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RESEARCH

Procalcitonin kinetics in the first 48 hours of ICU admission is associated with higher mortality in critically ill patients with community-acquired pneumonia in a setting of high HIV prevalence

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Background: Severe community acquired pneumonia (CAP) commonly results in ICU admission and is associated with significant morbidity and mortality. Procalcitonin (PCT) may assist risk stratification and prediction of aetiology but is not well studied in critically ill patients with a high HIV prevalence.
Methods: A retrospective observational study of patients admitted to ICU with a clinical diagnosis of CAP was undertaken. PCT on admission and at 48 hours was evaluated as a predictor of ICU outcome and pneumonia aetiology.
Results: A total of 100 patients were included; 62% were HIV positive. Overall ICU mortality was 61%. PCT at admission and 48 hours was not associated with any outcome variables. A significant association was found between mortality and patients whose PCT levels increased or remained >10 ng/ml at 48 hours, compared with those that remained unchanged or decreased (67% vs. 41% $p = 0.018$). The commonest aetiology identified was *Mycobacterium tuberculosis* ($n = 18$, 21.4%). Patients with admission PCT levels >10 ng/ml were more likely to have positive bacterial cultures (OR = 3.14; 95% CI 1.11–9.73).
Conclusions: Increasing or persistently elevated PCT predicts a higher mortality in critically ill patients with CAP. This suggests PCT kinetics may be useful in risk stratifying patients with CAP at 48 hours. While positive bacterial cultures are more likely in patients with high admission PCT, this assay does not allow for decisions to be made on antimicrobial management and is of limited clinical utility in critically ill patients with a high HIV prevalence and CAP.

Keywords: critical care, procalcitonin, intensive care, prognosis, severe community acquired pneumonia

Introduction

Severe community acquired pneumonia (CAP) remains a common cause for admission to the intensive care unit (ICU) and is associated with significant morbidity and mortality.[1] Numerous studies have explored factors used for diagnosis and prognosis in CAP.[2,3] Biomarkers are increasingly being investigated to aid in predicting aetiology and improving diagnosis and treatment of this condition. Procalcitonin (PCT) has emerged as one such biomarker. It is useful in differentiating bacterial CAP from other causes of CAP; differentiating infectious from inflammatory processes; guiding antibiotic therapy duration; characterising the severity of underlying disease; and predicting outcome.[4] In patients with severe CAP requiring admission to the intensive care unit, increased admission PCT levels and a trend of increasing PCT during the ICU stay has been shown to predict increased mortality and is associated with increased organ dysfunction.[5–7] Mortality amongst patients with severe CAP has remained extremely high and ICU-based studies have reported mortality rates between 20% and 50%.[8] Few studies have attempted to investigate the utility of PCT in CAP in South Africa and none of these have been in the ICU population.

Background

PCT is a precursor of the hormone calcitonin which is normally secreted from the parafollicular C cells of the thyroid gland.[9] In healthy individuals, circulating serum levels of procalcitonin are usually undetectable or low, generally < 0.1 ng/ml. In 1993, Assicot *et al*. described high serum concentrations of PCT in children with severe bacterial infections in comparison with those with no signs of infection.[10] Since then, it has been demonstrated that the variant PCT associated with infection can be produced by other tissues and studies have highlighted the value of PCT in differentiating bacterial from non-bacterial or non-infective causes of inflammation.[11,12]

There are numerous studies of PCT in patients with CAP in high-income countries.[5–7] In patients requiring admission to the ICU for severe CAP, increased levels of PCT have been associated with severity of illness and may be prognostic for morbidity and mortality.[7] Studies conducted in ICUs in Canada, the United States of America and Europe have all shown that initial admission PCT levels, maximum PCT and trends in PCT kinetics are associated with morbidity and mortality.[5,6]

In South Africa, CAP is a common cause of hospital admission, yet there is a paucity of data regarding the role of PCT in severe CAP, and none in the intensive care unit.[13–15] Patients with severe CAP in South Africa may differ from those in high-income countries. CAP is often encountered in younger patients.[13,15] This, combined with the high prevalence of the human immunodeficiency virus (HIV) in South Africa, has to alert the clinician to the possibility of atypical aetiological organisms.[13] The effect of immune deficiency on PCT in HIV-infected individuals has previously been investigated, and these studies have shown similarly increased serum PCT concentrations in bacterial sepsis.[16–18] In a study conducted in KwaZulu-Natal, *Mycobacterium tuberculosis* (MTB) was found to be the leading cause of CAP amongst both HIV and non-HIV infected individuals.[13] *Pneumocystis jirovecii* pneumonia (PJP) is another common cause of CAP in the HIV-infected population and PCT

has been shown to discriminate between pulmonary tuberculosis, PJP and bacterial causes of CAP.[14]

