Procalcitonin (PCT)

An introduction to sepsis and PCT
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What is sepsis?

Sepsis is a common and frequently fatal medical condition that is the result of the body’s inflammatory response to an infection.\(^1\) Angus, D. et al., reported in *Critical Care Medicine* that 751,000 severe sepsis cases occurred in the US in 1995 and mortality was 28.6%, or 215,000 deaths nationally.\(^1\)

Hall, M.J. et al., reported in a Centers for Disease Control and Prevention (CDC) NCHS Data Brief that US hospitalizations for septicemia or sepsis as the principal or a secondary diagnosis increased from 621,000 in 2000 to 1,141,000 in 2008 (ICD-9-CM diagnosis codes of 038.xx, 995.91 and 995.92).\(^2\)

In 2009, septicemia or sepsis was the single most expensive condition treated in U.S. hospitals. Costs for stays with a principal diagnosis of septicemia totaled nearly $15.4 billion.\(^3\)

Sepsis is defined as a documented or suspected infection together with two or more systemic inflammatory response syndrome (SIRS) criteria (see table below).\(^5,6\)

The importance of early intervention

Early identification and intervention is crucial to improving sepsis outcomes. A retrospective study by Kumar, A. et al., (1989 – 2004) showed that administration of an effective antimicrobial therapy within the first hour of documented hypotension was associated with a survival rate of 79.9%. Each hour of delay in antimicrobial administration over the ensuing 6 hours was associated with an average decrease in survival of 7.6%.\(^7\) However, early identification of sepsis can be challenging due to its non-specific symptoms.

What is Procalcitonin (PCT)?

PCT is the prohormone of calcitonin. Calcitonin is produced exclusively in the thyroid gland. In 2001, Muller, B. et al., found that PCT is ubiquitously and uniformly expressed in multiple tissues throughout the body in response to sepsis. Elevated circulating levels of PCT are important markers in response to microbial infections and a powerful tool in the early detection of sepsis.\(^8\)

When does Procalcitonin rise?

Following stimulus by a bacterial endotoxin or trauma, PCT plasma concentrations:\(^9,10\)

- Rise 3 – 6 hours after bacterial invasion
- Are significant after 6 hours
- Exhibit peak values between 12 – 48 hours
- Have an observed half-life of 24 hours

This rapid and sustained response to bacterially induced systemic inflammation is an important hallmark of PCT as a marker of sepsis risk.
PCT concentrations and sepsis risk\(^{1,12,13}\)

- **Less than 0.5 ng/mL** — Low risk for progression to severe sepsis and/or septic shock.
- **Between 0.5 and 2 ng/mL** — Sepsis should be considered.
- **Greater than 2 ng/mL** — High risk for progression to severe sepsis and/or septic shock.

PCT levels must always be interpreted in the clinical context.

Procalcitonin (PCT) values rise in relation to sepsis severity\(^{11,14}\)

How is PCT different than other biomarkers?

PCT vs. Cytokines

Meisner, M. et al., reported in *Laboratory Medicine* that PCT has a smooth increase over 12 hours and expresses prior to CRP, allowing rapid diagnosis. Unlike cytokines, PCT’s unique kinetics help physicians detect sepsis over a much wider time window than IL-6, IL-10, and TNF-\(\alpha\).\(^{15}\)

PCT vs. lactate and other markers

Lactate can be elevated in many disease states or in cases of poor tissue perfusion. Müller, B. et al. reported in *Critical Care Medicine* that serum PCT concentrations are more sensitive and are specific markers of sepsis as compared with serum lactate, CRP, and IL-6 levels.\(^{12}\)

Challenges with blood cultures for sepsis

The use of blood cultures as the assumed gold standard in sepsis lacks sensitivity or specificity, or both.\(^{16}\) Challenges with relying on blood cultures for sepsis include the delay for response, particularly for slow growing organisms, and limited sensitivity from patients already on antibiotics. Depending on the severity of the sepsis, only 30% – 50% of sepsis patients have positive blood cultures.\(^{17}\)

Important considerations when interpreting PCT results

Increased PCT levels may not always be related to systemic infection. These conditions include, but are not limited to:

- The first days after a major trauma, major surgical intervention, burns, treatment with OKT3 antibodies and other drugs stimulating the release of pro-inflammatory cytokines, small cell lung cancer, medullary C-cell carcinoma of the thyroid, neonates (first 2 days of life).\(^{13,18,19,20}\)
- Patients with prolonged or severe cardiogenic shock or prolonged severe organ perfusion anomalies.

Low PCT levels may also be observed during the early course of infection, in localized infections, and in subacute endocarditis. Therefore, follow-up and re-evaluation of PCT in cases of clinical suspicion of infection is pivotal. PCT values must always be evaluated in light of each patient’s clinical context.
References


2. Hall MJ, et al., Inpatient Care for Septicemia or Sepsis: A Challenge for Patients and Hospital, CDC NCHS Data Brief 2011 June;62.


