

The Value of Serum Procalcitonin, Thromboelastography Combined with Platelet Count in Predicting the Short-Term Progression of Septic Shock in the Intensive Care Unit

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Objective: By evaluating the level of serum procalcitonin (PCT), thromboelastography (TEG) and platelet count (PLT) of patients with septic shock in intensive care unit (ICU), the predictive value of the combination of the three indicators on the short-term progression was discussed, which provided a new basis for early clinical diagnosis and disease evaluation.

Methods: The clinical data of 130 patients with septic shock admitted to the IUC of our hospital from December 2021 to December 2023 were analyzed retrospectively. These subjects were divided into good prognosis group (n=78) and poor prognosis group (n=52) according to the 28 d deaths. The influencing factors were explored using the Multivariate logistic regression analysis. The value of single or combined PCT, PLT and TEG in predicting poor short-term prognosis was assessed using the receiver operating characteristic (ROC) curve.

Results: The patients in poor prognosis group had higher Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, serum PCT level, coagulation reaction time (R value) and coagulation formation time (K value), but lower PLT levels, final strength of coagulation (MA value) and coagulation formation rate (α angle) than those in good prognosis group ($P<0.001$). PCT, R value and K value were risk factors ($P<0.001$), while PLT, MA value and α angle were protective factors ($P<0.001$). The area under the curve (AUC) of PCT, PLT and TEG predicting poor short-term progression was 0.813, 0.658 and 0.752, respectively. The AUC of combined three indicators was 0.905, which had the highest predictive value.

Conclusion: Serum levels of PCT, PLT and TEG had certain value in predicting poor short-term progression of septic shock patients, and their combined diagnostic value was higher. Therefore, regular monitoring of these three indicators could provide certain guiding significance for the prevention and treatment of poor short-term prognosis in patients with septic shock.

Keywords: calcitoninogen, thromboelastography, platelet count, infectious shock, Disease progression, predictive value

Introduction

Septic shock is one of the serious complications of sepsis in the intensive care unit (ICU), which can further aggravate organ function damage, accumulation of toxic metabolites, and tissue cell hypoxia. In severe cases, multiple organ failure may occur, which is life-threatening. Hospital mortality rates of septic shock are as high as 40%–60%, which are the leading cause of death in ICU patients.^{1,2} Although the diagnosis and management of septic shock have been greatly improved, the prognosis is poor and the development of septic shock is rapid. Thus, early prediction of short-term progression and timely adjustment of treatment plans are of great significance for improving treatment effectiveness and prognosis.³

In recent years, more and more research has shown that^{4,5} specific and sensitive infection-related markers such as procalcitonin (PCT) not only have important reference value for the early diagnosis, evaluation of infection severity and prognosis of sepsis, but also can easily guide the use of antibiotics. High concentration of PCT may develop into severe bacterial sepsis or septic shock.⁶ At present, it has been found that coagulation dysfunction is the most fundamental pathophysiological change of systemic infections, which can affect the prognosis of the disease, so the evaluation of coagulation function changes is of great significance for clinical treatment.⁷ Platelet count (PLT) plays an important role in the process of hemostasis and coagulation in the human body, and is a common coagulation index in clinical practice. Research has shown that patients with sepsis have varying degrees of thrombocytopenia in the early stages of the disease and throughout the course of the disease, and thrombocytopenia is an independent predictor of disease severity and mortality risk in sepsis.⁸ Thrombocytopenia is an independent predictor of the severity of sepsis and the risk of death. Thromboelastography (TEG) is an emerging index of coagulation function in recent years, which has potential clinical value in the evaluation of coagulation dysfunction in patients with sepsis.⁹

In this study, 130 patients with septic shock admitted to the IUC of our hospital from December 2021 to December 2023 were chosen as the subjects. By analyzing the changes of serum PCT, PLT and TEG in patients with septic shock in ICU, their value in predicting the short-term progression of septic shock alone and in combination was explored, which provided clinicians with more effective diagnosis and treatment methods, thereby improving the survival rate and quality of life of patients, and also providing a theoretical basis and reference value for research in related fields.