Considering the evidence showing the value of PCT as a likely predictor of aetiology, its emerging role in predicting outcome, and the limited evaluation of PCT concentration in severe CAP in the ICU locally, this study aimed to establish the relationship between PCT and (i) ICU mortality; (ii) ICU length of stay (LOS); and (iii) duration of ventilation (DOV) in patients admitted to the intensive care unit with severe CAP. Secondary aims were to evaluate the ability of PCT to predict the aetiology of CAP, and its association with organ dysfunction.

Method

This study was a retrospective observational chart review of consecutive patients admitted to the ICU at King Edward VIII Hospital (KEH) in Durban, South Africa, over the period from January 2012 to August 2014. All patients were assessed for eligibility for the study. Inclusion criteria were based on the clinical diagnosis of CAP with the following five criteria at initial presentation or within 48 hours of hospitalisation:

(1) admission from the community;
(2) history of cough, dyspnoea, pleuritic chest pain, sputum production or constitutional symptoms;
(3) auscultatory findings on pulmonary examination of crackles or evidence of pulmonary consolidation or tachypnoea or hypoxaemia;
(4) white blood cell (WBC) count of $> 12.0 \times 10^9$/l or $<4.0 \times 10^9$/l or a raised C-reactive protein (CRP) or radiographic changes suggestive of pneumonia; and
(5) requiring mechanical ventilation.

Organ dysfunctions examined included PaO_2/FiO_2 ratio and acute kidney injury (AKI). AKI was defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, using serum creatinine levels.[19] Where baseline serum creatinine levels were unknown, the Modification of Diet in Renal Disease (MDRD) equation was used to calculate an assumed baseline, as described by KDIGO.

Exclusions included hospitalisation within 30 days prior to developing pneumonia; evidence of a pulmonary embolus, acute coronary syndrome, cardiac failure or chronic renal failure; post-surgical patients; trauma; and those in whom aspiration pneumonia was suspected.

Data collected on patients included in the study consisted of demographic data; co-morbidities; laboratory data; microbiological findings and ICU mortality outcome. The Brahms PCT-Q Immunochromatographic (Thermo Fischer Scientific, Waltham, MA, USA) test for the determination of procalcitonin in human serum and plasma was used. As procalcitonin is measured semi-quantitatively in this ICU, the PCT levels were reported in 1 of 4 groups: < 0.5 ng/ml; ≥ 0.5–2.0 ng/ml; > 2.0–10 ng/ml; and > 10 ng/ml. Admission PCT and 48-hour PCT (where available) were recorded. Microbiological aetiology was determined from endotracheal aspirates. In patients who had 'dry' endotracheal aspirates, a mini bronchoalveolar lavage was performed.

Statistical Package for the Social Sciences (SPSS IBM) 23 was used to analyse the data. Comparison of categorical parameters was performed using the chi square test or Fisher's exact test, where appropriate. Continuous, normally distributed data were analysed using the Student's T-test. Non-parametric data were analysed using the Mann-Whitney U or Kruskal-Wallis tests as appropriate.

Full ethics approval was obtained from the Biomedical Research Ethics Committee at the University of Kwazulu-Natal (BE090/14).

Results

Data were collected for 100 consecutive patients that met the study criteria. The baseline characteristics of the cohort are shown in Table 1. The patients were young (median 33 years, IQR 27–49) and predominantly female (62%). The majority of patients were HIV positive (62%), and 18 of the patients were either pregnant or in the early puerperium. The CD4 count was available for 56 patients infected with HIV with a median of 64 cells/μL (IQR 13–139). Only 19 patients (31% of known HIV-positive cohort) were on antiretroviral therapy. The incidence of other co-morbidities was relatively low. Overall ICU mortality was 61%. The median duration of ventilation was 4 days (IQR 3–8), with a median ICU length of stay of 6 days (IQR 3–9).

