Original Research

Diagnostic Utility of Plasma Procalcitonin for Nosocomial Pneumonia in the Intensive Care Unit Setting

John Dallas MD, Sarah M Brown PhD, Karl Hock, Mitchell G Scott PhD, Lee P Skrupky PharmD, Walter A Boyle III MD and Marin H Kollef MD

BACKGROUND: Nosocomial pneumonia is a difficult diagnosis to establish in the intensive care unit setting, due to the non-specific nature of the clinical and radiographic findings. Procalcitonin is a circulating biomarker that may become elevated in the presence of bacterial infection. METHODS: We conducted a prospective single-center cohort study at Barnes-Jewish Hospital, a 1,200-bed urban teaching hospital in St Louis, Missouri. In medical and surgical intensive care unit patients with suspected nosocomial pneumonia we measured plasma procalcitonin with an enzyme-linked fluorescent assay. RESULTS: We evaluated 104 consecutive patients with suspected nosocomial pneumonia, 67 (64%) of whom met our predefined clinical and microbiologic criteria for definite nosocomial pneumonia. Though the mean procalcitonin concentration was greater in the 67 patients with definite nosocomial pneumonia (18.3 ± 99.1 ng/mL, median 0.8 ng/mL, 5th percentile 0.0 ng/mL, 95th percentile 43.1 ng/mL) than in the 12 patients with definite absence of nosocomial pneumonia (1.7 ± 2.0 ng/mL, median 1.0 ng/mL, 5th percentile 0.0 ng/mL, 95th percentile 6.7 ng/mL), this difference was not statistically significant (*P* = .66). A procalcitonin cutoff value of > 1 ng/mL yielded a diagnostic sensitivity of 50% and a specificity of 49% for definite nosocomial pneumonia. Receiver operating curve and multivariate logistic regression analyses demonstrated that procalcitonin is inferior to clinical variables for diagnosing nosocomial pneumonia. However, compared to patients with an initial procalcitonin > 1 ng/mL, those with lower procalcitonin had fewer total antibiotic days (13.0 ± 10.3 d vs 19.7 ± 12.0 d, *P* < .001) and fewer antibiotic days for treatment of nosocomial pneumonia (10.0 ± 5.9 d vs 14.7 ± 7.4 d, *P* < .001). CONCLUSIONS: Plasma procalcitonin has minimal diagnostic value for nosocomial pneumonia. *Key words: nosocomial pneumonia; intensive care; procalcitonin; bacterial infection; enzyme-linked fluorescent assay.*
[Respir Care 2011;56(4):412–419.

Introduction

Nosocomial pneumonia is a common infection in the intensive care unit (ICU) setting and includes patients with healthcare-associated pneumonia, hospital-acquired pneumonia, and ventilator-associated pneumonia (VAP).[1,2] Nosocomial pneumonia is usually suspected when new or progressive infiltrates develop in a patient with fever, leukocytosis, or leukopenia, and purulent tracheobronchial secretions.[2,3] However, non-infectious conditions such as pulmonary embolism, atelectasis, congestive heart failure, and chemical aspiration can mimic the clinical and radiographic

SEE THE RELATED EDITORIAL ON PAGE 530

John Dallas MD and Marin H Kollef MD are affiliated with the Division of Pulmonary and Critical Care Medicine; and Sarah M Brown PhD, Karl Hock, Mitchell G Scott PhD are affiliated with the Division of Laboratory and Genomic Medicine; and Walter A Boyle III MD is affiliated with the Departments of Anesthesia and Surgery, Washington University School of Medicine, St Louis, Missouri. Lee P Skrupky PharmD is affiliated with the Department of Pharmacy, Barnes-Jewish Hospital, St Louis, Missouri.

The authors have disclosed a relationship with bioMérieux, which partly supported this research.

Correspondence: Marin H Kollef MD, Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8052, St Louis MO 63110. E-mail: mkollef@dom.wustl.edu.

DOI: 10.4187/respcare.00979

features of nosocomial pneumonia, making an accurate diagnosis problematic in many cases.[4,5] As a result, patients with pneumonia could have antibiotic therapy withheld if the correct diagnosis is not made, while patients with non-infectious conditions could receive needless antibiotic therapy.