Materials and Methods

General Materials

A total of 130 patients with septic shock admitted to IUC in our hospital from December 2021 to December 2023 were selected as the observation subjects, and the clinical data were retrospectively analyzed. Inclusion criteria: (1) Patients with septic shock met the clinical diagnostic criteria for septic shock;¹⁰ (2) Patient age > 18 years old; (3) Patients with a definite foci of infection; (4) The patient had systemic inflammatory response syndrome; (5) The patient's organs and tissues showed hypoperfusion:¹¹ Altered consciousness: irritability, apathy, delirium and coma were sensitive indicators of cerebral perfusion; Decreased urine output: the urine output was still < 0.5 mL/kg·h with adequate hydration, indicating decreased renal blood flow and circulatory volume depletion; Clinical manifestations such as clammy, cyanosis, pallor, and mottleness; Capillary filling time > 2s; (6) Patients with complete clinical data. Exclusion criteria: (1) Patients with severe dysfunction of important organs; (2) Pregnant or lactating women; (3) Patients undergoing blood purification therapy; (4) Patients with concurrent malignant tumors; (5) Patients who died within 24 hours; (6) Patients treated with anticoagulant drugs in the past one month. Patients were divided into the good prognosis group (n=78) and the poor prognosis group (n=52) according to the 28 d deaths.¹² There were 78 cases in the good prognosis group, including 40 males and 38 females, with an average age of (51.16 ± 5.85) years. There were 52 cases in the poor prognosis group, including 28 males and 24 females, with an average age of (52.08 ± 4.04) years. There was no significant statistical difference in age and gender between the two groups ($P > 0.05$). All operations in this study were ratified by the hospital Ethics Committee of the Yiyang Central Hospital Of Hunan (2021012).

Outcome Measures

Data collection: Age, gender, oxygenation index, central venous pressure, mean arterial pressure, cardiac index, and acute physiology and chronic health evaluation II (APACHE II) scores were collected from two groups of patients. The APACHE II score was based on 12 physiological indicators, age, and health status, with the score of 0–71. Higher score indicated more severe condition, worse prognosis, and the higher expected mortality rate.

Laboratory indicators: Fasting venous blood was collected from patients in the two groups in the morning after enrollment, and centrifuged at 3000 r/min for 10 minutes. The serum was carefully collected, and was stored at -40°C to avoid repeated freeze-thaw cycles. The PCT level was detected using immunochemiluminescent assay (ICMA). The reagent kit was purchased from Suzhou Beetle Biological Products Co., Ltd. in Suzhou, Jiangsu Province (Products No.

MZ095933). The COOLTER LH 780/LH 785 blood cell analyzer (Beckman Kurt International Trade (Shanghai) Co., Ltd) was used to detect the PLT levels.

TEG¹³ detection: 2 mL of blood was collected using a sodium citrate anticoagulant tube. The Coagulation Reaction Time (R value), Coagulation Formation Time (K value), Coagulation Formation Rate (α Angle) and final coagulation strength (MA value) levels were measured. The reference interval for R value was 4–9 minutes, indicating the time required from the start of testing to the formation of the initial clot. The R value reflected the rate at which platelets aggregated to form the first stable blood clot after prothrombin activation. The R value represented the overall activity of the coagulation factors, mainly reflecting whether the activity level of coagulation factors was normal. The reference interval for K value was 1–3 minutes, which represented the time taken for blood clot formation from the end of R time to an amplitude of 20 mm. The reference range of the α angle was 55~75°, which represented the angle between the point of blood clot formation and the maximum curvature of the curve as a horizontal line and tangent. α angle together with the K value reflected the level of fibrinogen and the function of some platelets. The reference ranged for MA value was 50~70 mm, which represented the maximum amplitude of thrombosis and reflected the maximum strength or hardness reached by the blood clot. The MA value also reflected the degree to which fibrin and platelets bound through GP IIb/IIIa receptors. According to the logistic regression equation, the prediction probability series was calculated according to the value of each TEG. This prediction probability series comprehensively reflected the diagnostic performance of each TEG index, and the receiver operating characteristic (ROC) curve could be plotted and the area under the curve (AUC) can be calculated by using the prediction probability series.

