

COMMENTARY

What procalcitonin brings to management of sepsis in the ICU

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See related research by Karlsson *et al.*, <http://ccforum.com/content/14/6/R205>

Abstract

In inflammatory states, particularly in response to infectious stimuli, local procalcitonin (PCT) production rises, and because these tissues cannot further process PCT into calcitonin, serum levels increase. In the critical care setting, PCT should be considered a useful tool to help physicians in some specific, although frequent, situations. Serial measurements of PCT levels may indicate the effectiveness of medical decisions such as the appropriateness of antibiotic therapy, the detection of new infections, and the exclusion of a diagnosis of sepsis. PCT-guided algorithms may also help to decrease the duration of antimicrobial therapy. However, the role of PCT as a prognostic marker in critically ill patients is controversial. In a study by Karlsson and colleagues, PCT concentrations did not differ between hospital survivors and nonsurvivors, but the outcome was better in patients whose PCT concentrations decreased more than 50%. The study of PCT kinetics thus could offer an individual risk assessment in patients with severe sepsis.

In this issue of *Critical Care*, Karlsson and colleagues [1] publish the results of a thorough prospective observational study of the predictive value of procalcitonin (PCT) in 24 intensive care units (ICUs) in Finland at ICU admission and 72 hours later. The success story of PCT in the ICU is based on this biomarker's relative specificity for bacterial infection and its easy and rapid measurement in serum. Although PCT is used in many ICUs every day, the question of whether this biomarker has real usefulness is worth investigating.

PCT for use in the critically ill has four main indications: diagnosis of severe bacterial infection, evaluation of sepsis severity, assessment of the appropriateness of therapy (antibiotics or surgery/drainage), and tailoring of antibiotic prescription (indication and duration) while keeping in mind that bacterial multidrug resistance has prompted the development of strategies to reduce antibiotic consumption. We want many things from biomarkers, perhaps too much! For example, we are still waiting for the ideal biomarker that could help us predict the individual outcomes of patients with severe sepsis and septic shock. Early detection of patients at high vital risk is of utmost importance.

The report by Karlsson and colleagues provides some interesting results but also some disappointing ones. First, the absolute serum PCT level had no direct impact on prognosis. PCT concentrations did not differ between survivors and nonsurvivors at either time point. Does that mean biomarkers are not useful tools to predict outcome? In a recent study of patients with community-acquired pneumonia (most of whom were not admitted to the ICU), PCT was higher in patients who died, but proadrenomedullin performed the best at predicting short- and long-term survival [2]. However, it is hard to imagine that a single biomarker could be a reliable predictor of outcome of patients with severe sepsis. Perhaps the combination of clinical data and several biomarkers would perform better.

Second, much more relevant than a single PCT level are serial PCT determinations after the therapeutic intervention. According to the authors, in-hospital mortality was lower for patients whose PCT concentrations diminished more than 50% by 72 hours compared with those with a decline of less than 50%; however, PCT decrease of more than 50% was not independently associated with outcome. These results mean that future studies should focus on PCT kinetics. Because daily measurement would raise costs, future research should use mathematical models to try to find the best predictive rule, requiring fewer PCT measurements.

Third, 15% of the patients with severe sepsis had low PCT levels. Indeed, it is well known that, in some

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situations (for example, locally restricted inflammatory reactions), PCT levels may stay within the normal range. When antimicrobials are initially withheld, clinical re-evaluation and repeated PCT measurements 6 to 12 hours later are recommended to detect a late peak of PCT level and to ensure that antibiotics are provided to patients who have true bacterial infections [3]. Karlsson and colleagues found that the median PCT concentrations on day 0 were 42% lower in patients with nosocomial infections (44% had pneumonia) in comparison with those with community-acquired infections. This observation is important as it suggests that PCT could be more useful for detection of infection and monitoring of therapeutic interventions in community-acquired infections. The usefulness of PCT as a tool to diagnose ventilator-associated pneumonia (VAP) yielded conflicting results. In one study, the areas under the receiver operating characteristic curves were 0.87 for PCT and 0.96 when PCT was combined with the clinical pulmonary infection score (CPIS) [4]. Another study found that including PCT in the CPIS did not increase its accuracy for the diagnosis of VAP [5], whereas increased PCT improved specificity but not sensitivity [6].

Finally, although high PCT levels may detect a subgroup of patients with positive blood cultures [7], the clinical relevance of this finding is uncertain and would not eliminate the need for drawing blood for cultures, which could be the only way to identify the microorganism.

Clearly, PCT is the most useful biomarker of bacterial infection available for routine use in the ICU. The study by Karlsson and colleagues has the merit of summarizing its advantages and limitations as a tool to diagnose severe sepsis and predict outcome.

Abbreviations

CPIS, clinical pulmonary infection score; ICU, intensive care unit; PCT, procalcitonin; VAP, ventilator-associated pneumonia.

Competing interests

The authors declare that they have no competing interests.

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