Procalcitonin as a sepsis marker: Experience of an intensive care setting in Malaysia

Basri MAT NOR [1], Azrina M RALIB [1], Abdul Hadi MOHAMED [1], Nor Zamzila ABDULLAH [2], [1] Department of Anaesthesiology and Intensive Care and [2] Department of Basic Medical Science, Kulliyyah of Medicine, International Islamic University Malaysia, Pahang, Malaysia

ABSTRACT

Introduction: During infection, there is increased expression of CALC-I gene resulting in ubiquitous release of procalcitonin (PCT). Since the expression of PCT is dependent on the genetic constituents of a population, this study aimed to validate the diagnostic performance of PCT in differentiating sepsis from noninfectious systemic inflammatory response syndrome (SIRS) in a Malaysian intensive care unit (ICU). **Materials and Methods:** Ninety-five patients fulfilling the criteria for SIRS were enrolled. Daily concentrations of PCT, C-reactive protein (CRP) and white cell count (WCC) were measured over three days. The diagnostic and predictive performance of these biomarkers were assessed using area under the curve of the ROC. **Results:** In this study, medical and surgical cohorts had similar PCT concentrations. Peak (p=0.02) and daily PCT (p<0.001) concentrations were significantly higher in patients with sepsis compared to SIRS. There were no significant differences in the CRP and WCC concentrations between the two groups. Peak PCT was significantly higher in patients with bacteraemia than those without (49.1 [19.3- 57] vs. 6.9 [1.1-25.6 ng/ml], p=0.001). PCT was diagnostic of sepsis and bacteraemia (AUC of 0.73 [0.64-0.83] and 0.80 [0.66-0.93] respectively). Peak PCT was significantly higher in septic patients with culture positive compared to culture negative (p=0.02). At the optimal cut-point of 10.68 ng/ml for peak PCT, sepsis was very likely with specificity of 86% and psotive predictive value (PPV) of 91%. There was a good correlation between PCT concentration and the Sequential Organ Failure Assessment (SOFA) score in the sepsis cohort (r=0.62, p<0.0001). **Conclusion:** PCT was better than CRP or WCC in differentiating sepsis from non-infectious SIRS in critically-ill patients. PCT is diagnostic of sepsis and bacteraemia, and is also useful as an indicator of severity of organ failure in sepsis.

Keywords: Sepsis, systemic inflammatory response syndrome, bacteraemia, procalcitonin, C-reactive protein

INTRODUCTION

In managing critically-ill patients, differentiating sepsis from non-infectious triggers of the systemic inflammatory response syndrome (SIRS) is crucial. The limitation of microbiological culture is the time required to isolate an organism. Cultures are also reported to be less sensitive under certain conditions, and these include slow growing and difficult to cul-

Correspondence author: Mohd Basri MAT NOR, Department of Anaesthesiology and Intensive Care, Kulliyyah of Medicine, International Islamic University Malaysia, Jalan Hospital Campus, 25100 Kuantan, Pahang, Malaysia.
E mail: basri.matnor@gmail.com

ture microorganisms. [1] Procalcitonin (PCT), a 116-amino-acid residue peptide has been studied extensively over the past decade as a promising diagnostic and prognostic biomarker for sepsis. [2]

PCT is encoded by the calcitonin I (CALC-I) gene located on chromosome 11. [3] It is a gene with six exons, although the first exon is not translated. In the absence of infection, transcription of the CALC-I gene in the non-endocrine tissue is suppressed, except in the C-cells of thyroid gland where its expression produces PCT, a precursor of calcitonin. [4, 5] In the normal physiological state, PCT is present at very low concentrations of <0.1 ng/ml. The presence of any microbial infection induces a ubiquitous increase in the CALC-I gene expression leading to release of PCT from all extra-thyroid neuroendocrine tissues and cell types throughout the body. Serum PCT concentrations increase significantly in severe systemic infections and may also be elevated in some non-infectious SIRS conditions. [6] There have been two meta-analyses published within the last five years assessing the diagnostic performance of PCT in critically-ill patients. [7, 8] A number of studies have also documented the ability of PCT to discriminate between bacterial sepsis and non-infectious SIRS. [8–10]

Since the expression of PCT depends on the genetic constituents of a population, its efficacy as a sepsis marker may vary between populations. To the best of our knowledge, there has been no published data on its usefulness as a marker of bacterial sepsis in a Malaysian population. The objectives of the study were to: a) assess and validate the performance of PCT in differentiating between sepsis and non-infectious SIRS in critically-ill patients, b) compare its performance with CRP in a Malaysian adult ICU setting. This with C-reactive protien (CRP); and c) determine the association between Sequential Organ Failure Assessment (SOFA) scores in a Malaysian adult ICU setting.