Biomarkers have been developed that may aid with the diagnosis of bacterial infections, including nosocomial pneumonia.[6] Procalcitonin is a precursor of calcitonin and is up-regulated during bacterial infection, and is a sensitive and specific marker of various bacterial infections.[7,8] However, based on studies to date, the diagnostic utility of procalcitonin in nosocomial pneumonia is controversial.[9-13] Potential explanations for the limited accuracy of procalcitonin for nosocomial pneumonia to date include the nonspecific diagnostic criteria employed for this infection, inaccuracy in the procalcitonin assay, use of arbitrary procalcitonin cutoff values, and the presence of unrecognized concurrent infection.[6,7]

Therefore, we conducted a clinical study to determine the utility of plasma procalcitonin concentration for diagnosing nosocomial pneumonia in the ICU, and to compare the predictive accuracy of procalcitonin concentration to that of the Clinical Pulmonary Infection Score (CPIS) for the diagnosis of nosocomial pneumonia.

Methods

Study Population and Data Collection

The study was conducted in the medical ICU (19 beds) and surgical ICU (24 beds) of Barnes-Jewish Hospital (1,200 beds), an urban teaching hospital in St Louis, Missouri. Between June 2009 and January 2010 we prospectively evaluated 104 consecutive adult patients with suspected nosocomial pneumonia. The Washington University School of Medicine institutional review board reviewed and approved the research protocol and waived the informed-consent requirement because we used plasma samples drawn for routine laboratory testing.

For all study patients, at the time nosocomial pneumonia was first suspected (baseline), we prospectively recorded age, sex, race, body temperature, leukocyte count, presence of purulent secretions, CPIS, P_{aO_2}/F_{IO_2}, and comorbid conditions (eg, COPD, congestive heart failure, diabetes, renal failure, cirrhosis, and malignancy). Respiratory secretion specimens, including bronchoalveolar lavage fluid, were processed using quantitative culture methods, as previously described.[14,15]

Plasma procalcitonin was assayed with a procalcitonin enzyme-linked fluorescent assay (BRAHMS assay, VIDAS analyzer, bioMérieux, Marcy l'Etoile, France), which has a functional detection limit (coefficient of variation 20%) of 0.09 ng/mL. The assay has a coefficient of variation of 6.2% at a mean concentration of 1.33 ng/mL and 6.4% at a mean concentration of 13.2 ng/mL ($n = 62$ and 2 reagent lot numbers). Excess plasma samples were obtained from the clinical laboratory. The samples were drawn at the time of initial suspicion of nosocomial pneumonia, and a second sample was drawn approximately 48 hours later. All the samples were analyzed within 24 hours of being obtained.

Definitions of Nosocomial Pneumonias

Patients with suspected nosocomial pneumonia were prospectively defined as individuals whose ICU treating physicians made a clinical diagnosis of healthcare-associated pneumonia, hospital-acquired pneumonia, or VAP and initiated antibiotics. On the basis of clinical, radiologic, and microbiologic data, these patients were assigned to 3 groups:[2,3]

- Definite Absence of Pneumonia: patients with non-infectious diseases (eg, interstitial lung disease, pulmonary edema, atelectasis, and acute respiratory distress syndrome), negative respiratory culture results, and who were not receiving antibiotics at the time respiratory cultures were obtained
- Indeterminate Pneumonia: patients with negative respiratory culture results who had received new or changed antibiotics for at least 24 hours prior to respiratory culture sampling
- Definite Pneumonia: patients with positive quantitative culture results for bacterial pathogens, no other more likely diagnosis identified, and clinical response to the antibiotics, defined as radiographic improvement within 3–5 days of beginning antibiotic treatment, accompanied by normalization of at least one of the abnormal clinical variables that suggested nosocomial pneumonia (hyperthermia or hypothermia, leukocytosis, purulent tracheobronchial secretions)

The concentration of microorganisms considered clinically important for the diagnosis of pneumonia was $> 10^3$ colony-forming units/mL in bronchoalveolar lavage fluid or $> 10^5$ colony-forming units/mL in tracheal aspirates or sputum.[5]

All classifications and CPIS scores were prospectively determined by one of us (JD) and confirmed by MHK. All investigators were blinded to the procalcitonin results until study completion.

