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Predictive Values of Semi-Quantitative Procalcitonin Test and Common Biomarkers for the Clinical Outcomes of Community-Acquired Pneumonia

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community-acquired pneumonia, semi-quantitative procalcitonin test, blood urea nitrogen, albumin, mortality, severity

Conflict of interest statement

None of the authors has any conflict of interest in connection with this article.

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Abstract

Background

The semi-quantitative serum procalcitonin (PCT) test (BRAHMS PCT-Q®) is available conveniently in clinical practice. However, there is little data on the relationship between this semi-quantitative PCT test results and clinical outcomes of community-acquired pneumonia (CAP). We investigated the usefulness of this PCT test for predicting the clinical outcomes of CAP in comparison with severity scoring systems and the blood urea nitrogen to serum albumin (B/A) ratio, which has been reported to be a simple but reliable prognostic indicator in our prior CAP study.

Methods

This retrospective study included data from subjects hospitalized for CAP from August 2010 through October 2012 in whom the semi-quantitative serum PCT test was performed on admission. The demographic characteristics, laboratory biomarkers, microbiological test results, pneumonia severity index (PSI), CURB-65, and A-DROP on admission were retrieved from their medical charts. The outcomes were mortality within 28 days of admission and the need for intensive care.

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Results

Of the 213 subjects with CAP enrolled, 20 died within 28 days of admission and 32 required intensive care. Mortality did not differ significantly among subjects with different semi-quantitative serum PCT levels; however, subjects with serum PCT levels ≥10.0 ng/mL were more likely to require intensive care than those with lower levels ($p < 0.001$). The elevation of semi-quantitative serum PCT levels was more frequently observed in subjects with proven etiology, especially pneumococcal pneumonia. Using the receiver-operating characteristic curves for mortality, the area under curve was 0.86 for PSI class, 0.81 for B/A ratio, 0.81 for A-DROP, 0.80 for CURB-65, and 0.57 for semi-quantitative PCT test.

Conclusion

The semi-quantitative serum PCT level on admission was less predictive of mortality from CAP as compared to the B/A ratio. However, the subjects with serum PCT levels ≥10.0 ng/mL were more likely to require intensive care than those with lower levels.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Introduction

Community-acquired pneumonia (CAP) is a serious illness and a common cause of death. Clinicians often wish to evaluate the disease severity and risk for mortality in patients with CAP. Therefore, many severity scoring systems for CAP have been introduced throughout the world. Of these scoring systems, pneumonia severity index (PSI) is recommended by the American Thoracic Society/Infectious Disease Society of America,[1] CURB-65, by the British Thoracic Society,[2] and A-DROP, by the Japanese Respiratory Society.[3] However, these scoring systems are subjective. It is often difficult to evaluate the mental status of patients with CAP who are elderly or have dementia, and the severity score assigned may therefore vary among clinicians.[4,5]

The quantitative serum procalcitonin (PCT) level has been reported to be a useful predictive prognostic marker in CAP.[6-8] However, in order to measure quantitative PCT levels, approximately 16 million yen is necessary as capital investment in Japan. Therefore, the facilities with capability to measure quantitative PCT levels immediately after blood sampling are limited due to the cost of the analysis. In clinical practice, a semi-quantitative serum PCT test kit (BRAHMS PCT-Q®, B.R.A.H.M.S GmbH, Hennigsdorf, Germany) is available conveniently and costs only 2,800 yen of each measurement without need for capital investment. This kit measures serum PCT levels using an immunochromatographic assay with an incubation

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

period of approximately 30 minutes, and categorizes the serum PCT levels as 1 of 4 grades (<0.5 ng/mL, 0.5–<2.0 ng/mL, 2.0–<10.0 ng/mL, or ≥10.0 ng/mL). On the other hand, there is little data on the usefulness of this semi-quantitative serum PCT test for predicting clinical outcomes of CAP. To our knowledge, only one report produced by Kasamatsu *et al.* showed that the semi-quantitative PCT test was useful for predicting mortality from CAP, but not as good as PSI, CURB-65, and A-DROP.[9] In short, the significance of performing this semi-quantitative serum PCT test for patients with CAP has not been yet revealed enough.

Of the commonly used laboratory biomarkers, earlier several studies showed that higher blood urea nitrogen levels and lower serum albumin levels indicate the poor clinical outcomes of CAP.[2,10-13] Moreover, our prior prospective observational study showed that the blood urea nitrogen to serum albumin (B/A) ratio was more accurate for predicting mortality and severity of CAP than blood urea nitrogen or serum albumin levels alone.[14]

In this single-center retrospective study, we investigated the predictive ability of the semi-quantitative serum PCT test for the clinical outcomes of CAP in comparison with severity scoring systems and commonly used laboratory biomarkers.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Materials and methods

Ethics

The informed consent obtained from all subjects was verbal, because this study protocol included no interventional procedure and used only a database that had guaranteed confidentiality. This study protocol and consent procedure were followed the statements of the Declaration of Helsinki and approved by the ethics committee of our hospital, called the Research Ethics Review Committee of Ichinomiya-Nishi Hospital (No. 20135).

