Comparison of procalcitonin and C-reactive protein as markers of sepsis

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Objective: To compare the clinical informative value of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations in the detection of infection and sepsis and in the assessment of severity of sepsis.

Design: Prospective study.

Setting: Medicosurgical intensive care unit.

Patients: Seventy consecutive adult patients who were admitted to the intensive care unit for an expected stay >24 hrs.

Interventions: None.

Measurements: PCT and CRP plasma concentrations were measured daily during the intensive care unit stay. Each patient was examined daily for signs and symptoms of infection and was classified daily in one of the following four categories according to the American College of Chest Physicians/Society of Critical Care Medicine criteria: negative, systemic inflammatory response syndrome, localized infection, and sepsis group (sepsis, severe sepsis, or septic shock). The severity of sepsis-related organ failure was assessed by the sepsis-related organ failure assessment score.

Main Results: A total of 800 patient days were classified into the four categories. The median plasma PCT concentrations in noninfected (systemic inflammatory response syndrome) and localized-infection patient days were 0.4 and 1.4 ng/mL ($p < .0001$), respectively; the median CRP plasma concentrations were 79.9 and 85.3 mg/L ($p = .08$), respectively. The area under the receiver operating characteristic curve was 0.756 for PCT (95% confidence interval [CI], 0.675–0.836), compared with 0.580 for CRP (95% CI, 0.488–0.672) ($p < .01$). The median plasma PCT concentrations in nonseptic (systemic inflammatory response syndrome) and septic (sepsis, severe sepsis, or septic shock) patient days were 0.4 and 3.65 ng/mL ($p < .0001$), respectively, whereas those for CRP were 79.9 and 115.6 mg/L ($p < .0001$), respectively. The area under the receiver operating characteristic curve was 0.925 for PCT (95% CI, 0.899–0.952), compared with 0.677 for CRP (95% CI, 0.622–0.733) ($p < .0001$). The linear correlation between PCT plasma concentrations and the four categories was much stronger than in the case of CRP (Spearman's rho, 0.73 vs. 0.41; $p < .05$). A rise in sepsis-related organ failure assessment score was related to a higher median value of PCT but not CRP.

Conclusion: PCT is a better marker of sepsis than CRP. The course of PCT shows a closer correlation than that of CRP with the severity of infection and organ dysfunction. (Crit Care Med 2003; 31:1737–1741)

Key Words: procalcitonin; C-reactive protein; infection; sepsis; sepsis-related organ failure assessment; organ dysfunction

Sepsis is a common cause of morbidity and mortality in intensive care unit (ICU), and delayed diagnosis is associated with increased mortality (1, 2). Clinical and laboratory signs of systemic inflammation including changes in body temperature, leukocytosis, and tachycardia are used for diagnosis of sepsis. However, they are neither specific nor sensitive for sepsis and can be misleading because critically ill patients often manifest a systemic inflammatory response syndrome (SIRS) without infection (3–7). Thus, diagnosis of sepsis is frequently difficult.

A marker that is able to distinguish the inflammatory response to infection from other types of inflammation would be of great clinical use. Unfortunately, the availability of a highly specific and sensitive marker of infection is still unsatisfied. This might be in part responsible for withholding, delaying, or overutilizing antimicrobial treatment in critically ill patients (8).

C-reactive protein (CRP) is commonly used as a marker of an acute inflammatory state, and its plasma concentration has been reported to parallel the clinical course of infection, the fall of the protein level indicating the resolution of infection (9). CRP plasma concentrations >50 mg/L have been reported to discriminate the inflammatory response to infection from other types of inflammation, even if with low specificity (10). Besides, the ideal marker should reflect not only the presence of infection but also its severity.

Recent investigations suggest that this goal might be better achieved by monitoring the procalcitonin (PCT) plasma concentration, which appears closely related to the severity and evolution of infection (11–20). Moreover, a recent report demonstrated that PCT plasma concentrations in septic patients are correlated with sepsis-related organ failure assessment (SOFA) score (21). However, other authors have questioned the clinical value of monitoring PCT concentrations: Ugarte et al. (22) did not find that PCT was better than CRP, although it can represent a useful adjunctive variable to identify infection and its severity; Suprin et al. (23) reported that both proteins are poor indicators of infection in critically ill patients. Until now, no study has compared daily PCT to CRP plasma concen-

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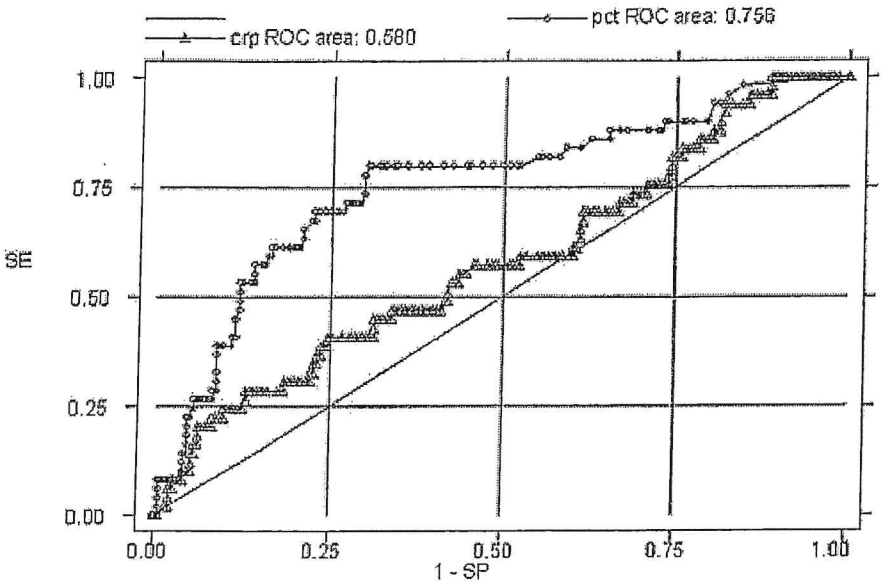

Figure 1. Receiver operating characteristic (*ROC*) curves comparing procalcitonin (*pct; circles*) and C-reactive protein (*crp; triangles*) for prediction of localized infection.

