

NEW BIOMARKERS IN SEPSIS: RECENT ADVANCES, CLINICAL READINESS, AND PERSONALIZED MEDICINE

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Background: Sepsis is a biologically complex and dynamic syndrome defined by a dysregulated host response to infection leading to organ dysfunction. Given its high clinical heterogeneity, conventional diagnostic approaches and static biomarkers often fail to capture real-time disease trajectories, leaving critical gaps in early identification, risk stratification, and targeted intervention.

Objective: To review emerging sepsis biomarkers across multiple biological domains, evaluate their dynamic prognostic and diagnostic capabilities, and assess their current clinical readiness within personalized care frameworks.

Key Domains & Findings:

- **Established vs. Point-of-Care (POC) Biomarkers:** Traditional markers (lactate, CRP, PCT) remain foundational for assessing hypoperfusion and guiding antibiotic de-escalation, though they lack specificity for sepsis endotypes [2, 8]. Novel POC and near-term markers (presepsin, MR-proADM, nCD64, calprotectin, PSP) offer rapid, high-accuracy signaling for early infection, severe endothelial stress, and acute clinical deterioration [4,5].
- **Prognostic Kinetics & Immunophenotyping:** Serial dynamics outperform static baseline measurements. Persistent elevations of cytokines such as IL-6 correlate with elevated 28-day mortality [1,9], whereas alterations in surface markers like mHLA-DR and sIL-7R identify distinct immunoparalysis phenotypes, laying the groundwork for phenotype-guided immunomodulatory therapies.
- **Omics, Epigenetics & Digital Health:** Next-generation tools—including organ-specific cfDNA methylation signatures for sepsis-associated AKI [10], non-coding RNAs like LncRNA HOTTIP [3], transcriptomic multigene panels [7], and targeted lipidomics—enable deep biological endotyping. When integrated with machine learning platforms, multi-omic profiles substantially improve risk prediction models compared to standard clinical scores [6].

Conclusion & Clinical Readiness: While routine markers remain the current standard, near-term biological tests (MR-proADM, presepsin, nCD64) demonstrate high diagnostic and prognostic value. High-dimensional omics and transcriptomic panels require further standardization of assays, prospective validation, and workflow integration before widespread adoption. Optimal clinical utility relies on combining rapid dynamic biomarker profiles, advanced multi-omics/AI modeling, and rigorous clinical assessment.

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