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LABORATORY EVALUATION OF PRESEPSIN AND PROCALCITONIN VERSUS C-REACTIVE PROTEIN AND WHITE BLOOD CELLS FOR SEPSIS DIAGNOSIS IN ADULTS

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Abstract

Background: Early and accurate discrimination of sepsis from non-infectious systemic inflammation is essential to guide antimicrobials and improve outcomes. Novel biomarkers presepsin (sCD14-ST) and procalcitonin (PCT) may outperform traditional markers (C-reactive protein [CRP], white blood cell count [WBC]). **Methods:** Following PRISMA principles, we synthesized eight investigator-provided original studies evaluating diagnostic performance of presepsin and/or PCT against CRP/WBC in adults with suspected infection across emergency and intensive-care settings (n=1,180 patients/samples). Primary outcomes were area under the ROC curve (AUC), sensitivity and specificity. Risk of bias was appraised qualitatively. Narrative synthesis was chosen due to between-study heterogeneity (assay platforms, thresholds, reference standards). **Results:** Presepsin showed high diagnostic accuracy in multiple cohorts: AUC 0.908 with sensitivity 87.8% and specificity 81.4% at 600 pg/mL; AUC 0.709 under Sepsis-3 in ED and differentiated septic shock from sepsis, correlating with SOFA. PCT generally exceeded CRP; in one ICU cohort, PCT AUC 0.776–0.816 depending on cut-off, while presepsin AUC 0.734. In severe sepsis/septic shock, presepsin AUCs 0.72–0.84 and prognostic value for mortality. **Conclusion:** Across heterogeneous adult populations, presepsin and PCT consistently outperform CRP/WBC for diagnosing sepsis, with presepsin offering additional severity/prognostic insights. Evidence supports using these biomarkers alongside clinical scores and cultures rather than in isolation.

Keywords: Sepsis; Presepsin; Procalcitonin; C-Reactive Protein; White Blood Cells; Diagnostic Accuracy; ROC.

INTRODUCTION

Rapid, reliable identification of sepsis remains challenging because clinical features over

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lap with sterile systemic inflammatory response syndromes; delayed recognition drives mortality and resource use. Traditional markers, CRP and WBC, are sensitive but non-specific, with slow kinetics and extensive elevation in non-infectious inflammation, limiting their rule-in value. Procalcitonin (PCT), a calcitonin prohormone induced by systemic bacterial stimuli, rises within hours, normalizes with recovery, and has been proposed to guide antibiotic decisions and differentiate bacterial from viral etiologies [1,2].

Presepsin (soluble CD14-subtype, sCD14-ST) represents a complementary host-response signal generated during monocyte/macrophage activation and bacterial phagocytosis; levels increase rapidly during bacterial infection and may reflect severity [3,4]. Because presepsin biology is tightly coupled to innate immune recognition (CD14/TLR signaling), it has been investigated as an early diagnostic and prognostic marker across ED and ICU cohorts, including under Sepsis-3 definitions [4].

Meta-analyses suggest that PCT generally outperforms CRP for diagnosing sepsis (summary AUC = 0.85 vs 0.73) [5], although accuracy varies with thresholds and populations. For presepsin, pooled estimates show moderate-to-high accuracy (AUC = 0.86–0.89), again with inter-study heterogeneity and caution against solitary use [6,7]. Comparative syntheses indicate presepsin performs similarly to PCT overall, with potential sensitivity advantages in ICU at the expense of specificity [8]. In the ED specifically, updated evidence still characterizes PCT as a moderately accurate early biomarker [9]. Given growing bedside availability of chemiluminescent assays and divergent results between settings (ED vs ICU), we synthesized eight original studies provided by the investigator, comparing presepsin and/or PCT to CRP/WBC against clinical and culture-based standards. We also used nine contemporary reviews/meta-analyses to contextualize diagnostic and prognostic implications [1–5]. Our objective was to describe the diagnostic accuracy and practical roles of these biomarkers and to highlight where each contributes beyond CRP/WBC.

METHODS

Design and protocol. We conducted a systematic review aligned with PRISMA principles focusing on diagnostic accuracy of presepsin and/or PCT versus CRP/WBC for adult sepsis. The review synthesized eight investigator-provided original studies.

Eligibility criteria. We included prospective/retrospective ED or ICU cohorts of adults with suspected infection that reported at least one diagnostic performance metric (AUC, sensitivity, specificity, likelihood ratios or odds ratios) for presepsin and/or PCT, with a clinical reference (Sepsis-2/Sepsis-3 adjudication, culture positivity, organ dysfunction) and/or bacteremia. Studies exclusively in neonates/children, purely prognostic analyses without diagnostic endpoints, or lacking comparators were excluded.

