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Original Article

Predictive value of procalcitonin for the therapeutic response of patients with uroseptic shock: a retrospective case-control study

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Abstract: Objectives: To evaluate the predictive value of procalcitonin (PCT) in assessing the therapeutic response of patients with uroseptic shock. Methods: This retrospective case-control study included 220 patients treated for uroseptic shock at Liyang People's Hospital between January 2018 and December 2023. Patients were classified into high-risk (HR) (n = 116) and low-risk (LR) (n = 104) groups based on their Sepsis-related Organ Failure Assessment (SOFA) scores after 14 days of treatment. Demographic, clinical, and laboratory data were collected, and PCT levels were measured using chemiluminescence. Correlation analysis and receiver operating characteristic (ROC) curve analysis were used to assess the predictive value of PCT. Results: The HR group had significantly higher PCT levels (25.33 ± 5.32 ng/mL) compared to the LR group (18.47 ± 2.88 ng/mL, $P < 0.001$). Elevated PCT levels were strongly correlated with poor therapeutic response (rho = -0.635, $P < 0.001$). Other markers, including hypertension (rho = -0.207, P = 0.002), CRP (rho = -0.224, $P < 0.001$), IL-6 (rho = -0.200, P = 0.003), TNF-α (rho = -0.151, P = 0.025), NEUT% (rho = -0.208, P = 0.002), GGT (rho = -0.160, P = 0.017), and BUN (rho = -0.198, P = 0.003), also showed significant negative correlations with treatment outcome. Conversely, PLT (rho = 0.156, P = 0.021) and the CD4+/CD8+ ratio (rho = 0.242, $P < 0.001$) were positively correlated with better treatment outcome. ROC analysis revealed an area under the curve (AUC) of 0.867 for PCT, indicating its strong predictive value. Conclusions: PCT level is a robust predictor of therapeutic response in uroseptic shock patients and may be integrated into clinical protocols for sepsis management.

Keywords: Uroseptic shock, procalcitonin, biomarker, therapeutic response, sepsis management

Introduction

Sepsis is a leading cause of global morbidity and mortality, particularly when it progresses to septic shock and multiple organ failure [1]. Among the various forms of sepsis, urosepsis - originating from urinary tract infections - presents a unique clinical challenge due to its rapid progression and high morbidity [2]. Timely diagnosis and effective management of septic shock, characterized by persistent hypotension and organ dysfunction despite adequate fluid resuscitation, are critical for improving patient outcome [3]. Identifying reliable biomarkers that predict therapeutic response and guide treatment decisions is of paramount importance [4].

Procalcitonin (PCT) has gained attention as a promising biomarker for diagnosing and managing systemic bacterial infections and sepsis [5]. Produced primarily by extrathyroidal tissues in response to pro-inflammatory cytokines and bacterial endotoxins, PCT rises significantly in severe bacterial infections and sepsis, correlating with infection severity and systemic inflammation [6]. Despite its diagnostic utility, the prognostic value of PCT for predicting treatment responses, particularly in uroseptic shock, remains uncertain [7].

The Sepsis-related Organ Failure Assessment (SOFA) score is widely used to quantify organ dysfunction in sepsis, providing an objective measure of patient deterioration and recovery [8]. Combining PCT level with SOFA score may

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enhance predictive accuracy for therapeutic responses in uroseptic shock, enabling clinicians to better stratify risk and tailor interventions [9]. However, few studies have systematically evaluated PCT as a predictive tool in this context, particularly within case-control frameworks that allow robust comparative analysis [10].

Existing research has demonstrated that dynamic monitoring of PCT levels reflects the host's response to antimicrobial treatment, offering real-time insight into infection control and systemic inflammation [11]. However, most studies focus on septic populations without considering the specific pathophysiologic mechanisms of uroseptic shock, where urinary tract obstruction and anatomical alterations can influence immune responses and bacterial proliferation differently from other sepsis sources [12]. Thus, a focused investigation into the predictive value of PCT in uroseptic shock was needed to address these matters [13].

Our study aimed to retrospectively examine the predictive value of PCT for assessing therapeutic response in patients with uroseptic shock. We integrated PCT with other clinical data to provide a comprehensive assessment of patient status, emphasizing the importance of a multifactorial approach for guiding personalized treatment strategy.

Materials and methods

Case selection

This study explored the predictive accuracy of PCT in assessing therapeutic response in patients with uroseptic shock. A retrospective analysis was conducted on 220 patients treated for uroseptic shock at Liyang People's Hospital between January 2018 and December 2023. Treatment response was assessed based on the SOFA score. Patients were classified into the high-risk (HR) group (116 cases, SOFA score > 2) and the low-risk (LR) group (104 cases, SOFA score ≤ 2) based on their SOFA score after 14 days of treatment. Demographic and laboratory data were collected from the medical record system. Additionally, 83 patients were included as a test set for external validation, following the same inclusion and grouping criteria.

This study was approved by the Institutional Review Board and Ethics Committee of Liyang People's Hospital. As a retrospective study using de-identified patient data with no risk to patient care, informed consent was waived in accordance with regulatory and ethical guidelines for retrospective research.

Inclusion and exclusion criteria

Inclusion criteria: 1) Diagnosis of urosepsis based on the criteria established by the European Association of Urology (EAU) in 2001 [14], with septic shock characterized by persistent hypotension despite fluid resuscitation. 2) Age between 40 and 85 years. 3) Complete medical records.

