

Procalcitonin: A New Tool for Sepsis

White Paper

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Why is procalcitonin (PCT) needed?

Early initiation of therapy in sepsis patients has been shown to reduce the relative mortality risk 0.26–0.8¹ and is associated with improved patient outcomes. Identification of sepsis remains a clinical challenge, often resulting in a late diagnosis and delayed treatment. Clinical studies have suggested that procalcitonin (PCT) has utility as a biomarker of sepsis, as an aid in both diagnosis and prognosis. Increased levels of PCT are associated with a greater likelihood of an adverse outcome.²

Who is at risk for sepsis?

Everyone has some level of risk for developing sepsis: patients with acute and chronic diseases, the very young and the very old, those with indwelling prostheses or medical devices, and the previously healthy. Individuals with underlying health conditions are at higher risk for developing and dying from sepsis. Without timely and appropriate treatment even the previously healthy can die from sepsis.

What is PCT?

PCT is a 116-amino-acid prohormone of the hormone calcitonin. PCT can be produced by several cell types in response to inflammation or infection.^{3,4,5} The exact biological role of PCT remains unknown; however, recent experimental studies suggest that PCT may play a pathologic role in sepsis.³ Bacterial endotoxins and proinflammatory cytokines (IL-1, IL-2, IL-6, TNF α) are powerful stimuli for PCT production.^{3,5,6,7}

How is sepsis defined?

The broad term sepsis encompasses several degrees of disease severity that include SIRS, and are defined as sepsis, severe sepsis, and septic shock (Table 1).^{8,9} These classifications also denote mortality risk. The mortality risk for sepsis increases with disease severity: SIRS<sepsis<severe sepsis<septic shock (Figure 1).

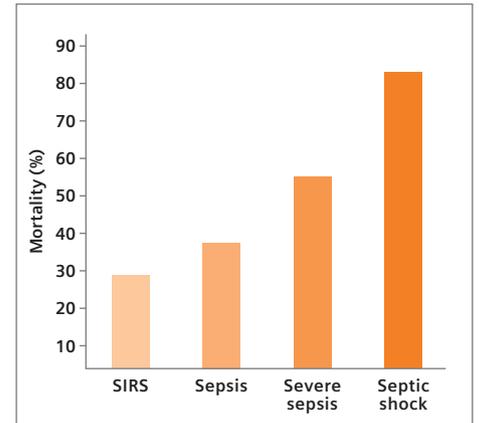


Figure 1. Mortality rates of ICU patients with SIRS, sepsis, severe sepsis, and septic shock.¹⁰

Table 1. Consensus definitions for SIRS, sepsis, severe sepsis, and septic shock.^{8,9}

Condition	Definition
Systemic inflammatory response syndrome (SIRS)	Manifested by two or more of the following conditions: 1. temperature >38°C or <36°C 2. heart rate >90 beats per minute 3. respiratory rate >20 breaths per minute or PaCO ₂ , <32 mm Hg 4. white blood cell count >12,000/ μ L, <4,000/ μ L, or >10% immature (band) forms
Sepsis	Systemic inflammatory response (SIRS) in the presence of a confirmed or suspected infection
Severe sepsis	Sepsis associated with organ dysfunction, hypoperfusion, or hypotension
Septic shock	Sepsis-induced hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities

How do PCT levels relate to disease severity?

PCT measurements can aid clinicians in the diagnosis of sepsis¹¹ (Figure 2) and provide information about the patient's prognosis (Figure 3).² PCT levels typically increase within ~3 to 6 hours of the stimulus.^{3,6} PCT levels are progressively more elevated in SIRS, sepsis, severe sepsis, and septic shock; the highest PCT levels are found in patients with severe sepsis and septic shock (Figure 4).^{2,11} High and increasing PCT levels are associated with poorer prognosis (Figure 3). PCT concentrations can increase up to 1000 ng/mL in patients with sepsis, severe sepsis, or septic shock.^{5,7}

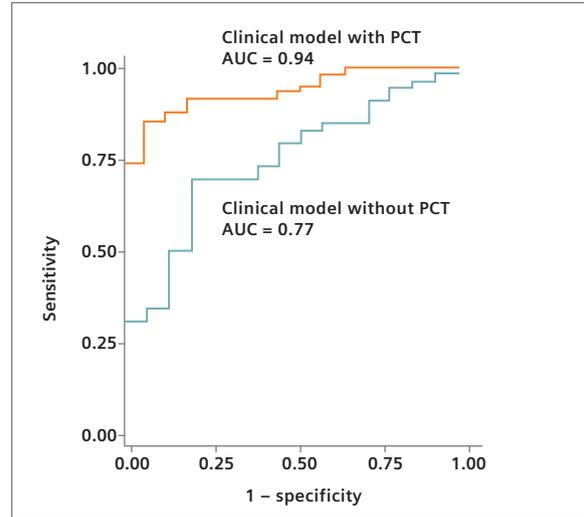


Figure 2. In ROC analysis, the AUC* for diagnosis of sepsis was improved from 0.77 to 0.94 when PCT was included.¹¹