Biochemical data collected on admission and 48 hours post-ICU admission are given in Table 2. Admission PCT data were available for all 100 patients, and for 86 patients at 48 hours. Over the first 48 hours of ICU admission, 17 patients (20%) had a decrease in PCT, and 30 (35%) showed an increase in PCT. A PCT persistently > 10 ng/ml was noted in 24 (28%) patients, and 11 (13%) had a PCT that remained < 0.5 ng/ml. In all

Table 1: Baseline demographic data and comorbidities

Item	All ($n = 100$)	Survived ($n = 39$)	Died ($n = 61$)	p-value
Demographics:				
Age (years)	33 (27–49)	32(23–53)	33(28–47)	0.684
Gender (M/F)	38/62	17/22	21/40	0.402
Co-morbidities, n (%):				
Diabetes	7 (7.0)	3 (7.7)	4 (6.6)	1.0
Cardiovascular disease	18 (18.0)	7 (17.9)	11 (18.0)	1.0
COPD	7 (7.0)	4 (10.3)	3 (4.9)	0.427
Asthma	5 (5.0)	1 (2.6)	4 (6.6)	0.646
HIV status, n (%):				0.031
Positive	62 (62)	19 (48.7)	43 (70.5)	
Negative	19 (19)	11 (28.2)	8 (13.1)	
Unknown	19 (19)	9 (23.1)	10 (16.4)	

COPD = CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Table 2: Biochemical data

Factor		Admission *n* (%) or median (IQR)	48 Hours *n* (%) or median (IQR)
Procalcitonin (ng/ml)	< 0.5	23 (23.0)	17 (19.8)
	0.5–2.0	24 (24.0)	14 (16.3)
	> 2.0–10	18 (18.0)	9 (10.5)
	> 10	35 (35.0)	46 (53.5)
White blood cell count ($\times 10^9$/l)		11.54 (8.20–16.97)	12.49 (9.03–16.75)
C-reactive protein (mg/l)		168 (109–269)	113 (66–151)
Platelets ($\times 10^9$/l)		239 (162–369)	206 (129–292)
PaO_2/FiO_2 ratio		128 (90–214)	172 (117–232)
PaO_2/FiO_2 ratio	> 300	8 (11.6)	8 (12.9)
	200– ≤ 300	11 (15.9)	15 (24.2)
	100– ≤ 200	27 (39.1)	28 (45.2)
	≤ 100	23 (33.3)	10 (17.7)

analyses performed there was no significant difference between the 0.5–2.0 ng/ml and the 2.0–10.0 ng/ml PCT categories and thus these categories were combined for further data presentation purposes (Table 3).

Microbiological data were available for 78% of the cohort of which 37 (47.4%) had no organism identified. The commonest organism found was MTB; other specific organisms identified are shown in Figure 1.

Mortality

Patients whose PCT increased or remained > 10 ng/ml had a significantly higher ICU mortality than those in whom the PCT decreased or remained unchanged (66.7% vs. 40.6%, OR = 2.92; 95% CI 1.18–7.22, $p = 0.018$) (Table 5). There were no other significant associations between PCT and mortality.

Inflammatory variables

There was a statistically significant association between admission and 48-hour platelet (PLT) count and admission and 48-hour PCT, with the median platelet count decreasing as PCT category increased (Table 3). The median admission and 48-hour platelet count was significantly lower in patients whose PCT remained < 0.5 ng/ml.

Microbiological data

There was no significant association between admission or 48-hour PCT categories and microbiological data (Table 3). An analysis performed exploring the association between positive bacterial cultures and an admission PCT of > 10 ng/ml or < 10 ng/ml revealed a significantly lower incidence of positive bacterial cultures in patients with a PCT < 10 ng/ml (13.7%) as opposed to a PCT > 10 ng/ml (33.3%), $p = 0.041$; OR = 3.14; 95% CI 1.11–9.73. An admission PCT of > 10 ng/ml had PPV of 56.3% and an NPV of 86.3% for a positive bacterial culture from an endotracheal aspirate with a sensitivity and specificity of 56.3% and 71.0% respectively. 59 patients received antimicrobial therapy prior to ICU admission, 12 patients had no antimicrobial therapy, and in the remaining 29 patients this was unknown.

