(REVIEW ARTICLE)

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The precision of procalcitonin as a biomarker for sepsis in adult emergency department visits: A systematic review

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Abstract

Background: Sepsis is a life-threatening condition and a significant cause of mortality among patients presenting to emergency departments (EDs). Early diagnosis is essential to initiate treatment and improve outcomes. Procalcitonin (PCT), level increase in response to bacterial infection, has been recently examined for its role in diagnosing and prognosticating sepsis. This systematic review aimed to evaluate the diagnostic accuracy of PCT in adult patients with suspected sepsis in the ED setting.

Methods: The review was conducted in accordance with PRISMA guidelines. We conduct a literature search of PubMed, Scopus, Web of Science, and Google Scholar for studies published between 2015 and 2024. Studies were included if they investigated serum PCT levels in adult ED patients with sepsis and reported diagnostic or prognostic outcomes. Nine eligible original studies were included.

Results: Procalcitonin show a moderate to high specificity in differentiating sepsis from non-infectious conditions. Elevated PCT on admission were associated with higher risks of septic shock, bacteremia, and mortality. Sensitivity differs depending on disease stage and patient population. PCT was enhanced when combined with other biomarkers or scoring systems such as IL-6, MDW, or qSOFA.

Conclusion: PCT is a useful biomarker for early sepsis detection in emergency settings. Its use in combination with clinical tools provide better diagnostic accuracy and improve patient management.

Keywords: Procalcitonin; Sepsis, Biomarkers; Emergency Department; Diagnosis; Prognosis; Systematic Review; Sepsis-3; Qsofa; Bacterial Infection

1. Introduction

Sepsis is a major health problem and leading cause of morbidity and mortality in emergency departments (EDs). Early recognition is important in improving outcomes for patients with sepsis. Early diagnosis is challenging due to the nonspecific clinical signs and delays in microbiological confirmation. Recently, biomarkers were regarded as valuable investigation in addition to clinical assessment. Procalcitonin (PCT) shown a good improvement in the diagnostic accuracy in sepsis management (Cong et al. 2021). PCT is a precursor of calcitonin, normally produced by thyroid C-cells, and upregulated in response to systemic bacterial infections. PCT is less affected by non-infectious inflammation and rises earlier in bacterial infections, giving a good method for early detection of sepsis in the ED setting (Song et al.

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2019). This biomarker get attention for its diagnostic accuracy and its utility in guiding antibiotic stewardship (Nazer et al. 2024).

A multicenter prospective study found that monocyte distribution width (MDW) had a good performance in sensitivity, and PCT had better specificity in adult ED patients suspected of sepsis (Hausfater et al. 2021). PCT differentiate infectious from non-infectious causes of systemic inflammation, it had better specificity when compared to IL-6 and CRP for sepsis diagnosis, its sensitivity differs depending on disease severity and time of measurement (Lee et al. 2022). PCT is useful in predicting progression to septic shock or mortality. Elevated PCT levels upon admission associated with worse outcomes in patients meeting Sepsis-3 criteria (Jekarl et al. 2019). Its utility is limited in specific populations, such as immunocompromised individuals or those with malignancies, where inflammatory responses differ (Moisa et al. 2023). Previous literature suggests the use of PCT in clinical protocols for the evaluation of sepsis in the ED. It can be used as a biomarker for early detection and a tool to improve clinical decision-making in urgent situations (Yan and Zhang 2021). Our systematic review aimed to evaluate the effectiveness of procalcitonin for sepsis diagnosis in adult emergency department patients.

2. Method

Our systematic review was conducted to discuss the effectiveness of procalcitonin (PCT) in adult patients with sepsis. The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.1. Search Strategy and Study Selection

We conduct a comprehensive literature to identify peer-reviewed studies examined the role of PCT in the diagnosis and prognosis of sepsis. We searched for English articles published in the period from 2015 to 2024 in electronic databases (PubMed, Web of Science, Scopus, and Google Scholar). Search terms used include a combination of (procalcitonin, PCT, sepsis, diagnosis, prognosis, mortality, and biomarker). Two authors screened titles and abstracts, and another two authors assessed the full-text articles for eligibility. We reviewed reference lists of included studies to identify any relevant publications. We include 9 original research articles met the inclusion criteria in the final review (Fig 1).

2.2. Inclusion and Exclusion Criteria

Studies were included if they; involved adult patients (≥18 years) with suspected or confirmed sepsis; measured serum procalcitonin levels as a diagnostic or prognostic biomarker; reported diagnostic accuracy, or outcomes such as mortality, septic shock, or bacteremia; used observational (prospective or retrospective) or interventional designs. We exclude studies on pediatric populations or pregnant women; non-original research such as reviews, editorials, and case reports; studies not reporting specific PCT-related outcomes.