The antibiotic days for the treatment of nosocomial pneumonia was the number of days on new antibiotic treatment from the day that nosocomial pneumonia was first suspected to the day that the nosocomial pneumonia antibiotics were stopped. Total antibiotic days were

Table 1. Baseline Patient Characteristics (n = 104)

	Pneumonia Definitely Absent (n = 12)	Pneumonia Indeterminate (n = 25)	Pneumonia Definitely Present (n = 67)
Age (mean ± SD y)	51.8 ± 22.8	58.4 ± 20.2	54.0 ± 18.5
Male, no. (%)	7 (58)	15 (60)	42 (63)
Race, no. (%)			
White	9 (75)	16 (64)	43 (64)
Other	3 (25)	9 (36)	24 (36)
Body mass index (mean ± SD kg/m^2)	30.2 ± 11.2	28.9 ± 10.4	29.8 ± 10.7
Pneumonia Type, no. (%)			
Healthcare-associated	1 (8)	11 (44)	4 (6) $P < .001$*
Hospital-acquired	6 (50)	8 (32)	13 (19)
Ventilator-associated	5 (42)	6 (24)	50 (75)
ICU Type, no. (%)			
Medical	7 (58)	18 (72)	25 (37) $P = .009$*
Surgical	5 (42)	7 (28)	42 (63)
COPD, no. (%)	3 (25)	6 (24)	17 (25)
Congestive heart failure, no. (%)	4 (33)	5 (20)	9 (13)
Diabetes, no. (%)	3 (25)	11 (44)	17 (25)
End-stage renal disease, no. (%)	2 (17)	7 (28)	5 (8) $P = .04$*
Cirrhosis, no. (%)	2 (17)	2 (8)	0 (0) $P = .01$*
Malignancy, no. (%)	0 (0)	3 (12)	11 (16)
APACHE II score (mean ± SD)	22 ± 9	22 ± 6	26 ± 8 $P = .03$*

* Compared to pneumonia indeterminate.
ICU = intensive care unit
APACHE = Acute Physiology and Chronic Health Evaluation

the number of days from the day that nosocomial pneumonia was first suspected to the day that all antibiotics were stopped (ie, after the nosocomial pneumonia antibiotics were stopped).

Statistical Analysis

All comparisons were unpaired, and all tests of significance were 2-tailed. We compared continuous variables with the Student t test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. We compared categorical variables with the chi-square test or Fisher exact test. For all analyses we considered a 2-tailed P value $< .05$ statistically significant. We constructed receiver operating characteristic (ROC) curves to illustrate the performance differences of plasma procalcitonin concentration and CPIS for diagnosing pneumonia. We conducted multivariate logistic regression analysis to determine independent risk factors for definite pneumonia. We entered variables predictive of definite pneumonia (by bivariate analysis with a P value $< .15$) into the model, in a stepwise manner. We performed the analyses with statistics software (SPSS 11.0, SPSS, Chicago, Illinois).

Results

Patient Characteristics

We enrolled 104 consecutive ICU patients with suspected nosocomial pneumonia (Table 1). Sixty-one (59%) had suspected VAP, 27 (26%) had suspected hospital-acquired pneumonia, and 16 (15%) had suspected healthcare-associated pneumonia. Patients with VAP were significantly more likely to be classified as having definite pneumonia (82%) than patients with hospital-acquired pneumonia (48%, $P = .001$) or those with healthcare-associated pneumonia (25%, $P < .001$). Patients classified as having definite pneumonia had statistically greater Acute Physiology and Chronic Health Evaluation II score and were more likely to be in the surgical ICU than the patients classified as indeterminate pneumonia.

Among the 67 patients with definite pneumonia, 18 (27%) had polymicrobial infections. The pathogens identified in these patients included *Pseudomonas aeruginosa* (n = 17), methicillin-susceptible *Staphylococcus aureus* (n = 11), methicillin-resistant *S. aureus* (n = 9), *Acinetobacter* species (n = 8), *Klebsiella* species (n = 8), *Enterobacter* species (n = 7), *Streptococcus pneumoniae* (n = 7), Haemophilus influenza (n = 6), *Serratia* species