Study population

Patients with CAP, who were admitted to Ichinomiya-Nishi Hospital (a 400-bed teaching hospital, Ichinomiya City, Aichi, Japan) from August 2010 through October 2012 and in whom the semi-quantitative serum PCT test on admission were enrolled in this study. CAP was diagnosed in patients aged ≥18 years, who were admitted from the community including a nursing home, were not exposed to antibiotics during the 14 days prior to enrollment, had not been hospitalized in the 90 days prior to enrollment, presented with a new radiographic infiltrate, and exhibited at least 2 compatible clinical symptoms (e.g., body temperature >38ºC, productive cough, chest pain, shortness of breath, and crackles on auscultation). Patients were excluded if they were chronically immunosuppressed (i.e., undergoing chemotherapy or other therapy with

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

corticosteroids or other immunosuppressive agents or infected with human immunodeficiency virus), had advanced liver disease, or had received hemodialysis or been found to have a serum creatinine level ≥1.5 mg/dL due to chronic kidney disease.

Study design

The following variables were retrieved from medical charts: (1) demographic characteristics (age and sex); (2) coexisting illnesses; (3) clinical data at the time of admission (body temperature, respiratory rate, percutaneous oxygen saturation, blood pressure, cardiac frequency, and mental status); (4) laboratory and radiographic findings on admission; (5) PSI, CURB-65 and A-DROP scores on admission; (6) causative pathogens; (7) intravenous initial antibiotic regimens; and (8) clinical outcomes.

The clinical outcomes were mortality within 28 days of admission and the requirement for intensive care, defined as the necessity of employing mechanical ventilation or vasopressor therapy against shock. The A-DROP is a 5-point scoring system similar to CURB-65 and includes confusion, blood urea nitrogen >20 mg/dL, percutaneous oxygen desaturation <90 %, systolic blood pressure <90 mmHg, and age ≥70 years for men or ≥75 years for women.[3] Causative pathogens were diagnosed as the following criteria: (1) for *Streprococcus pneumonia*, 3+ growth of sputum culture or the presence of antigen in urine; (2) for *Legionella pneumophila*,

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

the presence of antigen in urine; and (3) for other bacteria, 3+ growth of sputum culture.

The endpoints of this study was to evaluate the predictive ability of severity scoring systems and laboratory biomarkers for the clinical outcomes of CAP, according to the guideline of standards for the reporting of diagnostic accuracy studies (STARD).[15]

Methods

PCT was measured using an immunochromatographic semi-quantitative PCT test kit (BRAHMS PCT-Q®) that categorizes the serum PCT levels as 1 of 4 grades (<0.5 ng/mL, 0.5–<2.0 ng/mL, 2.0–<10.0 ng/mL, or ≥10.0 ng/mL). Blood urea nitrogen was measured using the enzymatic method with urease and glutamate dehydrogenase (Shino-Test Corporation, Tokyo, Japan). Serum C-reactive protein (CRP) level was measured using the latex nephelometric assay (Nittobo Medical, Tokyo, Japan). Serum albumin level was measured using the bromocresol green method (Shino-Test Corporation) from August 2010 through December 2011 and the bromocresol purple method (Kainos Laboratories, Tokyo, Japan) from January through October 2012. The normal range of the serum albumin level is the same for both of methods. Other biochemical markers were assayed using standard methods. Routine sampling to detect the causative pathogens included sputum and urinary antigen tests for *Streptococcus pneumoniae* (Binax Inc., Portland, ME) and *Legionella pneumophila* serogroup 1 (Binax Inc.).

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Statistical analysis

Data are expressed as numbers or the median (25th–75th percentile range). Differences between 2 groups were tested using the non-parametric Mann-Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables. Receiver-operating characteristic (ROC) curve analysis and the calculation of the area under the curve (AUC) were performed to assess the diagnostic ability of each potential indicator and identify the optimal cutoff values for predicting mortality and the requirement for intensive care. A two-tailed probability value of <0.05 was considered significant.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Results

Clinical characteristics

A total of 376 patients with CAP were admitted to our hospital during the study period. Of these patients, 163 were excluded because no semi-quantitative PCT measurement was performed on admission (n = 149) or because of chronic kidney disease (n = 13) or advanced liver disease (n = 1). The remaining 213 subjects were enrolled in this study (Figure 1). Their demographic characteristics are shown in Table 1. Fifty-nine subjects (27.7%) were admitted from a nursing home. Twenty subjects (9.4%) died within 28 days of admission and 32 subjects (15.0%) required intensive care. The elevation of semi-quantitative serum PCT level (≥0.5 ng/mL) was observed in 110 subjects (51.6%).