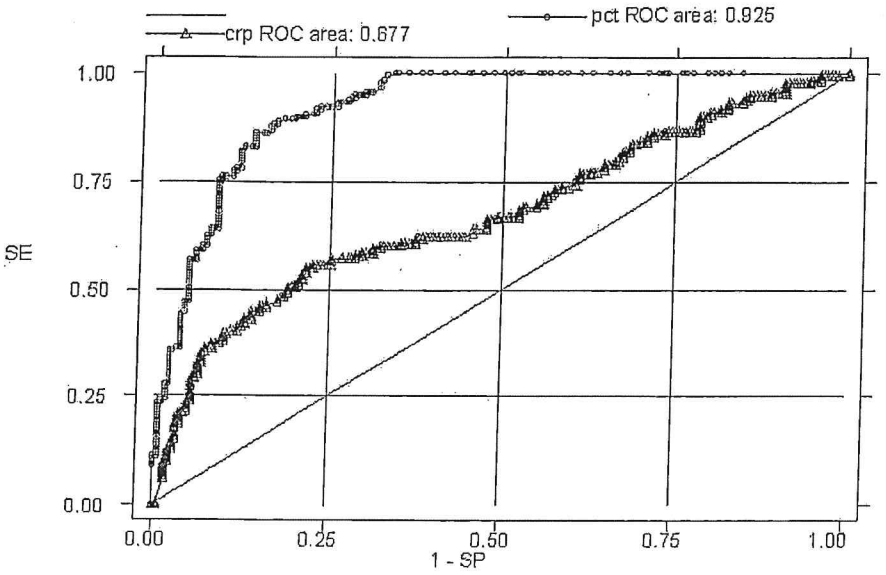

Figure 2. Receiver operating characteristic (*ROC*) curve comparing procalcitonin (*pct; circles*) and C-reactive protein (*crp; triangles*) for prediction of sepsis.

Table 2. PCT and CRP plasma concentrations in the diagnostic classes

Classes	PCT Median (Interquartile Range)	CRP Median (Interquartile Range)
Negative	0.1 (0.09–0.3)	50.4 (25.3–87.6)
SIRS	0.4 (0.2–0.7)	79.9 (52.9–103.4)
Localized infection	1.3 (0.6–2.0)	85.5 (58.5–132.4)
Sepsis group	3.6 (1.7–6.6)	115.9 (69.7–171.2)
Sepsis	3.1 (1.4–5.2)	125.6 (79.4–174.6)
Severe sepsis	3.2 (1.7–7.4)	73.6 (60.9–148.9)
Septic shock	10.7 (2.9–33.2)	108.0 (62.9–167.5)

PCT, procalcitonin; CRP, C-reactive protein; SIRS, systemic inflammatory response syndrome.

SOFA Score: Comparison Between PCT and CRP. We obtained three groups of SOFA scores: a) 1–6; b) 7–12; and c) 13–18. No patient had a SOFA score >18. PCT and CRP concentrations in the three SOFA score groups are shown in Table 3. A rise in SOFA score group was related to a higher median value of PCT but not CRP. Indeed, CRP concentrations were highly elevated also at low SOFA scores and showed no significant differences among the three groups.

DISCUSSION

Early identification of infection has a major impact on the clinical course, management, and outcome of critical patients. Thus, the effort of many investigating groups has been to find a reliable marker to discriminate the inflammatory response to infection from other types of inflammation.

High PCT plasma concentrations were first described by Assicot et al. (11), who in a prospective study conducted on 79 children with suspected infections found that PCT levels were very low (<0.1 ng/mL) in those with no infections and very high (6–53 ng/mL) in those with severe infections. Resolution of infections with antibiotic therapy led to decreases in PCT levels. Both localized bacterial infections without systemic manifestations and viral infections produced only moderate increases (0.3–1.5 ng/mL). Since then, many studies have been performed to determine whether PCT is a specific marker of infection and sepsis, but they yielded conflicting results. On one hand, a number of studies suggested that PCT could be an attractive variable to provide early diagnosis of sepsis, both in pediatric (12) and in adult patients in different medical (13–18, 20) and postsurgical (19, 20) conditions. On the other hand, some investigators questioned the diagnostic accuracy of PCT in detecting infection-related conditions (22, 23, 29, 30). In particular, Ugarte et al. (22) concluded that PCT is not a better marker of infection than CRP in critically ill patients, and Suprin et al. (23) performed a prospective study on 77 infected patients and 24 patients with SIRS due to other causes and reported that both markers had poor sensitivity and specificity for the diagnosis of infection. Moreover, Mimoz et al. (29) described an early and transient PCT plasma level increase after severe trauma that was proportional to the severity of tissue injury and hypovolemia, yet unre-