2.3. Data Extraction and Synthesis

Data were extracted from each study, including study design, population characteristics, PCT cut-off values, diagnostic tools compared, and key outcomes. Due to heterogeneity in study designs and outcome reporting, a qualitative synthesis was performed. Methodological quality and risk of bias were assessed narratively by evaluating inclusion criteria clarity, sample size, and use of appropriate statistical methods.
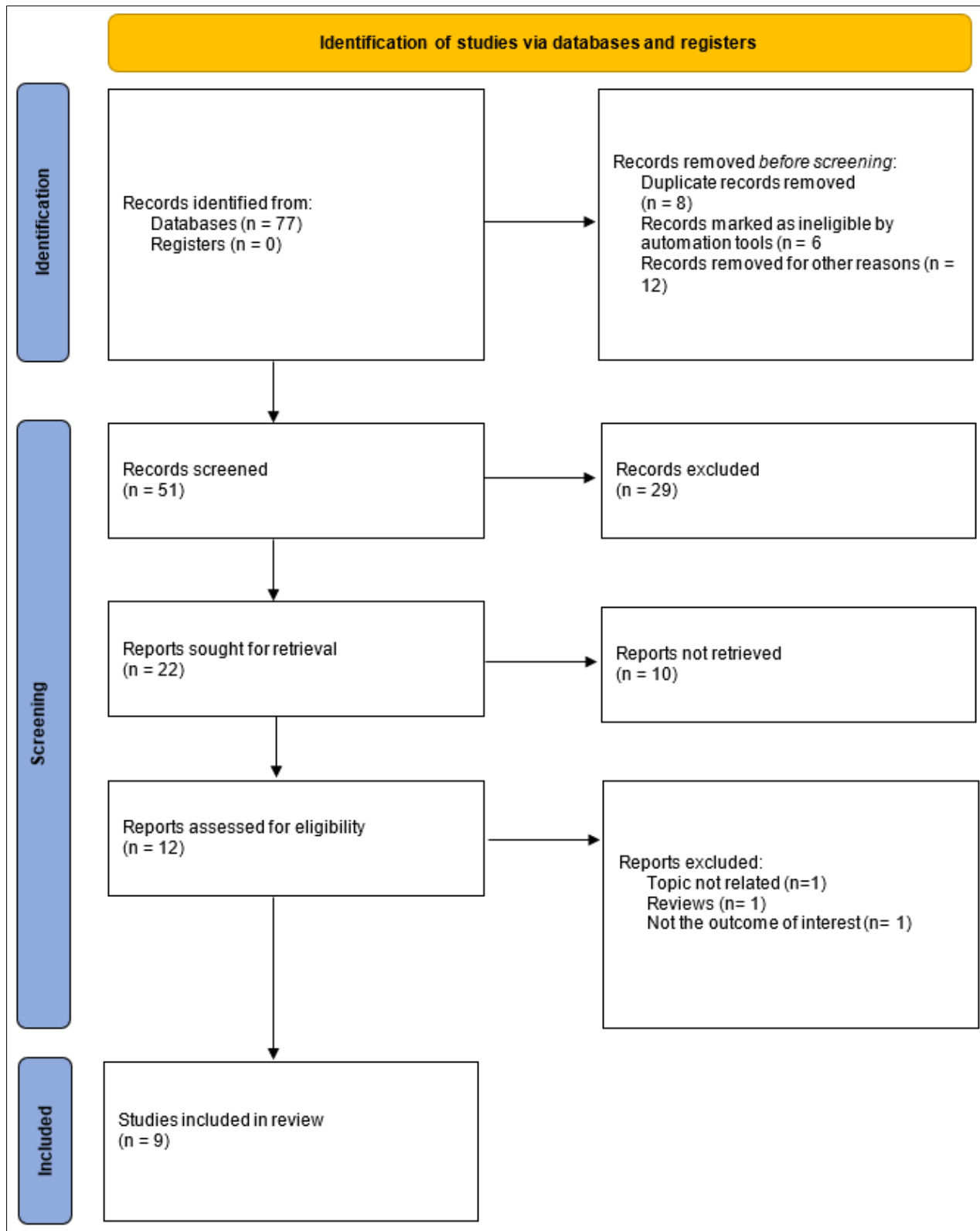
Figure 1 PRISMA consort chart of selected studies

3. Result and discussion

The findings of this study discussed the diagnostic and prognostic utility of procalcitonin (PCT) in the management of sepsis. PCT show moderate to high accuracy in differentiating sepsis from non-infectious conditions and guiding early intervention strategies. A recent systematic review and meta-analysis, conclude that PCT is a reliable biomarker for early diagnosis of sepsis in emergency department patients. The meta-analysis, included nearly 3,000 patients, found that elevated PCT levels correlated with bacterial infections, providing a practical tool to distinguish sepsis from non-infectious SIRS in ED (Zaki et al. 2024). This systematic review found that PCT show a high sensitivity and specificity in multiple cohorts, mainly in distinguishing bacterial sepsis from systemic candidiasis or viral illnesses.

