Procalcitonin as a Marker of Bacterial Sepsis: Time for a Reappraisal?

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] It is frequently leading to death from septic shock and multi organ failure worldwide. Sepsis can be caused by any infection, either fungal, viral, parasitic, or bacterial, and not all of these pathogens can be cultured. In around half of patients with sepsis, no pathogen is identified.[2] For every hour delayed treatment the risk of mortality from sepsis increases by 4-9%.[3] Sepsis takes 11 million lives around the world each year, contributing to 20% of all deaths globally and taking more lives than cancer.[4] There is more than 20 deaths every minute.[5] Before the onset of organ dysfunction, infections should be identified and this requires a rapid diagnosis and a prompt initiation of treatment.

The signs and symptoms of sepsis are nonspecific and overlap with signs of SIRS of non-infectious origin like burns, poly trauma or severe acute pancreatitis (or an infectious syndrome of nonbacterial origin), making detection of sepsis a clinical challenge. In addition, as traditional standard culture methods are time-consuming, accurate microbial diagnosis can be delayed. Thus, delaying diagnosis and initiating treatment of sepsis is responsible for increased mortality.

The lack of a gold standard test to diagnose specific infection as well as the nonspecific clinical features of sepsis led the continuous development of sepsis biomarkers to help in predicting the diagnosis and prognosis of sepsis and monitoring treatment responses. So far, a large number of trials have identified potential biomarkers. More than 170 biomarkers have been studied for use in evaluation of sepsis including C-reactive protein, procalcitonin, various cytokines, and cell surface markers,[6] among them PCT and CRP being the most frequently studied.

Procalcitonin is considered to have pivotal role in the guidance of antibiotic stewardship. Procalcitonin levels along with clinical evaluation may facilitate the diagnosis of serious bacterial infections and early initiation of antimicrobial agents. In a meta-analysis of 30 studies (3,244 patients), procalcitonin had a pooled sensitivity of 77% and specificity of 79% for sepsis in critically ill patients.[7] Direct evidence from three RCTs that compared procalcitonin-guided protocols for antibiotic initiation vs usual care.[8-10] A meta-analysis of the three trials (n = 1,769 ICU patients) found no difference in short-term mortality, length of ICU stays or length of hospitalization. Long-term mortality, readmission rates, and hospital-free days were not reported in any of the trials, and no relevant studies on the costs associated with use of procalcitonin were found.[11] Guideline of the American Thoracic Society and Infectious Diseases Society of America for the management of community acquired pneumonia recommend initiation of antimicrobials for patients with community acquired pneumonia regardless of procalcitonin level.[12] Elevated PCT levels are also found after surgery, cardiogenic shock, heat shock, acute graft-versus-host disease, and immunotherapy, which could limit its usefulness as a sepsis biomarker.[13] Published guideline issued a weak recommendation against using procalcitonin to guide antimicrobial initiation in addition to clinical evaluation considering no apparent benefit, unknown costs, and limited availability in some settings including low and middle income countries (LMICs).[11] In spite of controversial role in diagnosis it is suggested to use procalcitonin along with clinical evaluation to decide when to discontinue antimicrobials in adults with an initial diagnosis of sepsis or septic shock.

There is an increasing demand for fast and adequate infectious disease diagnostic tests,[14] and special attention should be focused on the features of an ideal diagnostic test—ASSURED— affordable, sensitive, specific, user-friendly, rapid, equipment-free, and delivered to those in need.[15]

Though Numerous biomarkers have been evaluated for clinical use in sepsis, with moderate to good sensitivity and specificity for diagnosis and prognosis, the results of measuring a single biomarker are inconclusive in

clinical settings. In absence of ideal biomarkers which could play a role in sepsis screening, early diagnosis, risk stratification, critical assessment, and prognosis prediction, combination approaches measuring multiple biomarkers along with "Scoring systems", which use both clinical and laboratory biomarkers can guide healthcare professionals to improve outcome of sepsis.

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