Exclusion criteria: 1) Severe underlying conditions such as end-stage renal diseaseor advanced cancer. 2) Kidney transplant recipients. 3) Patients with an ICU stay of less than 24 hours. 4) Patients who have used immunomodulatory drugs in the past month or received antibiotic treatment in the past week. 5) Patients with conditions that may cause abnormal inflammatory marker changes, such as systemic lupus erythematosus or rheumatoid arthritis. 6) Incomplete clinical data.

Treatment approach

All patients received treatment according to established sepsis guidelines [15].

Fluid Resuscitation: In the initial phase, fluid administration was based on central venous pressure (CVP) readings. Patients received at least 1000 mL of crystalloid or 300-500 mL of colloid solution within the first 30 minutes until the CVP reached 8-12 mm H_2O. For patients on mechanical ventilation with reduced ventricular compliance, the CVP target was set at 12-15 mm H_2O.

Antibiotic Therapy: For patients with high fever, blood and midstream urine samples were collected for culture and susceptibility testing. Intravenous broad-spectrum antibiotics were administered initially, with adjustments made based on culture results.

Oxygenation Support: Oxygen saturation (SaO_2/SpO_2) was maintained between 88% and 95% using mechanical ventilation or high-flow oxygen therapy.

Renal Support: Patients with stable blood pressure but renal impairment were treated with

Table 1. SOFA scores

SOFA score	1	2	3	4
Respiration PaO_2/FiO_2, mmHg	< 400	< 300	< 200	< 100
Coagulation Platelets × $10^3/mm^3$	< 150	< 100	< 50	< 20
Liver Bilirubin, mg/dL (μmol/L)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	> 12.0 (< 204)
Cardiovascular Hypotension	MA*P* < 70 mmHg	Dopamine ≤ 5 or dobutamine (any dose)[a]	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine > 15 Or epinephrine > 0.1 or norepinephrine > 0.1
Central nervous system Glasgow Coma Score	13-14	10-12	6-9	< 6
Renal Creatinine, mg/dl (μmol/L) or urine output	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440) or < 500 ml/day	> 5.0 (> 440) or < 200 ml/day

Note: a, Adrenergic agents administered for at least 1 h (doses given were in gg/kg-min). Note: SOFA, Sepsis-related Organ Failure Assessment; PaO_2, Partial Pressure of Oxygen in Arterial Blood; FiO_2, Fraction of inspiration O_2; MAP, mean arterial pressure.

intravenous furosemide (20-69 mg/day; Approval No. H41020310, Henan Runhong Pharmaceutical Co., Ltd., China) to maintain urine output. Other patients received deslanoside (0.2-0.4 mg/day; Approval No. H31021178, Shanghai Xudong Haipu Pharmaceutical Co., Ltd., China) and hydrocortisone (200-300 mg/day; Approval No. H41020789, Henan Runhong Pharmaceutical Co., Ltd., China) until blood pressure stabilized.

Hemoglobin and Coagulation Management: If hemoglobin levels dropped below 90 g/L, red blood cell transfusions (600-1200 mL) were administered to improve coagulation function.

Post-Stabilization Care: After vital signs stabilized, patients received treatments focused on preventing complications and supporting rehabilitation.

Each patient underwent SOFA scoring for fourteen consecutive days [16].

Organ Limitation: The SOFA assessment focused on six key organs. While gastrointestinal dysfunction/failure was considered important, it was excluded due to its complexity.

Scoring System: Each organ was evaluated and assigned a score (0-4: normal to severe). The worst daily values were recorded.

Risk Group Stratification: On day 14, patients were categorized into two groups based on their SOFA scores: those with scores greater than 2 were placed in the HR group (n = 116), and those with scores of 2 or less were placed in the LR group (n = 104). The SOFA score is presented in **Table 1**.

Data collection

Basic clinical information was extracted from the electronic medical record system of Liyang People's Hospital and included the following:

General Information: Age, gender, smoking and alcohol history, etiology, number of comorbidities, oral medications, and any surgical procedures related to urinary tract infections after admission.

Laboratory data on PCT, C-reactive protein (CRP), white blood cell (WBC) count, neutrophil percentage (NEUT%), platelet count (PLT), serum albumin (ALB), total bilirubin (TBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), blood urea nitrogen (BUN), and serum creatinine (Scr) were collected. The most adverse values for each measurement were recorded.

Blood data

A 5 mL fasting blood sample was collected from the antecubital vein in the morning. After centrifugation at 3000 rpm for 5 minutes, the supernatant was analyzed for the following indicators [17]. PCT levels were measured by chemiluminescence on the iFlash3000 instrument (AutoBi Fengxiang Medical Technology Co., Ltd., Shenzhen, China). CRP was assessed using nephelometry with a Siemens BNII or BN Pro analyzer (Siemens, Germany), employing reagents (batch number 16573C). WBC, NEUT%, PLT, monocytes, lymphocytes, and natural killer (NK) cells were analyzed via flow cytometry on a BC-6800 Plus hematology ana-

lyzer (Mindray, Shenzhen, China). ALB, TBIL, ALT, AST, GGT, BUN, and Scr were measured by scattering on an AU5800 automated biochemistry analyzer (Beckman Coulter, Brea, CA, USA).

