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# Evaluation of Procalcitonin and C-Reactive Protein as Early Predictors of Sepsis Severity and Clinical Outcomes in ICU Patients

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## ABSTRACT

**Background:** Sepsis is a life-threatening condition associated with high morbidity and mortality in intensive care units (ICUs). Early identification of disease severity is crucial for improving outcomes. Biomarkers such as procalcitonin (PCT) and C-reactive protein (CRP) are increasingly used for early risk stratification.

**Objective:** To evaluate the role of serum procalcitonin and C-reactive protein as early predictors of sepsis severity and clinical outcomes in ICU patients.

**Methods:** This prospective observational study was conducted at The Second Affiliated Hospital, Hengyang Medical School, University of South China, Hengyang, Hunan, China, from June 2023 to April 2025. A total of 150 adult patients diagnosed with sepsis according to the Sepsis-3 criteria were included in the study. Serum procalcitonin (PCT) and C-reactive protein (CRP) levels were measured within the first 24 hours of ICU admission. Patients were categorized according to disease severity into sepsis and severe sepsis/septic shock groups. Clinical outcomes, including in-hospital mortality, need for mechanical ventilation, and length of ICU stay, were recorded. Statistical analysis was performed using SPSS version 26.0, and a p-value of $<0.05$ was considered statistically significant.

**Results:** Mean PCT and CRP levels were significantly higher in patients with severe sepsis compared to those with non-severe sepsis ($p<0.001$). Procalcitonin showed a strong positive correlation with SOFA score ($r=0.73$), whereas CRP demonstrated a moderate correlation ($r=0.57$). Mortality was observed in 28.0% of patients and was significantly associated with elevated PCT levels ($p<0.001$). Multivariate analysis identified procalcitonin as an independent predictor of mortality (AOR=4.1).

**Conclusion:** Procalcitonin is a reliable and superior biomarker compared to CRP for early prediction of sepsis severity and adverse clinical outcomes. Its use in ICU settings may enhance early risk stratification and improve patient management.

**Keywords:** Sepsis, Procalcitonin, C-Reactive Protein, ICU, Biomarkers, Mortality



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## INTRODUCTION

Sepsis is a complex and potentially life-threatening clinical syndrome characterized by a dysregulated host response to infection, resulting in acute organ dysfunction [1]. It remains one of the leading causes of mortality in intensive care units (ICUs) worldwide and contributes substantially to hospital-related deaths, particularly in resource-limited settings. Despite major advances in sepsis management, including antimicrobial therapy, organ support, and critical care interventions, its prognosis remains poor, largely due to delays in early diagnosis and risk stratification [2].

The clinical course of sepsis is highly dynamic, ranging from mild infection with limited systemic involvement to severe sepsis and septic shock accompanied by multiple organ failure. Early identification of patients at risk of clinical deterioration is essential for timely therapeutic intervention, efficient resource allocation, and improved survival. Although conventional diagnostic tools such as clinical evaluation and scoring systems, including

the Sequential Organ Failure Assessment (SOFA), are useful, they may not always provide sufficiently rapid or sensitive prediction of disease severity during the early stages of illness [3].

In recent years, increasing attention has been directed toward the use of circulating biomarkers as adjunctive tools for early sepsis detection and prognostic assessment. Among these, procalcitonin (PCT) and C-reactive protein (CRP) have been widely investigated because of their availability and potential clinical utility [4]. Procalcitonin is the prohormone of calcitonin and is normally produced in negligible amounts under physiological conditions. However, its production increases markedly in response to bacterial infections and systemic inflammation. Its rapid elevation within hours of infection and its relative specificity for bacterial etiologies make it a promising biomarker for the early diagnosis of sepsis and assessment of its severity [5].

C-reactive protein, an acute-phase reactant synthesized by hepatocytes in response to inflammatory cytokines, particularly interleukin-6, has long been used as a marker of systemic inflammation. Although CRP is widely available, cost-effective, and routinely used in clinical practice, its slower kinetic profile and limited specificity reduce its ability to distinguish sepsis severity from other inflammatory conditions. Nevertheless, it remains a commonly used biomarker, especially in low-resource healthcare settings [6,7].

