The utility of procalcitonin in critically ill trauma patients

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BACKGROUND: Procalcitonin (PCT), the prohormone of calcitonin, has an early and highly specific increase in response to systemic bacterial infection. The objectives of this study were to determine the natural history of PCT for patients with critical illness and trauma, the utility of PCT as a marker of sepsis versus systemic inflammatory response syndrome (SIRS), and the association of PCT level with mortality.

METHODS: PCT assays were done on eligible patients with trauma admitted to the trauma intensive care unit (ICU) of a Level I trauma center from June 2009 to June 2010, at hours 0, 6, 12, 24, and daily until discharge from ICU or death. Patients were retrospectively diagnosed with SIRS or sepsis by researchers blinded to PCT results.

RESULTS: A total of 856 PCT levels from 102 patients were analyzed, with mean age of 49 years, 63% male, 89% blunt trauma, mean Injury Severity Score of 21, and hospital mortality of 13%. PCT concentration for patients with sepsis, SIRS, and neither were evaluated. Mean PCT levels were higher for patients with sepsis versus SIRS ($p < 0.0001$). Patients with a PCT concentration of 5 ng/mL or higher had an increased mortality when compared with those with a PCT of less than 5 ng/mL in a univariate analysis (odds ratio, 3.65; 95% confidence interval, 1.03–12.9; $p = 0.04$). In a multivariate logistic analysis, PCT was found to be the only significant predictor for sepsis (odds ratio, 2.37; 95% confidence interval,1.23–4.61, $p = 0.01$).

CONCLUSION: PCT levels are significantly higher in ICU patients with trauma and sepsis and may help differentiate sepsis from SIRS in critical illness. An elevated PCT level was associated with increased mortality. (*J Trauma Acute Care Surg*. 2012;73: 413–418. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Prognostic study, level II.

KEY WORDS: Procalcitonin; trauma; intensive care unit; sepsis; biomarker.

Trauma care in the United States has evolved substantially with regionalized, designated trauma centers providing care to approximately 700,000 injured patients annually. Sepsis remains a major challenge in the critically injured patient with a recent systematic review reporting a prealence of 17%.[1] Microbiologic culturing and clinical judgment remain the criterion standard for the diagnosis of sepsis. However, a number of limitations surrounding this method exist. Cultures are time consuming, typically requiring 24 hours to 48 hours to be finalized; negative cultures do not necessarily exclude infection; and contamination from skin microorganisms is not infrequent.[2,3] The early recognition and treatment of septic patients with antibiotics is one of the most effective interventions for improved prognosis in the patient with critical illness.[4–6] Use of a biomarker that is sensitive and specific for sepsis and whose results are available in real time would be an appealing addition to the clinical assessment of such patients. A biomarker would be considered ideal if it was sensitive for early diagnosis, specific for bacterial origin, and if clinicians would easily be able to monitor it during the patient's course of illness.[7] Certain biomarkers such as C-reactive protein (CRP) have been evaluated as indicators for infectious processes. The lack of specificity has made them less than ideal.[8] Procalcitonin (PCT), a biomarker of bacterial infection, has been at the forefront of sepsis research recently as a proposed tool to be added to our clinical armamentarium.[9–11]

PCT is a 116 amino acid polypeptide prohormone of calcitonin, which is the hormone that regulates calcium homeostasis.[12–13] In healthy individuals, PCT is produced by C cells in the thyroid and neuroendocrine cells in the lung.[13] However, in the presence of bacterial infection, serum PCT levels are elevated.[9] This "septic" release of PCT occurs from a wide variety of tissues that typically do not produce significant amounts of PCT in healthy individuals. Animal studies have demonstrated PCT in the following tissues: thyroid, adrenal gland, spleen, spine, brain, lung, liver, kidney, pancreas, colon, small intestine, muscle, visceral fat, testes, skin, and stomach.[13–15] Healthy individuals typically have PCT levels less than 0.05 ng/mL, whereas concentrations exceeding 0.5 ng/mL are considered abnormal.[7,16] Numerous studies have found PCT to have an early and highly specific increase in response to systemic bacterial infection and sepsis.[17–22] Recently, studies have also shown that PCT might not be as useful as initially thought in this setting.[23–25] The type of analyzer used for the PCT assay can influence the test's accuracy. Most of the studies have used the LUMI test (BRAHMS Diagnostics, Hennigsdorf, Germany) that