Organ dysfunction

There was a significant association between admission PCT category and the need for inotropic support within the first 48 hours of admission, with only 34.8% of patients with an admission PCT of < 0.5 ng/ml requiring inotropic support, as opposed to 64.3% with a PCT 0.5–10 ng/ml (OR = 3.38; 95% CI 1.16–9.79, $p = 0.025$) and 74.3% (OR = 5.42; 95% CI 1.72–17.02, $p = 0.004$) with a PCT > 10 ng/ml (Table 4). There was a similar association between 48-hour PCT and an increasing incidence of inotropic support with increasing PCT category: PCT of 0.5–10.0 ng/ml (OR = 5.77; 95%CI 1.06–31.27, $p = 0.042$) and PCT of >10 ng/ml (OR = 35.63; 95% CI 6.77–187.50, $p < 0.001$). In addition, there was a significantly lower need for inotropic support in patients whose PCT remained < 0.5 ng/ml (OR 0.05; 95% CI 0.01–0.44, $p = 0.001$); and a significantly greater need for inotropic support in patients whose PCT increased or remained >10 ng/ml (OR 13.96; 95% CI 4.80–40.63, $p < 0.001$) (Table 5).

There was a similar association between PCT category and AKI, with an increasing incidence of AKI with increasing PCT category (see Table 4) and a lower incidence of AKI in patients whose PCT remained < 0.5 ng/ml and a higher incidence in those whose PCT increased or remained > 10 ng/ml (see Table 5).

There was no significant association between PCT category and admission PaO_2/FiO_2 ratios (see Table 4); however, patients with a PCT < 0.5 ng/ml had a significantly lower PaO2/FiO2 ratio at 48 hours.

Discussion

The study population described is demographically different from previous studies examining CAP in the ICU. It is a remarkably young cohort with a high incidence of HIV disease and low incidence of other co-morbidities, when compared with similar studies conducted in Europe and North America.[5–7] The study population had significant respiratory dysfunction, contributing to their admission to the ICU for ventilatory support. A large proportion of patients were admitted to the ICU with PaO_2/FiO_2 ratios < 200 and for the majority this remained low even at 48 hours post-admission. Despite the absence of other co-morbidities that could have contributed to further organ dysfunction, the high incidence of circulatory shock and AKI indicates the severity of the disease process in these patients. The high incidence of HIV-positive individuals in the study cohort highlights a unique group of patients who may pose further diagnostic and therapeutic challenges. The median CD4 count was low, indicating a population at high risk for opportunistic infections. Although there were limitations with obtaining microbiological data, there was a high incidence of microbiologically proven MTB, fungi and viruses in keeping with the

Table 3: Biochemistry and microbiology analysed with admission and 48-hour procalcitonin

	Admission PCT (ng/ml)				PCT at 48 hours (ng/ml)			
	< 0.5	0.5–10	> 10	*p*-value	< 0.5	0.5–10	> 10	*p*-value
Admission:								
WBC count ($\times 10^9$/l) median (IQR)	12.11 (10.57–18.61)	11.04 (7.79–14.06)	11.59 (4.00–21.10)	0.401	11.09 (8.41–12.32)	11.93 (10.52–18.07)	11.48 (7.39–15.85)	0.711
CRP (mg/l) median (IQR)	126 (38–180)	166 (111–196)	219 (113–290)	0.166	115 (40–169)	125 (102–290)	176 (159–286)	0.049
Platelets ($\times 10^9$/l) median (IQR)	410 (209–462)	257 (142–353)	184 (137–265)	0.001	387 (206–416)	271 (142–416)	224 (150–290)	0.017
48 hours post-admission:								
WBC count ($\times 10^9$/l) median (IQR)	12.09 (9.79–13.47)	12.15 (8.04–16.75)	13.35 (10.00–18.01)	0.627	10.51 (7.17–12.49)	12.09 (9.64–13.92)	13.70 (9.72–17.83)	0.053
CRP (mg/l) median (IQR)	73 (28–102)	116 (68–152)	139 (112–179)	0.048	65 (40–147)	95 (54–153)	135 (113–169)	0.061
Platelets ($\times 10^9$/l) median (IQR)	284 (206–405)	221 (146–325)	159 (88–220)	<0.001	252 (184–406)	215 (176–325)	185 (118–251)	0.019
CD4 count (cells/μl) median (IQR)	32 (12–89)	52 (13–196)	100 (36–139)	0.234	40 (13–52)	75 (12–111)	99 (17–226)	0.339
HIV-positive, *n* (%)	15 (88.2)	27 (73.0)	20 (74.1)	0.439	10 (76.9)	10 (55.6)	31 (81.6)	0.113
Microbiology, *n* (%)								
Mycobacterium tuberculosis	2/22 (9.1)	8/34 (23.5)	8/28 (28.6)	0.231	0/17 (0.0)	5/21 (23.8)	11/39 (28.2)	0.053
Bacterial	3/20 (15.0)	4/31 (12.9)	9/27 (33.3)	0.123	2/15 (13.3)	3/19 (15.8)	9/38 (24.7)	0.620
Fungal	2/20 (10.0)	6/31 (19.4)	2/26 (7.7)	0.384	4/15 (26.7)	2/19 (10.5)	4/37 (10.8)	0.288
Viral	2/20 (10.0)	4/31 (12.9)	2/26 (7.7)	0.812	3/15 (20.0)	1/19 (5.3)	3/37 (8.1)	0.314
Negative microbiology	12/20 (45.2)	14/31 (45.2)	11/27 (40.7)	0.403	9/15 (60.0)	9/19 (47.4)	17/38 (44.7)	0.601