Statistical Analysis

SPSS 20.0 software was used to analyze the data of this study. Measurement data such as age, PCT and PLT were shown as ($\bar{x} \pm s$) and compared using *t*-test. Enumeration data were shown in the form of (%) and compared using χ^2 test. Multivariate logistic regression analysis was adopted to investigate the influencing factors of poor short-term progression in patients with septic shock. Pearson correlation analysis was used to investigate the correlation between serum PCT, PLT, TEG indicators and APACHE II score. ROC curve was used to evaluate the predictive value of individual or combined PCT, PLT, TEG for short-term poor disease progression in patients with septic shock. The statistical results were statistically significant if $P < 0.05$.

Results

Comparison of General Information Between Two Groups

There was no statistically significant difference in age, gender, oxygenation index, central venous pressure, mean arterial pressure, and cardiac index between the two groups ($P > 0.05$). Patients with poor prognosis had much higher APACHE II score than those with good prognosis ($P < 0.001$, Table 1).

Table 1 Comparison of General Information Between Two Groups ($\bar{x} \pm s$, %)

General Data		Good Prognosis (n=78)	Poor Prognosis (n=52)	χ^2/t	P
Gender	Male	40 (51.28)	28 (53.85)	0.082	0.774
	Female	38 (48.72)	24 (46.15)		
Age (year)		51.16±5.85	52.08±4.04	0.987	0.325
Oxygenation index (mmHg)		152.33±29.72	145.25±26.40	1.390	0.167
Central venous pressure (mmHg)		7.88±1.43	7.42±1.65	1.689	0.094
Mean arterial pressure (mmHg)		72.80±6.50	71.19±7.31	1.316	0.191
Cardiac index		4.11±0.58	4.12±0.68	0.090	0.929
APACHE II (score)		22.64±2.18	26.95±2.83	9.788	<0.001

Notes: χ^2 was the comparison of the counting data between the two groups; *t* was the comparison of the continuous data between the two groups; *P* value was the statistical significance of the hypothesis test.

Table 2 Comparison of Serum PCT and PLT Levels Between Two Groups ($\bar{x} \pm s$)

Groups	Cases	PCT (ng/mL)	PLT ($\times 10^9/L$)
Good prognosis group	78	8.48 \pm 1.08	175.96 \pm 42.16
Poor prognosis group	52	14.37 \pm 3.16	131.25 \pm 28.74
<i>t</i>		15.207	6.678
<i>P</i>		<0.001	<0.001

Notes: *t* was the comparison of the continuous data between the two groups; *P* value was the statistical significance of the hypothesis test.

Comparison of Serum PCT and PLT Levels Between Two Groups

Patients in the poor prognosis group had higher serum PCT level and lower PLT levels than those in the good prognosis group ($P < 0.001$, Table 2 and Figure 1).

Comparison of TEG Indicators Between Two Groups

Patients in the poor prognosis group had higher R value and K value and lower MA value and α angle than those in the good prognosis group ($P < 0.001$, Table 3 and Figure 2).

The Correlation Between Serum PCT, PLT, TEG Indicators and APACHE II Score

The Pearson correlation analysis indicated that APACHE II score was positively correlated with serum PCT, R value and K value ($P < 0.001$), and was negatively correlated with PLT, MA value and α angle ($P < 0.001$, Table 4 and Figure 3).

Multivariate Analysis of Short-Term Disease Progression in Patients with Septic Shock

Multivariate logistic regression analysis showed that PCT, R value and K value were risk factors ($P < 0.001$), while PLT, MA value and α angle were protective factors for short-term poor progression in patients with septic shock ($P < 0.001$, Table 5).

Value Analysis of Predicting Short-Term Disease Progression in Patients with Septic Shock

The ROC curve showed that the AUC of PCT, PLT and TEG predicting poor short-term progression in patients with septic shock was 0.813, 0.658 and 0.752, respectively. The AUC of combined three indicators was 0.905, which had the highest predictive value (Table 6 and Figure 4).

