

Biomarkers Update on Management of Sepsis

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ABSTRACT

Background: Emergency department (ED) overcrowding is a major global health challenge and is associated with increased morbidity and mortality, particularly in septic patients. Delays in diagnosis and treatment contribute to adverse outcomes.

Objective: This review summarizes recent evidence on novel sepsis biomarkers and their role in improving early recognition, risk stratification, and prognosis in ED settings.

Methods: Evidence from international studies, clinical trials, and biomarker research presented in Singapore (October 2025) was analyzed, focusing on procalcitonin (PCT), presepsin, bio-adrenomedullin (bio-ADM), proenkephalin (PenKid), and dipeptidyl peptidase 3 (DPP3).

Results: PCT and Presepsin demonstrated superior specificity for bacterial infections compared to conventional markers. bio-ADM levels correlated with endothelial dysfunction and predicted septic shock. PenKid was validated as an early predictor of acute kidney injury (AKI), independent of comorbidities. DPP3 was identified as a harmful mediator released during cellular damage, strongly associated with circulatory failure and mortality. Clinical trials such as ALBIOS, FROG-ICU, and AdrenOSS confirmed their prognostic and therapeutic implications.

Conclusion: A multimarker approach that combines traditional and emerging biomarkers may enhance sepsis management in overcrowded EDs, enabling timely interventions and improving patient outcomes. Further validation is required before routine clinical implementation.

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Introduction

Overcrowding in emergency departments (EDs) is a critical international issue, with direct implications for patient safety and outcomes [1]. In septic patients, delays in diagnosis and initiation of treatment significantly increase mortality. Conventional diagnostic approaches, including microbiological cultures, are often slow, with results available only after 48 hours or longer. This delay is incompatible with the need for rapid decision-making in sepsis, a condition characterized by heterogeneous and non-specific symptoms that can rapidly progress to multi-organ failure.

To overcome these limitations, research has increasingly focused on biomarkers capable of providing fast, reliable, and clinically relevant information at the point of care. Among them, procalcitonin (PCT), presepsin, bio-adrenomedullin (bio-ADM), proenkephalin (PenKid), and dipeptidyl peptidase 3 (DPP3) have emerged as promising tools for early diagnosis, risk stratification, and outcome prediction.

Methods

This narrative review is based on evidence presented at the Singapore Symposium (October 2025), integrating findings from published literature, randomized trials, and observational studies. Biomarkers were evaluated according to their biological mechanisms, diagnostic and prognostic accuracy, and potential role in guiding clinical management in septic patients presenting to overcrowded EDs.

Results

Procalcitonin (PCT)

PCT, a prohormone of calcitonin, is not normally detectable in the bloodstream of healthy individuals but increases significantly in bacterial infections [2]. Compared with C-reactive protein (CRP), PCT demonstrates greater specificity and correlates more closely with sepsis severity and outcome.

Presepsin

Presepsin (sCD14-ST) is a soluble fragment of CD14 generated during bacterial infections. Several studies have shown its infection-specific expression and potential superiority over traditional markers in differentiating sepsis from other inflammatory conditions [3].

Bio-Adrenomedullin (bio-ADM)

Bio-ADM is a vasoactive peptide involved in endothelial integrity and vascular tone regulation [4]. Elevated bio-ADM levels are associated with vascular leakage, vasopressor use, and mortality in septic shock. Importantly, increases in bio-ADM precede clinical manifestations of shock, suggesting its value for early therapeutic decision-making.

Proenkephalin (PenKid)

PenKid has been validated as a reliable marker of renal function, predicting acute kidney injury (AKI) even in patients with comorbidities. Studies have demonstrated its superiority over

neutrophil gelatinase-associated lipocalin (NGAL) in predicting renal outcomes in septic patients [5,6].

Dipeptidyl Peptidase 3 (DPP3)

DPP3 is an intracellular enzyme released into circulation upon cellular damage. When elevated, DPP3 inactivates key cardiovascular hormones, leading to cardiac depression and circulatory failure. High DPP3 levels are strongly correlated with mortality across multiple cohorts, including burn patients and septic shock (AdrenOSS-1; FROG-ICU).

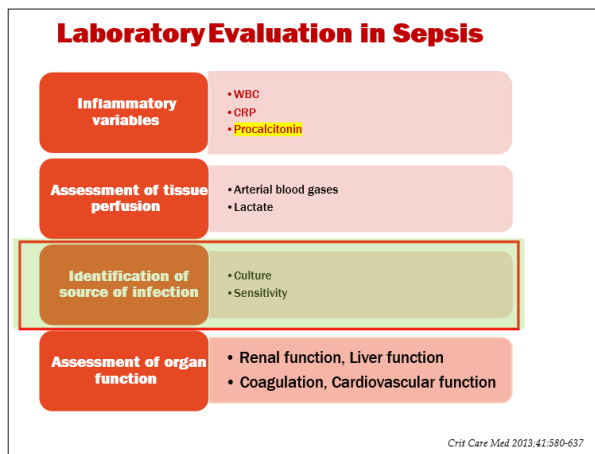
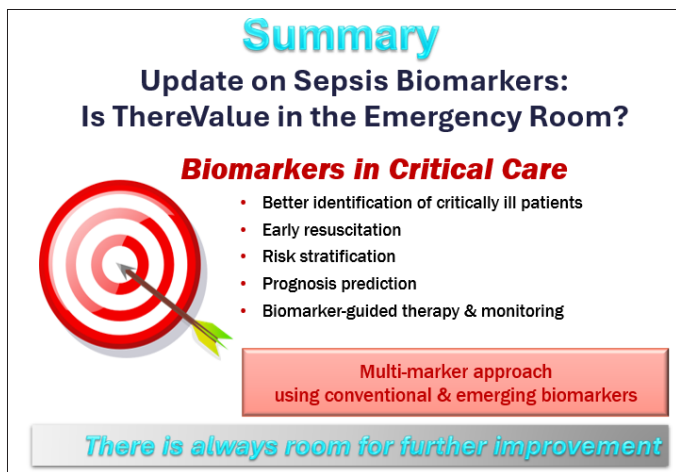


Figure 1: Sepsis and Biomarker Involvement (Placeholder)

Table 1: Summary of key Sepsis Biomarkers and their Clinical Applications (see Results Section)



Discussion

The integration of novel biomarkers into ED practice could substantially improve sepsis care by enabling faster diagnosis, risk stratification, and personalized treatment strategies. While PCT and presepsin aid in early infection detection, bio-ADM provides prognostic information on shock development, PenKid supports renal risk assessment, and DPP3 identifies patients at risk of cardiovascular collapse.

However, challenges remain. The clinical utility of these biomarkers depends on validation in large, multicenter studies, cost-effectiveness analyses, and integration into point-of-care platforms. Moreover, biomarker-guided therapy must be standardized to avoid variability in interpretation.

Conclusion

Sepsis remains a life-threatening condition in overcrowded EDs, where delays in recognition and treatment contribute to poor outcomes. Emerging biomarkers-including PCT, presepsin, bio-ADM, PenKid, and DPP3-show promise in addressing these challenges. A multimarker approach could revolutionize sepsis management, but widespread adoption requires further validation and integration into clinical workflows.

References

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