A large retrospective study of febrile hospitalized patients supports the early PCT measurement. The authors found that in patients with qSOFA scores ≥2, early PCT determination was associated with reduced in-hospital mortality (Covino et al. 2021). This supports our finding about early assessment of PCT levels which can provide outcome prediction. Our reviewed studies, including Ko et al. and Mustafić et al., showed that timely measurement of PCT at ED presentation has prognostic value, in predicting septic shock or mortality.

Among HIV populations, PCT has shown similar prognostic relevance. A recent study found that elevated PCT levels (≥0.5 ng/mL) associated with increased in-hospital mortality among HIV-positive patients with fever (Celani et al. 2025). This finding accentuates the biomarker's role in immunocompromised individuals, though caution must be exercised in such subgroups due to variability in immune response. Our findings reflected challenges in immunocompromised populations, in the study by Keçe et al., PCT and lactate showed modest diagnostic performance among cancer patients, which indicate that biomarker thresholds need adjustment in such cohorts.

Our findings support PCT's diagnostic capabilities, and indicate its limitations as a standalone marker. This view is supported by another systematic review, which investigate combinations of biomarkers and clinical scoring systems for mortality prediction in sepsis. The review concluded that PCT, achieved the highest predictive value when integrated with lactate or IL-6 and clinical scores like SAPS-2 or qSOFA (Tong-Minh et al. 2021). This go in line with our analysis of studies like Xie et al. and Woo et al., where PCT's accuracy improved substantially when used with additional markers or clinical scoring tools. These multimodal strategies provide a comprehensive picture of patient status and improve clinical decision-making.

It is important to note that newer biomarkers such as IL-6 and calprotectin emerged. In a recent prospective study, CRP and IL-6 perform better that PCT in identifying infection in patients with suspected sepsis in the ED (Christensen et al. 2022). PCT had a good diagnostic accuracy, but its later peak in comparison to IL-6 limited its use in early detection. Our findings support this conclusion about PCT good specificity, but it was not the most sensitive marker and underachieve in early-stage detection compared to newer indicators like MDW.

Our review supported PCT role in monitoring dynamic changes over time. Several studies, such as Webb et al., indicated the prognostic implications of serial PCT measurements. This dynamic utility was matched in the longitudinal design of Christensen et al., where biomarkers including PCT were tracked throughout the first week of hospitalization. PCT peaked later than IL-6, its tendency over time provided complementary information that helped refine infection recognition and antibiotic management strategies. Characteristics of the included studies presented in (Table 1), intervention and main findings of the included studies presented in (Table 2).

Table 1 characteristics of the included studies

Citation	Study Design	Study Aim	Inclusion Criteria	Methodology
Miglietta et al. 2015	Retrospective cohort	Assess accuracy of PCT, CRP, LDH, and platelet count as early markers for differentiating SIRS, bacterial sepsis, and systemic candidiasis.	ICU patients with ≥2 SIRS criteria and clinical signs of sepsis.	Retrospective analysis; ROC curve analysis for biomarkers differentiation.
Ko et al. 2016	Retrospective cohort	Evaluate initial procalcitonin level as a predictor for progression to septic shock in patients with sepsis from acute pyelonephritis (APN) due to ureteral stones.	Patients presenting to ED with sepsis due to APN from ureteral calculi.	Clinical variables analysis; logistic regression; ROC curves.
Li et al. 2022	Prospective cohort	Compare diagnostic accuracy of monocyte distribution width (MDW) and procalcitonin (PCT) in diagnosing sepsis.	ED patients categorized into non-infection, infection without SIRS, infection with SIRS, and sepsis-3.	Prospective data collection; ROC curves; sensitivity/specificity analysis.
Webb et al. 2020	Retrospective cohort	Evaluate initial and subsequent PCT levels for predicting positive blood cultures, in-hospital mortality, and septic shock.	Patients presenting to ED diagnosed with severe sepsis.	Retrospective review; correlation of PCT levels with clinical outcomes.
Mustafić et al. 2018	Prospective cohort	Evaluate predictive value of PCT in diagnosing sepsis, predicting positive blood cultures, and mortality in septic patients.	Hospitalized patients meeting ≥2 SIRS criteria.	Prospective evaluation; ROC curve analysis.
Keçe et al. 2016	Prospective case-control	Compare diagnostic and prognostic utilities of lactate and PCT in sepsis among adult cancer patients.	Cancer patients in ED with ≥2 SIRS criteria.	Prospective data collection; ROC curve analysis for lactate and PCT.
Xie et al. 2020	Retrospective cohort	Identify biomarkers combination to predict 28-day mortality in sepsis patients upon ED arrival.	ED patients meeting Sepsis-3 criteria.	Multivariate logistic regression; ROC analysis of biomarker combinations.
Lin et al. 2017	Retrospective cohort	Evaluate diagnostic value of PCT, lactate, and hs-CRP in predicting bacteremia in adult ED patients.	Adult patients suspected of having sepsis in the ED.	ROC analysis; sensitivity, specificity, and diagnostic odds ratio evaluations.
Woo et al. 2021	Prospective cohort	Compare monocyte distribution width (MDW) with CRP and PCT for early sepsis detection.	Adults (18-80 years) visiting the ED.	Prospective data collection; ROC analysis; diagnostic performance analysis.