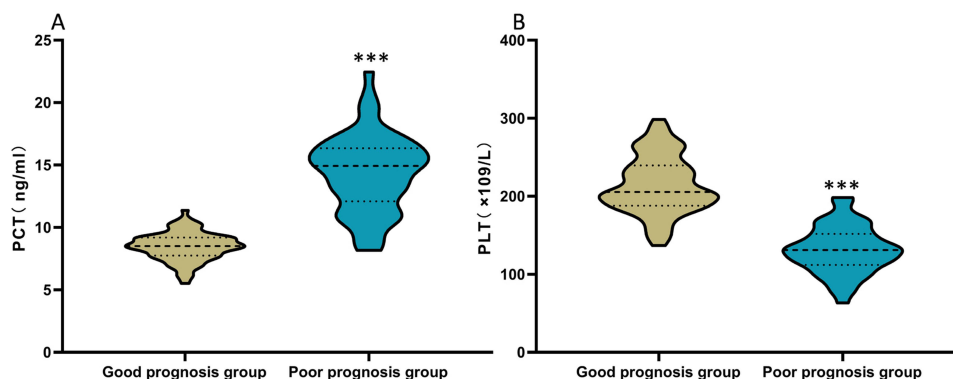


Figure 1 Comparison of serum PCT and PLT levels between two groups. (A) Comparison of PCT levels between two groups; (B) Comparison of PLT levels between two groups.

Note: *** $P < 0.001$ compared with the good prognosis group.

Table 3 Comparison of TEG Indicators Between Two Groups ($\bar{x} \pm s$)

Group	Cases	R value (min)	MA value (mm)	α Angle (°)	K value (min)
Good prognosis group	78	5.19±1.69	67.42±5.38	75.48±13.16	1.15±0.21
Poor prognosis group	52	9.84±3.13	49.62±7.85	53.12±10.24	4.08±0.61
<i>t</i>		10.955	15.348	10.338	39.146
<i>P</i>		<0.001	<0.001	<0.001	<0.001

Notes: *t* was the comparison of the continuous data between the two groups; *P* value was the statistical significance of the hypothesis test.

Discussion

Infectious shock is a serious systemic disease caused by sepsis, characterized by circulatory failure and abnormal cellular metabolism. The condition progresses rapidly and can lead to multiple organ failure with poor prognosis.¹⁴ According to previous research, the hospitalization mortality rate of septic shock is close to 40%–60%, which seriously endangers the patient's life.¹⁵ Early evaluation of the development direction of septic shock can help provide targeted treatment strategies and improve patient prognosis.

The occurrence and development mechanism of septic shock is relatively complex. Currently, research suggests that inflammation, immunity, infection, and coagulation dysfunction are closely related to the occurrence and development of septic shock.^{16,17} PCT is a common biological indicator for clinical diagnosis of systemic infections, with higher sensitivity and specificity compared to other indicators such as white blood cell (WBC) and C-reactive protein (CRP). Under normal circumstances, PCT is only produced by the thyroid gland and is mostly converted into calcitonin, resulting in lower levels of PCT in the body. When the body experiences trauma or infection, substantial tissues such as the lungs, liver, kidneys, and muscles secrete a large amount of PCT to cope with the infection. Meanwhile, substantive