The semi-quantitative serum PCT levels and causative pathogens

Causative pathogens were detected in 99 subjects (46.5%) and are listed in Table 2. The most frequently detected pathogen was *Streptococcus pneumoniae* (n = 43, 20.2%). The elevation of semi-quantitative serum PCT levels (≥0.5 ng/mL) was more frequently observed in subjects whose causative pathogen was detected than in those without proven etiology (59.6% versus 44.7%, p = 0.039). In particular, significantly more subjects with pneumococcal etiology had the elevation of semi-quantitative serum PCT levels (67.4%, p = 0.013).

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Predictive value for mortality

Table 3 shows a comparison of the demographic and clinical characteristics between the deceased and surviving subjects. The deceased subjects were more likely to be of advanced age and nursing home inhabitants, have required intensive care, and have been treated with anti-pseudomonal beta-lactam agents as initial antibiotics. Concerning severity scoring systems, the deceased subjects were more likely to have high PSI risk class, high CURB-65 scores, and high A-DROP scores. Comparison of the commonly used laboratory biomarkers between the groups showed that the deceased subjects had higher blood urea nitrogen levels, higher B/A ratios, and lower serum albumin levels than surviving subjects. Mortality did not differ significantly according to the subjects' semi-quantitative serum PCT levels (Table 3, Figure 2A).

The ROC curves for predicting mortality within 28 days from admission are shown in Figure 3A. The area under the curve (AUC) values were 0.86 (95% confidence interval [CI] 0.78–0.94) for the PSI class, 0.81 (95% CI 0.72–0.91) for the B/A ratio, 0.81 (95% CI 0.74–0.89) for the A-DROP score, 0.80 (95% CI 0.73–0.88) for the CURB-65 score, 0.74 (95% CI 0.63–0.84) for the serum albumin level, 0.73 (95% CI 0.61–0.85) for the blood urea nitrogen level, 0.57 (95% CI 0.44–0.71) for the semi-quantitative serum PCT test, and 0.54 (95% CI 0.40–0.67) for the

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

serum CRP level.

Predictive value for the need for intensive care

Table 4 shows a comparison of the demographic and clinical characteristics of subjects who did or did not receive intensive care. The subjects who required intensive care were more likely to be of advanced age and nursing home inhabitants and have been treated with anti-pseudomonal beta-lactam agents as initial antibiotics. Concerning severity scoring systems, the subjects who required intensive care were more likely to have high PSI risk class, high CURB-65 scores, and high A-DROP scores. Comparison of the commonly used laboratory biomarkers between the groups showed that subjects who required intensive care had higher blood urea nitrogen levels, higher B/A ratios, and lower serum albumin levels than those who did not require intensive care. Subjects with serum PCT levels ≥10.0 ng/mL were significantly more likely to require intensive care than those with levels <10.0 ng/mL ($p < 0.001$, Figure 2B).

The ROC curves for predicting the need for intensive care are shown in Figure 3B. The AUC was 0.87 (95% CI 0.80–0.93) for the PSI class, 0.86 (95% CI 0.81–0.92) for the A–DROP score, 0.86 (95% CI 0.80–0.92) for the CURB-65 score, 0.85 (95% CI 0.79–0.91) for the B/A ratio, 0.82 (95% CI 0.74–0.90) for the blood urea nitrogen level, 0.72 (95% CI 0.62–0.82) for the semi-quantitative serum PCT test, 0.67 (95% CI 0.57–0.76) for the serum albumin level, and

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

0.56 (95% CI 0.44–0.67) for the serum CRP level.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Discussion

In the present CAP study, we showed that (1) the semi-quantitative serum PCT test performed on admission had little predictive value for mortality, (2) a semi-quantitative serum PCT level ≥10.0 ng/mL on admission indicated a high probability for requiring intensive care, (3) the elevation of semi-quantitative serum PCT level was more frequently observed in subjects with proven pathogen, particularly pneumococcal pneumonia, and (4) the B/A ratio on admission was as accurate as CURB-65 and A-DROP scores for predicting mortality and the need for intensive care.