Commercial enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA) were used to quantify IL-1β (ab214025, Abcam, UK), IL-6 (ab178013, Abcam, UK), IL-8 (ab214030, Abcam, UK), TNF-α (ab181421, Abcam, UK), IP-10 (ab289906, Abcam, UK), and MCP-1 (ab179886, Abcam, UK).

Data cleaning and management

A standardized data cleaning process was applied before analysis to identify and correct any inconsistencies, errors, or missing values. This involved reviewing the dataset for duplicates, correcting data entry errors, and addressing missing values. Missing data were imputed using the Impyute library in Python 3.6.0 with the K-nearest neighbors (KNN) method. Initially, basic mean imputation was applied, followed by constructing a KDTree to calculate nearest neighbors and their weighted averages.

To minimize selection bias, missing data accounted for less than 5% of the dataset. Sensitivity analyses were performed by treating missing outcomes as both the worst and best possible cases. No significant differences were found in the conclusions, indicating minimal effect from the missing data. The final dataset was produced with imputed values.

Statistical analysis

A post hoc analysis was conducted using G*Power 3.1.9.7 with the "Means: Difference between two independent means (two groups)" option under t tests. The following settings were used: two-tailed mode, effect size d = 0.5, $\alpha = 0.05$. The sample sizes of the two groups were input, yielding a Power of 0.958.

Data analysis was performed using SPSS 29.0 software (SPSS Inc., Chicago, IL, USA). Categorical data were presented as [n (%)]. The chi-square test was used when the sample size was ≥ 40 and $T \geq 5$ (test statistic: χ^2). For $1 \leq T < 5$, a corrected chi-square test was applied. For sample sizes < 40 or $T < 1$, Fisher's exact test was used.

Continuous variables were first tested for normality using the Shapiro-Wilk test. Normally distributed data were expressed as mean ± standard deviation ($\bar{x} \pm s$), with statistical significance defined as $P < 0.05$.

Pearson correlation analysis was used for assessing the relationship between continuous variables, while Spearman correlation analysis was used for categorical variables. Initial correlation analysis was performed to evaluate relationships between variables.

Independent predictors were identified through logistic regression analysis. The accuracy of PCT for predicting the treatment response in patients with uroseptic shock was evaluated using receiver operating characteristic (ROC) analysis to calculate the area under the curve (AUC).

Results

Comparison of baseline characteristics

The mean ages of the two groups were similar, with the HR group averaging 69.83 ± 12.98 years and the LR group 70.36 ± 13.24 years (P = 0.765) (**Table 2**). Gender distribution was not significantly different, with males comprising 50.00% of the HR group and 40.38% of the LR group (P = 0.153). Body mass index (BMI) was also similar between the groups, with averages of 22.11 ± 2.35 kg/m^2 in the HR group and 22.36 ± 2.44 kg/m^2 in the LR group (P = 0.430). There were no significant differences in lifestyle factors, including smoking and alcohol consumption, as well as marital status (all P > 0.05).

Conditions contributing to uroseptic shock, such as urinary tract infections, abscesses, skin or soft tissue infections, benign prostatic hyperplasia, urinary calculi, and urinary catheter placement, were also similar between the two groups. The SOFA scores prior to treatment were slightly higher in the HR group (3.56 ± 0.73) than the LR group (3.37 ± 0.80), though this difference did not reach significance (P = 0.064).

Comparison of comorbidities

Among comorbidities, a significant difference was observed in the prevalence of hypertension, with the HR group having a higher inci-

Table 2. Comparison of baseline characteristics

Item	HR group (n = 116)	LR group (n = 104)	t/χ^2	P
Age (years)	69.83 ± 12.98	70.36 ± 13.24	0.300	0.765
Gender (Male/Female)	58 (50.00%)	42 (40.38%)	2.045	0.153
Body Mass Index (kg/m^2)	22.11 ± 2.35	22.36 ± 2.44	0.790	0.430
Drinking history [n (%)] (Y/N)	37 (31.90%)	29 (27.88%)	0.420	0.517
Smoking history [n (%)] (Y/N)	42 (36.21%)	37 (35.58%)	0.009	0.923
Marital status			0.477	0.788
Unmarried [n (%)]	2 (1.72%)	1 (0.96%)		
Married with spouse [n (%)]	103 (88.79%)	95 (91.35%)		
Divorced or widowed [n (%)]	11 (9.48%)	8 (7.69%)		
Conditions causing urosepsis shock				
Urinary tract infection [n (%)]	58 (50.00%)	50 (48.08%)	0.081	0.776
Abscess [n (%)]	22 (18.97%)	18 (17.31%)	0.101	0.750
Skin or soft tissue infection [n (%)]	8 (6.90%)	8 (7.69%)	0.051	0.820
BPH [n (%)]	28 (24.14%)	23 (22.12%)	0.126	0.723
Urinary calculi [n (%)]	42 (36.21%)	33 (31.73%)	0.489	0.484
Placement of urinary catheter [n (%)]	61 (52.59%)	55 (52.88%)	0.002	0.965
Unknown or other [n (%)]	5 (4.31%)	3 (2.88%)	0.041	0.839
SOFA score before treatment	3.56 ± 0.73	3.37 ± 0.80	1.859	0.064

Note: BPH, Benign Prostatic Hyperplasia; SOFA, Sepsis-related Organ Failure Assessment; HR, high risk; LR, low risk.