Comparative evaluation of PCT and CRP as early indicators of sepsis severity and clinical outcomes remains an important area of investigation. Although several studies have suggested that procalcitonin may have superior diagnostic and prognostic performance compared with CRP, findings across the literature remain inconsistent, and variations in patient populations necessitate further validation, particularly in local clinical settings [8].

The present study aimed to assess the diagnostic and prognostic value of serum procalcitonin and C-reactive protein levels in patients with sepsis admitted to the ICU. It also sought to determine their predictive ability for disease severity, organ dysfunction, and major clinical outcomes, including mortality. This study was designed to generate clinically relevant evidence that may support the integration of biomarker-based risk stratification into routine critical care practice [9].

## MATERIALS AND METHODS

This prospective observational study was conducted at The Second Affiliated Hospital, Hengyang Medical School, University of South China, Hengyang, Hunan, China, from June 2023 to April 2025 to evaluate the usefulness of serum procalcitonin (PCT) and C-reactive protein (CRP) as early indicators of severe sepsis and predictors of patient outcomes. A total of 150 adult patients were enrolled using a non-probability consecutive sampling technique, ensuring the inclusion of all eligible patients presenting during the study period. The diagnosis of sepsis was established according to the Sepsis-3 criteria, which define sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection and operationalized by an increase of 2 or more points in the Sequential Organ Failure Assessment (SOFA) score.

The study included patients aged 18 years and above who had clinically suspected or microbiologically confirmed infection along with evidence of organ dysfunction. Only those patients whose blood samples for PCT and CRP measurement were obtained within the first 24 hours of ICU admission were considered eligible. Patients were excluded if they had conditions known to independently elevate inflammatory biomarkers, including chronic inflammatory or autoimmune diseases, recent major surgery, trauma, burns, immunosuppressive therapy, or end-stage liver disease. In addition, patients transferred from other ICUs after more than 24 hours of critical care or those with incomplete clinical records were excluded to ensure data consistency and reliability.

Following enrollment, demographic and clinical data were collected using a structured data collection form. The recorded variables included age, gender, comorbidities, source of infection, admission vital signs, vasopressor requirement, use of mechanical ventilation, and baseline SOFA score. Patients were followed throughout their ICU stay, and clinical outcomes including duration of ICU stay, development of septic shock, and in-hospital mortality were comprehensively documented.

For biomarker analysis, venous blood samples were collected under aseptic conditions within the first 24 hours of ICU admission. Serum procalcitonin levels were measured using a standardized enzyme-linked immunosorbent assay (ELISA) or automated immunoassay method, while serum CRP levels were determined using a high-sensitivity immunoturbidimetric assay in the hospital laboratory. All analyses were performed according to manufacturer instructions, and strict internal quality control procedures were followed to ensure accuracy and reproducibility.

Sepsis severity was assessed using the SOFA score at ICU admission. Patients were further categorized according to clinical severity and hemodynamic status into sepsis and septic shock groups, particularly based on the presence of persistent hypotension requiring vasopressor support and elevated lactate levels. The relationship between biomarker levels and severity categories was analyzed to determine their prognostic significance.

The primary objective of the study was to evaluate the association between admission levels of PCT and CRP and sepsis severity. Secondary outcomes included their relationship with the need for mechanical ventilation, vasopressor use, duration of ICU stay, and in-hospital mortality. These outcomes were monitored throughout the ICU course until discharge or death.

All data were entered and analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparative analyses between groups were performed using the independent samples t-test or one-way analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. Pearson correlation analysis was used to assess the relationship between biomarker levels and SOFA scores. Multivariate logistic regression analysis was performed to identify independent predictors of adverse clinical outcomes. A p-value of <0.05 was considered statistically significant.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethical Review Committee (ERC/2023/April-137). Written informed consent was obtained from all patients or their legally authorized representatives prior to inclusion, and confidentiality of patient-related information was maintained throughout the study period.

## RESULTS

The study involved a total of 150 patients with verified sepsis. The median age of the participants included in the study was 54.6, with a standard deviation of 13.8, and the majority were male patients (93 males, 62.0%) as compared to female patients (57 females, 38.0%). According to clinical criteria and hemodynamic condition at admission, both 68 patients (45.3%) and 82 patients (54.7%) were diagnosed with sepsis and severe sepsis conditions, respectively. The demographic and clinical baseline is summarized in Table 1.