PCT is well-known as a systemic inflammatory protein induced under bacterial infection and a diagnostic biomarker for estimating the likelihood of septic infection. The serum PCT level shows a strong positive correlation with the severity of sepsis.[16,17] Septic shock, the most severe form of sepsis, is defined as sepsis-induced hypotension that persists despite adequate fluid resuscitation and requires treatment with vasopressor agents.[18] Many patients with septic shock have been reported to have serum PCT levels ≥10.0 ng/mL.[16,17] Moreover, many critically ill patients progressing to acute respiratory distress syndrome had serum PCT levels ≥10.0 ng/mL.[19] Similarly, the present study revealed that subjects with semi-quantitative serum PCT levels ≥10.0 ng/mL required intensive care, including vasopressor administration or mechanical

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

ventilation, more frequently than those with levels <10.0 ng/mL. However, over a half of subjects who needed intensive care had semi-quantitative serum PCT levels of <10.0 ng/mL. In particular, 21.9% of them had its negative value (<0.5 ng/mL). A former CAP study showed that while a positive correlation was observed between the probability of intensive care unit admission and serum PCT levels, about a half of patients who were admitted to intensive care units had serum PCT levels of <0.5 ng/mL.[20] In short, the semi-quantitative serum PCT levels ≥10.0 ng/mL might indicate the high probability of need for intensive care, but the lower levels of semi-quantitative serum PCT could not exclude the possibility of need for intensive care.

The quantitative serum PCT level at the time of admission has been shown to be a reliable prognostic indicator in patients with CAP.[6,8,21] However, in the present study, we did not find the semi-quantitative serum PCT test to be useful for predicting mortality from CAP. We propose 2 explanations for this discrepancy. The first, the semi-quantitative serum PCT test may be inaccurate; a study in a pediatric emergency department found that 103 out of 359 pairs of BRAHMS PCT-Q® and quantitative PCT measurements were discordant.[22] Another study found that the BRAHMS PCT-Q® was frequently 1 grade higher or lower than would be indicated by the quantitative measurement.[23] The second explanation is that the grades defined by the semi-quantitative serum PCT test may be too coarse to be useful in patients with CAP. The

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

elevation of the serum PCT level in patients with CAP unless sepsis is generally minimal.[24] Shuetz *et al.* showed that while the serum PCT level was significantly higher in non-survivors of CAP than in survivors, the difference between the median values was very small (0.39 ng/mL).[20] In contrast, the BRAHMS PCT-Q® categorizes serum PCT levels into only 4 grades (<0.5 ng/mL; 0.5–<2.0 ng/mL; 2.0–<10.0 ng/mL; ≥10.0 ng/mL). These wide ranges may be inadequate for predicting mortality due to CAP.

Unlike the present study, Kasamatsu *et al.* showed that the semi-quantitative PCT measurement was useful for predicting mortality from CAP.[9] We can propose 2 possible explanations for this discrepancy. First, the timing of blood sampling differed between the two studies. We only included subjects whose semi-quantitative PCT measurement had been performed on admission, while the prior study included subjects whose measurement had been done within 24 hours from admission. The change of serum PCT level is drastic in systemic bacterial infection. A study using healthy volunteers demonstrated that the concentration of serum PCT was peaked at 6 hours after injection of endotoxin.[25] On the other hand, the decline of serum PCT level was observed within 24 hours from the start of appropriate treatment.[26] Some earlier studies on septic patients showed that the serum PCT levels after 24 hours from admission predicted mortality more accurately than those of admission time.[27,28] In short, the

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

PCT levels after 24 hours from admission may have already reflected patients' clinical course. Second, the study population differed between the two studies. For example, we excluded the subjects who had advanced liver diseases or chronic kidney diseases to evaluate the prognostic value of commonly used laboratory biomarkers. The serum PCT level tends to be higher in patients with cirrhosis or renal impairment.[29,30] These comorbidities may have affected the results in both studies.

PSI is based on patient characteristics, co-morbid illnesses, physical examination, radiographic findings, and laboratory findings.[1] Consistent with the present study, PSI has been shown to perform as a reliable predictor of mortality and severity of CAP, but it may be complex to calculate and difficult to implement in routine clinical practice.[31] Therefore, other simple indicators that perform as well as PSI should be considered in CAP. CURB-65 and A-DROP are simple and widely used severity scoring systems for CAP.[2,3] In the present study, these simple severity scores showed good abilities of predicting mortality and severity of CAP. However, these severity scoring systems have some weaknesses. First, it is difficult for clinicians to evaluate the change in mental status due to pneumonia in old patients.[5] Second, these scoring systems can underestimate the potential severity of CAP in young patients.[32]