Table 2 Intervention and main findings of the included studies

Citation	Demographic Characteristics	Intervention	Outcome	Main Findings
Miglietta et al. 2015	145 ICU patients, mean age 63 years	Measurement of PCT, CRP, LDH, Platelets	Differentiation accuracy among SIRS, bacterial sepsis, candidiasis	PCT and CRP significantly higher in bacterial sepsis than in SIRS and candidiasis
Ko et al. 2016	49 patients with ureteral stones, mean hospitalization =12 days	Initial procalcitonin measurement	Prediction of septic shock	High initial PCT level independently predicts progression to septic shock
Li et al. 2022	402 ED patients, divided into 4 groups	Monocyte distribution width and PCT measurement	Diagnostic accuracy for sepsis	Combination of MDW and WBC provides better sensitivity and specificity compared to PCT alone
Webb et al. 2020	ED patients with severe sepsis; median initial PCT 0.58 ng/mL	Initial and subsequent PCT measurement	Predictive correlation with positive blood cultures, mortality, and septic shock	PCT >2.0 ng/mL significantly correlates with positive blood cultures, mortality, and septic shock
Mustafić et al. 2018	106 hospitalized patients with ≥2 SIRS criteria	PCT, CRP, lactate measurement	Sepsis diagnosis accuracy and 28-day mortality prediction	PCT shows excellent predictive value for sepsis diagnosis and mortality prediction
Keçe et al. 2016	86 cancer patients, mean age 61 years	Measurement of lactate and PCT	Diagnostic/prognostic utility in sepsis	Neither lactate nor PCT alone reliably differentiates sepsis from non-infectious SIRS
Xie et al. 2020	90 sepsis patients, 28-day follow-up	IL-6, PCT, lactate, neutrophil-to-WBC ratio	28-day mortality prediction	Combination of IL-6, PCT, lactate, NWR provides best predictive accuracy for mortality
Lin et al. 2017	886 ED patients suspected of sepsis	Measurement of PCT, lactate, hs-CRP	Prediction of positive blood bacterial culture	PCT outperforms lactate and hs-CRP in predicting positive blood cultures
Woo et al. 2021	549 ED patients (18-80 years)	Measurement of MDW, CRP, PCT	Diagnostic accuracy for early sepsis	MDW comparable to CRP and PCT; combination with qSOFA enhances sepsis detection accuracy

List of abbreviations

- PCT: procalcitonin,
- ED: emergency department,
- SIRS: systemic inflammatory response syndrome,
- CRP: C-reactive protein,
- IL-6: interleukin-6,
- MDW: monocyte distribution width,
- qSOFA: quick Sequential Organ Failure Assessment,
- ICU: intensive care unit,
- AUC: area under the curve,
- PLWH: people living with HIV,
- DDD: defined daily dose,
- ROC: receiver operating characteristic,
- WBC: white blood cell,
- COVID-19: coronavirus disease 2019,
- SAPS-2: Simplified Acute Physiology Score II.

4. Conclusion

PCT is validated in multiple settings as a good biomarker for sepsis diagnosis, severity assessment, and prognosis. It provides high specificity and better than clinical scoring systems or other biomarkers like MDW, IL-6, or WBC. Future researches should focus on PCT multimodal diagnostic algorithms to improve early detection and guide therapeutic interventions more effectively.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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