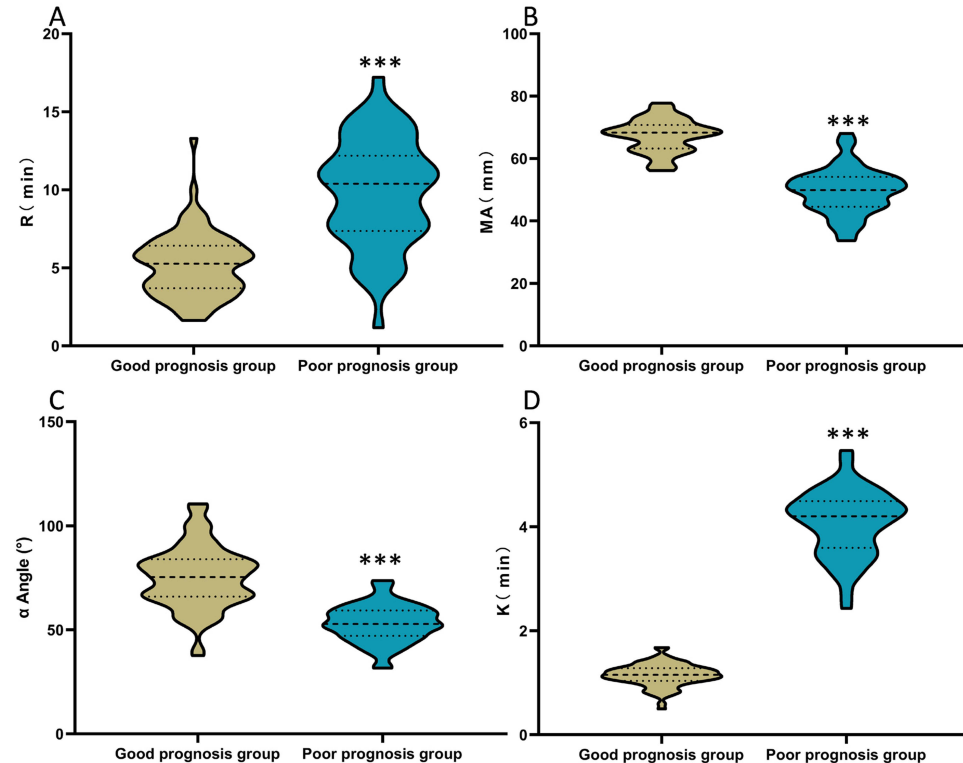


Figure 2 Comparison of TEG indicators between two groups. (A) Comparison of R values of two groups; (B) Comparison of MA values of two groups; (C) Comparison of α angle between two groups; (D) Comparison of K values of two groups.

Note: *** $P < 0.001$ compared with the good prognosis group.

Table 4 The Correlation Between Serum PCT, PLT, TEG Indicators and APACHE II Score

Indicators	APACHE II Score	
	<i>r</i>	<i>P</i>
PCT (ng/mL)	0.501	<0.001
PLT ($\times 10^9/L$)	-0.476	<0.001
R value (min)	0.373	<0.001
MA value (mm)	-0.502	<0.001
α angle ($^{\circ}$)	-0.406	<0.001
K value (min)	0.595	<0.001

Notes: *r* represented the statistic of the degree and direction of linear correlation between two random variables; *P* value was the statistical significance of the hypothesis test.

organizations lack the ability to decompose PCT, resulting in a significant accumulation of PCT within the body.^{18,19} The concentration of PCT in the plasma of patients with systemic bacterial infection rises earlier than other inflammatory factors, usually sharply between 2 and 6 hours, and maintains a high level within 8 to 24 hours.²⁰ Vishalashi SG et al²¹ believed that in patients with severe sepsis, changes in serum PCT levels can guide antibiotic treatment plans, help reduce the length of stay in ICU, and reduce the incidence rate of secondary infection and other related diseases, which can further promote antibiotic management. In this study, the serum PCT levels of patients with poor prognosis were much higher than those with good prognosis, indicating that changes in serum PCT levels in septic shock patients were closely related to short-term disease progression. Similar to the findings of Tocu G et al,²² this study suggested a positive correlation between PCT and 28-day mortality in septic shock patients, which could be used to predict the prognosis of

