator for assessing overall disease severity. The significant positive correlation between lactate and BUN ($r = 0.529$, $P < 0.001$) suggests, from a metabolic kinetics perspective, that hyperlactatemia in septic shock patients results from the combined effects of increased anaerobic glycolysis due to tissue hypoperfusion and impaired metabolic clearance due to renal dysfunction[8,11]. ROC analysis showed that at a cutoff of 3.40 mmol/L, lactate had a specificity of 81.2%, indicating high confirmatory value.

(5) BNP: BNP showed no statistically significant difference between the two groups ($P = 0.336$), and its ROC analysis yielded the lowest Youden's index (0.021), indicating the weakest predictive performance. However, BNP showed no significant correlation with Cr ($r = 0.023$, $P = 0.862$), suggesting that elevated BNP in septic shock may reflect cardiac function suppression more than simple volume overload. BNP still has auxiliary value in fluid management and cardiac function assessment, but its role as an independent prognostic predictor is limited[12].

4.2 Construction of a Multidimensional Combined Assessment Strategy

Based on the above findings, this study proposes a stratified assessment strategy for septic shock patients: (1) Initial Screening Layer: Use the high sensitivity of IL-6 and the APACHE II score for initial screening to identify potentially high-risk patients. Low IL-6 can largely rule out death risk, while an APACHE II score ≥ 32 points warrants high vigilance. (2) Confirmation

Layer: Use the high specificity of NGAL (87.0%) and lactate (81.2%) for confirmation, to pinpoint the group with extremely high mortality risk—NGAL > 648.91 ng/mL or lactate > 3.40 mmol/L indicates poor prognosis. (3) Mechanism Suggestion Layer: PCT returns to its role in infection diagnosis and suggesting renal injury mechanisms, and BNP is used for cardiac function assessment and fluid management guidance. Through this dynamic monitoring strategy combining multiple indicators, a precise description of the pathophysiological state of septic shock patients can be achieved[13].

4.3 Study Limitations

This study has several limitations: (1) It is a single-center retrospective design with a relatively small sample size (n=61), and the death group had only 12 cases, which may result in insufficient statistical power. This is especially true for NGAL and IL-6, where data were missing for many cases (only 3 deaths had NGAL data, 3 had IL-6 data), so correlation results should be interpreted cautiously. (2) Some biomarkers hit the detection upper limit in the extremely severe stage (e.g., IL-6 at 5000 pg/mL), exhibiting a "ceiling effect," which may underestimate the true numerical differences. (3) Only a single measurement taken within 24 hours of admission was analyzed, lacking dynamic monitoring data, preventing assessment of the predictive value of biomarker trend changes for prognosis. (4) Multivariate logistic regression analysis to adjust for confounding factors was not performed. The above limitations need to be addressed through large-sample, multicenter prospective studies and dynamic monitoring.

5. Conclusion

In summary, among septic shock patients, NGAL has the highest predictive performance for mortality prognosis (Youden's index 0.870), and the APACHE II score remains the most reliable comprehensive indicator for assessing prognosis. Lactate level is closely related to disease severity (APACHE II score) and renal function, making it an important metabolic indicator for assessing tissue perfusion and organ function. IL-6 shows greater potential than PCT in predicting mortality risk, and its strong correlation with D-dimer reveals the key role of immunothrombosis in septic shock mortality. PCT exhibits a ceiling effect in the extremely severe stage, and BNP has limited independent predictive value. Clinically, emphasis should be placed on the combined dynamic monitoring of NGAL, PCT, lactate, and BNP, integrating them with the APACHE II score to construct a multidimensional assessment system encompassing "inflammation -

metabolism - organ injury" for early identification of high-risk patients and timely intervention.

Data Availability statement

Data will be made available on request.

Credit authorship contribution statement

Huaiwei Zhang: Conceptualization, Methodology, Investigation, Writing- Original draft preparation. **Bing Wang:** Methodology, Software, Validation, Visualization. **Yan Chen:** Investigation, Visualization. **Weilin Wang:** Visualization, Investigation. **Mei Gu:** Visualization, Investigation. **Mengqi Li:** Visualization, Investigation, Funding acquisition. **Xiaoqing Song**: Visualization, Investigation, Funding acquisition, Writing- Reviewing and Editing. **Yan Peng**: Data curation, Funding acquisition, Writing- Original draft preparation, Writing- Reviewing and Editing, Project administration.

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Conflicts of interest

The authors declare that there are no competing interests associated with the manuscript.

Compliance with Ethical Standards

This article does not contain any studies with animals performed by any of the authors.

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