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has a functional sensitivity of 0.5 ng/mL.[26] However, levels below this reference number might be subject to error. The Kryptor-PCT, a newer generation analyzer used in this study, performs an automated immunofluorescent assay with TRACE (Time Resolved Amplified Cryptate Emission) technology and has a much higher functional sensitivity of 0.06 ng/mL, reaching levels seen in healthy individuals. Patients with trauma demonstrate a transient increase in PCT levels after injury, with some suggestion of levels being useful for this population of patients when septic.[27–33] The severity of injury seems to have a positive correlation with PCT level. The duration of detectable levels of PCT after injury and the impact of using PCT level as a marker for sepsis in a critically ill trauma population has not been clearly elucidated. Using PCT may have an impact on therapeutic decision making and potentially result in cost reduction.[34] Because sepsis is a major determinant of outcome for patients with critical injury in the intensive care unit (ICU), PCT levels may be used as an early prognostic indicator for these patients.[35,36] Our objectives were to determine the following for patients with critical illness and trauma: (1) the natural history of PCT, (2) the utility of PCT as a marker of sepsis versus systemic inflammatory response syndrome (SIRS), and (3) the association of PCT level with mortality.

PATIENTS AND METHODS

This prospective observational cohort study was conducted between June 2009 and June 2010 in the trauma ICU (TICU) at Inova Fairfax Hospital, an American College of Surgeons–verified Level I trauma center. Burn patients are not admitted to our trauma center. The study was approved by the hospital institutional review board. PCT results were not used in clinical care, and clinicians were blinded to results.

Patients

Inclusion criteria were age of 18 years or older, partial or full trauma team activation (as defined by our trauma center's criteria consistent with American College of Surgeons Committee on Trauma standards), and direct admission to the TICU from the trauma bay or from the trauma bay via the operating room. Exclusion criteria were identification of patients as a Jehovah's Witness (to allow conservation of blood), special populations (pregnancy, inmates), transfer from an outside facility, preexisting renal failure, TICU stay under 24 hours, and no consent after the second blood draw. For patients who were not conscious or otherwise unable to consent to the study and when no legally authorized representative was available, permission was granted by the institutional review board to obtain the first two blood draws without consent. If the patient or legally authorized representative was not able to consent before the third blood draw or they did not want to participate in the study, the patients were immediately withdrawn from the study, and any existing specimens were discarded.

PCT Measurements

PCT assays were done upon admission to the TICU (0 hour), at 6 hours, 12 hours, 24 hours, and daily thereafter. Assays were taken up to 30 days, until transfer from TICU or death. A minimum of 1 mL of blood was drawn, with at least 50 μL needed for analysis. Specimens were immediately labeled and refrigerated. Specimens were centrifuged, and plasma was drawn off and frozen within 24 hours of refrigeration. PCT assays were performed in batches on a weekly basis using the Kryptor-PCT (BRAHMS Diagnostics) analyzer. To minimize measurement error throughout the study, only three of the investigators (J.V.S., C.P.M., R.R.) performed the PCT analysis. Before patient enrollment, a trial period of 2 weeks was implemented in which blood samples with known PCT values and control specimens were analyzed, to establish quality control.

Definitions

The SIRS was defined as per the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference.[37] Sepsis was defined as the presence of SIRS and a diagnosed infection. Patients were allocated to three groups post hoc (1) SIRS, (2) sepsis, (3) neither sepsis nor SIRS (the *neither* group).

