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Clinical usefulness of biomarkers for diagnosis and prediction of prognosis in sepsis and septic shock

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Abstract

Sepsis is a life-threatening condition and remains a major cause of mortality. The aim of this study was to evaluate the role of biomarkers in the diagnosis of sepsis and septic shock in patients admitted to the emergency department (ED). Medical records of patients who underwent measurement of serum biomarkers including lactic acid, C-reactive protein, procalcitonin (PCT), and presepsin in the ED between May 2019 and May 2020 were retrospectively reviewed. Patients were subdivided into 3 groups; non-sepsis, sepsis, and septic shock according to the new definition using the sequential organ failure assessment score. The mean age was 69.3 years, and 55.8% of the study population was female. Of 249 subjects, 98 patients confined to sepsis group, and 35.7% of them were septic shock. In the multivariable analysis, a high level of PCT was an independent predictor of sepsis (odds ratio [OR], 1.028; 95% confidence interval [CI], 1.006–1.051; $P = .011$) along with a simplified acute physiology score III (SAPS III) (OR, 1.082; 95% CI, 1.062–1.103, $P < .001$). PCT was also an independent risk factor for septic shock (OR, 1.043; 95% CI, 1.016–1.071, $P = .02$). In the receiver operating characteristic curve analysis, the area under the curve of PCT to predict sepsis and septic shock were 0.691 ($P < .001$) and 0.734 ($P < .001$), respectively. The overall 30-days mortality rate was 8.8%, and the mortality rate was significantly higher in the sepsis group (sepsis vs non-sepsis, 15.3% vs 4.6%; $P = .004$). In the multivariate Cox analysis, a higher level of lactic acid (hazard ratio [HR], 1.328; 95% CI, 1.061–1.663, $P = .013$), predisposing chronic pulmonary diseases (HR, 7.035; 95% CI, 1.687–29.341, $P = .007$), and a high SAPSIII value (HR, 1.046; 95% CI, 1.015–1.078, $P = .003$) were independent risk factors for mortality in sepsis patients. PCT was a useful biomarker for predicting sepsis and septic shock in the ED. A higher level of lactic acid, predisposing chronic pulmonary diseases, and a high SAPS III score were associated with a greater mortality risk in patients with sepsis.

Abbreviations: AKI = acute kidney injury, APACHE II = acute physiology and chronic health evaluation II, AUC = area under the curve, CI = confidence interval, CRP = C-reactive protein, ED = emergency department, HR = hazzard ratio, OR = odds ratio, ROC = receiver operating characteristic, SAPS III = simplified acute physiology score III, SOFA = sequential organ failure assessment score.

Keywords: biomarkers, procalcitonin, prognosis, sepsis, septic shock

1. Introduction

Sepsis is a major cause of morbidity and mortality that results in life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] Sepsis and septic shock account for a large portion of the death in intensive care unit, and the reported incidence is increasing as a major public health concern.[2] As a medical emergent condition, early diagnosis and appropriate treatment are crucial for better outcomes in the emergency department (ED).[3,4] However, accurate and early diagnosis of sepsis is still challenging in real clinical practice. Definite diagnosis based on blood culture usually takes days and often yield negative result.[5,6]

Serum biomarkers have the advantage of convenience to test, quick result time and repeatability. Several biomarkers have been widely used in clinical setting, and efforts and research for

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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developing new biomarker are ongoing.[7–9] Among biomarker, C-reactive protein (CRP) have been used as an inflammation-based biomarker.[10] Procalcitonin (PCT) is a representative marker used for sepsis and especially bacteremia with the highest sensitivity.[11] Recently, there is increasing reports about presepsin, a subtype of soluble cluster of differentiation 14, for usefulness of diagnosis and predicting prognosis in sepsis since 1st report in 2005.[12,13] However, there is no absolute biomarkers for diagnosis of sepsis with false negative or positive result.[14,15]

The aim of this study was to evaluate the role of biomarkers in the diagnosis of sepsis and septic shock in patients admitted to the emergency department (ED).