Data items & outcomes. We abstracted sample size, care setting, biomarker assays and thresholds, and diagnostic metrics (AUC; sensitivity/specificity; OR for sepsis; bacteremia prediction). Where multiple thresholds were reported, we prioritized widely used cut-offs (PCT 0.25/0.5/1.0 ng/mL; presepsin 500–700 pg/mL) [10–13].

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Risk of bias. Two reviewers qualitatively considered QUADAS-2 domains (patient selection, index test, reference standard, flow/timing). Heterogeneity was anticipated given differing case mixes (ED vs ICU), definitions (Sepsis-2 vs Sepsis-3), and platforms (PATHFAST vs ELISA) [4].

Synthesis. We performed narrative synthesis with structured tables because of heterogeneous designs and endpoints and because the objective was a focused review of the provided studies rather than a de-novo meta-analysis.

RESULTS

Study characteristics

Eight studies (2012–2023) across ED and ICU settings evaluated presepsin and/or PCT against traditional markers (Table 1). Sample sizes ranged from 73 ICU patients [16] to 2,697 consecutive hospital samples [17]; several used PATHFAST chemiluminescent presepsin assays; others used ELISA [15].

Table 1: Included study characteristics (index tests, setting, sample size, reference standard)

Study (year)	Setting / population	Index tests	n	Reference & notes
Endo et al. (2012)	Multicenter suspected sepsis	Presepsin, PCT, IL-6	207	Clinical adjudication; ROC & cut-off 600 pg/mL [11].
Nargis et al. (2014)	Mixed ICU (Bangladesh)	PCT vs CRP	73	ACCP criteria; multiple serial measurements [16].
Joen & Ji (2015)	Hospitalized pts; lab dataset	PCT vs CRP	2,697 samples	Retrospective; culture-positive vs negative comparison [17].
Juneja et al. (2023)	Medical ICU (India)	Presepsin, PCT, CRP	100	Sepsis per guidelines; AUCs & mortality prognostics [12].
Behnes et al. (2014)	ICU severe sepsis/septic shock	Presepsin, PCT, IL-6, CRP, WBC	116	Day 1/3/8 kinetics; severity & mortality prognostics [13].
Ulla et al. (2013)	ED SIRS/sepsis	Presepsin vs PCT	189 (106 suspected sepsis + 83 SIRS)	Time-0/24/72 h sampling; mortality [14].
Contenti et al. (2019)	ED suspected infection (Sepsis-3)	Presepsin, PCT, CRP, lactate	359	Sepsis & bacteremia; predefined cut-points [10].
Aliu-Bejta et al. (2020)	ICU sepsis vs septic shock	Presepsin, PCT, CRP; SOFA	100	Sepsis-3; ELISA presepsin; severity correlation [15].

Diagnostic accuracy, presepsin

In the landmark multicenter cohort, presepsin discriminated bacterial vs non-bacterial disease with AUC 0.908, sensitivity 87.8%, specificity 81.4% at 600 pg/mL; PCT AUC was similar (0.905) and IL-6 lower (0.825) [11]. Blood-culture sensitivity was 35.4% versus presepsin 91.9%, highlighting host-response advantages for early diagnosis [11].

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In ED populations adjudicated by Sepsis-3, presepsin AUC was 0.709, comparable to PCT (0.711), and the predefined 500 pg/mL cut-point yielded an odds ratio of 3.19 for sepsis; adding presepsin to PCT did not materially improve the AUC [10]. Ulla et al. observed lower presepsin diagnostic AUC (0.701) than PCT (0.875) at ED presentation, but presepsin was prognostic for 60-day mortality whereas PCT was not [14].

In ICU cohorts enriched for severe sepsis/shock, presepsin levels increased with severity, achieving diagnostic AUC 0.72–0.84 for severe phenotypes across days 1–8 and demonstrating prognostic AUCs 0.64–0.71 for 30-day/6-month mortality. Quartile analyses showed markedly higher death risk in the highest presepsin quartile [13]. Aliu-Bejta et al. further showed presepsin (ELISA) distinguished septic shock from sepsis at admission (mean ± SD 128.5 ± 47.6 ng/mL vs 88.6 ± 65.6 ng/mL) and correlated strongly with SOFA across serial measures [15].

Diagnostic accuracy, procalcitonin vs traditional markers

Across multiple settings, PCT outperformed CRP as a diagnostic marker of sepsis. In a mixed ICU, PCT sensitivity/specificity were 76%/72%, with positive likelihood ratio 2.75 and lower negative likelihood ratio than CRP; both markers rose with sepsis severity, but PCT's kinetics favored earlier diagnosis and monitoring [16]. In a large hospital dataset, PCT's AUC was 0.743 (threshold 0.5 ng/mL) compared to CRP's 0.540; both differed between culture-positive and culture-negative subsets [17]. Juneja et al. (ICU) compared all three: for sepsis diagnosis, PCT AUCs were 0.776 (cut-off 0.5 ng/mL) and 0.816 (1.0 ng/mL), while presepsin AUC was 0.734 and CRP 0.725; none predicted ICU mortality with high accuracy, reinforcing diagnostic rather than prognostic use for PCT/CRP [12].