CD4 count; WBC count; CRP and platelets reported as median (IQR). HIV positive; microbiological results reported as *n* (%).

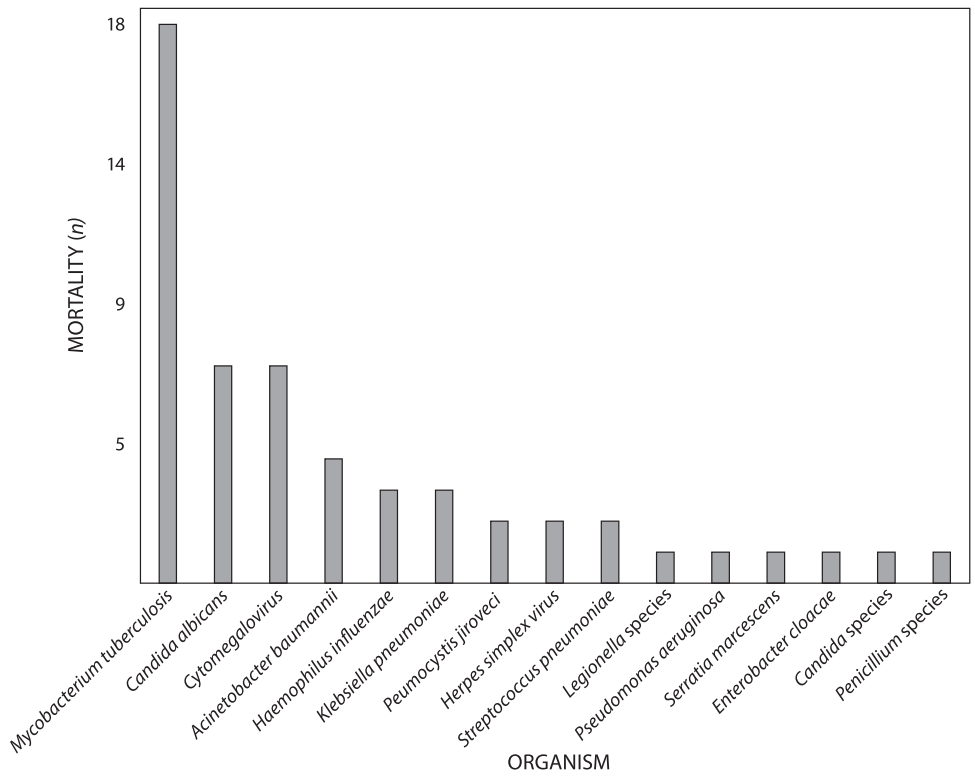

Figure 1: Positive microbiological results from endotracheal aspirates.