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Among the many possible laboratory biomarkers, several serum markers such as the D-dimer,[33] cortisol,[34] B-type natriuretic peptide,[35] mid-regional proatrial natriuretic peptid,[36] and copeptin [37] levels correlate well with the clinical outcomes of CAP. However, these parameters are unsuitable for routine use in patients with CAP due to the cost of the assays or the retrospective nature of the results. In contrast, the blood urea nitrogen and serum albumin levels are commonly tested, can be measured quickly, and has been reported as prognostic indicators of CAP.[2,10-13] We have previously shown that the combination of blood urea nitrogen and serum albumin was more accurate for predicting mortality and severity of CAP than each of them.[14] Blood urea nitrogen is frequently elevated in patients with dehydration, while low serum albumin levels occur in those with malnutrition and inflammation.[38,39] Therefore, a high B/A ratio is associated with critical illness. In the present study, we have shown that the B/A ratio is a good indicator of both the risk for mortality from and the severity of CAP, with predictive value comparable to those of CURB-65 and A-DROP scores. The sensitivity, specificity, and positive and negative predictive value of the B/A ratio for mortality and the need for intensive care are presented in Supplemental Table 1. The optimal cutoff value of the B/A ratio for predicting mortality was 14.65 mg/g, with 50.0 % sensitivity, 96.4% specificity, a positive predictive value of 58.8%, and a negative predictive value of 94.9%. Similarly, the optimal cutoff value of the B/A ratio for predicting the need for intensive care was 9.85 mg/g, with

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

59.4 % sensitivity, 89.0% specificity, a positive predictive value of 48.7%, and a negative predictive value of 92.5%.

We must note several limitations of our current study. First, this study cohort included a limited number of subjects because it was a single-center study. To prove the usefulness of the semi-quantitative serum PCT test and B/A ratio on admission for predicting the clinical outcomes of CAP, additional studies involving a large number of subjects are needed. Second, we excluded about 40% of admitted patients from this analysis due to the absence of semi-quantitative PCT measurement on admission. No significant differences were observed between the excluded patients and included subjects in age, gender, mortality, and the need for intensive care. However, we could not deny that such a high rate of exclusion might influence the results of our present study. Third, most subjects in our study cohort were of advanced age. Therefore, our mortality rate may be higher compared to that in other earlier CAP studies. To evaluate the clinical significance of the semi-quantitative serum PCT test and B/A ratio on admission in CAP, additional studies including younger patients are needed.

In conclusion, the semi-quantitative serum PCT level on admission had little predictive value for mortality in patients with CAP. However, patients with serum PCT levels ≥10.0 ng/mL had a

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

high probability of requiring intensive care. In addition, the B/A ratio on admission was a reliable predictor of the risk for mortality from and severity of CAP.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

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RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Figure legends

Figure 1. Flow diagram explaining recruitment of study population. CAP: community-acquired pneumonia; PCT: procalcitonin.

Figure 2. Distribution of subjects with different semi-quantitative serum procalcitonin levels. (A) Relation with mortality. Significant differences were not observed between any 2 concentration groups. (B) Relation with the requirement for intensive care. Subjects with serum procalcitonin levels ≥10.0 ng/mL were significantly more likely to require intensive care than those with levels <10.0 ng/mL ($p < 0.001$).

Figure 3. Analysis of the receiver-operating characteristics curves. (A) For predicting mortality. The area under the curve values were 0.86 for the PSI class, 0.81 for the B/A ratio, 0.80 for the CURB-65, and 0.57 for the semi-quantitative PCT test. (B) For predicting the requirement for intensive care. The area under the curve values were 0.87 for the PSI class, 0.86 for the CURB-65, 0.85 for the B/A ratio, and 0.72 for the semi-quantitative PCT test. PSI: pneumonia severity index; B/A ratio: blood urea nitrogen to serum albumin ratio; PCT: procalcitonin.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Table 1. Baseline characteristics of enrolled subjects

Characteristics	Values
Total	213
Age, years	82 (74–88)
Male patients	127 (59.6)
From nursing home	59 (27.7)
Identification of pathogen	99 (46.5)
Death within 28 days	20 (9.4)
Intensive care requirement	32 (15.0)
Co-existing illnesses	
Chronic lung disease	30 (14.1)
Diabetes mellitus	32 (15.0)
Heart failure	39 (18.3)
Neoplastic disease	4 (1.9)
Intravenous initial antibiotics	
Anti-Pseudomonal beta-lactams	156 (73.2)
Tetracyclines	62 (29.1)
Fluoroquinolones	18 (8.5)
Clindamycin	16 (7.5)
Macrolides	3 (1.4)
Antibiotic combination therapy	84 (39.4)
PSI class	
1–2	24 (11.3)
3	56 (26.3)
4	87 (40.8)
5	46 (21.6)
CURB-65	
0–1	66 (31.0)
2	64 (30.0)
≥3	83 (39.0)
A-DROP	
0–1	76 (35.7)