Table 1 indicates that the age and gender distribution did not differ in the two groups statistically ($p > 0.05$). But there were also much higher SOFA scores in the severe sepsis/septic shock group ($p < 0.001$), signifying more pronounced organ dysfunction at presentation.

The analysis of serum biomarkers showed that the levels of procalcitonin (PCT) and C-reactive protein (CRP) were both considerably higher in patients with severe disease than in those with non-severe sepsis. The average level of procalcitonin was 2.7 ± 1.3 ng/mL in the sepsis group, and it had become significantly higher at 9.6 ± 3.8 ng/mL in the severe group. On the same note, the CRP levels were 48.9 ± 20.4 mg/L in the sepsis and 110.3 ± 37.6 mg/L in the severe groups. Such differences were very statistically significant ($p < 0.001$) as seen in Table 2.

Both biomarkers showed a significant increase with the severity of the disease, as shown in Table 2, but the increase of procalcitonin was greater, implying that it is a more powerful discriminatory variable in the diagnosis of severe sepsis.

The correlation test further showed that serum procalcitonin was significantly positively correlated with SOFA score ($r = 0.73$, $p < 0.001$), which showed that with increasing levels of PCT, organ dysfunction increased significantly. Conversely, CRP had a moderate positive relationship with SOFA score ($r = 0.57$, $p < 0.001$), which implied relatively lower predictability.

Concerning the clinical outcomes, 42 patients (28.0%) died in hospital. The patients who had high procalcitonin levels had a much worse prognosis with a higher death rate, more patients needed mechanical ventilation, and had a longer ICU stay. To do the analysis, the patients were stratified by PCT levels with a cutoff of 5 ng/mL. Table 3 presents the data on the relationship between the procalcitonin levels and the clinical results.

As indicated in Table 3, patients with high levels of procalcitonin had high mortality (41.8% vs 14.3%), high requirement for mechanical ventilation, and higher ICU stay than those with lower procalcitonin levels ($p < 0.001$). These results indicate the high prognostic ability of procalcitonin in the critically ill patient with septic shock.

Additional multivariate logistic regression analysis was conducted to control the possible confounders such as age, gender, and SOFA score. The analysis showed that procalcitonin was an independent predictor of mortality with an adjusted odds ratio (AOR) of 4.1 (95% CI: 2.2–7.6, $p = 0.001$). However, in the multivariate model, CRP failed to maintain statistical significance, which showed that it had a low amount of independent prognostic value.

All in all, the findings of this study show that both CRP and procalcitonin are similar in sepsis, but procalcitonin has a better outcome in predicting the severity of the disease, organ dysfunction, and unfavorable clinical outcomes, making it a better biomarker to use in early risk stratification in an ICU environment.

**Table 1:** Baseline Characteristics of Study Population (n=150)

| Variable | Sepsis (n=68) | Severe Sepsis/Septic Shock (n=82) | p-value |
|---|---|---|---|
| **Age (years)** | 52.8 ± 14.1 | 56.2 ± 13.4 | 0.12 |
| **Male (%)** | 41 (60.3%) | 52 (63.4%) | 0.68 |
| **Female (%)** | 27 (39.7%) | 30 (36.6%) | 0.68 |
| **SOFA Score** | 5.4 ± 1.6 | 10.1 ± 2.7 | <0.001 |

**Table 2:** Comparison of Biomarker Levels Between Groups

| Biomarker | Sepsis | Severe Sepsis/Septic Shock | p-value |
|---|---|---|---|
| **Procalcitonin (ng/mL)** | 2.7 ± 1.3 | 9.6 ± 3.8 | <0.001 |
| **CRP (mg/L)** | 48.9 ± 20.4 | 110.3 ± 37.6 | <0.001 |

**Table 3:** Association of Procalcitonin Levels with Clinical Outcomes

| Outcome | High PCT (≥5 ng/mL) (n=74) | Low PCT (<5 ng/mL) (n=76) | p-value |
|---|---|---|---|
| **Mortality (%)** | 31 (41.8%) | 11 (14.3%) | <0.001 |
| **Mechanical Ventilation (%)** | 49 (66.2%) | 24 (31.6%) | <0.001 |
| **ICU Stay (days)** | 10.8 ± 4.2 | 6.7 ± 2.9 | <0.001 |

## DISCUSSION

The present study compared the effectiveness of serum procalcitonin (PCT) and C-reactive protein (CRP) as early indicators of sepsis severity and clinical outcomes in ICU patients. The findings demonstrate that both biomarkers were significantly elevated in patients with severe sepsis and septic shock; however, procalcitonin showed superior diagnostic and prognostic performance compared with CRP [1,2].