Table 2. Procalcitonin Concentrations and Clinical Pulmonary Infection Scores

	Pneumonia Definitely Absent (n = 12)			Pneumonia Indeterminate (n = 25)			Pneumonia Definitely Present (n = 67)		
	Mean ± SD	Median	5th–95th percentiles	Mean ± SD	Median	5th–95th percentiles	Mean ± SD	Median	5th–95th percentiles
Procalcitonin (ng/mL)									
At first suspicion	1.7 ± 2.0	1.3	0.2–6.7	9.7 ± 40.3	0.8	0.1–144.8	18.3 ± 99.1	0.9	0.1–44.5
48 h later	6.3 ± 12.2	0.9	0.3–42.6	5.3 ± 14.8	1.8	0.1–65.4	10.1 ± 50.9	0.7	0.1–47.5
Difference	4.5 ± 10.6	0.2	–2.5 to 35.9	–4.4 ± 26.1	0.2	–91.9 to 11.0	–8.8 ± 51.4*†	–0.2	–28.2 to 4.8
Clinical Pulmonary Infection Score									
At first suspicion	5.7 ± 1.8	5.5	3.0–8.0	6.3 ± 1.6	6.0	3.3–9.7	6.2 ± 1.6	6.0	4.0–9.0
48 h later	3.3 ± 2.1	2.5	1.0–6.0	4.9 ± 2.1*	5.0	1.3–8.7	5.1 ± 1.6*	5.0	2.4–8.0
Difference	–2.3 ± 2.0	–2.0	–7.0 to 1.0	–1.4 ± 1.6	–1.0	–3.7 to 1.0	–1.1 ± 1.8*	–1.0	–4.0 to 2.0

* P = .050 for procalcitonin difference, .049 and .01 for CPIS at 48 hours, and .048 for CPIS difference, compared to pneumonia definitely absent.
† P = .014 for procalcitonin difference, compared to pneumonia indeterminant.

(n = 4), *Escherichia coli* (n = 4), *Citrobacter* species (n = 1), *Achromobacter* species (n = 1), and *Stenotrophomonas maltophilia* (n = 1).

Procalcitonin Assay

The mean duration between the 2 plasma samples for procalcitonin measurement was 56.1 ± 8.9 hours (minimum 28.8 h, maximum 73.9 h). Though the mean baseline procalcitonin concentration was greater in the 67 patients with definite pneumonia (18.3 ± 99.1 ng/mL, median 0.8 ng/mL 5th percentile 0.0 ng/mL, 95th percentile 43.1 ng/mL) than in the 12 patients with definite absence of pneumonia (1.7 ± 2.0 ng/mL, median 1.0 ng/mL, 5th percentile 0.0 ng/mL, 95th percentile 6.7 ng/mL]) (Table 2), this difference was not statistically significant (P = .66).

No best procalcitonin cutoff value for the diagnosis of nosocomial pneumonia could be established. A procalcitonin cutoff value of 1 ng/mL at the time pneumonia was first suspected yielded a diagnostic sensitivity of 50%, a specificity of 49%, a positive predictive value of 64%, and a negative predictive value of 35% for definite pneumonia. The corresponding values when the 25 patients classified as indeterminate were excluded were sensitivity 50%, specificity 40%, positive predictive value 84%, and negative predictive value 11%.

Procalcitonin cutoff values of 0.5 ng/mL and 2.0 ng/mL resulted in similar operating characteristics for the assay. The median procalcitonin concentration values obtained 48 hours after the initial suspicion of pneumonia did not change significantly in any of the 3 groups, compared to the baseline values, and most of the individual procalcitonin concentration values overlapped between the groups at both the initial and the 48-hour time point (Fig. 1). Patients classified as having definite pneumonia had decreases in procalcitonin concentration between the 2 measurements that were statistically greater than in the patients classified as definite absence of pneumonia or indeterminate pneumonia (see Table 2).

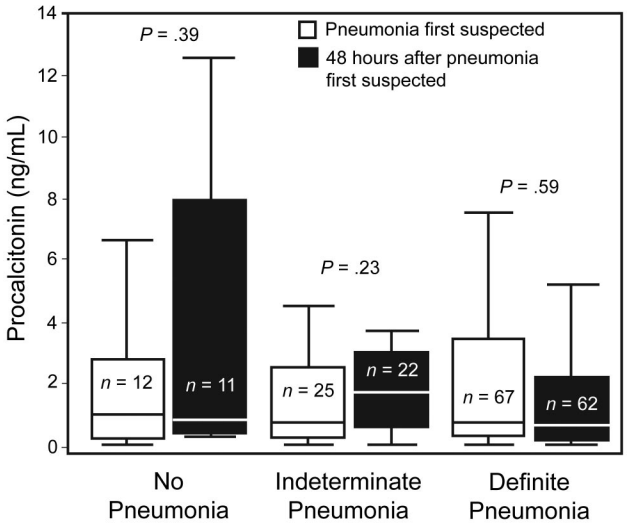

Fig. 1. Plasma procalcitonin concentration at first suspicion of nosocomial pneumonia and 48 hours later, versus presence/absence of pneumonia determined via culture of respiratory-tract secretions. In each bar, the horizontal line indicates the median, the top and bottom of the bar indicate the 25th and 75th percentiles (ie, the interquartile range), and the whiskers indicate the 5th and 95th percentiles. The P values are for comparison of the procalcitonin concentration in each pneumonia category.