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

2	55 (25.8)
≥3	82 (38.5)
Semi-quantitative PCT	
<0.5 ng/mL	103 (48.4)
0.5–< 2.0 ng/mL	48 (22.5)
2.0–< 10.0 ng/mL	33 (15.5)
≥10.0 ng/mL	29 (13.6)
Leukocyte count, 10^9 cells/L	10.8 (8.4–13.5)
Hematocrit, %	36.7 (33.4–39.7)
C-reactive protein, mg/dL	15.10 (7.04–21.23)
Sodium, mEq/L	139 (136–141)
Glucose, mg/dL	125 (106–152)
Creatinine, mg/dL	0.78 (0.64–1.06)
Blood urea nitrogen, mg/dL	19.9 (14.8–27.9)
Albumin, g/dL	3.4 (3.0–3.8)
B/A ratio, mg/g	6.14 (4.24–8.92)

Data are expressed as number (%) or median (25th–75th range). PSI: pneumonia severity index;

PCT: procalcitonin; B/A ratio: blood urea nitrogen to serum albumin ratio.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Table 2. Causative pathogens

Micro-organism	**Number**	**PCT ≥0.5 ng/mL**	**p value***
Identification of pathogen	99 (46.5)	59	0.039
Streptococcus pneumoniae	43 (20.2)	29	0.013
Klebsiella pneumoniae	13 (6.1)	7	0.569
Pseudomonas aeruginosa	11 (5.2)	5	>0.999
Staphylococcus species	8 (3.8)	6	0.144
Haemophilus influenzae	7 (3.3)	3	>0.999
MRSA	6 (2.8)	5	0.096
Escherichia coli	4 (1.9)	2	>0.999
Moraxella catarrhalis	2 (0.9)	0	0.503
Legionella pneumophila	1 (0.5)	1	0.452
Enterobacter species	1 (0.5)	1	0.452
Acinetobacter baumannii	1 (0.5)	0	>0.999
Proteus mirabilis	1 (0.5)	0	>0.999
Stenotrophomonas maltophilia	1 (0.5)	0	>0.999
Unknown	114 (53.5)	51	Reference

Data are expressed as number (%). PCT: procalcitonin; MRSA: methicillin-resistant *Staphylococcus aureus*. *: comparison with patients whose causative pathogen was unknown.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Table 3. Comparison of the characteristics between deceased and surviving subjects with CAP

	Deceased (n = 20)	Surviving (n = 193)	P value
Age, years	87 (83–89)	81 (73–87)	0.004
Male patients	10 (50.0)	117 (60.6)	0.473
From nursing home	12 (60.0)	47 (24.4)	<0.001
Identification of pathogens	13 (65.0)	86 (44.6)	0.1
Intensive care requirement	14 (70.0)	18 (9.3)	<0.001
Co-existing illness	10 (50.0)	81 (42.0)	0.489
Intravenous initial antibiotics			
Anti-Pseudomonal beta-lactams	19 (95.0)	137 (71.0)	0.018
Tetracyclines	6 (30.0)	56 (29.0)	>0.999
Fluoroquinolones	2 (10.0)	16 (8.3)	0.68
Clindamycin	1 (5.0)	15 (7.8)	>0.999
Macrolides	0	3 (1.6)	>0.999
Antibiotic combination therapy	8 (40.0)	76 (39.4)	>0.999
PSI class	5 (5–5)	4 (3–4)	<0.001
CURB-65	3 (3–4)	2 (1–3)	<0.001
A-DROP	3 (3–4)	2 (1–3)	<0.001
Semi-quantitative PCT			
<0.5 ng/mL	8 (40.0)	95 (49.2)	
0.5–< 2.0 ng/mL	4 (20.0)	44 (22.8)	>0.999*
2.0–< 10.0 ng/mL	3 (15.0)	30 (15.5)	0.728*
≥10.0 ng/mL	5 (25.0)	24 (12.4)	0.158*
Leukocyte count, 10^9 cells/L	10.7 (8.6–14.7)	10.8 (8.3–13.4)	0.555
Hematocrit, %	35.6 (29.5–38.9)	37.2 (33.7–39.9)	0.165
C-reactive protein, mg/dL	15.22 (8.31–23.70)	15.06 (6.78–20.52)	0.573
Sodium, mEq/L	141 (134–148)	139 (136–141)	0.23
Glucose, mg/dL	116 (101–153)	126 (107–152)	0.379
Creatinine, mg/dL	0.78 (0.62–1.46)	0.77 (0.65–1.02)	0.349
Blood urea nitrogen, mg/dL	33.8 (18.5–51.3)	19.5 (14.7–26.6)	0.001
Albumin, g/dL	3.1 (2.2–3.4)	3.5 (3.1–3.9)	0.001