2. Materials and methods

2.1. Study participants

From May 2019 to May 2020, patients who visited the ED at Haeundae Paik hospital in South Koreas and had blood test, were screened for this study. Of 55,077 patients, total 249 patients who were suspected sepsis and had all biomarkers including PCT, presepsin, CRP, lactate at the ED were included. The diagnosis of sepsis was confirmed according to the new definition using the sequential organ failure assessment (SOFA) score.[1]

This study was approved by the Institutional Review Board of Haeundae Paik Hospital (approval number: 2020-06-016), and conducted in accordance with the ethical standards of the Declaration of Helsinki. Requirement for written informed consent was waived due to the retrospective nature of this study.

2.2. Data collection

Clinical and laboratory data for all patients during hospitalization were obtained from medical records. At the ED, initially measured biomarkers including presepsin, PCT, CRP, lactate were collected. After reviewing medical records, enrolled patients were classified into 2 group of non-sepsis and sepsis. Sepsis is defined as the presence of organ dysfunction, evaluated by an acute change in the SOFA score of ≥ 2 points secondary to infection. Among sepsis patients, septic shock group was subdivided by definition of a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain mean arterial pressure ≥ 65mmHg and having a serum lactate level ≥ 2mmol/L despite adequate volume resuscitation. Among patients with sepsis, the primary disease of sepsis and cause of death were collected. The acute physiology and chronic health evaluation II (APACHE II) score and the simplified acute physiology score III (SAPS III) were also calculated from patients' data at the ED to classify the disease severity and predict mortality. For mortality analysis, overall survival was defined as the time from hospital admission to death and 30-days mortality was defined as the death in 30 days from hospital admission.

2.3. Sample size calculation

The aim of this study was to evaluate the role of biomarkers in the diagnosis of sepsis and septic shock. An area under the curve (AUC) of biomarker in detecting sepsis or septic shock is expected to be 0.7 compared to an AUC of 0.5 that is equivalent to randomly classifying patients. Given alpha of 0.05 and power of 0.80, a total of 62 study patients (31 patients per group) is required. For sample size calculation, MedCalc® Statistical Software version 20.009 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021). This study was explorative in nature and therefore no adjustment for multiple testing was applied.

2.4. Statistical analysis

The data are presented frequency and percentage for categorical variables and mean ± standard deviation for numeric variables. The independent *t*-test or Mann-Whitney's U test was used to analyze continuous data, and chi-square test or Fisher's exact test was used to analyze categorical data. To check if its distribution is normal, we used Shapiro-Wilk's test. Univariate and multivariate analyses, using logistic regression, were performed to identify prognostic factors which are independently related to sepsis and septic shock. Prognostic factor for mortality were analyzed using a Cox proportional hazard model. Overall survival was estimated using the Kaplan-Meier curve. The receiver operating characteristic (ROC) curve analysis was performed to assess the sensitivity and specificity procalcitonin for predicting sepsis and septic shock. Optimal cutoff point using maximum Youden index from ROC curve for differentiation of the 2 groups with sensitivity and specificity. All statistical analyses were carried out using R 4.0.2, SPSS 25.0 (IBM Corp, Armonk, NY), and p values < 0.05 was considered statistically significant.

3. Results

3.1. Baseline clinical characteristics

A total of 249 patients was included in this study. The baseline characteristics in enrolled subjects are presented in Table 1. Median patient age was 69.3 years, and 55.8% were female. About a quarter of the patients had cardiovascular disease, followed by chronic kidney disease (22.1%), malignancy (17.3%) and chronic pulmonary disease (12.4%) as underlying diseases. 88 (35.3%) patients had acute kidney injury and about 1 in 5 patients had bacteremia. Sepsis was diagnosed in 98 (39.4%) patients, and septic shock was diagnosed in 35 (14.1%) patients. Most common cause of sepsis was urologic disease (35.7%), followed by pulmonary disease (26.5%) and gastrointestinal disease (26.5%). In comparison between sepsis and non-sepsis group, sepsis group showed older age, higher incidence of acute kidney injury (AKI) and bacteremia, higher levels of serum biomarkers and higher scores in APACHE II and SAPS III according to severity.