Bacteremia prediction and combined strategies

Where assessed, PCT better predicted bacteremia than presepsin, with AUC 0.835 versus lower values for other markers [10]. Presepsin often added severity/prognostic signal [14,13,15]. Combining presepsin with PCT did not improve ED diagnostic AUC beyond PCT alone [10], but serial presepsin trajectories in ICU may stratify risk over the first week [13].

Table 2: Selected diagnostic performance metrics

Study	Biomarker (cut-off)	AUC	Sens	Spec	Notable findings
Endo 2012	Presepsin (600 pg/mL)	0.908	87.8%	81.4%	PCT AUC 0.905; cultures sens 35.4% vs presepsin 91.9% [11].
Contenti 2019	PCT (0.25 ng/mL)	0.711	—	—	OR 2.51 for sepsis; bacteremia AUC 0.835 [10].
Contenti 2019	Presepsin (500 pg/mL)	0.709	—	—	OR 3.19 for sepsis; combo with PCT no AUC gain [10].
Nargis 2014	PCT	—	76%	72%	Better LR– than CRP; earlier kinetics [16].

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Joen & Ji 2015	PCT (0.5 ng/mL)	0.743	—	—	CRP AUC 0.540; culture subgroup differences [17].
Juneja 2023	PCT (0.5/1.0 ng/mL)	0.776 / 0.816	—	—	Presepsin AUC 0.734; CRP 0.725 [12].
Behnes 2014	Presepsin	0.72–0.84	—	—	Severity & mortality prognostics; day 1–8 profiling [13].
Aliu-Bejta 2020	Presepsin (ELISA)	—	—	—	Higher in shock vs sepsis; strong SOFA correlation [15].

Risk of bias and applicability

Some ED studies applied Sepsis-3 with pre-specified cut-points [10], whereas earlier ICU studies used Sepsis-2/ACCP-SCCM and diverse reference standards. Retrospective designs and sample-level analyses may inflate precision [17], and single-center ICU cohorts limit generalizability [12]. Assay heterogeneity (PATHFAST vs ELISA) may affect presepsin values [4].

DISCUSSION

This review in eight cohorts shows consistent superiority of host-response biomarkers over traditional inflammatory markers. PCT repeatedly outperformed CRP on accuracy and timeliness, aligning with meta-analytic evidence [5,9]. Presepsin's performance varied by setting: very strong in multicenter suspected sepsis [11] and in ICU severe phenotypes with prognostic value [13,15], but only moderate in ED under Sepsis-3 [10] and lower than PCT in one ED cohort [14].

Our findings mirror broader syntheses: pooled presepsin AUCs near 0.86–0.89 with modest LR+ (=3–5) and LR– (=0.2) support its use as an adjunct rather than a stand-alone rule-in test [6,7]. Comparative meta-analysis shows presepsin ≈ PCT overall, with ICU-specific sensitivity advantages but lower specificity, consistent with our ICU signal for severity tracking [8,13,15]. Mechanistically, presepsin reflects monocyte/macrophage CD14-mediated activation and may capture a facet of host response distinct from PCT's systemic pro-inflammatory signature [3,4].

Clinically, PCT is a practical first-line biomarker to aid early risk assessment and antimicrobial stewardship, especially in ED, while presepsin adds value for ICU severity stratification and potential mortality prediction, and in scenarios where culture sensitivity is low or time-to-result is critical [11,1]. Importantly, meta-evidence and reviews emphasize integrating biomarkers with clinical scores (SOFA/qSOFA) rather than replacing bedside assessment [3,1].

Heterogeneity in thresholds (presepsin 500–700 pg/mL; PCT 0.25–1.0 ng/mL), platforms (chemiluminescent vs ELISA), and case mix limits cross-study comparability [4]. Retrospective and single-center designs, sample-level analyses, and variable reference standards (Sepsis-2 vs Sepsis-3) introduce bias [14,17].

Use PCT to guide early decisions, particularly when CRP/WBC are non-discriminatory; consider presepsin where available to complement diagnosis and to stratify

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severity/prognosis, especially in ICU and in serial measurements, recognizing that neither should be used in isolation [3,8,1].

CONCLUSION

Presepsin and procalcitonin consistently outperform CRP and WBC for diagnosing sepsis across adult ED and ICU populations. PCT is a pragmatic first-line diagnostic adjunct with better accuracy than CRP and useful antimicrobial-stewardship roles, while presepsin provides comparable diagnostic performance in many cohorts and adds severity/prognostic information, particularly in ICU. Given heterogeneity in thresholds, assays and case mix, clinicians should integrate these biomarkers with clinical scores and microbiology rather than relying on any single test. Future work should standardize cut-offs and evaluate combined, serial biomarker-plus-score strategies under Sepsis-3 frameworks.

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