Comparison of Procalcitonin to CPIS

CPIS obtained 48 hours after the initial suspicion of pneumonia was statistically greater in patients classified as

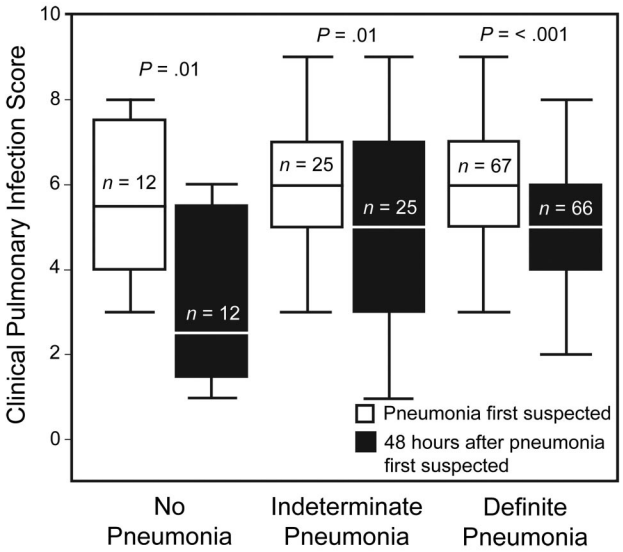

Fig. 2. Clinical Pulmonary Infection Score at first suspicion of nosocomial pneumonia and 48 hours later, versus presence/absence of pneumonia determined via culture of respiratory-tract secretions. In each bar, the horizontal line indicates the median, the top and bottom of the bar indicate the 25th and 75th percentiles (ie, the interquartile range), and the whiskers indicate the 5th and 95th percentiles. The *P* values are for comparison of the procalcitonin concentration in each pneumonia category.

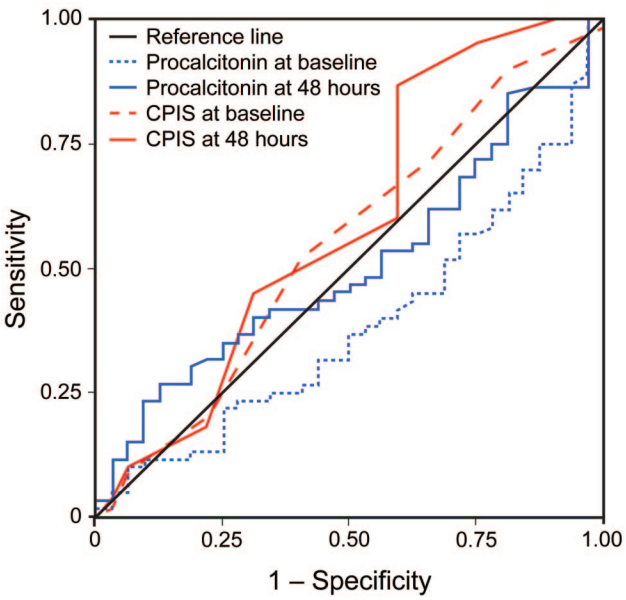

Fig. 3. Receiver operating characteristic curves of procalcitonin concentration and Clinical Pulmonary Infection Score at first suspicion of nosocomial pneumonia and 48 hours later, reflecting the correlation with pneumonia confirmed via culture of respiratory-tract secretions.

definite pneumonia and indeterminate pneumonia, compared to those classified with definite absence of pneumonia (see Table 2). CPIS obtained 48 hours after the initial suspicion of pneumonia was statistically lower, compared to CPIS obtained at baseline for all 3 pneumonia categories; however, most of the individual CPIS values again overlapped between groups (Fig. 2). There was also significant overlap of procalcitonin concentration for all individual CPIS values at baseline and 48 hours later ($r = -0.011$ and 0.139 respectively, $P = .67$ and .15, respectively). A CPIS cutoff value of > 6 had a diagnostic sensitivity of 48%, a specificity of 60%, a positive predictive value of 68%, and a negative predictive value of 39%. A similar analysis with a CPIS cutoff value of > 6 obtained 48 hours after the initial suspicion of pneumonia yielded a sensitivity of 18%, a specificity of 81%, a positive predictive value of 63%, and a negative predictive value of 36%.