3.2. Discriminatory ability of biomarkers for sepsis

In the univariate logistic regression analysis, older age, predisposing chronic kidney disease, presence of bacteremia and AKI, higher level of blood urea nitrogen, lactate dehydrogenase, presepsin, PCT, and higher scores of APACHE II and SAPS III were significant predictive factors for sepsis (Table 2). In the multivariate analysis, procalcitonin and high score of SAPS III were only independent predictive factors for sepsis in the ED. In the receiver operation characteristic (ROC) curve analysis, high level of procalcitonin was useful in predicting for sepsis (AUC = 0.691, 95% CI: 0.623–0.759, $P < .001$) in patients at the ED. The best cutoff level was 0.595 with a sensitivity of 75.3% and specificity of 54.7% (Fig. 1). Comparison of AUC among biomarkers for predicting sepsis are shown in Figure 2.

3.3. Discriminatory ability of biomarkers for septic shock

In the univariate logistic regression analysis, predisposing chronic kidney disease, presence of malignancy and AKI, higher level of blood urea nitrogen, lactate dehydrogenase, presepsin, PCT, and higher scores of APACHE II and SAPS III were significant predictive factors for septic shock (Table 3). In the multivariate analysis, high level of procalcitonin among biomarkers and high score of APACH II were only independent predictive factors for septic shock. In the ROC curve analysis, high level

Table 1

Baseline characteristics of enrolled patients.

Characteristics	Non-sepsis (N = 151)	Sepsis (N = 98)	All-patients (N = 249)	*P* value
Age, yrs	66.76 ± 17.48	73.24 ± 14.24	69.31 ± 16.56	.006
Male	64 (42.4)	46 (46.9)	110 (44.2)	.480
Underlying disease				
Cardiovascular	39 (25.8)	21 (21.4)	60 (24.1)	.428
Cerebrovascular	12 (7.9)	14 (14.3)	26 (10.4)	.110
Chronic pulmonary	15 (9.9)	16 (16.3)	31 (12.4)	.136
Chronic kidney	27 (17.9)	28 (28.6)	55 (22.1)	.047
Chronic liver	10 (6.6)	9 (9.2)	19 (7.6)	.457
Malignancy	21 (13.9)	22 (22.4)	43 (17.3)	.081
Bacteremia	25 (16.6)	27 (27.6)	52 (20.9)	.037
AKI	39 (25.8)	49 (50.0)	88 (35.3)	<.001
Laboratory findings				
WBC (10^3/μL)	12.84 ± 5.96	11.98 ± 7.09	12.50 ± 6.43	.217
Total bilirubin (mg/dL)	1.04 ± 1.36	1.05 ± 1.03	1.05 ± 1.24	.158
BUN (mg/dL)	22.90 ± 18.32	32.86 ± 23.50	26.82 ± 21.04	<.001
Creatinine (mg/dL)	1.38 ± 1.35	1.71 ± 1.24	1.51 ± 1.31	.004
LDH (U/L)	281.23 ± 145.05	342.10 ± 209.07	305.38 ± 175.45	<.001
Lactate (mmol/L)	5.25 ± 16.32	2.65 ± 2.23	3.62 ± 10.13	.382
PaO_2 (mm Hg)	75.75 ± 35.96	85.95 ± 51.04	82.58 ± 46.70	.737
Presepsin (pg/mL)	825.19 ± 954.25	1124.59 ± 1109.47	943.50 ± 1026.75	.006
CRP (mg/dL)	12.93 ± 11.04	14.57 ± 10.86	13.57 ± 10.98	.192
Procalcitonin (ng/mL)	4.84 ± 14.34	17.27 ± 28.48	9.72 ± 21.86	<.001
APACHE II	4.18 ± 9.30	19.61 ± 9.87	10.25 ± 12.14	<.001
SAPS III	11.35 ± 23.64	58.66 ± 16.81	30.00 ± 31.38	<.001

Values are presented as mean ± standard deviation or number (%).

AKI = acute kidney injury, APACHEII = acute physiology and chronic health evaluationII, BUN = blood urea nitrogen, CRP = C-reactive protein, LDH = lactate dehydrogenase, PaO_2 = partial pressure of oxygen, SAPS III = simplified acute physiology score III, WBC = white blood cell.

Table 2

Predictive factors for sepsis.