MATERIALS AND METHODS

Ninety-five consenting patients above 18 years old with established SIRS admitted to the ICU in a University Hospital from July 2011 to June 2012 were prospectively enrolled. This hospital is a 12-bed mixed medical -surgical ICU with approximately 800 ICU admissions per year. Patients who received antimicrobial therapy for more than 24 hours before the first blood sample could be taken were excluded. Ethic approval were obtained from the University Ethic Committee for the study.

SIRS and sepsis were defined according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) Consensus conference. [11] SIR is defined as an inflammatory state affecting the body (typically multi-system) as a response of the immune system to triggers that can be infective or non-infective. Sepsis is present when there are two or more SIRS criteria, along with a culture proven or clinically identified or suspected infection. Data regarding demographics, Simplified Acute Physiology II Score (SAPS II), SOFA score, length of ICU and hospital stay, duration of mechanical ventilation, requirement for renal replacement therapy (RRT), and death before hospital discharge were also recorded. Clinical parameters such as body temperature, heart rate, white cell count (WCC) and clinical signs of

infection were recorded. At least one set of blood, sputum or broncho-alveolar lavage (BAL) and urine were taken on the day of recruitment. Daily blood samples for PCT and CRP measurement were collected over three consecutive days, starting from the day of ICU admission. Collected serum was frozen at -80^{o}C and analysed in batches. At the time of the study, PCT was not used as part of patient management. ICU doctors completed a questionnaire **(Appendix 1:** *available as Supplementary Text***)** for each patient on admission and day 3 to define the clinical suspicion of sepsis. Finally, patients were grouped into non-infectious SIRS if there was a low clinical suspicion of infection on day 1 and day 3 and all culture results are negative. In this study, sepsis is a clinical diagnosis with or without any positive cultures in SIRS population. [6]

Measurements of PCT and CRP: PCT was measured by BRAHMS Kryptor compact (Germany), which used time-resolved amplified cryptate emission technology assay. It provides a sensitive PCT measurement with improved functional assay sensitivity of 0.06 ng/ml and quantitative result in 19 minutes. Serum CRP was determined by immunoturbidimetric method (Thermo Scientific).

Statistical Analysis: Statistical analysis was performed using PASW version 18.0 (IBM, USA) licensed to the International Islamic University Malaysia. Results are presented as mean ± SD for normally distributed variables or median (inter-quartile range) for non-normally distributed variables. Comparison of variables between the two groups was analysed using the independent *t*-test for normally distributed variables, or the Mann-Whitney test for non-normally distributed variables. Categorical variables were compared with Chi-Square test. The diagnostic and predictive performance of biomarkers was assessed by the area under the curve of receiver operating characteristic curve (AUC) of the sensitivity over 1-specificity. Good diagnostic performance is defined as AUC of more than 0.7. The optimal threshold was defined as the biomarker concentration closest to the point on the ROC curve where sensitivity = 1 and specificity = 1. This concentration was used as a cut-point to calculate sensitivity (true positive), specificity (false positive), PPV (positive predictive value) and NPV (negative predictive value) of the biomarkers.

RESULTS

Ninety-five ICU patients were enrolled and of these, 67 patients had sepsis. The baseline demographics and clinical characteristics are shown in Table 1. Patients with sepsis were more ill and had significantly higher SAPS II and SOFA scores than those with SIRS (p=0.02 and p=0.003 respectively). A majority of the patients were from the medical category.

The median PCT concentrations between the Surgical and Medical groups were not significantly different throughout three days study period (Table 2).

Overall, 28 (29.5%) patients required renal replacement therapy (RRT), and 30 (31.6%) died in hospital. Patients with sepsis had a higher rate of RRT and hospital mortality and higher baseline and peak PCT levels compared to those with SIRS. Summary of outcomes, baseline (day 1) and maximum (peak) concentrations of PCT and CRP are shown in Table 3.

Table 1: Demographic and clinical characteristics.