Figure 3 shows the ROC curves for the correlation of definite pneumonia to procalcitonin and CPIS at baseline and 48 hours. The area under the ROC curve for CPIS was greater than that for procalcitonin concentration, at baseline (0.548, 95% CI 0.421–0.674, versus 0.506, 95% CI 0.386–0.626, respectively, $P = .35$) and at 48 hours (0.590, 95% CI 0.459–0.721, versus 0.385, 95% CI 0.268–0.503, $P = .07$).

Figure 4 shows the ROC curves for the procalcitonin and CPIS differences between baseline and 48 hours. The area under the ROC curve for the CPIS difference was statistically greater than that for the procalcitonin difference (0.582, 95% CI 0.462–0.702, versus 0.321, 95% CI 0.201–0.441, $P < .004$). Logistic regression analysis identified CPIS > 6 (adjusted odds ratio 4.1, 95% CI 2.2–7.7, $P = .02$) and the difference in CPIS score (adjusted odds ratio 1.5, 95% CI 1.2–1.8, $P = .03$) as the only independent predictors of definite pneumonia.

Antibiotic Duration, Hospital and ICU Stay, and Hospital Mortality

Table 3 shows the prognostic value of procalcitonin and CPIS for hospital and ICU stay, duration of mechanical ventilation, and antibiotic duration. Compared to patients with an initial procalcitonin value > 1 ng/mL, those with lower procalcitonin values had fewer total antibiotic days and fewer antibiotic days for treatment of nosocomial pneumonia. Similarly, compared to patients with an initial CPIS > 6, those with lower CPIS had fewer total antibiotic days and fewer antibiotic days for treatment of nosocomial pneumonia.

Hospital mortality was greater in patients with procalcitonin > 1 ng/mL when pneumonia was first suspected

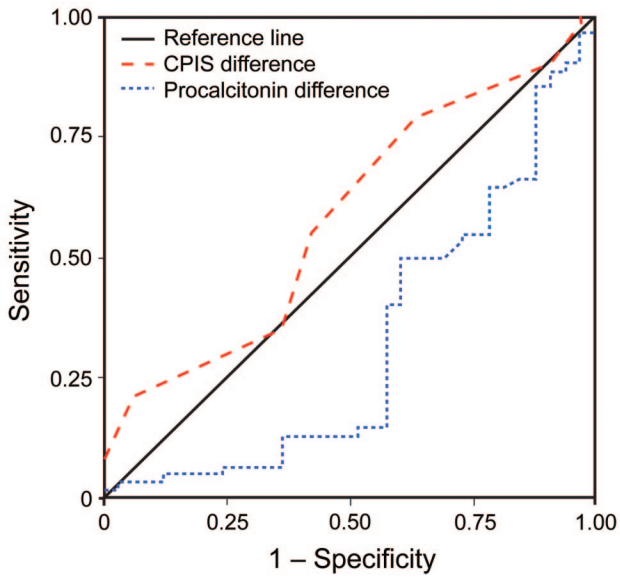

Fig. 4. Receiver operating characteristic curves of the difference in procalcitonin concentration and the difference in Clinical Pulmonary Infection Score between first suspicion of nosocomial pneumonia and 48 hours after first suspicion of nosocomial pneumonia, reflecting the correlation with pneumonia confirmed via culture of respiratory-tract secretions. The area under the ROC curve for the CPIS difference is statistically greater than that for the procalcitonin difference (P = .004).

(31% vs 16%, P = .07) and after 48 hours (37% vs 10%, P = .002), compared to patients with procalcitonin ≤ 1 ng/mL. Hospital mortality was similar in patients with CPIS > 6 when pneumonia was first suspected (28% vs 19%, P = .31) and after 48 hours (21% vs 23%, P = .86), compared to patients with CPIS ≤ 6.

Logistic regression analysis identified increasing Acute Physiology and Chronic Health Evaluation II scores (1-point increments) (adjusted odds ratio 1.11, 95% CI 1.06–1.15, P = .008) and procalcitonin > 1 ng/mL 48 hours after the first suspicion of pneumonia (adjusted odds ratio 7.2, 95% CI 3.1–16.9, P = .02) as independent predictors of hospital mortality.

Discussion

This study found that serum procalcitonin concentration was not a good predictor of definite nosocomial pneumonia in ICU patients. By ROC curve analysis and logistic regression analysis, CPIS and the CPIS difference were better predictors of definite pneumonia than was procalcitonin concentration.