	Univariate analysis		Multivariate analysis	
Variable	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Age, yr	1.026 (1.009–1.044)	.003		
Male	1.230 (0.721–2.005)	.480		
Underlying diseases				
Cardiovascular	0.783 (0.428–1.434)	.428		
Cerebrovascular	1.931 (0.853–4.371)	.115		
Chronic pulmonary	1.769 (0.831–3.767)	.139		
Chronic kidney	1.837 (1.004–3.362)	.049		
Chronic liver	1.426 (0.558–3.646)	.459		
Malignancy	1.792 (0.925–3.472)	.084		
Bacteremia	1.917 (1.034–3.552)	.039		
AKI	2.872 (1.677–4.919)	<.001		
Laboratory findings				
WBC (10^3/μL)	0.979 (0.940–1.020)	.304		
Total bilirubin (mg/dl)	1.004 (0.818–1.233)	.967		
BUN (mg/dL)	1.024 (1.010–1.037)	<.001		
Creatinine (mg/dl)	1.211 (0.986–1.487)	.068		
LDH (U/L)	1.002 (1.000–1.004)	.015		
Lactate (mmol/L)	0.970 (0.924–1.019)	.223		
PaO_2 (mm Hg)	1.005 (0.997–1.014)	.232		
Presepsin (pg/ml)	1.000 (1.000–1.001)	.030		
CRP (mg/dL)	1.014 (0.990–1.037)	.250		
Procalcitonin (ng/ml)	1.031 (1.014–1.047)	<.001	1.028 (1.006–1.051)	.011
APACHE II	1.154 (1.114–1.195)	<.001		
SAPS III	1.076 (1.059–1.094)	<.001	1.082 (1.062–1.103)	<.001

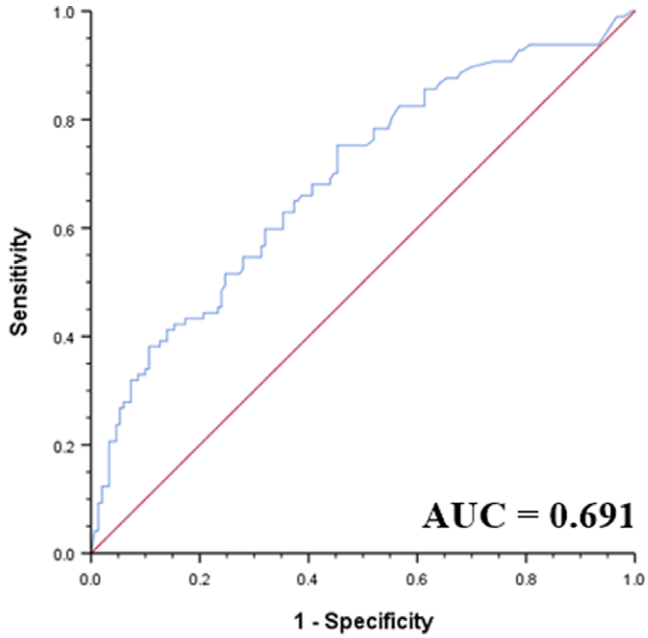
Values are presented as mean ± standard deviation or number (%).

AKI = acute kidney injury, APACHE II = acute physiology and chronic health evaluation II, BUN = blood urea nitrogen, CRP = C-reactive protein, LDH = lactate dehydrogenase, PaO_2 = partial pressure of oxygen, SAPS III = simplified acute physiology score III, WBC = white blood cell.

of procalcitonin was a useful in predicting for septic shock (AUC = 0.734, 95% CI: 0.633–0.836, $P < .001$) in patients at the ED. The best cutoff level was 9.1 ng/mL with a sensitivity of 48.6% and specificity of 89.3% (Fig. 3).

3.4. Survival analysis and prognostic biomarkers for mortality in sepsis

Overall 30-days mortality rate was 8.8% in this study, and mortality rate was significantly higher in the sepsis group (sepsis vs



Variable	Cut-Point Value	group		AUC (p)	95% CI	Sensitivity	Specificity
		Sepsis	Non-sepsis				
Procalcitonin	≥0.595	73	68	0.691 (<.001)	0.623-0.759	75.3%	54.7%
	<0.595	24	82				

Figure 1. ROC curve of procalcitonin to predict sepsis. ROC = receiver operating characteristic, AUC = area under the curve, CI = confidence interval.