Table 3. Comparison of comorbidities

Item	HR group (n = 116)	LR group (n = 104)	X^2	P
Diabetes [n (%)]	71 (61.21%)	55 (52.88%)	1.552	0.213
Hypertension [n (%)]	63 (54.31%)	35 (33.65%)	9.472	0.002
CKD [n (%)]	19 (16.38%)	20 (19.23%)	0.306	0.580
CAD [n (%)]	33 (28.45%)	40 (38.46%)	2.480	0.115
CHF [n (%)]	23 (19.83%)	17 (16.35%)	0.447	0.504
Pulmonary disease/COPD [n (%)]	16 (13.79%)	11 (10.58%)	0.527	0.468

Note: CKD, chronic kidney disease; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HR, high risk; LR, low risk.

dence (54.31%) compared to the LR group (33.65%; P = 0.002) (**Table 3**). Other comorbidities did not show significant differences. The prevalence of diabetes was 61.21% in the HR group and 52.88% in the LR group (P = 0.213), while chronic kidney disease was present in 16.38% of the HR group and 19.23% of the LR group (P = 0.580). Coronary artery disease was found in 28.45% of the HR group and 38.46% of the LR group (P = 0.115). The prevalence of congestive heart failure was 19.83% in the HR group and 16.35% in the LR group (P = 0.504), and pulmonary diseases, including COPD, were observed in 13.79% of the HR group and 10.58% of the LR group (P = 0.468).

Comparison of inflammatory markers

The HR group exhibited significantly elevated levels of PCT, with a mean of 25.33 ± 5.32 ng/mL, compared to the LR group (18.47 ± 2.88 ng/mL; P < 0.001) (**Figure 1**). CRP was also higher in the HR group (12.17 ± 3.36 mg/L) than of the LR group (11.02 ± 2.14 mg/L; P = 0.002).

Levels of interleukin-6 (IL-6) were significantly higher in the HR group (124.88 ± 15.26 pg/mL) compared to the LR group (119.70 ± 13.52 pg/mL; P = 0.009). Tumor necrosis factor-alpha (TNF-α) levels were also significantly higher in the HR group (15.31 ± 2.36 pg/mL) compared