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

B/A ratio, mg/g	12.00 (8.11–18.28)	5.74 (4.14–8.58)	<0.001

Data are expressed as number (%) or median (25th–75th percentile range). PSI: pneumonia severity index; PCT: procalcitonin; B/A ratio: blood urea nitrogen to serum albumin ratio. *: comparison with semi-quantitative PCT levels of <0.5 ng/mL.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Table 4. Comparison of the characteristics between subjects with and without intensive care

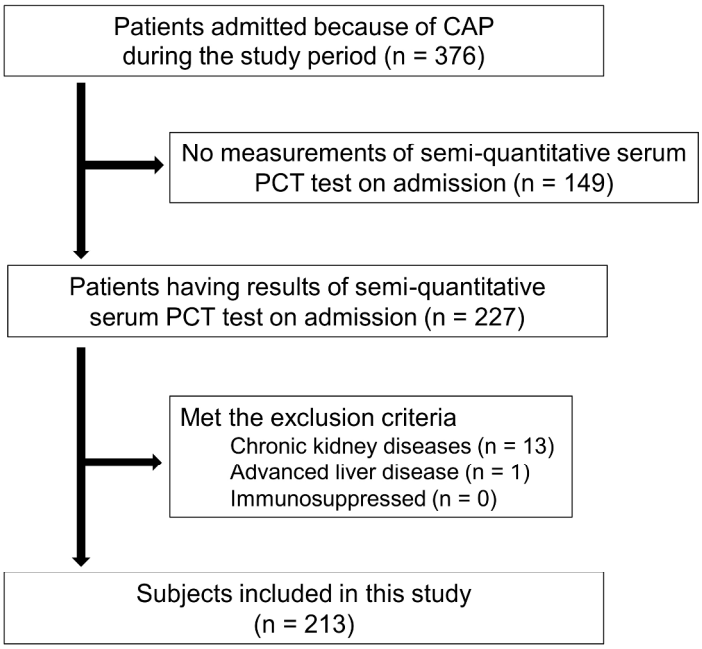
	IC requirement (n = 32)	No requirement (n = 181)	P value
Age, years	85 (82–90)	80 (72–87)	0.001
Male patients	20 (62.5)	107 (59.1)	0.846
From nursing home	17 (53.1)	42 (23.2)	0.001
Identification of pathogens	18 (56.3)	81 (44.8)	0.253
Co-existing illness	17 (53.1)	74 (40.9)	0.245
Intravenous initial antibiotics			
Anti-Pseudomonal beta-lactams	30 (93.8)	126 (69.6)	0.004
Tetracyclines	10 (31.3)	52 (28.7)	0.833
Fluoroquinolones	5 (15.6)	13 (7.2)	0.158
Clindamycin	3 (9.4)	13 (7.2)	0.714
Macrolides	0	3 (1.7)	>0.999
Antibiotic combination therapy	15 (46.9)	69 (38.1)	0.433
PSI class	5 (5–5)	4 (3–4)	<0.001
CURB-65	4 (3–4)	2 (1–3)	<0.001
A-DROP	4 (3–4)	2 (1–3)	<0.001
Semi-quantitative PCT			
<0.5 ng/mL	7 (21.9)	96 (53.0)	
0.5–<2.0 ng/mL	7 (21.9)	41 (22.7)	0.14*
2.0–<10.0 ng/mL	4 (12.5)	29 (16.0)	0.461*
≥10.0 ng/mL	14 (43.8)	15 (8.3)	<0.001*
Leukocyte count, 10^9 cells/L	11.0 (7.7–13.3)	10.8 (8.4–13.6)	0.89
Hematocrit, %	35.4 (31.6–38.8)	37.2 (33.9–39.9)	0.15
C-reactive protein, mg/dL	15.68 (7.05–25.86)	15.06 (7.04–20.44)	0.312
Sodium, mEq/L	140 (135–145)	139 (136–141)	0.161
Glucose, mg/dL	122 (101–155)	125 (107–152)	0.686
Creatinine, mg/dL	1.06 (0.66–1.15)	0.76 (0.62–0.98)	0.056
Blood urea nitrogen, mg/dL	33.1 (26.3–50.0)	18.6 (14.4–25.4)	<0.001
Albumin, g/dL	3.2 (2.7–3.5)	3.5 (3.1–3.9)	0.003
B/A ratio, mg/g	11.42 (8.14–17.33)	5.57 (4.08–7.90)	<0.001

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Data are expressed as number (%) or median (25th–75th percentile range). IC: intensive care; PSI: pneumonia severity index; PCT: procalcitonin; B/A ratio: blood urea nitrogen to serum albumin ratio. *: comparison with semi-quantitative PCT levels of <0.5 ng/mL.