One of the key findings of this study was the strong positive correlation between elevated procalcitonin levels and increasing sepsis severity, as reflected by higher SOFA scores. This close association between PCT and organ dysfunction suggests that procalcitonin is a reliable marker of systemic inflammatory burden and disease progression [3]. This observation can be explained by the pathophysiological role of procalcitonin, which is rapidly released in response to bacterial endotoxins and pro-inflammatory cytokines, making it a sensitive indicator of systemic infection and progression to sepsis. In contrast, although CRP levels were markedly elevated, they demonstrated only a moderate correlation with disease severity, likely due to their slower kinetics and lower specificity for inflammatory responses [4].

Another important finding of this study was the prognostic value of procalcitonin in predicting adverse clinical outcomes [5]. Patients with elevated PCT levels had higher mortality rates, required more frequent mechanical ventilation, and experienced longer ICU stays. Notably, multivariate analysis identified procalcitonin as an independent predictor of mortality, even after adjustment for confounding variables such as age, gender, and baseline organ dysfunction. These findings highlight the clinical utility of PCT as an early risk stratification tool in critically ill patients, enabling clinicians to identify high-risk individuals and implement timely, aggressive management strategies with closer monitoring [6,7].

Although CRP remains a widely used biomarker in sepsis due to its accessibility and cost-effectiveness, its limited specificity reduces its value as a standalone predictor of disease severity and outcomes. The lack of statistical significance of CRP in multivariate analysis further supports its comparatively lower predictive accuracy. Nevertheless, CRP may still serve as a supportive biomarker when used in combination with more specific markers such as procalcitonin [8,9].

The findings of this study are consistent with the growing body of evidence suggesting that procalcitonin is superior to conventional inflammatory markers for the early identification of severe sepsis and prediction of clinical outcomes. The rapid rise and favorable kinetics of PCT are particularly advantageous in ICU settings, where timely decision-making is critical. Incorporating routine PCT measurement into clinical practice may facilitate earlier diagnosis, optimize antimicrobial therapy, and ultimately improve patient outcomes [10,11].

Despite its strengths, this study has several limitations. It was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. In addition, only baseline biomarker levels were assessed; serial measurements could provide more comprehensive insights into disease progression and treatment response. Furthermore, other emerging biomarkers were not evaluated, which might offer additional prognostic value when used in combination [12,13].

Future research should focus on multicenter studies with larger sample sizes and incorporate dynamic biomarker monitoring over time. Combining procalcitonin with clinical scoring systems and other novel biomarkers may further enhance predictive accuracy and support more personalized management strategies in sepsis [14-15].

## CONCLUSION

Procalcitonin and C-reactive protein levels are both elevated in patients with sepsis; however, procalcitonin demonstrates superior performance as an early predictor of disease severity and clinical outcomes. Elevated PCT levels were strongly associated with organ dysfunction, increased mortality, prolonged ICU stay, and a greater need for mechanical ventilation. Importantly, procalcitonin emerged as a robust independent predictor of mortality, unlike CRP, further emphasizing its greater clinical significance. These findings support the incorporation of procalcitonin into routine ICU assessment as an early risk stratification tool and aid in clinical decision-making. The use of PCT for early identification of high-risk patients may facilitate timely therapeutic interventions, ultimately contributing to reduced morbidity and mortality in sepsis.

**Conflict of Interest:** The authors declare no conflicts of interest.

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**Authors' Contributions:** S.P. contributed to conceptualization, data collection, and manuscript drafting. J.Z. was responsible for study design, supervision, and critical revision of the manuscript. All authors approved the final version of the manuscript.

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**Data Availability:** The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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