Funding

Funding was obtained through a $15,000 Seed Grant from the Inova Research Center. The Kryptor-PCT analyzer manufactured by BRAHMS Diagnostics was donated to the Inova Regional Trauma Center for exclusive use in this study for the duration of the research period. BRAHMS Diagnostics supplied reagents and PCT kits. BRAHMS Diagnostics had no input in the design, execution, or analysis of the study and did not have access to the patient data or PCT results.

Data Analysis

Demographics are presented as means with 95% confidence interval (CI). Nonparametric analysis of variance (Wilcoxon rank sum test) was used to detect differences in PCT levels among groups. Proportions were compared using χ^2 methods. The multivariate logistic regression was used to identify independent predictors of sepsis. A receiver operating characteristic (ROC) curve was calculated. A $p < 0.05$ was considered to be statistically significant. All analyses were performed using SAS software (version 9.2, SAS Institute, Cary, NC).

RESULTS

There were 102 eligible patients. Most were male (63%), and blunt mechanism (89%) predominated. Mean age was

TABLE 1. Demographics (n = 102)

Variable	Mean (95% CI)
Age, y	49 (44–53)
ISS	21 (19–23)
GCS score	10 (9–11)
Ventilator days	7 (4–9)
ICU LOS, d	8 (6–10)
Hospital LOS, d	16 (12–20)

LOS, length of stay.

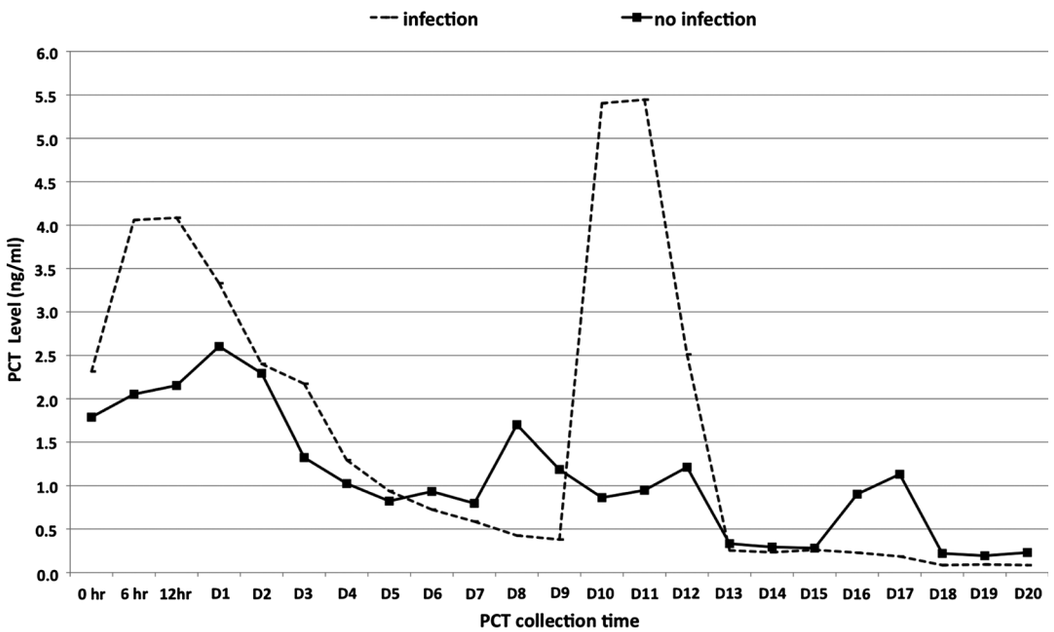

Figure 1. Trend of PCT in patients with critical illness and trauma: infected (n=33) versus noninfected (n=47). Both groups (n = 80).

49 years (95% CI, 44–53 years). Mean Injury Severity Score (ISS) was 21 (95% CI, 19–23), whereas mortality was 13%. Sepsis was present in 33% of the patients. Patient demographics and study factors are shown in Table 1.