RESPIRATORY CARE Paper in Press. Published on October 29, 2013 as DOI: 10.4187/respcare.02807

Figure 1



Flow diagram explaining recruitment of study population. CAP: community-acquired pneumonia; PCT: procalcitonin.
254x190mm (300 x 300 DPI)

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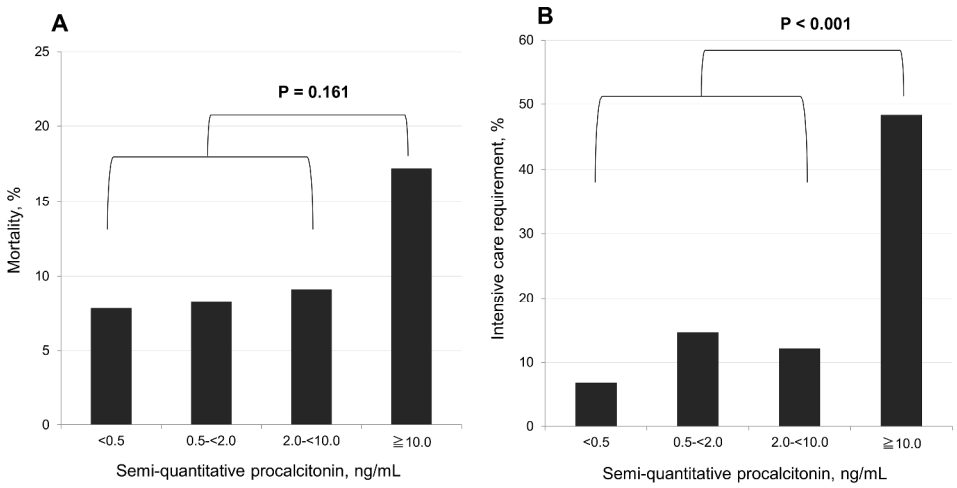
Figure 2



Distribution of subjects with different semi-quantitative serum procalcitonin levels. (A) Relation with mortality. Significant differences were not observed between any 2 concentration groups. (B) Relation with the requirement for intensive care. Subjects with serum procalcitonin levels ≥10.0 ng/mL were significantly more likely to require intensive care than those with levels <10.0 ng/mL ($p < 0.001$).
420x297mm (300 x 300 DPI)

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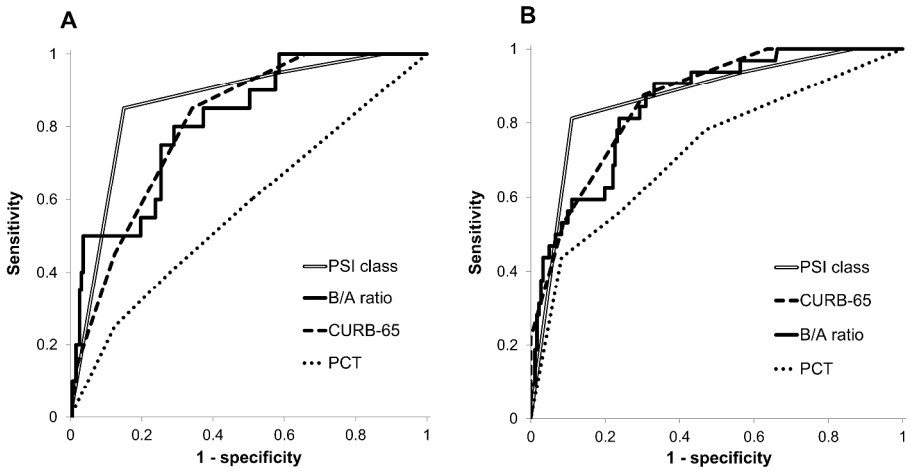
Figure 3



Analysis of the receiver-operating characteristics curves. (A) For predicting mortality. The area under the curve values were 0.86 for the PSI class, 0.81 for the B/A ratio, 0.80 for the CURB-65, and 0.57 for the semi-quantitative PCT test. (B) For predicting the requirement for intensive care. The area under the curve values were 0.87 for the PSI class, 0.86 for the CURB-65, 0.85 for the B/A ratio, and 0.72 for the semi-quantitative PCT test. PSI: pneumonia severity index; B/A ratio: blood urea nitrogen to serum albumin ratio; PCT: procalcitonin.
420x297mm (300 x 300 DPI)