Luyt et al evaluated 73 suspected VAP episodes and found that procalcitonin concentration and rise in procalcitonin had poor diagnostic value for VAP.[13] Using a cutoff of 0.5 ng/mL, procalcitonin had a sensitivity of 72% and a specificity of 24% for the diagnosis of VAP. However, Luyt et al also found that patients with VAP and sustained elevated procalcitonin had greater hospital mortality than patients with VAP but whose procalcitonin decreased.[11] Similarly, Seligman et al found that serial elevated procalcitonin was an independent predictor of outcome in patients with VAP.[12] Gibot et al found that other serum markers (tumor necrosis factor alpha and interleukin-1β) were not as accurate as CPIS for diagnosing VAP.[10] Duffo et al found that serum procalcitonin, but not alveolar procalcitonin, might be useful for diagnosing VAP.[9] However, using a procalcitonin cutoff of 3.9 ng/mL yielded a sensitivity of 41% and a specificity of 100%. Taken together with our results, the available data suggest that procalcitonin is not useful for diagnosing nosocomial pneumonia.[9,11,12]

Procalcitonin has also been used to guide antibiotic therapy in patients with respiratory infections.[16] Schuetz et al found that serial procalcitonin measurement, with predefined cutoff ranges for starting and stopping antibiotics, reduced antibiotic duration by 3 days in patients with lower-respiratory-tract infections.[17] Similarly, Bouadma et al used predefined procalcitonin cutoff ranges for starting and stopping antibiotics in patients with infection requiring ICU admission, resulting in approximately the same number of antibiotic-free days for the procalcitonin-

Table 3. Prognostic Value of Procalcitonin Concentration and Clinical Pulmonary Infection Score

	Procalcitonin Concentration			Clinical Pulmonary Infection Score		
	≤ 1 ng/mL	> 1 ng/mL	P	≤ 6	> 6	P
Hospital days	22.6 ± 16.6	27.0 ± 21.7	.24	23.9 ± 20.9	25.5 ± 16.9	.29
ICU days	13.9 ± 12.0	18.3 ± 12.4	.03	14.7 ± 11.9	17.5 ± 12.8	.17
Ventilator days	11.7 ± 14.0	15.3 ± 10.9	.02	11.6 ± 12.4	15.5 ± 13.0	.03
Total antibiotic days	13.0 ± 10.3	19.7 ± 12.0	< .001	13.8 ± 11.5	18.8 ± 11.1	.004
Nosocomial pneumonia antibiotic days	10.0 ± 5.9	14.7 ± 7.4	< .001	10.5 ± 6.9	14.2 ± 6.7	.002

ICU = intensive care unit

managed patients as found in the study by Schuetz et al.[18] However, those 2 studies focused primarily on patients with respiratory-tract infections, and the results may not be applicable to patients with other infections, including severe sepsis.[19] Additionally, it is not clear how rigorously antibiotics were managed in the control arms of those studies.[20] A previous investigation found that a pharmacist-driven protocol had a similar effect on reducing the duration of antibiotics in the ICU setting.[21]

Limitations

First, we included patients with healthcare-associated pneumonia, hospital-acquired pneumonia, and VAP, so our diagnostic classification may not have been as accurate as if we had included only patients with VAP. However, our findings were similar to those of Luyt et al,[11,13] and we found similar results when we excluded the patients with healthcare-associated pneumonia and hospital-acquired pneumonia from the analysis (data not shown).[13]

Second, most of our patients were classified as having definite pneumonia, which may have influenced the results if some of those patients were misclassified. Nevertheless, the patients with definite pneumonia met all the clinical and microbiologic criteria for the classification, as determined by 2 blinded investigators. Third, our study may have been underpowered to identify all the variables associated with definite pneumonia and hospital mortality. Fourth, although we excluded patients with any clinically identifiable concurrent infection, we cannot exclude the possibility that some patients had occult concurrent infections that were not clinically identified. Fifth, the procalcitonin change in patients with definite pneumonia may reflect the influence of antibiotic therapy. However, we did not attempt to assess the impact of various antibiotic regimens on procalcitonin or procalcitonin changes.

Conclusions

Our findings suggest that procalcitonin does not assist in diagnosing nosocomial pneumonia. However, the relationship between procalcitonin and antibiotic duration supports procalcitonin as a potential guide for starting and stopping antibiotics in ICU patients.[16,17,22] Additional studies are needed to assess procalcitonin as a tool for managing antimicrobial therapy in patients with nosocomial pneumonia.