Figure 1 shows the mean PCT levels for septic versus the SIRS/*neither* group in the overall population. There was a transient increase in PCT level in both groups during the first 24 hours to 48 hours after admission. A second peak, with even higher PCT levels, was seen in septic patients between days 9 and 13. The type of infections that were found, starting with the most prevalent, was ventilator-associated pneumonia, blood stream infections, urinary tract infections, and other. Elevated PCT levels were not seen in the SIRS and the *neither* group.

Twenty-two patients had PCT levels measured for less than 48 hours and were removed from the subgroup analysis leaving a total of 80 patients. When comparing the sepsis group with the SIRS and the *neither* group (Table 2), there were no statistically significant differences in Glasgow Coma Scale (GCS) score, body mass index, sex, and mechanism. The ISS was slightly higher in the septic group (mean [95% CI], 25 [21–29] vs. SIRS 20 [16–23] and the *neither* 20 [17–24]; p = 0.07). The sepsis group was younger than the SIRS or the *neither* groups (39 [32–46] vs. 55 [46–64] vs. 51 [43–60], respectively; p = 0.01). Ventilator days were significantly higher in the sepsis group versus the SIRS and the *neither* group (15 [9–20] vs. 2 [0.5–2.0] vs. 6 [2–10], respectively;

TABLE 2. Comparison of *Neither*, SIRS, and Sepsis Groups (n = 80)

Clinical Group	*Neither* (n = 23)	SIRS (n = 24)	Sepsis (n = 33)	
Variable	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	*p*
ISS	20 (17–24)	20 (16–23)	25 (21–29)	0.07
Age, y*	51 (43–60)	55 (46–64)	39 (32–46)	0.01
GCS score	10 (8–12)	11 (9–13)	8.0 (6–10)	0.16
Ventilator days†	6.0 (2–10)	2.0 (0.5–2.0)	15 (9–20)	<0.0001
Hospital days‡	16 (9–24)	8.0 (6–10)	28 (18–39)	<0.0001
BMI	26 (24–28)	27 (24–30)	25 (23–27)	0.48
ICU LOS‡	8.0 (5–11)	5.0 (4–6)	17 (12–22)	<0.0001
PCT level, ng†	0.2 (0.1–0.4)	0.9 (0.2–1.5)	6.6 (2.7–10.5)	<0.0001
Male, %	74	67	61	0.32
Blunt injury, %	96	79	91	0.83
Mortality, %	9	17	12	0.83

*Sepsis < SIRS = *neither*.
†Sepsis > SIRS = *neither*.
‡Sepsis = *neither* > SIRS.
BMI, body mass index; LOS, length of stay.

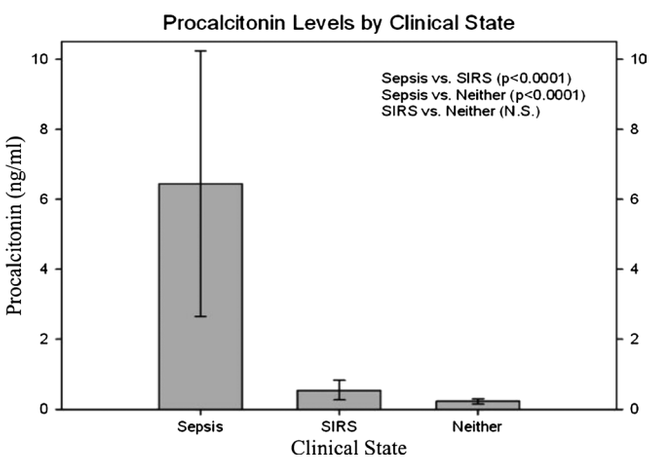

Figure 2. Comparison of groups by PCT level (n = 80).

$p < 0.0001$). ICU lengths of stay (days) were also significantly higher in the sepsis group versus the SIRS and the *neither* group (17 [12–22] vs. 5 [4–6] vs. 8 [5–11], respectively; $p < 0.0001$). Hospital days demonstrated a similar increase in the sepsis group versus the SIRS and the *neither* group (28 [18–39] vs. 8 [6–10] vs. 16 [9–24], respectively; $p < 0.0001$).