Variables	All patients (n= 95)	SIRS (n=28)	Sepsis (n=67)	*p*
Age (years)	44 ± 16	41 ± 17	45 ± 16	0.26
Gender (male)	66 (69.5)	19 (67.9)	47 (70.1)	0.83
Weight (kg)	67 ± 16	69 ± 22	66 ± 13	0.45
Height (cm)	159 ± 18	155 ± 31	161 ± 8	0.14
Baseline SAPS II Score	39 ± 16	33 ± 13	41 ± 16	0.02
Baseline SOFA Score	7.2 ± 4.3	5.2 ± 2.6	8.0 ± 4.7	0.003
Admission category				
Medical	56 (58.9)	12 (42.9)	44 (65.7)	0.003
Surgical	39 (41.1)	16 (51.1)	23 (34.3)	0.04
Primary Diagnoses				
Cardiovascular	6 (6.3)	2 (7.1)	4 (6.0)	
Endocrine/Metabolic	3 (28.6)	0 (0)	3 (4.5)	
Gastrointestinal/Hepatobiliary/Pancreas	7 (7.4)	1 (3.6)	6 (9.0)	
Infective	18 (18.9)	0 (0)	18 (26.9)	
Renal	4 (4.2)	2 (7.1)	2 (3.0)	
Neurological	12 (12.6)	3 (10.7)	9 (13.4)	0.001
Respiratory	20 (21.1)	6 (21.4)	14 (20.9)	
Trauma	15 (15.8)	11 (39.3)	4 (6.0)	
Postoperative surgical	4 (4.2)	3 (10.7)	1 (1.5)	
Connective tissue/autoimmune	2 (2.1)	0 (0)	2 (3.0)	
Maternity/Gynaecological	3 (3.2)	0 (0)	3 (4.5)	
Drug overdose/Poisoning	1 (1.1)	0 (0)	1 (1.5)	
Baseline co-morbidities				
Hypertension	35 (36.8)	8 (28.6)	27 (40.3)	0.28
Ischaemic heart disease	13 (13.7)	3 (10.7)	10 (14.9)	0.58
Chronic lung disease	16 (16.8)	5 (17.9)	11 (16.4)	0.86
Diabetes Mellitus	22 (23.2)	4 (14.3)	18 (26.9)	0.19
Cancer	3 (3.2)	1 (3.6)	2 (3.0)	0.88
Chronic immunosuppression/HIV	2 (2.1)	0 (0)	2 (3.0)	0.36
Chronic liver failure	1 (1.1)	0 (0)	1 (1.5)	0.52
Others	17 (17.9)	5 (17.9)	12 (17.9)	0.99

Data expressed as mean ± SD, n (%), or median (lower quartile – upper quartile). Comparison of variables between the two groups was analysed using the independent t test for normally distributed variables or the Mann-Whitney test for non-normally distributed variables. Categorical variables were compared with Chi-Square test.
Legends: SAPS II Score: Simplified Acute Physiological II Score, SOFA Score: Sequential Organ Failure Assessment Score, SIRS; systemic inflammatory response syndrome, HIV; Human immune deficiency virus

Comparisons of the daily PCT, CRP and WCC levels are demonstrated in Figure 1 (Whiskers plots). PCT concentrations were consistently higher in sepsis patients throughout the first three days of ICU admission. In contrast, serum CRP and WCC were unable to discriminate between the infectious and noninfectious groups.

Table 2: PCT as a function of Medical vs. Surgical groups.

	Medical		Surgical		p
	n	PCT concentration	n	PCT concentration	
Day 1	56	4.0 (0.5 – 18.0)	39	6.6 (0.9 – 42.3)	0.48
Day 2	54	7.6 (0.9 – 23.3)	34	5.8 (0.6 – 25.2)	0.84
Day 3	48	5.7 (0.6 – 18.9)	25	3.1 (0.5 – 11.4)	0.75
Peak PCT	56	10.0 (1.7 – 35.8)	39	8.3 (1.1 – 44.5)	0.81

Data presented as median (interquartile range). Comparison was made using the Mann Whitney test.
Legend: PCT; procalcitonin.

Table 3: Comparison of outcomes, PCT and C-Reactive protein (CRP) concentration between the SIRS and sepsis groups.