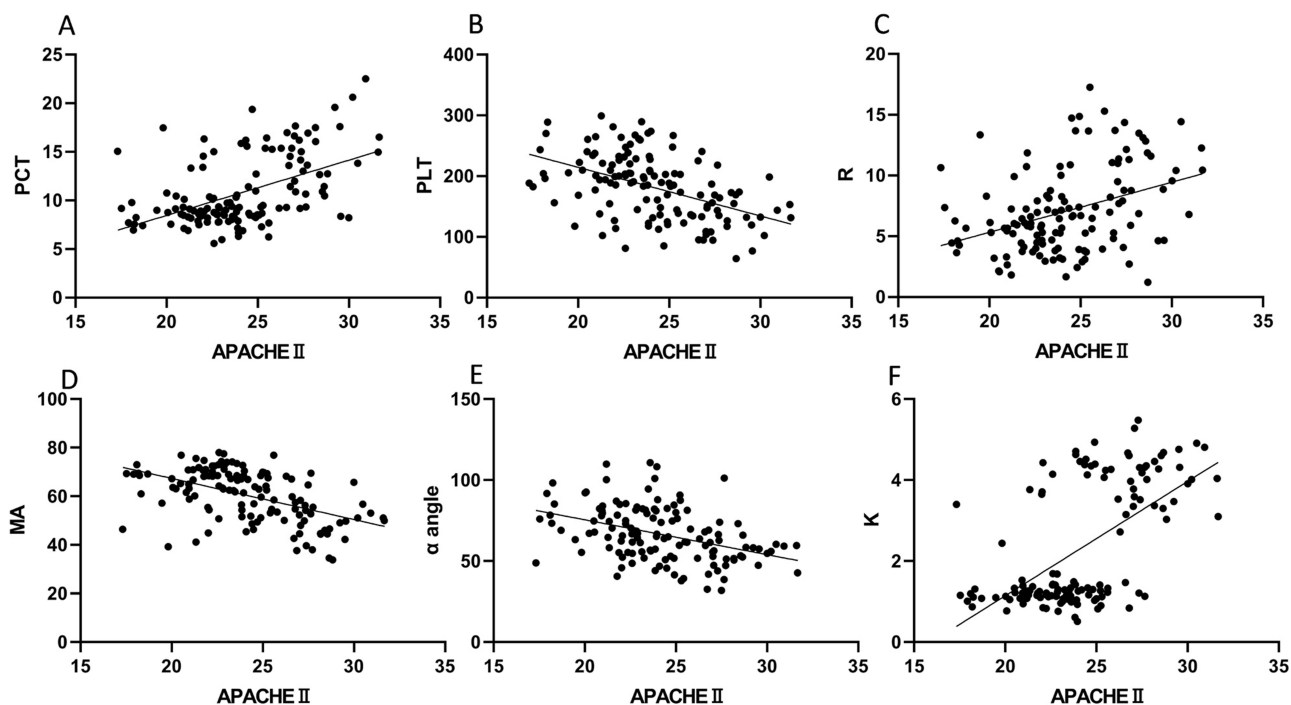


Figure 3 The correlation between serum PCT, PLT, TEG indicators and APACHE II score. (A) The correlation between serum PCT and APACHE II score; (B) The correlation between PLT and APACHE II score; (C) The correlation between R value and APACHE II score; (D) The correlation between MA value and APACHE II score; (E) The correlation between α angle and APACHE II score; (F) The correlation between K value and APACHE II score.

Table 5 Multivariate Analysis of Short-Term Disease Progression in Patients with Septic Shock

Indicators	β	SE	Wald χ^2 value	P value	OR value	95% CI
PCT (ng/mL)	2.334	0.415	31.630	<0.001	10.319	4.577–23.266
PLT ($\times 10^9/L$)	-0.958	0.236	16.478	<0.001	0.383	0.241–0.610
R value (min)	1.167	0.337	11.992	<0.001	3.212	1.658–6.221
MA value (mm)	-1.024	0.418	6.001	<0.001	0.359	0.158–0.815
α angle ($^\circ$)	-0.967	0.312	9.606	<0.001	0.358	0.206–0.701
K value (min)	0.820	0.274	8.956	<0.001	2.270	1.327–3.885

Notes: β was regression coefficient; SE was standard error; Wald χ^2 value was chi-square value; P value was the statistical significance of the hypothesis test; OR value was odds ratio; 95% CI was 95% confidence interval.