PCT levels were significantly higher in the sepsis group versus the SIRS and the *neither* group (6.6 ng/mL [2.7–10.5] vs. 0.9 [0.2–1.5] vs. 0.2 [0.1–0.4], respectively; $p < 0.0001$) (Fig. 2). In a univariate analysis, patients with a PCT level of 5 ng/mL or higher had a significantly increased mortality compared with that of patients with a level less than 5 ng/mL (odds ratio [OR], 3.65; 95% CI, 1.03–12.9; $p = 0.04$). In a multivariate logistic regression, PCT remained a significant predictor of sepsis (OR, 2.37; 95% CI, 1.23–4.61; $p = 0.01$) (Table 3). Using an ROC curve analysis, a PCT level of 0.82 ng/mL or less was found to produce an optimal sensitivity (87%) and specificity (82%) for sepsis with an area under the curve of 92% (Fig. 3).

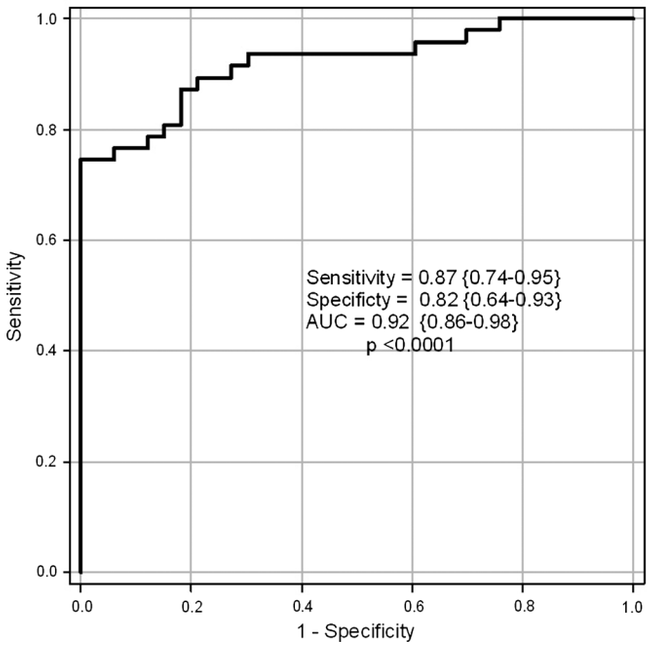

Figure 3. ROC curve modeling PCT for cohort of sepsis versus SIRS and the *neither* group using a cutoff level of 0.82 ng/mL or lower. AUC, area under the curve.

DISCUSSION

This is the first study in the United States investigating the utility of PCT in the critically ill trauma population. In this group of patients with critical illness and trauma in the ICU, PCT levels strongly correlated with infection, with elevated levels occurring in patients with sepsis, whereas patients with SIRS and those with neither had low PCT levels. The concept of having a biomarker to help differentiate sepsis from noninfectious systemic inflammatory response is appealing to the clinician. Furthermore, the early recognition of sepsis may allow the implementation of early goal-directed therapy that has demonstrated an improvement in outcomes.[4–6]

Cytokines have been evaluated in the past for the detection of sepsis with the primary problem being the lack of specificity. PCT has been compared with CRP and interleukin 6 with most of the studies finding PCT to be more useful.[33,38] Although multiple studies have shown that PCT is specific for systemic bacterial infection,[17–22] only a few studies have evaluated the utility of PCT in the trauma population.[27–33]

The present study demonstrates that PCT levels rise almost immediately after injury and remain elevated for approximately 2 days. These findings are consistent with other studies that have demonstrated similar elevations.[27] Given the elevation of PCT levels that occurs in nearly all injured patients, it is difficult to use PCT to differentiate sepsis from SIRS in the initial period after the injury based on these results. Previous studies[39] have shown that admission or baseline PCT is not meaningful prognostically, and this further reinforces the benefit of serial measurements as was performed in this study. This may also argue for deferring testing for PCT levels in the first 48 hours after injury.