Variables	Cohort (n = 95)	SIRS (n = 28)	Sepsis (n = 67)	p
Renal Replacement Therapy (RRT)	28 (29.5)	4 (14.3)	24 (35.8)	0.04
Hospital Mortality	30 (31.6)	3 (10.7)	27 (40.3)	0.008
Mechanical Ventilation (MV)	87 (91.6)	25 (89.3)	62 (92.5)	0.60
Length of Mechanic Ventilation (days)	4.8 (1.8 – 9.9)	4.7 (1.0 – 9.5)	4.9 (2.1 – 13.0)	0.41
Length of ICU stay (days)	7.0 (2.9 – 14.6)	6.8 (2.7 – 10.3)	7.0 (3.2 – 15.8)	0.46
Length of hospital stay (days)	12.3 (6.6 – 18.2)	12.4 (6.4 – 17.4)	12.3 (6.6 – 19.2)	0.73
Baseline PCT (ng/ml)	5.3 (0.8 – 19.8)	2.3 (0.3 – 7.8)	7.6 (1.0 – 37.7)	0.02
Peak PCT (ng/ml)	8.8 (1.1 – 39.7)	3.4 (0.6 – 8.2)	20 (1.9 – 49.1)	<0.0001
Baseline CRP (mg/l)	85 (14 – 145)	105 (26 – 147)	81 (11 – 145)	0.37
Peak CRP (mg/l)	136 (87 – 183)	139 (56 – 170)	136 (89 – 188)	0.50
Baseline WCC ($x10^3$)	15 (12 – 22)	17 (14 – 17)	15 (12 – 21)	0.28
Peak WCC ($x10^3$)	18 (14 – 22)	19 (14 – 22)	18 (13 – 23)	0.78

Data expressed as mean ± SD, n (%), or median (lower quartile – upper quartile). Comparison between the two groups was analysed using the Chi-Square test for categorical variables, and Mann-Whitney test for continuous variables.
Legends: ICU; Intensive care unit, PCT; procalcitonin, CRP; C-reactive protein, WCC; white cell count, SIRS; systemic inflammatory response syndrome

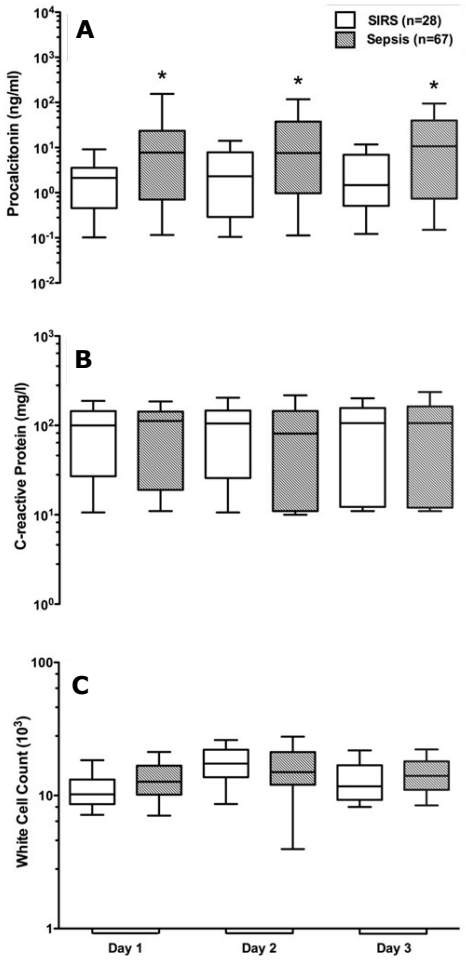

Fig. 1: Daily concentration of PCT (A), CRP (B) and, WCC (C) in sepsis and SIRS cohorts. *Mann Whitney test between sepsis and SIRS: p values (A), 0.02 (day 1) 0.002 (day 2), 0.03 (day 3) , (B) 0.37 (day 1), 0.68 (day 2), 0.74 (day 3), and (C) 0.28 (day 1), 0.25 (day 2) and 0.5 (day 3).

Differences in the peak PCT level between the genders, mortality and positive cultures groups are shown in Table 4. The peak PCT concentrations were higher in men, death in hospital, patients with any positive culture, positive blood culture and positive blood culture sepsis, but not positive tracheal culture. Overall, the peak PCT concentrations were seven times higher in patients with bacteraemia (p=0.001), 3.7 times higher in those with positive culture of any kind overall (p=0.002) and more than twice in patients with patients culture positive sepsis (p=0.02) as shown in Table 4.

The receiver operating characteristic curves (ROC) of maximum PCT and CRP concentrations were for sepsis, bacteraemia and

Table 4: Differences in peak procalcitonin (PCT) in gender, mortality and positive cultures.