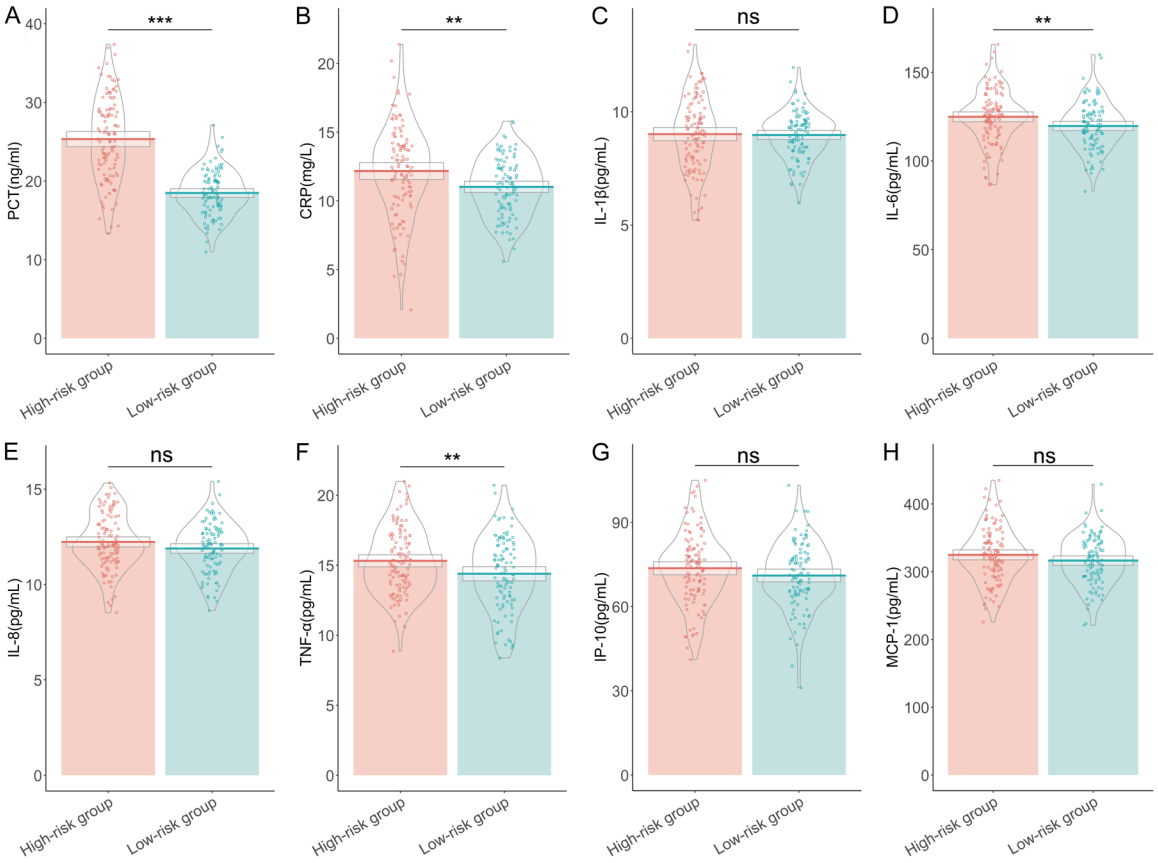

Figure 1. Comparison of inflammatory markers between the two groups of patients. A. PCT (ng/ml); B. CRP (mg/L); C. IL-1β (pg/mL); D. IL-6 (pg/mL); E. IL-8 (pg/mL); F. TNF-α (pg/mL); G. IP-10 (pg/mL); H. MCP-1 (pg/mL). Note: PCT, Procalcitonin; CRP, C-reactive protein; IL-1β, Interleukin-1 beta; IL-6, Interleukin-6; IL-8, Interleukin-8; TNF-α, Tumor Necrosis Factor alpha; IP-10, Interferon gamma-induced Protein 10 kDa; MCP-1, Monocyte Chemoattractant Protein-1; ns, no significant difference; **, $P < 0.01$; ***, $P < 0.001$.

to the LR group (14.39 ± 2.65 pg/mL; P = 0.007).

However, there were no significant differences in interleukin-1 beta (IL-1β), interleukin-8 (IL-8), interferon gamma-induced protein 10 kDa (IP-10), or monocyte chemoattractant protein-1 (MCP-1) levels between the two groups (all P > 0.05).

Comparison of blood cell counts

The HR group had a significantly higher NEUT with a mean of 80.33 ± 5.40%, compared to 77.86 ± 6.24% in the LR group (P = 0.002) (**Figure 2**). PLT was significantly lower in the HR group (98.11 ± 10.38 × 10^9/L) compared to the LR group (102.26 ± 12.55 × 10^9/L; P = 0.009).

The CD4+/CD8+ ratio was also significantly reduced in the HR group (0.96 ± 0.21) compared to the LR group (1.08 ± 0.30; P = 0.001). There were no significant differences in white blood cell (WBC) count, monocyte count, lymphocyte count, CD4+ percentage, or NK cell levels between the groups. These results suggest that NEUT%, PLT, and the CD4+/CD8+ ratio differentiated between the HR and LR groups.

Comparison of liver and renal function

The HR group had significantly higher levels of GGT (70.01 ± 10.75 U/L) and BUN (11.32 ± 3.00 mmol/L) compared to the LR group (GGT: 67.09 ± 8.37 U/L, P = 0.025; BUN: 10.27 ± 2.15 mmol/L, P = 0.003) (**Table 4**). However, no significant differences were observed between the groups for other liver and renal function markers, including ALB, TBIL, ALT, AST, and Scr (all P > 0.05).