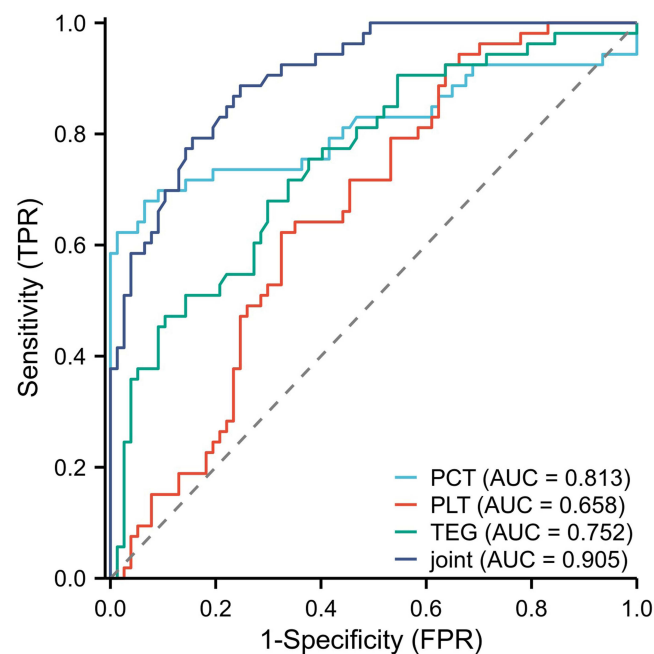
Table 6 ROC Curve Analysis of PCT, PLT, and TEG in Predicting Short-Term Disease Progression in Patients with Septic Shock

Indicators	AUC	Cut-off value	95% CI	P value	Sensitivity	Specificity	Youden Index
PCT (ng/mL)	0.813	12.05 ng/mL	0.726–0.900	0.001	67.93	93.51	0.614
PLT ($\times 10^9/L$)	0.658	$147.22 \times 10^9/L$	0.568–0.751	0.042	62.26	67.53	0.278
TEG	0.752	-	0.666–0.837	0.001	67.93	70.13	0.381
Combined detection	0.905	-	0.856–0.954	0.001	88.68	75.33	0.640

Notes: AUC was area under the curve; 95% CI was 95% confidence interval; P value was the statistical significance of the hypothesis test.

septic shock patients. From this, it could be seen that the detection of serum PCT in the intensive care unit could help doctors quickly identify septic shock and win valuable treatment time for patients. Meanwhile, monitoring changes in serum PCT levels may also help guide the rational use of antibiotics and reduce mortality.

Previous studies have suggested that coagulation abnormalities and microthrombus are closely related to the occurrence and development of septic shock. Coagulation dysfunction is a common and critical complication of

**Figure 4** ROC curve analysis of PCT, PLT, and TEG in predicting short-term disease progression in patients with septic shock.

sepsis.²³ A study has found²⁴ that endothelial cells, platelets, white blood cells, and red blood cells jointly participate in the formation of immune thrombotic effects in sepsis, which can clinically manifest as thrombosis dominated by hypercoagulability and bleeding dominated by hypocoagulability. At present, research^{25,26} suggests that sepsis induced coagulation dysfunction is mainly manifested in endothelial cell damage, excessive release of procoagulant substances, impaired physiological anticoagulant mechanisms, and fibrinolysis inhibition. There are literature reports²⁷ that conventional coagulation tests cannot fully reflect the effects of factors such as cellular interactions and thrombin production in whole blood on coagulation function, especially the hypercoagulable state induced by sepsis is not easily detected. TEG detection can instantly record the continuous changes in viscoelasticity indicators during the process of fibrin aggregation in whole blood samples at the bedside, reflecting the effects of plasma and cellular components on coagulation at different stages of coagulation. TEG detection can qualitatively and quantitatively comprehensively evaluate the overall coagulation process.²⁸ Sivula et al²⁹ found that TEG had potential clinical value in evaluating coagulation dysfunction in patients with sepsis. However, the occurrence of sepsis induced coagulation dysfunction is not limited to the dysfunction of the coagulation system itself, but is also intertwined and mutually promoted with systemic immune dysfunction, inflammatory response imbalance, and multi organ damage.³⁰ Through retrospective analysis, Guo et al³¹ found that the hospital had clear clinical characteristics of neonatal sepsis patients with bloodstream infections, and found that about 29% of newborns experienced thrombocytopenia during hospitalization. Among them, the incidence of thrombocytopenia was higher in patients with sepsis caused by *Klebsiella pneumoniae* or *Candida*, at 53% and 65%, respectively. Claushuis et al³² analyzed the characteristics of 931 patients with sepsis and found that patients with reduced platelet count ($<100 \times 10^9/L$) had more severe conditions, higher acute physiological and chronic health scores and pSOFA scores, making them more prone to shock and organ failure. In this study, the patients in the poor prognosis group had much lower serum PLT levels, much lower MA value and α angle and much higher R and K values than those in the good prognosis group. These above results indicated that there existed a certain correlation between changes in coagulation function with the progression of the disease in patients with septic shock. In routine coagulation function, PLT is a quantitative count of fibrinogen concentration and platelets in the body, and cannot analyze and evaluate the function of fibrinogen and platelets. The MA value is a comprehensive evaluation of the number and function of fibrinogen and platelets involved in the formation of blood clots in the blood. Abnormal quantity or function can lead to abnormal MA values, so MA values can better reflect the functional status of platelets than PLT.³³ α angle and K value are both indicators for detecting fibrinogen function, so changes in the count and function of fibrinogen and platelet can be analyzed in a timely manner based on the results.³⁴ The above results all suggested that TEG could help comprehensively evaluate the coagulation function status of sepsis patients, and could detect coagulation function abnormalities in patients earlier and more sensitively than conventional coagulation indicators.