Variables		n	Peak PCT (ng/ml)	*p*
Gender	Male	66	15.3 (2.0 – 41.3)	0.08
	Female	29	3.9 (0.73 – 25.9)	
Death in hospital	Yes	30	31.1 (3.5 – 91.1)	0.002
	No	65	7.2 (1.0 – 19.3)	
Positive culture anywhere	Yes	32	22.7 (4.8 – 80.7)	0.002
	No	63	6.2 (1.0 – 20.9)	
Positive blood culture	Yes	13	49.1 (19.3 – 257)	0.001
	No	82	6.9 (1.1 – 25.6)	
Culture positive sepsis	Yes	30	26.5 (8.0 – 89.6)	0.02
	No	37	11.7 (1.0 – 40.0)	
Positive tracheal culture	Yes	17	11.3 (1.6 – 41.3)	0.93
	No	78	8.4 (1.1 – 39.9)	

for other cultures are shown in Figure 2. The AUC (95% CI) for diagnosis of sepsis, bacteraemia and other cultures are shown in Table 5.

The peak PCT was diagnostic of sepsis with an AUC of 0.73 (0.64-0.83) and bacteraemia with AUC of 0.80 (0.66-0.93) (Table 5). The AUC for peak PCT (0.73, $p<0.0001$) and its 95% confidence interval did not encompass 0.50, thus demonstrating PCT to have a good diagnostic ability. In contrast, the AUC for peak CRP and its 95% confidence interval encompassed 0.5, hence were not diagnostic of sepsis. Using these curves, the optimal cut-point that maximises sensitivity and specificity of PCT was 10.68 ng/ml. At this cut-off point, peak PCT had a specificity of 86% and PPV of 91% for diagnosing sepsis (Table 6).

The contributions of PCT or CRP were assessed using multivariable logistic regression model. Variables found to be significant on univariate analysis (Table 7) were included in the analysis. Peak PCT over the three days period remained independently diagnostic of sepsis (Odd ratio [OR] 1.07, 95% Confidence internal [95% CI] 1.02-1.13), $p=0.008$), along with the SOFA score (OR 1.20, 95% CI

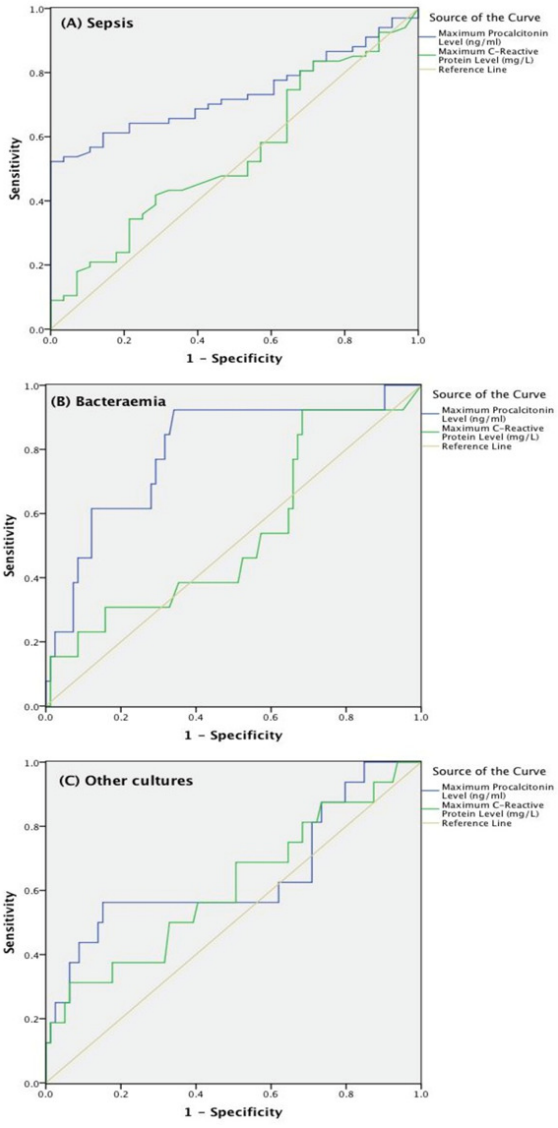

Fig. 2: Receiver operating characteristics (ROC) curves of peak PCT (blue line), and peak CRP (green line) for sepsis (A), bacteraemia (B) and other cultures (C).

1.00-1.44, p=0.05) but not SAPS II score (Table 7). Addition of peak PCT concentration to the reference model increased the diagnostic performance of the reference model, from AUC of 0.68 (0.67-0.79) to 0.75 (0.65-0.85).