In contrast to previous studies that used the older generation analyzer LUMItest,[26] we used the Kryptor-PCT that is eight times more sensitive. This provided a better detection method and possibly a more accurate assessment when attempting to differentiate sepsis versus noninfectious SIRS. As shown in other studies,[27,32] we demonstrated a statistically significant increase in PCT level in the sepsis group compared with both the SIRS and the *neither* groups. Given that PCT level in our multivariate logistic regression was an independent predictor of sepsis, clinicians can potentially use PCT in the clinical workup of patients with suspected sepsis. We found that the specificity of PCT as a predictor of sepsis was 82%. This high specificity also has been demonstrated in numerous nontrauma studies[17–22] and has been missing in evaluation of other biomarkers (i.e., CRP, interleukin 6) in sepsis research. In addition, falling PCT levels after an episode of sepsis may indicate control of infection and the ability to discontinue antibiotics.

The mortality rate in our study was 13%. We found an increased mortality for patients with elevated PCT levels; however, the difference was found to be marginally statistically significant. Our sample size was likely not large enough to demonstrate a more substantial difference.

TABLE 3. Multivariate Logistic Regression—Predictors of Sepsis

Variable	OR (95% CI)	*p*
ISS	0.98 (0.89–1.07)	0.60
Age, y	0.96 (0.91–1.00)	0.65
GCS score	0.98 (0.84–1.13)	0.07
Ventilator days	0.98 (0.85–1.12)	0.77
ICU LOS	1.17 (0.69–1.99)	0.57
Hospital LOS	0.94 (0.84–1.05)	0.29
PCT	2.37 (1.23–4.61)	0.01

LOS, length of stay.

Our study has some inherent limitations. As a prospective cohort study, the lack of randomization may have allowed the influence of unmeasured confounding factors on our results. Our study group was relatively small, and despite defined inclusion criteria, selection bias cannot be excluded.

The ability to use a specific biomarker in conjunction with clinical assessment to aid in the diagnosis of sepsis in patients with critical illness and trauma would be an important advance in critical care. Our study contributes to the current body of literature showing that PCT holds promise as a biomarker to differentiate sepsis from noninfectious SIRS. PCT has been shown in mixed critical care populations to effectively guide the early discontinuation of antibiotics when infection has resolved.[40] A need also exists for larger randomized studies of patients with critical illness and trauma evaluating antibiotic stewardship both before and after sepsis. One might hypothesize that someday, the use of PCT elevation may prompt investigation for/treatment of sepsis in patients with critical illness and trauma.

In conclusion, PCT levels of 0.82 ng/mL or higher are significantly more common in injured ICU patients with sepsis. An increase in PCT level is seen transiently after injury, with levels returning to baseline within 2 days. PCT levels should be considered as an important parameter in the clinical workup of those patients suspected of developing sepsis. More robust and larger scale studies are needed to determine the exact role of PCT measurement in the care of patients with critical illness and trauma.

AUTHORSHIP

J.V.S., M.J.S., C.P.M., and S.M.F. designed this study. J.V.S., C.P.M., and T.W. conducted the literature search. J.V.S., C.P.M., R.R., T.W., A.R., and M.G. collected data, which M.J.S., J.V.S., C.P.M., and T.A. analyzed. J.V.S., M.J.S., C.P.M., S.M.F., T.A., and A.R. performed data interpretation. All authors participated in writing and revising the manuscript. J.V.S., M.J.S., C.P.M., T.A., and S.M.F. provided figures and tables.