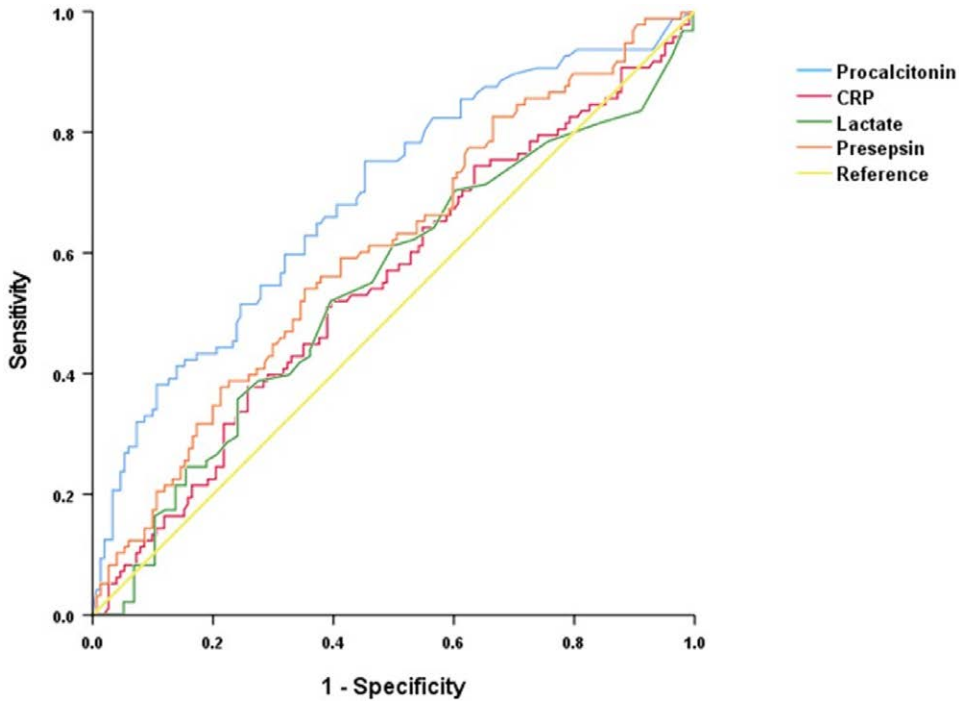


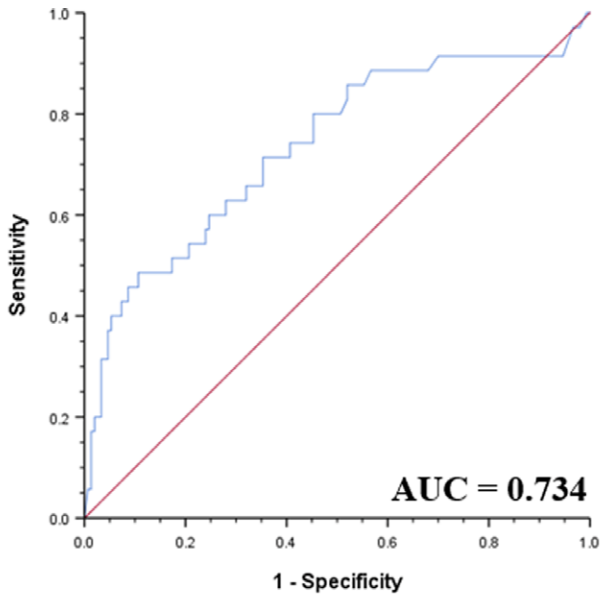
Figure 2. Comparison of AUC in ROC curves of biomarkers to predict sepsis. AUC, area under the curve; ROC, receiver operating characteristic; CRP, C-reactive protein.

Table 3

Predicting factor for Septic shock.