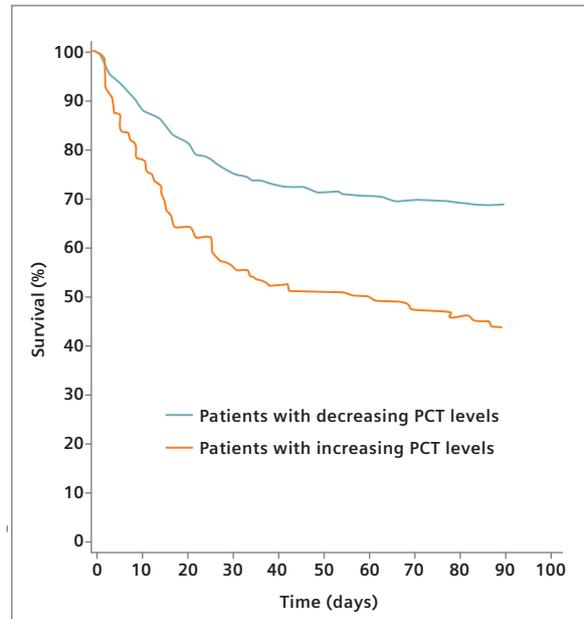


Figure 3. Increasing PCT levels are associated with lower survival.²

*In ROC analysis, the AUC is a measure of diagnostic accuracy: the closer the value is to 1 the more accurate the test.

How can PCT values be interpreted?

In healthy individuals, plasma PCT concentrations are typically below 0.05 ng/mL; PCT concentrations exceeding 0.5 ng/mL are generally considered abnormal.^{5,6} Values in the range of 0.5 to 2 ng/mL may identify patients at risk for sepsis but generally represent a gray zone in terms of the assessment of sepsis and related conditions.^{5,6} PCT levels greater than 2 ng/mL are associated with a high risk of progression to severe sepsis and septic shock in ICU patients (Table 2 and Figure 4).

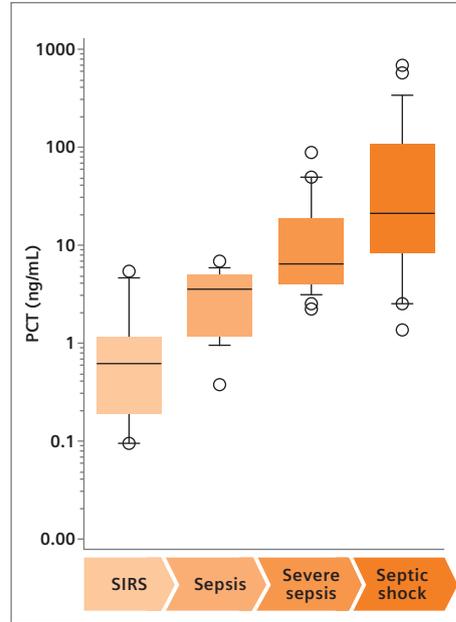


Figure 4. In ROC analysis, the AUC^{*} for diagnosis of sepsis was improved from 0.77 to 0.94 when PCT was included.¹¹

Table 2. PCT levels and possible interpretations.^{6,12,13,14,15}

PCT (ng/mL)	Possible interpretations
<0.05	<ul style="list-style-type: none"> • Normal values • Local inflammation or infection is possible; systemic inflammatory response unlikely
<0.5	<ul style="list-style-type: none"> • On the first day of ICU admission this indicates a low risk for progression to severe sepsis and/or septic shock • Local inflammation or infection is possible; systemic inflammatory response unlikely
≥0.5 and <2.0	<ul style="list-style-type: none"> • Systemic inflammatory response present due to infection, severe trauma, major surgery, or cardiogenic shock • If the patient has a proven infection it could be sepsis
≥2.0 and <10	<ul style="list-style-type: none"> • Likely to be sepsis (systemic inflammatory response associated with infection) • On the first day of ICU admission this indicates a high risk for progression to severe sepsis and/or septic shock
≥10	<ul style="list-style-type: none"> • Severe sepsis or septic shock • Organ dysfunction • High risk of death



Conclusion

Additional tools to aid clinicians in the diagnosis of sepsis are needed because diagnosis, especially early diagnosis, can be challenging. Furthermore, therapy is most effective when administered early. PCT measurements can aid clinicians in making the diagnosis of sepsis and can provide information about patient prognosis.

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