The correlation between PCT concentrations and SOFA score was studied with the Spearman's correlation test and the scatterplot is shown in Figure 3. There was a stronger correlation between PCT concentration and SOFA score in sepsis cohort, Spearman's correlation coefficient, r=0.62 (p<0.0001) compared to overall patients, r=0.57 (p<0.001). There was no correlation between SOFA score and PCT in the SIRS cohort (r=0.05, p=0.80).

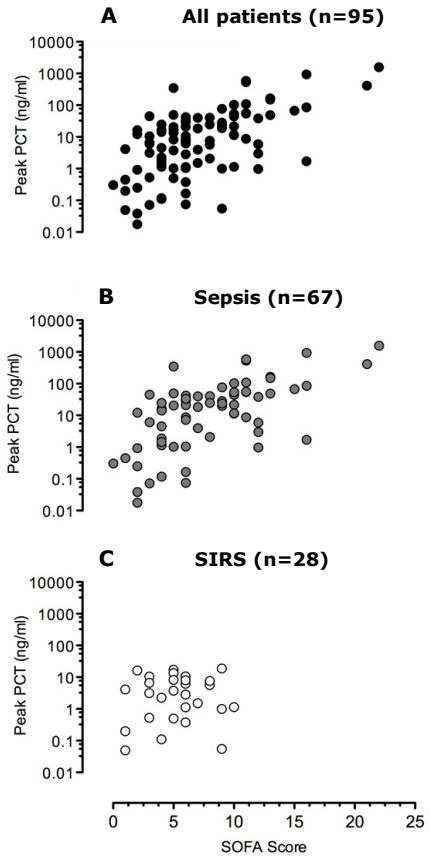

Fig. 3: Correlations between Peak PCT concentration and SOFA score. PCT concentrations were in a $\log_{10}$ scale. Spearman correlations (A) r=0.57, p<0.0001 (B) r=0.62, p<0.0001 and (C) r=0.05, p=0.80.

DISCUSSION

Since the expression of PCT is regulated by the CALC-I gene, we undertook a validation study to assess its diagnostic accuracy of PCT in diagnosing sepsis in a Malaysian ICU setting. In this study, patients who received antibiotics for more than 24 hours were excluded as serum PCT concentrations may rapidly normalise after administration of antibiotics [12] and this increase the rate of false negatives. PCT starts to rise four hours after the start of sepsis and peaks between eight and 24 hours, whereas CRP rises slowly and peaks at 36 hours after endotoxin challenge. [13] However, in some patients, the PCT and CRP concentrations do not peak until the second or third day after developing sepsis. [14] In order to avoid these errors, we measured their concentrations from the first 24 hours the patient fulfilled SIRS criteria and continued for three days. The peak concentrations obtained during this period were assessed.

Table 5: AUC for diagnosis of sepsis, bacteraemia and other cultures.

	Sepsis (n = 67)	Bacteraemia (n = 13)	Other Cultures (n = 26)
Peak PCT	0.73 (0.64 to 0.83)	0.80 (0.66 to 0.93)	0.50 (0.37 to 0.64)
Peak CRP	0.54 (0.42 to 0.67)	0.54 (0.37 to 0.71)	0.58 (0.45 to 0.71)

Legend: AUC; Area under the curve, PCT; procalcitonin, CRP; C-reactive protein

Table 6: Optimal cut-point, sensitivity, specificity, PPV and NPV of PCT, and CRP for sepsis.

Biomarkers	Optimal Cut-point	Sensitivity	Specificity	PPV	NPV
Peak PCT	10.68 (ng/ml)	0.61 (0.5 to 0.73)	0.86 (0.73 to 0.99)	0.91 (0.83 to 0.99)	0.48 (0.34 to 0.62)
Peak CRP	148 (mg/ml)	0.42 (0.3 to 0.54)	0.71 (0.55 to 0.88)	0.78 (0.64 to 0.91)	0.34 (0.22 to 0.46)

Legends: PCT; procalcitonin, CRP; C-reactive protein, PPV; positive predictive value, NPV; negative predictive value