REFERENCES

1. Anand N, Kollef MH. The alphabet soup of pneumonia: CAP, HAP, HCAP, NHAP, and VAP. Semin Respir Crit Care Med 2009;30(1):3-9.
2. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165(7):867-903.
3. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388-416.
4. Wunderink RG, Woldenberg LS, Zeiss J, Day CM, Ciemins J, Lacher DA. The radiologic diagnosis of autopsy-proven ventilator-associated pneumonia. Chest 1992;101(2):458-463.
5. Rea-Neto A, Youssef NC, Tuche F, Brunkhorst F, Ranieri VM, Reinhart K, Sakr Y. Diagnosis of ventilator-associated pneumonia: a systematic review of the literature. Crit Care 2008;12(2):R56.
6. Schuetz P, Christ-Crain M, Müller B. Biomarkers to improve diagnostic and prognostic accuracy in systemic infections. Curr Opin Crit Care 2007;13(5):578-585.
7. Yealy DM, Fine MJ. Measurement of serum procalcitonin: a step closer to tailored care for respiratory infections? JAMA 2009;302(10):1115-1116.
8. Dubos F, Korczowski B, Aygun DA, Martinot A, Prat C, Galetto-Lacour A, et al. Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children: a European multicenter case cohort study. Arch Pediatr Adolesc Med 2008;162(12):1157-1163.
9. Duflo F, Debon R, Monneret G, Bienvenu J, Chassard D, Allaouchiche B. Alveolar and serum procalcitonin: diagnostic and prognostic value in ventilator-associated pneumonia. Anesthesiology 2002;96(1):74-79.
10. Gibot S, Cravoisy A, Levy B, Bene MC, Faure G, Bollaert PE. Soluble triggering receptor expressed on myeloid cells and the diagnosis of pneumonia. N Engl J Med 2004;350(5):451-458.
11. Luyt CE, Guérin V, Combes A, Trouillet JL, Ayed SB, Bernard M, et al. Procalcitonin kinetics as a prognostic marker of ventilator-associated pneumonia. Am J Respir Crit Care Med 2005;171(1):48-53.
12. Seligman R, Meisner M, Lisboa TC, Hertz FT, Filippin TB, Fachel JM, Teixeira PJ. Decreases in procalcitonin and C-reactive protein are strong predictors of survival in ventilator-associated pneumonia. Crit Care 2006;10(5):R125.
13. Luyt CE, Combes A, Reynaud C, Hekimian G, Nieszkowska A, Tonnellier M, et al. Usefulness of procalcitonin for the diagnosis of ventilator-associated pneumonia. Intensive Care Med 2008;34(8):1434-1440.
14. Anand NJ, Zuick S, Klesney-Tait J, Kollef MH. Diagnostic implications of soluble triggering receptor expressed on myeloid cells-1 in BAL fluid of patients with pulmonary infiltrates in the ICU. Chest 2009;135(3):641-647.
15. Kollef MH, Bock KR, Richards RD, Hearns ML. The safety and diagnostic accuracy of minibronchoalveolar lavage in patients with suspected ventilator-associated pneumonia. Ann Intern Med 1995;122(10):743-748.
16. Brown JS. Biomarkers and community-acquired pneumonia. Thorax 2009;64(7):556-558.
17. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. JAMA 2009;302(10):1059-1066.
18. Kollef MH. Will procalcitonin reduce antibiotic use in intensive care? Lancet 2010;375(9713):435-436.
19. Bouadma L, Luyt CE, Tubach F, Cracco C, Alvarez A, Schwebel C, et al. Use of procalcitonin to reduce patients' exposure to antibiotics

in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet 2010;375(9713):463-474.
20. Venkatesh B, Kennedy P, Kruger PS, Looke D, Jones M, Hall J, Barruel GR. Changes in serum procalcitonin and C-reactive protein following antimicrobial therapy as a guide to antibiotic duration in the critically ill: a prospective evaluation. Anaesth Intensive Care 2009;37(1):20-56.
21. Micek ST, Ward S, Fraser VJ, Kollef MH. A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. Chest 2004;125(5):1791-1799.
22. Procalcitonin guidance and reduction of antibiotic use in acute respiratory tract infection. Burkhardt O, Ewig S, Haagen U, Giersdorf S, Hartmann O, Wegscheider K, et al. Eur Respir J 2010;36(6):601-607.