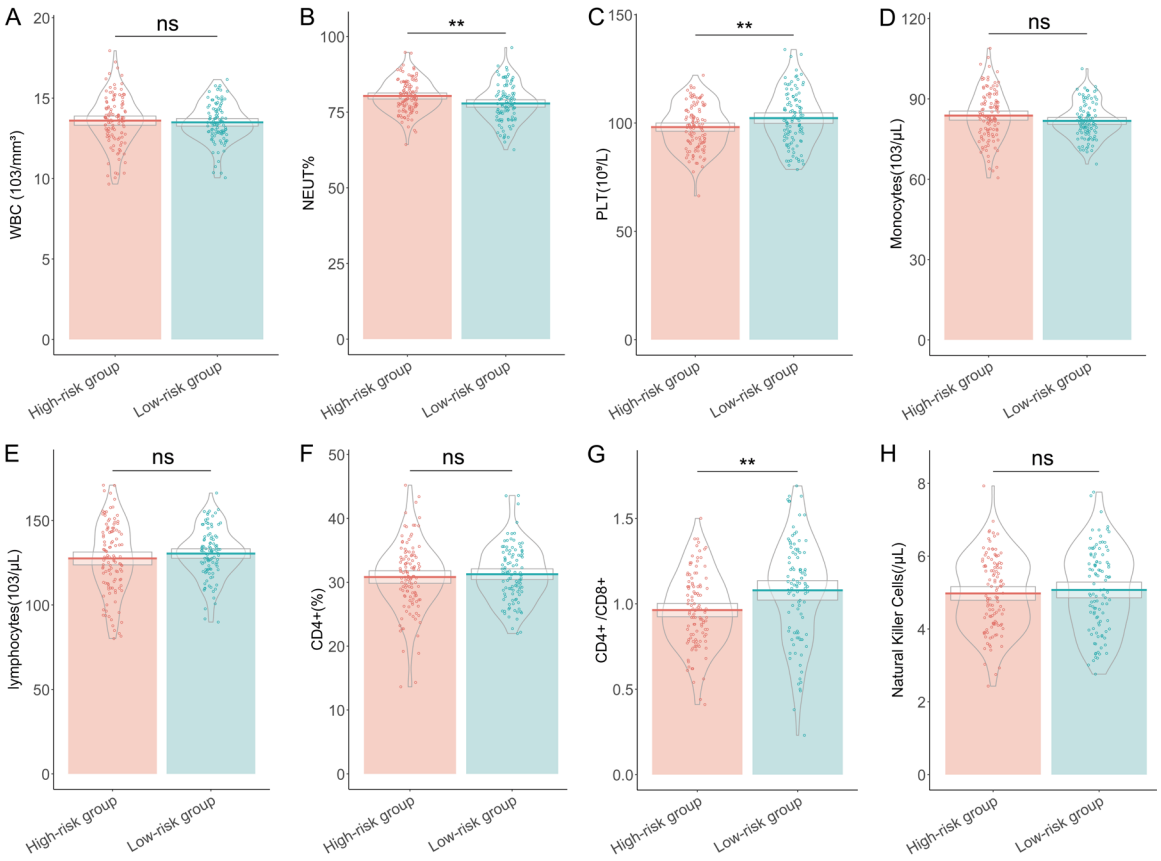

Figure 2. Comparison of blood cell counts between the two groups of patients. A. WBC (10^3/mm^3); B. NEUT (%); C. PLT (10^9/L); D. Monocytes (10^3/μL); E. lymphocytes (10^3/μL); F. CD4+ (%); G. CD4+/CD8+; H. Natural Killer Cells (/μL). Note: WBC, white blood cell count; NEUT%, neutrophil percentage; PLT, platelet count; CD4+, Cluster of Differentiation 4 Positive; CD8+, Cluster of Differentiation 4 Positive; ns, no significant difference; **, $P < 0.01$.

Table 4. Comparison of liver and renal function indicators

Item	HR group (n = 116)	LR group (n = 104)	t	P
ALB (g/L)	27.86 ± 3.22	28.30 ± 4.02	0.882	0.379
TBIL (μmol/L)	24.36 ± 4.15	23.87 ± 3.65	0.930	0.353
ALT (U/L)	55.73 ± 10.61	53.36 ± 8.69	1.821	0.070
AST (U/L)	57.35 ± 9.83	56.06 ± 5.97	1.195	0.233
GGT (U/L)	70.01 ± 10.75	67.09 ± 8.37	2.264	0.025
BUN (mmol/L)	11.32 ± 3.00	10.27 ± 2.15	3.005	0.003
Scr (μmol/L)	107.58 ± 10.24	105.33 ± 11.86	1.509	0.133

Note: ALB, serum albumin; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; BUN, blood urea nitrogen; Scr, serum creatinine; HR, high risk; LR, low risk.

Comparison of medication use

Furosemide was administered to 46.55% of the HR group and 50.00% of the LR group (P = 0.609) (**Table 5**). Hydrocortisone use was nearly identical between the groups (HR: 45.69%, LR: 45.19%; P = 0.941), and Lanatoside C was used by 14.66% of HR patients versus 12.50% in LR patients (P = 0.642).

Comparison of tolerance to treatment (adverse reactions)

Adverse reactions were comparable between the groups. Rigor, chills, and a temperature elevation exceeding 1°C were reported in 17.24% of the HR group and 15.38% of the LR group (P = 0.710) (**Table 6**). Vomiting occurred in 3.45% of HR patients compared to 1.92% in

Table 5. Comparison of medication use

Medication	HR group (n = 116)	LR group (n = 104)	X^2	P
Furosemide [n (%)]	54 (46.55%)	52 (50.00%)	0.261	0.609
Hydrocortisone [n (%)]	53 (45.69%)	47 (45.19%)	0.005	0.941
Lanatoside C [n (%)]	17 (14.66%)	13 (12.50%)	0.216	0.642

Note: HR, high risk; LR, low risk.

Table 6. Comparison of adverse reactions

Item	HR group (n = 116)	LR group (n = 104)	X^2	P
Rigor, chills, and elevation of temperature (> 1°C) [n (%)]	20 (17.24%)	16 (15.38%)	0.138	0.710
Vomiting [n (%)]	4 (3.45%)	2 (1.92%)	0.078	0.780
Anaphylactic/allergic reactions [n (%)]	2 (1.72%)	0 (0.00%)	0.402	0.526
Severe haemolytic complications [n (%)]	3 (2.59%)	1 (0.96%)	0.156	0.693
TRALI [n (%)]	1 (0.86%)	2 (1.92%)	0.009	0.924
TACO [n (%)]	2 (1.72%)	0 (0.00%)	0.402	0.526

Note: TRALI, Transfusion associated acute lung injury; TACO, Transfusion associated circulatory overload; HR, high risk; LR, low risk.

Table 7. Correlation analysis of each factor and patients' response to treatment

Item	rho	P
Hypertension [n (%)] (Y/N)	-0.207	0.002
PCT (ng/ml)	-0.635	< 0.001
CRP (mg/L)	-0.224	< 0.001
IL-6 (pg/mL)	-0.200	0.003
TNF-α (pg/mL)	-0.151	0.025
NEUT%	-0.208	0.002
PLT (10^9/L)	0.156	0.021
CD4+/CD8+	0.242	< 0.001
GGT (U/L)	-0.160	0.017
BUN (mmol/L)	-0.198	0.003

Note: PCT, Procalcitonin; CRP, C-reactive protein; IL-6, Interleukin-6; TNF-α, Tumor Necrosis Factor alpha; NEUT%, neutrophil percentage; PLT, platelet count; CD4+, Cluster of Differentiation 4 Positive; CD8+, Cluster of Differentiation 4 Positive; GGT, gamma-glutamyl transferase; BUN, blood urea nitrogen; Scr, serum creatinine.

the LR group (P = 0.780). Anaphylactic reactions were observed in 1.72% of HR patients, with no occurrences in the LR group (P = 0.526). Severe hemolytic complications were noted in 2.59% of HR patients versus 0.96% of LR patients (P = 0.693), while transfusion-associated acute lung injury and transfusion-associated circulatory overload were rare and showed no significant differences between groups (both P > 0.05).