Our study population was a mixed medical-surgical patients with a diverse admission diagnoses and baseline co-morbidities. When we compared the medical and surgical patients, there were no significant differences in the baseline and peak PCT concentrations. This is important as induction of PCT after surgery may interfere with the validity and reliability of using PCT as a parameter for 'monitoring infection'. [15, 16] Serum PCT was significantly higher in patients with sepsis compared to SIRS, and the median PCT concentration remained significantly elevated throughout the three days study period. Therefore it is a reliable marker to differentiate sepsis from non-infectious SIRS during early ICU admission. In contrast, CRP and WCC failed to show significant differences during the first three days of daily assessment. The rapid up-regulation and sustained elevation of the PCT concentrations in the serum during infection suggest that it is a more reliable biomarker than CRP and WCC group. Not only was PCT significantly higher in the bacteraemia group, its median peak concentrations were seven times higher that than the other SIRS patients with sterile blood cultures. Other studies have also shown that septic patients with bacteraemia to have higher PCT concentrations than those without bloodstream infection. [21, 22] However, it was not useful in patients with positive tracheal cultures. This may be explained by the fact that some positive cultures are actually due to colonisation or localised infection or presence of other concomitant infections.

Table 7: Multivariable logistic regression for diagnosis of sepsis after inclusion of PCT or CRP.

Variables	Odds Ratio (95% CI)	p-value
SOFA	1.20 (1.00 to 1.44)	0.05
SAPS II	1.01 (0.96 to 1.06)	0.76
Peak CRP 3-days	1.00 (0.99 to 1.01)	0.98
Peak PCT 3-days	1.07 (1.02 to 1.13)	0.008

Legends: SOFA; Sequential Organ Failure Assessment, SAPS II; Simplified Acute Physiology Score II, CRP; C=reactive protein and PCT; procalcitonin

In this study, peak PCT concentration was more useful for diagnosing sepsis and bacteraemia than CRP. For clinical use, the cut-point chosen will depend on the aim of the biomarker, whether it is used as a screening test or a diagnostic marker. At a cut-point of 10.68 ng/ml, PCT was superior with a specificity of 86% and PPV of 91%. This optimal cut-point identified 12 of 13 patients with bacteraemia. Therefore as a diagnostic marker, concentrations over a certain range (10.68 ng/ml in our study, but 10 ng/ml in other studies) [12] should prompt a search for the source of sepsis and appropriate treatment instituted. After controlling for the SOFA and SAPS II scores, peak PCT remained diagnostic for sepsis. This result supports the ability of PCT to identify sepsis in addition to what is obvious from clinical data. In our mixed medical-

surgical ICU patients with sepsis, we found a good correlation between the SOFA score and PCT concentration. The PCT concentration was able to predict the severity of sepsis as was shown by the degree of organ dysfunction based on the SOFA score. Therefore, combining PCT with the SOFA score can increase the diagnostic performance of the SOFA score to predict the incidence of sepsis.

Based on our study, we believe that PCT has a role as a biomarker in our local ICU setting. It has a better discrimination and diagnostic accuracy than CRP for bacterial sepsis. We also found PCT to be specific for diagnosing sepsis and bacteraemia at the earlier stages in critically-ill patients with SIRS. Our study was designed as a real-life study with a diverse group of patients, thus closely resembling clinical practice in the ICU. Although it is a single centre study, our study showed the importance of serum PCT in managing SIRS patients in early admission to ICU. Incorporating PCT into our local practice can improve decision making, especially in patients with conflicting clues on the presence or absence of sepsis. The test can be performed within an hour and gives valuable information long before culture results are available.

This study has several limitations. PCT is also known to increase systemic inflammation without infection such as burns, pancreatitis, mechanical traumas or major surgeries. However, in the non-infectious group, the median or peak concentrations are usually lower than those patients with severe sepsis. [23] In septic shock. [23] our study, we included patients who had received any antibiotics but not more than 24 hours after the first dose. Given that the half-life of PCT in the systemic circulation is approximately 22 to 35 hours, [24] a single dose of antibiotic is not likely to affect the PCT concentrations.

In our centre, we have been using quantitative PCT concentration in the management of patients with severe sepsis admitted to our ICU since 2008. However, its use is not currently routine due to the high cost associated with the test. This test is also not available in other government hospitals in Malaysia. We have observed that the use of PCT assisted in the management of critically-ill patients and reduced the need of antibiotic use. However, we are not able to quantify the impact on survival, and overall outcome. This could only be adequately addressed in a randomised controlled trial comparing management with and without PCT test in our local population.