Table 4: Correlation between outcomes and admission and 48-hour procalcitonin

	Admission PCT (ng/ml)				PCT at 48 hours (ng/ml)			
	< 0.5 (*n* = 33)	0.5–10 (*n* = 42)	> 10 (*n* = 35)		< 0.5 (*n* = 17)	0.5–10 (*n* = 23)	> 10 (*n* = 46)	
	n (%) or median (IQR)	*n* (%) or median (IQR)	*n* (%) or median (IQR)	*p*-value	*n* (%) or median (IQR)	*n* (%) or median (IQR)	*n* (%) or median (IQR)	*p*-value
ICU mortality	12 (52.2)	25 (59.5)	24 (68.6)	0.442	7 (41.2)	12 (52.2)	30 (65.2)	0.200
DOV	6 (2–7)	4 (3–9)	4 (2–8)	0.705	7 (4–11)	6 (3–8)	5 (3–9)	0.564
LOS	6 (2–9)	6 (4–9)	4 (3–9)	0.569	7 (6–11)	7 (4–9)	7 (3–9)	0.317
Inotropic support (48 hours)	8 (34.8)	27 (64.3)	26(74.3)	0.009	2(11.8)	10(43.5)	38(82.6)	< 0.001
AKI	4 (17.4)	19 (45.2)	24 (68.6)	0.001	2 (11.8)	8 (34.8)	32 (69.6)	< 0.001
PaO_2/FiO_2 ratio admission	133 (89–188)	128 (87–265)	125 (93–215)	0.942	120 (90–188)	120 (102–258)	149 (88–247)	0.905
PaO_2/FiO_2 ratio (48 hours)	119 (79–170)	190 (126–237)	196 (130–275)	0.035	118 (107–176)	190 (158–246)	196 (121–275)	0.023

DOV = days of ventilation; LOS = length of stay in ICU; AKI = acute kidney injury.

aforementioned findings. As a consequence of all of the above, the ICU mortality was remarkably high at 61%, reflecting a group with severe disease.

Early outcome prediction in critically ill patients is challenging. Previous studies in ICU populations have shown that increased admission PCT levels could be predictors of mortality and cut-off values of 1.1 ng/ml and > 2 ng/ml have been reported.[5,6] We found semi-quantitative admission procalcitonin levels were not associated with ICU mortality in our study. However, there was a significantly higher mortality associated with PCT levels that increased or remained above 10 ng/ml at 48 hours. This is in keeping with similar studies that found an increase in PCT from day 1 to day 3 in ICU to be an independent risk factor for mortality.[6,20] This may reflect a failure of response to empiric antimicrobial therapy and it may be argued that this should prompt an alteration of such therapy.

Deciding on empiric antimicrobial therapy in immunocompromised patients with CAP is challenging. The ability to rapidly determine aetiology and direct treatment may offer outcome advantages as patients would get early appropriate therapy and would avoid side effects of unnecessary antimicrobial therapy. PCT may assist in determining aetiology of infection,

Table 5: Correlation between outcomes and procalcitonin trends

	PCT remaining < 0.5 ng/ml			PCT increased/remaining above 10 ng/ml		
	No ($n = 75$)	Yes ($n = 11$)		PCT decreased/ unchanged ($n = 32$)	Increased/remained >10 ng/ml ($n = 54$)	
	n (%) or median (IQR)	*n* (%) or median (IQR)	*p*-value	*n* (%) or median (IQR)	*n* (%) or median (IQR)	*p*-value
ICU mortality	44 (58.7)	5 (45.5)	0.409	13 (40.6)	36 (66.7)	0.018
DOV	5 (3–9)	7 (4–9)	0.310	5 (3–8)	6 (4–9)	0.792
LOS	7 (4–9)	7 (6–12)	0.207	7 (4–9)	7 (4–9)	0.640
Inotropic support (within 48 hours)	49 (65.3)	1 (9.1)	0.001	7 (21.9)	43 (79.6)	< 0.001
AKI	42 (56.0)	0 (0.0)	0.001	6 (18.8)	36 (66.7)	< 0.001
PaO_2/FiO_2 ratio (admission)	135 (90–258)	104 (90–188)	0.702	120 (102–188)	146 (86–258)	0.822
PaO_2/FiO_2 ratio (48 hours)	190 (130–242)	117 (99–146)	0.017	160 (117–232)	180 (121–270)	0.822

DOV = days of ventilation; LOS = length of stay in ICU; AKI = acute kidney injury.

with a low PCT being indicative of a non-bacterial infection and a high PCT indicating a bacterial infection.[10,14] Our study showed that patients with an admission PCT > 10.0 ng/ml were indeed significantly more likely to have a positive bacterial culture (33.3% vs. 13.7%, $p = 0.041$). While statistically significant, this finding has limited utility in directing empiric antimicrobial therapy however. With the exception of the above finding, admission and 48-hour PCT were not significantly associated with CAP aetiology in our study. An admission PCT > 10 ng/ml also had a good NPV of 86.3%. This could suggest that in patients with admission PCT < 10 ng/ml investigation for non-bacterial aetiologies should be more comprehensive.