Correlation analysis

Correlation analysis revealed significant associations between various factors and treatment response in uroseptic shock patients. Higher levels of PCT, CRP, IL-6, and TNF-α were negatively correlated with treatment response (PCT: rho = -0.635, P < 0.001; CRP: rho = -0.224, P < 0.001; IL-6: rho = -0.200, P = 0.003; TNF-α: rho = -0.151, P = 0.025). Additionally, NEUT% (rho = -0.208, P = 0.002), GGT (rho = -0.160, P = 0.017), and BUN (rho = -0.198, P = 0.003) showed negative correlations with treatment response. Conversely, the PLT and CD4+/CD8+ ratio were positively correlated with treatment response (PLT: rho = 0.156, P = 0.021; CD4+/CD8+: rho = 0.242, P < 0.001). Hypertension also showed a significant negative correlation (rho = -0.207, P = 0.002) (**Table 7**).

ROC analysis

ROC analysis was conducted to assess the predictive value of various markers on therapeutic response in uroseptic shock patients (**Figure 3**). PCT exhibited a high AUC of 0.867, indicating that it was a strong predictor of treatment response. This suggests that PCT could serve as a valuable biomarker for assessing the efficacy of therapeutic intervention in these patients.

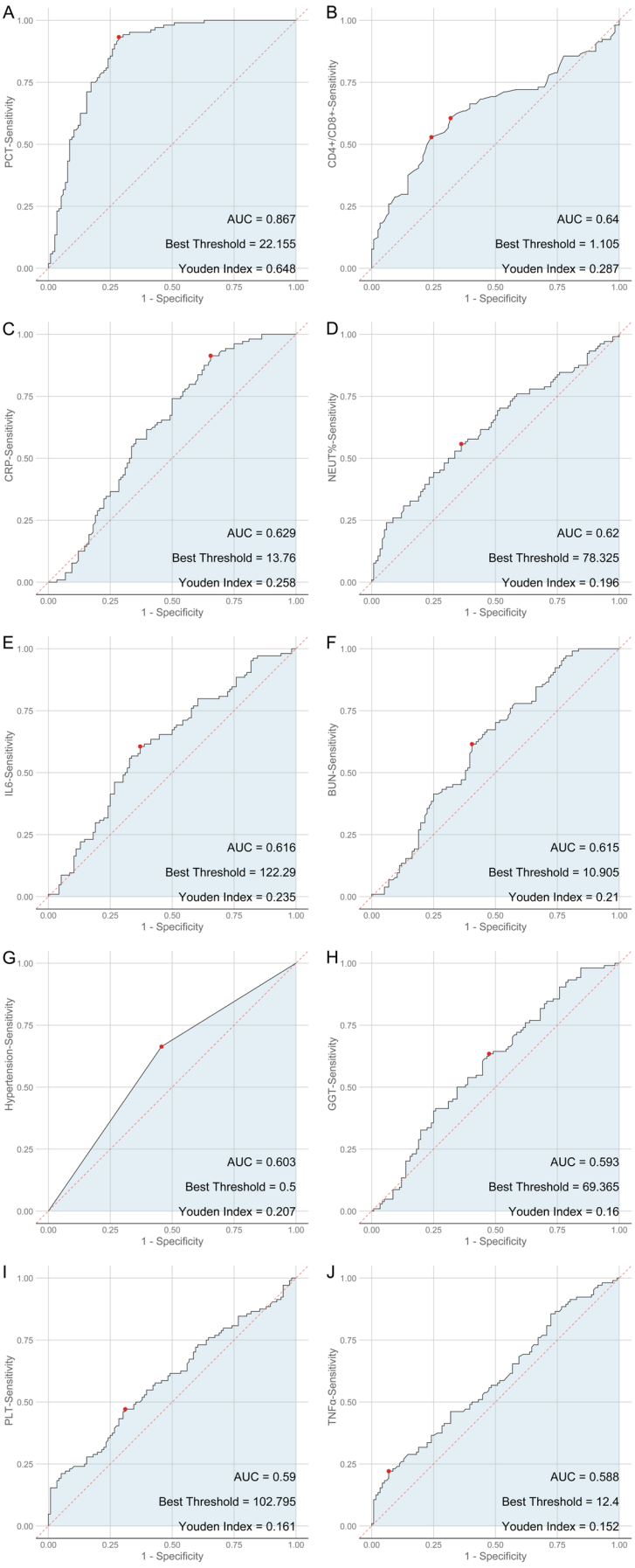

Figure 3. Prognostic value of each index for treatment response of patients with urogenic septic shock. A. PCT; B. CD4+/CD8+; C. CRP; D. NEUT%; E. IL-6; F. BUN; G. Hypertension; H. GGT; I. PLT; J. TNF-α. Note: PCT, Procalcitonin; CD4+, Cluster of Differentiation 4 Positive; CD8+, Cluster of Differentiation 4 Positive; CRP, C-reactive protein; NEUT%, neutrophil percentage; IL-6, Interleukin-6; BUN, blood urea nitrogen; GGT, gamma-glutamyl transferase; PLT, platelet count; TNF-α, Tumor Necrosis Factor alpha.

