Biomarkers in Sepsis

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KEYWORDS

• Sepsis • Biomarkers • Procalcitonin • Omics technologies • Transcriptomics • Diagnosis • Prognosis

KEY POINTS

- A biomarker is a characteristic by which a pathophysiologic process can be identified.
- In the clinical setting, a biomarker needs to quickly assist physicians confronted with an ill patient in their decision on the best possible treatment.
- Biomarkers can be of diagnostic value, prognostic value, and in the future may be of theranostic value.
- The omics field of systems biology provides a promising tool for the discovery of novel biomarkers.
- Biomarkers, measured in simply obtainable samples with limited hands-on time or need for specialized laboratories, may be the key to personalized targeted treatment in the future clinical management of sepsis.

INTRODUCTION

Sepsis is characterized by complex pathophysiology and heterogeneous phenotypes of affected patients regarding their symptoms, response to treatment, and outcomes. At present there is no gold standard to diagnose sepsis; no tool to select, evaluate, and de-escalate treatment; and no reliable way to assign risk profiles or predict outcome.[1] Biomarkers can be the key to personalized medicine in sepsis whereby patients receive tailored treatment based on their unique characteristics.[2,3]

Biomarkers are naturally occurring molecules, genes, or other characteristics by which particular physiologic or pathologic processes can be identified. In the clinical setting a biomarker is useful once it can aid decision making. The ideal biomarker has

Disclosure: The authors have nothing to disclose.

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Crit Care Clin ■ (2017) ■–■
http://dx.doi.org/10.1016/j.ccc.2017.08.010 criticalcare.theclinics.com

fast kinetics, high sensitivity and specificity, can be identified by fully automated technology, has a short turnaround time, and is available as a point-of-care test with low production costs.[1] A biomarker therefore needs to quickly assist physicians confronted with an ill patient in their decision on the best possible treatment. Current clinical biomarkers can be roughly divided into 2 types: diagnostic and prognostic markers (**Fig. 1**). Biomarkers that can discriminate sepsis from noninfectious critical illness or can differentiate between causative organisms in sepsis can be regarded as diagnostic biomarkers. A diagnostic biomarker can diminish improper use of antibiotics and could be used for antibiotic stewardship. Although pathogen detection remains the gold standard in establishing the cause of infection, blood cultures are only positive in 30% to 40% of the sepsis cases and in one-third of (clinically defined) sepsis cases all cultures are sterile.[4,5] In addition, the presence of a pathogen does not prove the presence of disease and infections can be caused by multiple pathogens, further showing the need for biomarkers that indicate infection. Prognostic biomarkers can help predict outcomes in patients with sepsis by assigning risk profiles. In addition, biomarkers can aid in stratifying patients in subgroups based on specific pathophysiologic features, thereby paving the way to personalized therapy with biomarker-guided follow-up of response to treatment.[6] The approach to using biomarker tests to select and evaluate specific therapies is known as theranostics and is seen as a main tool in the future management of many diseases.[7] Such biomarker tests should be applicable on easily obtained samples such as urine or blood. Rapid testing should identify subgroups of patients that would benefit from certain targeted therapies. The biomarker test could further be of use by evaluating the effect of the therapy on its target.

Biomarkers have been implemented in clinical practice in various fields of medicine, including cardiology (eg, troponin T in myocardial infarction), vascular medicine (eg, D-dimer in patients suspected of pulmonary embolism), and in particular oncology

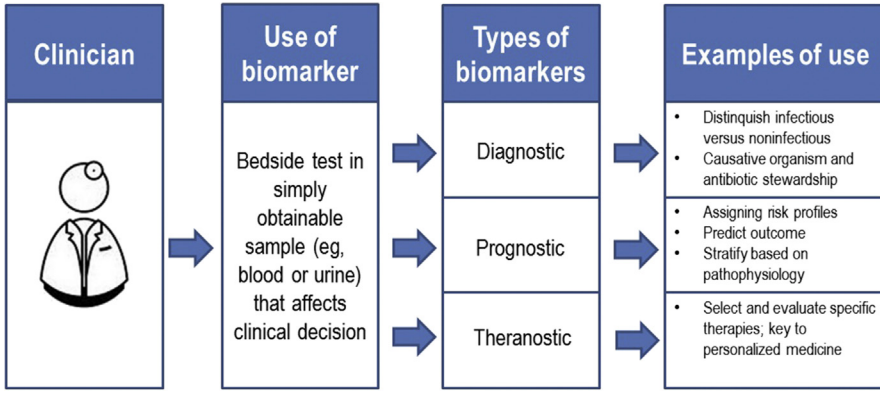

Fig. 1. What is a biomarker? Biomarkers are host characteristics, such as molecules or genes, by which particular physiologic or pathologic processes can be identified. When developing and validating novel biomarkers their potential clinical use is of utmost importance. Biomarkers can be used to distinguish sepsis from noninfectious critical illness or to determine causative pathogens to initiate the best possible treatment, thereby contributing to antibiotic stewardship. Furthermore, biomarkers can help stratify patients based on risk profiles, and predict outcome or identify pathophysiologic pathways that can be the target for personalized therapy. Biomarker tests that select and monitor specific therapies are known as theranostics and are seen as a future aid for a targeted personalized approach in patients with sepsis.