Meanwhile, multiple logistic regression analysis in this study showed that PCT, R value, and K value were risk factors for poor short-term disease progression in patients with septic shock. PLT, MA value and α angle were protective factors, which further demonstrated that PCT, PLT, and TEG were involved in the short-term progression of septic shock. The ROC curve showed that the combined prediction of PCT, PLT, and TEG had an AUC of 0.905 for short-term disease progression in septic shock patients, which was higher than the AUC of a single indicator, indicating that PCT, PLT, and TEG had certain value in predicting short-term disease progression in septic shock patients. Specifically, an increase in serum PLT levels indicates an exacerbation of inflammatory response. Abnormal TEG reflects coagulation dysfunction, while decreased PLT indicates microcirculation disorders. The changes in these indicators can sensitively reflect the fluctuations of the condition, and regular monitoring can help predict the development of septic shock, guide treatment plans, and improve prognosis.

The results of this study will help clinicians more accurately predict the short-term disease progression of patients with septic shock and provide patients with more timely and effective treatment measures. By identifying the risk of exacerbation early, the mortality rate of patients in the intensive care unit can be reduced and the cure rate can be improved. In addition, this study also provides new research ideas for researchers in related fields, which is helpful for further exploring the biomarkers of septic shock assessment. In today's era of rapid development of medical technology, early recognition and intervention of septic shock in ICU have become the key to clinical treatment. Serum PCT, PLT and TEG, as commonly used detection methods, have important clinical value in the diagnosis and evaluation of septic shock. In this study, the results of the joint study of these three indicators have met expectations and are consistent with the original research objectives. The combined

detection of serum PCT, PLT and TEG has a wide range of applications in the short-term prediction of septic shock in the ICU. This approach helps clinicians understand the patient's condition in a timely manner and develop a more precise treatment plan, thereby improving the cure rate and reducing the mortality rate. In addition, this method can also provide strong support for clinical research and provide a new research direction for the treatment of septic shock.

Conclusions

In general, serum levels of PCT, PLT, and TEG in patients with septic shock have certain value in predicting short-term poor disease progression in patients with septic shock, and regular monitoring can help guide the treatment of patients with septic shock. There were still certain limitations in this study. The number of patients included in this study was relatively small, which might affect the universality of the results. We can further explore the effect of co-detection with other biomarkers in the future.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

All procedures performed in studies involving animals were in accordance with the ethical standards of the ethics committee of the Yiyang Central Hospital of Hunan (2021012).

Consent for Publication

Informed consent was obtained from all individual participants included in the study. The patients participating in the study all agree to publish the research results.

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Disclosure

Xianhui Zeng and Yuxi Yin are co-first authors for this study. The authors declare that they have no competing interests in this work.

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