Discussion

The present retrospective case-control study investigated the predictive value of PCT in assessing therapeutic responses in patients with uroseptic shock, offering new insights that contribute to the ongoing discourse in critical care and infectious disease management. Given the complexity of sepsis, particularly uroseptic shock, early identification and monitoring of disease progression and therapeutic response are crucial for improving patient outcomes.

Several studies have explored the role of PCT in sepsis [18, 19]. For example, an analysis by Kyriazopoulou et al. [20] found PCT to be a reliable marker for distinguishing long-term infections. As a precursor of the hormone calcitonin, PCT increases significantly in response to systemic bacterial infections and sepsis [21]. In line with this, our study found elevated PCT levels were significantly associated with suboptimal therapeutic responses in patients. This is consistent with the understanding that PCT is released in response to pro-inflammatory stimuli, particularly those triggered by bacterial endotoxins and cytokines such as interleukin-1β and TNF-α. The marked elevation of PCT likely mirrors the systemic inflammatory response syndrome seen in sepsis, where the body initiates a widespread inflamma-

tory response to combat bacterial proliferation and dissemination [22].

This study also reveals significant associations between PCT levels and other inflammatory markers, such as CRP, IL-6, and TNF-α. These cytokines and acute-phase proteins play integral roles in the host's immune response, and their elevated levels further underscore the heightened inflammatory state in patients with poor therapeutic outcome [23]. The interplay between these markers and PCT may be explained by their roles in the inflammatory cascade [24, 25]. For instance, IL-6 is a key mediator that stimulates the liver to produce acute-phase proteins like CRP and induces PCT production in various tissues [26, 27]. This interconnectedness of inflammatory markers highlights the complexity of the immune response and suggests that PCT may serve as a downstream indicator of primary immune responses [28, 29].

Interestingly, the correlation analysis highlights a negative relationship between PCT and treatment response, suggesting that elevated PCT levels could signal treatment failure or an increased risk of progression to severe outcomes. This finding is supported by Godínez-Vidal et al. [30], who demonstrated that persistently elevated PCT levels are associated with higher mortality in septic patients. This underscores the clinical importance of PCT, as it could reflect the efficacy of interventions aimed at controlling the underlying infection and managing systemic inflammation in real-time [31]. Moreover, the high AUC for PCT in the receiver operating characteristic (ROC) analysis supports its significant prognostic value, reinforcing the utility of serial PCT measurements in dynamic monitoring strategies for critically ill patients. In contrast to the general sepsis population studied by Zaki et al. [25], our focus on uroseptic shock provides more specific insight into this subset of patients, where pathophysiology may differ due to the infection's origin and possible anatomic obstructions.

It is noteworthy that hypertension emerged as a significant negative predictor of treatment response in this cohort. This association can be explained by the fact that systemic hypertension alters vascular structure and function, impairing microcirculation and exacerbating organ dysfunction in septic contexts. Hypertensive patients may also experience differential expression of inflammatory responses, potentially influencing the progression and severity of septic shock [32].

Despite these clear associations, the study also highlighted other less commonly discussed factors, such as GGT and BUN, which were negatively correlated with treatment response. Elevated GGT levels, often indicative of liver dysfunction, may reflect hepatic stress or broader systemic oxidative stress responses. Similarly, increased BUN can indicate renal impairment, a common complication of severe sepsis and septic shock [33, 34], which impairs the body's ability to eliminate metabolic waste, further worsening the patient's overall condition.

In addition to the inflammatory markers, the study found a positive correlation between PLT and the CD4+/CD8+ ratio with treatment response. Platelets play a critical role in hemostasis and are increasingly recognized for their role in the immune response to sepsis, possibly through interaction with leukocytes and modulation of microvascular inflammation. The CD4+/CD8+ lymphocyte ratio has been proposed as a marker of immune status, where a normal or elevated ratio suggests better immune surveillance and a more robust capacity to respond to infection, enhancing prognosis [35, 36].

The findings of this study emphasize the importance of integrating PCT with other clinical meaurements in the multifactorial context of sepsis. While elevated PCT levels serve as a valuable biomarker for assessing infection and inflammation, understanding patient-specific factors, such as comorbidities and immune status, is equally crucial for optimizing personalized treatment strategy.

While our study offers valuable insight into the predictive value of PCT in assessing therapeutic responses in patients with uroseptic shock, several limitations must be acknowledged. First, the retrospective nature of the study limits control over data collection and the potential influence of confounding variables, which may affect the generalizability of the findings. The reliance on a single-center dataset may not represent broader populations or diverse

healthcare settings. Additionally, variability in treatment protocols and timing of PCT measurements could influence the observed associations. Finally, the study did not account for the effects of concurrent infections or underlying conditions that may independently alter PCT levels. Further research is needed to establish causal relationships and validate these findings in diverse and prospective cohorts.

In conclusion, our study supports the predictive value of PCT levels for assessing therapeutic responses among patients with uroseptic shock. These findings suggest that PCT measurement should be incorporated into standard practice for managing sepsis, aiding in the differentiation between responders and non-responders to therapy and guiding timely adjustments in treatment strategy. Future research should focus on prospective studies to validate these relationships in larger populations, exploring the mechanistic pathways through which PCT correlates with disease severity and treatment outcome.

Disclosure of conflict of interest

None.

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