In conclusion, our study demonstrated that serum PCT is a better biomarker than CRP and WCC in differentiating sepsis from noninfectious SIRS in critically-ill patients. It is more useful in early diagnosis of sepsis and bacteraemia. It is useful as an indicator of severity of organ failure in patients with sepsis as measured by the SOFA score. These findings can be used as a reference for further studies, such as PCT-guided antibiotic stewardship in the management of sepsis in our local population.

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REFERENCES

1: Chan T, Gu F. Early diagnosis of sepsis using serum biomarkers. Expert Rev Mol Diagn. 2011; 11:487–96.

2: Foushee JA, Hope NH, Grace EE. Applying biomarkers to clinical practice: a guide for utilizing procalcitonin assays. J Antimicrob Chemother. 2012; 67:2560–9.

3: Jin M, Khan AI. Procalcitonin: Uses in the clinical laboratory for the diagnosis of sepsis. Lab Medicine. 2010; 41:173–7.

4: Becker KL. Procalcitonin and the calcitonin gene family of peptides in inflammation, infection, and sepsis: a journey from calcitonin back to its precursors. J Clin Endocrinol Metab. 2004; 89:1512–25.

5: Müller B, White JC, Nylén ES, et al. Ubiquitous expression of the calcitonin-i gene in multiple tissues in response to sepsis. J Clin Endocrinol Metab. 2001; 86:396–404.

6: Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. Crit Care Med. 2008; 36:941–52.

7: Uzzan B, Cohen R, Nicolas P, et al. Procalcitonin as a diagnostic test for sepsis in critically-ill adults and after surgery or trauma: a systematic review and meta-analysis. Crit Care Med. 2006; 34:1996–2003.

8: Tang BMP, Eslick GD, Craig JC, et al. Accuracy of procalcitonin for sepsis diagnosis in critically-ill patients: systematic review and meta-analysis. Lancet Infect Dis. 2007; 7:210–7.

9: Bell K, Wattie M, Byth K, et al. Procalcitonin: a marker of bacteraemia in SIRS. Anaesth Intensive Care. 2003; 31:629–36.

10: Sudhir U, Venkatachalaiah RK, Kumar TA, et al. Significance of serum procalcitonin in sepsis. Indian J Crit Care Med. 2011; 15:1–5.

11: Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992; 20:864–74.

12: Assicot M, Gendrel D, Carsin H, et al. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet. 1993; 341:515–8.

13: Reinhart K, Karzai W, Meisner M. Procalcitonin as a marker of the systemic inflammatory response to infection. Intensive Care Med. 2000; 26:1193–200.

14:Shehabi Y, Seppelt I. Pro/Con debate: Is procalcitonin useful for guiding antibiotic decision making in critically-ill patients? Crit Care. 2008; 12:211.

15: Meisner M, Tschaikowsky K, Hutzler A, et al. Postoperative plasma concentrations of procalcitonin after different types of surgery. Intensive Care Med. 1998;24:680–4.

16: Molter GP, Soltész S, Kottke R, et al. Procalcitonin plasma concentrations and systemic inflammatory response following different types of surgery. Anaesthesist. 2003; 52:210–7.

17: Simon L, Gauvin F, Amre DK, et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis. 2004; 39:206–17.

18: Simon L, Saint-Louis P, Amre DK, et al. Procalcitonin and C-reactive protein as markers of bacterial infection in critically-ill children at onset of systemic inflammatory response syndrome. Pediatr Crit Care Med. 2008; 9:407–13.

19: Ruiz-Alvarez M, Garcia-Valdecasas S, De Pablo R, et al. Diagnostic efficacy and prognostic value of serum procalcitonin concentration in patients with suspected sepsis. J Intensive Care Med. 2009; :63–71.

20: Aikawa N, Fujishima S, Endo S, et al. Multicenter prospective study of procalcitonin as an indicator of sepsis. J Infect Chemother. 2005; 11:152–9.

21: Blommendahl J, Janas M, Laine S, et al. Comparison of procalcitonin with CRP and differential white blood cell count for diagnosis of culture-proven neonatal sepsis. Scan J Infect Dis. 2002; 34:620–2.

22: Clec'h C, et al. Diagnostic and prognostic value of procalcitonin in patients with septic shock. Crit Care Med. 2004; 32:1166–9.

23: Brunkhorst FM, Wegscheider K, Forycki ZF, et al. Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis, and septic shock. Intensive Care Med. 2000; 26 Suppl 2:S148 –S152.

24: Meisner M. Pathobiochemistry and clinical use of procalcitonin. Clin Chim Acta. 2002; 328:17–9.