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DISCLOSURE

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REFERENCES

1. Mann EA, Baun MM, Meininger JC, Wade CE. Comparison of mortality associated with sepsis in the burn, trauma, and general intensive care unit patient: a systematic review of the literature. *Shock*. 2011.
2. Kim MH, Lim G, Kang SY, et al. Utility of procalcitonin as an early diagnostic marker of bacteremia in patients with acute fever. *Yonsei Med J*. 2011;52:276–281.
3. Mitaka C. Clinical laboratory differentiation of infectious versus noninfectious systemic inflammatory response syndrome. *Clin Chim Acta*. 2005;351:17–29.
4. Parrillo JE. Pathogenetic mechanisms of septic shock. *N Engl J Med*. 1993;328:1471–1477.
5. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34:1589–1596.
6. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med*. 2008;36:296–327.
7. Schneider HG, Lam QT. Procalcitonin for the clinical laboratory: a review. *Pathology*. 2007;39:383–390.
8. Clyne B, Olshaker JS. The C-reactive protein. *J Emerg Med*. 1999;17:1019–1025.
9. Assicot M, Gendrel D, Carsin H, et al. High serum procalcitonin concentrations in patients with sepsis and infection. *Lancet*. 1993;341:515–518.
10. Uzzan B, Cohen R, Nicolas P, et al. Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis. *Crit Care Med*. 2006;34:1996–2003.
11. Ventetuolo CE, Levy MM. Biomarkers: diagnosis and risk assessment in sepsis. *Clin Chest Med*. 2008;29:591–603.
12. Weglohner W, Struck J, fischer-Schulz C, et al. Isolation and characterization of serum procalcitonin from patients with sepsis. *Peptides*. 2001;22:2099–2103.
13. Jacobs JW, Lund PK, Potts JT Jr, et al. Procalcitonin is a glycoprotein. *J Biol Chem*. 1981;256:2803–2807.
14. Meisner M, Muller V, Khakpour Z, et al. Induction of procalcitonin and proinflammatory cytokines in an anhepatic baboon endotoxin shock model. *Shock*. 2003;19:187–190.
15. Muller B, White JC, Nylen ES, et al. Ubiquitous expression of the calcitonin-1 gene in multiple tissues in response to sepsis. *J Clin Endocrinol Metab*. 2001;86:396–404.
16. Morgenthaler NG, Struck J, Fischer-Schulz C, et al. Detection of procalcitonin (PCT) in healthy controls and patients with local infection by a sensitive ILMA. *Clin Lab*. 2002;48:263–270.
17. Harbarth S, Holeckova K, Froidevaux C, Pittet D, Ricou B, Grau GE, Vadas L, Pugin J. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. *Am J Respir Crit Care Med*. 2001;164:396–402.
18. Muller B, Becker KL, Schachinger H, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. *Crit Care Med*. 2000;28:977–983.
19. Brunkhorst FM, Wegscheider K, Forycki ZF, Brunkhorst R. Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis, and septic shock. *Intensive Care Med*. 2000;26(Suppl 2):S148–S152.
20. Luzzani A, Polati E, Dorizzi R, Rungatscher A, Pavan R, Merlini A. Comparison of procalcitonin and C-reactive protein as markers of sepsis. *Crit Care Med*. 2003;31:1737–1741.
21. Endo S, Aikawa N, Fujishima S, Sekine I, Kogawa K, Yamamoto Y, et al. Usefulness of procalcitonin serum level for the discrimination of severe sepsis from sepsis: a multicenter prospective study. *J Infect Chemother*. 2008;14:244–249.
22. Christ-Crain M, Jaccard-Stolz D, Bingisser R, et al. Effect of procalcitonin-guided treatment of antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. *Lancet*. 2004;363:600–607.
23. Luyt CE, Combes A, Reynaud C, et al. Usefulness of procalcitonin for the diagnosis of ventilator-associated pneumonia. *Intensive Care Med*. 2008;34:1434–1440.
24. Mongardon N, Lemiale V, Perbet S, et al. Value of procalcitonin for diagnosis of early onset pneumonia in hypothermia-treated cardiac arrest patients. *Intensive Care Med*. 2010;36:92–99.
25. Jensen J, Hein L, Lundgren B, et al. Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial. *Crit Care Med*. 2011;39:2048–2058.
26. Becker K, Snider R, Nylen E. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. *Crit Care Med*. 2008;36:941–952.
27. Wanner GA, Keel M, Steckholzer U, et al. Relationship between procalcitonin plasma levels and severity of injury, sepsis, organ failure, and mortality in injured patients. *Crit Care Med*. 2000;28:950–957.
28. Meisner M, Adina H, Schmidt J. Correlation of procalcitonin and C-reactive protein to inflammation, complications, and outcome during the intensive care unit course of multiple-trauma patients. *Crit Care*. 2006;10:R1.

