

Personalizing Sepsis Care

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KEYWORDS

• Sepsis • Personalized medicine • Precision medicine • Biomarker • Theranostic

KEY POINTS

- Although sepsis represents a syndrome of organ dysfunction related to a dysregulated host response to infection, it covers a wide range of causative microorganisms and sites of infection in heterogeneous patient populations with differing comorbidities, clinical features, illness severity, and outcomes.
- A 1-size-fits-all approach, adopting a rigid, homogenized treatment approach, is unlikely to offer optimal care to individual patients.
- Biological signatures are increasingly being unraveled that can identify subsets of septic patients who may either respond positively or negatively to therapeutic interventions.
- Rapid access to such biomarker information will allow identification of suitable patients and titration of therapy to optimal effect

PROTOCOLS, GUIDELINES, AND PROCESS OF CARE

The term, *evidence-based guidelines*, first appeared in press in a series of articles in *JAMA* in 1990.¹ These articles differentiated between guidelines based on consensus, evidence, outcomes, and preference and proposed that evidence based should take precedence over the other forms. Sackett and colleagues² later described evidence-based medicine as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.” Crucially, they continued, “Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients.”²

Eddy³ promoted this personalized, educational, bedside-based philosophy, coining the description of “Evidence-based individual decision-making (EBID).” He contended that EBID should be undertaken “by individual physicians, using implicit and personal methods, to make decisions about individual patients and directly determine their care.” He distinguished EBID from evidence-based guidelines, where generic

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guidelines and other policies address the needs of institutions and groups of people and thus affect individual patients indirectly. He argued, “guidelines need to be tailored to individual cases, and EBID improves physicians’ ability to do this. Many problems fall through the cracks of guidelines, and EBID is the only way to get evidence-based medicine to them. Physicians work on guideline teams, and the educational approach of EBID enables them to be better participants. EBID also helps physicians understand the rationale for evidence-based guidelines, which greatly improves their acceptance, especially when the evidence contradicts a time-honored practice.”³

Evidence-based guidelines have been incorporated into clinical practice within critical care, in particular, the management of sepsis and septic shock within the Surviving Sepsis Campaign guidelines.^{4–7} These guidelines perhaps have not taken sufficient note of Sackett and colleagues’ and Eddy’s strictures that individual expertise be brought to bear to guide management of individual patients. Didactic recommendations suit populations but may not be best suited to individuals. Although aiming to raise mediocre or poor practice and offering a framework for management, especially among practitioners who may be inexperienced in dealing with critically ill patients, there is a significant risk that strict adherence to guidelines may, in some cases, detract from best care. This is particularly pertinent when the bulk of recommendations is based on a poor evidence base and, often, a weak strength of recommendation because full consensus could not be achieved among the guidelines committee members. Strict blood pressure targets, fluid resuscitation volumes, and duration of antibiotic therapy are examples of rigid directives applied to patients and situations where a more tailored approach is likely preferable.

Guidelines should perhaps be differentiated from protocols. Although protocols may be viewed as mandatory, guidelines can be perceived as advisory. A protocolized approach can be reasonably applied to processes of care that should happen automatically. This includes, for example, a daily methodical clinical examination, daily review of drug chart and fluid balance, good infection control practices, and an individualized management plan reviewed at least daily. On the other hand, advisory guidelines should incorporate Eddy’s EBID dictum, as described previously. This allows clinicians to be aware of the wider evidence base and follow appropriate general recommendations. Yet it still permits a more flexible management approach that varies according to a patient’s age, comorbidities, condition (cause of sepsis and affected organs), and initial response to treatment.

INDIVIDUALIZED PHYSIOLOGIC ENDPOINTS

As with any critically ill patient, septic or otherwise, one size does not — should not — fit all. Didactic treatment endpoints and management strategies serve a general population but not necessarily individuals. Thus, a hypertensive patient may benefit from a higher targeted blood pressure in sepsis.^{8,9} In other patients, however, a lower-than-recommended mean blood pressure (eg, 55–60 mm Hg) may still be compatible with adequacy of tissue perfusion, thereby avoiding unnecessary and potentially deleterious vasopressor therapy (or high dosing). Avoidance of a rigid mindset and a stepwise evaluation of the adequacy of tissue perfusion at different pressures are key to a likely more beneficial individualized approach. Similarly, fluid resuscitation should not involve fixed-volume administration because patients vary markedly in requirements.¹⁰ Some patients may require much less than 30 mL/kg over the first few hours of sepsis presentation, especially in the presence of significant sepsis-induced myocardial depression because this may be compromised further by

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