Patients with a low PCT had significantly lower PaO_2/FiO_2 ratios at 48 hours. Despite the microbiological findings discussed above, this may reflect differences in aetiology, with the patients in the low PCT group suffering from pneumonias of non-bacterial aetiology such as PJP. These may not have been detected microbiologically. In addition, these patients may also represent a non-infectious aetiology such as lymphoma, Kaposi's sarcoma, or bronchiolitis obliterans organising pneumonia (BOOP) that may have resulted in progressive respiratory disease, non-responsive to antimicrobial therapy.

We found no significant difference in PCT between HIV-positive and HIV-negative patients. There have been concerns that HIV-positive patients may not mount a PCT response; however, in a study conducted by Schleicher *et al*., it was found that elevated PCT in HIV-positive patients admitted with CAP was highly predictive of pneumococcal infection.[15] Our study confirms that HIV-positive patients do mount a PCT response. Until this is evaluated further this suggests that PCT may be used similarly in HIV-positive and HIV-negative patients.

This study highlights a number of significant associations between PCT and mortality and organ dysfunction in our cohort of patients. Despite these associations, there appears to be limited clinical utility of early semi-quantitative PCT in the clinical care of these patients in terms of determining aetiology, directing antimicrobial therapy or assisting with triage. It is unclear if this is due to the limited utility of PCT in general, limited utility of the semi-quantitative test or due to limitations of the study. The findings of this study suggest that a similar study using quantitative PCT and alternative thresholds be performed.

Limitations

This study was a retrospective observational study using routinely collected ICU data. While this has numerous well-known limitations the authors believe that it reflects 'real-world' care of this challenging subset of ICU patients.

No objective scoring system was utilised in the study ICU and thus describing and controlling for severity of illness using standard scoring systems was not possible. However, the organ dysfunction data presented highlight the severity of illness of the study population. In addition, standard scoring systems have not been validated in a similar population and the validity of using them in this study population could rightly be questioned.

Similar studies evaluating the use of PCT in critical care use quantitative PCT; the use of semi-quantitative PCT remains the real-world alternative in many instances. The semi-quantitative PCT is an immunochromatographic test that uses visual detection of the colour of a band to determine the PCT category. It is rapid and relatively low-tech and does not require a potentially costly analyser. It was thus deemed important to evaluate its utility in the early treatment of critically ill patients with CAP. Our study population may be considered small, but comparable studies conducted in other intensive care units have had similar numbers of study subjects.[2,3]

Microbiological diagnosis was made on endotracheal aspiration specimens. In 22 patients, there were no microbiological results obtained and in 37 patients microbiology was negative. Factors contributing to this include technical difficulties in obtaining specimens; inadequate samples with a low yield of organisms; and the timing of specimens obtained in relation to antibiotic dosing. Many of these difficulties reflect the real-world difficulties in obtaining accurate microbiological specimens from critically ill patients suffering from CAP.

Serum PCT can be difficult to interpret in a patient suffering from AKI,[21] as PCT is renally excreted. The kinetics of PCT clearance while on renal replacement therapy (RRT) are also variable. As the use of RRT was not captured as part of our data collection, it is unknown if this influenced the 48-hour PCT results.

Conclusion

Patients who had a PCT that increased or remained above 10.0 ng/ml at 48 hours had a significantly higher mortality

than those in whom the PCT decreased or remained low at 48 hours. Patients with CAP requiring ICU admission with an elevated semi-quantitative PCT of > 10.0 ng/ml on admission had significantly increased odds of having a positive bacterial culture on endotracheal aspirate when compared with patients with a PCT of < 10.0 ng/ml. Despite this result, a significant number of patients had positive microbiology with a low initial procalcitonin and this finding may have limited clinical applicability with regard to antimicrobial therapy. Further studies evaluating the use of quantitative and semi-quantitative PCT, for other indications and as a component of a risk prediction model, are warranted in this population of patients with CAP.

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