29. Oconnor E, Venkatesh B, Mashongonyika C, et al. Serum procalcitonin and C-reactive protein as markers of sepsis and outcome in patients with neurotrauma and subarachnoid haemorrhage. *Anaesth Intensive Care*. 2004;32:465–470.
30. Hensler T, Sauerland S, Lefering R, et al. The clinical value of procalcitonin and neopterin in predicting sepsis and organ failure after major trauma. *Shock*. 2003;20:420–426.
31. Castelli GP, Pognani C, Meisner M, et al. Procalcitonin and C-reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction. *Crit Care Med*. 2004;R234–R242.
32. Castelli GP, Pognani C, Cita M, et al. Procalcitonin as a prognostic and diagnostic tool for septic complications after major trauma. *Crit Care Med*. 2009;37:1845–1849.
33. Haasper C, Kalmbach M, Dikos GD, et al. Prognostic value of procalcitonin (PCT) and/or interleukin-6 (IL-6) plasma levels after multiple trauma for the development of multi organ dysfunction syndrome (MODS) or sepsis. *Technol Health Care*. 2010;18:89–100.
34. Christ-Crain, M, Stolz, D, Bingisser, R, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. *Am J Respir Crit Care Med*. 2006;174:84–93.
35. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001;29:1303–1310.
36. Selassie AW, Fakhry SM, Ford D. Population-based study of the risk of in-hospital death after traumatic brain injury: the role of sepsis. *J Trauma*. 2011;71:1226–1234.
37. ACCP-SCCM Consensus Conference. Definitions of sepsis and multiple organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med*. 1992;20:864–874.
38. Chan YL, Tseng CP, Tsay PK, et al. Procalcitonin as a marker of bacterial infection in the emergency department: an observational study. *Crit Care Med*. 2005;33:894–895.
39. Jensen JU, Heslet L, Jensen TH, et al. Procalcitonin increase in early identification of critically ill patients at high risk of mortality. *Crit Care Med*. 2006;24:2596–2602.
40. Kopterides P, Siempos II, Tsangaris I, et al. Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: a systematic review and meta-analysis of randomized controlled trials. *Crit Care Med*. 2010;38:2229–2241.

EDITORIAL CRITIQUE

The authors have addressed a problem faced daily in the ICU, differentiating sepsis from SIRS. The reported prevalence of SIRS in a surgical ICU is 93%, but only about 40% of those patients will have infection as a cause. An ideal biomarker would allow us to easily differentiate between infection and SIRS, which would lead to more directed antibiotic use. The authors specifically sought to determine the effect of increased sensitivity of the procalcitonin (PCT) assay on its predictive abilities and its ability to predict infection and mortality.

The authors showed that the critical thresholds for mortality and infection were both detectable with the LUMITest, so there was no advantage to the increased sensitivity of their PCT assay. The PCT levels were higher in patients who died, but the authors imply that it was not an independent predictor of mortality. They also showed that septic patients had a significantly higher PCT level, which was also an independent predictor of sepsis. This finding has two limitations. First the authors do not report the temporal relationship of the PCT rise and the diagnosis of infection. The second they do not report how they defined infections. There are many sources of criteria for diagnosing infections, but they vary in their purpose and accuracy.

There is one other curious finding in this study. Both groups had an elevated PCT for the first few days. On subsequent days the uninfected group often had means above the 0.82 ng/ml threshold for infection. Furthermore, the septic group showed a large increase in PCT from day 9 to 13. Did all or most of the infections occur on these 5 days?

The authors have contributed to our knowledge of PCT in trauma patients, but have only begun to explore how it might be useful in the trauma ICU.

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