	Univariate analysis		Multivariate analysis	
Variable	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Age, yr	1.003 (0.981–1.025)	.786		
Male	1.284 (0.614–2.684)	.507		
Underlying disease				
Cardiovascular	0.851 (0.357–2.029)	.716		
Cerebrovascular	0.702 (0.150–3.289)	.653		
Chronic pulmonary	1.876 (0.671–5.245)	.230		
Chronic kidney	4.863 (2.223–10.637)	<.001		
Chronic liver	1.819 (0.536–6.181)	.337		
Malignancy	2.476 (1.041–5.888)	.040		
Bacteremia	1.745 (0.730–4.169)	.210		
AKI	4.308 (1.998–9.287)	<.001		
Laboratory finding				
WBC (10^3/μL)	1.010 (0.958–1.065)	.715		
Total bilirubin (mg/dL)	0.895 (0.626–1.280)	.544		
BUN (mg/dL)	1.023 (1.005–1.041)	.013		
Creatinine (mg/dL)	1.247 (0.986–1.577)	.065		
LDH (U/L)	1.003 (1.001–1.006)	.004		
Lactate (mmol/L)	0.991 (0.954–1.029)	.644		
PaO_2 (mm Hg)	1.010 (1.000 1.020)	.042		
Presepsin (pg/mL)	1.000 (1.000–1.001)	.009		
CRP (mg/dL)	1.012 (0.981–1.045)	.439		
Procalcitonin (ng/mL)	1.036 (1.018–1.054)	<.001	1.043 (1.016–1.071)	0.002
APACHE II	1.179 (1.123–1.237)	<.001	1.188 (1.124–1.256)	<.001
SAPS III	1.064 (1.044–1.085)	<.001		

AKI = acute kidney injury, APACHEII = acute physiology and chronic health evaluationII, BUN = blood urea nitrogen, CRP = C-reactive protein, LDH = lactate dehydrogenase, PaO_2 = partial pressure of oxygen, SAPSIII = simplified acute physiology score III, WBC = white blood cell.



Variable	Cut-Point Value	group		AUC (p)	95% CI	Sensitivity	Specificity
		Septic-shock	Non-sepsis				
Procalcitonin	≥9.1	17	16	0.734 (<.001)	0.633-0.836	48.6%	89.3%
	<9.1	18	134				

Figure 3. ROC curve of procalcitonin to predict septic shock. ROC = receiver operating characteristic, AUC = area under the curve, CI = confidence interval.

non-sepsis: 15.3% vs 4.6%, $P = .004$). The 30-days mortality rates of sepsis groups without and with septic shock were 1.6% and 25.7%, respectively (Fig. 4).

In a multivariable Cox analysis, predisposing chronic pulmonary disease (hazzard ratio [HR] 7.035, 95% CI: 1.687–29.341, $P = .007$), high level of serum lactate (HR 1.328, 95% CI: 1.061–1.633, $P = .013$), and high scores of SAPS III (HR 1.046, 95% CI: 1.015–1.078, $P = .003$) were found to be an independent factor affecting overall survival (Table 4).

4. Discussion

In our study, PCT was a most useful biomarker for predicting sepsis and septic shock among biomarkers in patients at the ED. Also clinical score system of SAPS III and APACHE II showed discriminative power for predicting sepsis and septic shock, respectively. The 30-days mortality rates of sepsis groups without and with septic shock were 1.6% and 25.7%, respectively. An high level of lactate, predisposing chronic pulmonary disease, and high score of SAPS III at the ED was a useful predictor of mortality.

Despite recent advances and efforts in medical science and system, sepsis remains a major cause of morbidity and mortality. Considering increasing mortality in septic shock, early diagnosis and accurate early treatment is essential for better outcome in patients at the ED. Therefore, there have been lots of research to find most useful biomarkers for predicting sepsis. Among many kind of biomarkers, there are increasing reports about presepsin, and presepsin has been available in clinical practice since relatively recent years. This study was originally designed to evaluate the efficacy of presepsin as a new biomarker for predicting sepsis, and compare the predictive values among previously well-known biomarkers. In comparison of biomarkers for diagnostic accuracy of sepsis, Aliu-Bejta et al, in 100 patients with sepsis, showed that serum concentration of presepsin had a good ability to diagnosis sepsis and distinguish sepsis; however, CRP and PCT were not.[12] Liu et al also reported that plasma level of presepsin were superior for reflecting the severity of sepsis compared to PCT based on the values of AUC (0.820 vs 0.724).[16] However, our study showed opposite results suggesting a higher predictive ability of PCT compared to presepsin. A previous prospective observation study, in 93 patients with suspected sepsis, reported that PCT showed a better diagnostic accuracy for bacteremia in patient suspected sepsis than presepsin (AUC: 0.875 vs 0.788).[17] Ulla et al, in 106 patients with suspected sepsis at the ED, reported that the AUC of PCT for diagnostic accuracy of sepsis showed a better diagnostic accuracy than presepsin (AUC 0.875 vs 0.701).[18] This conflicting result might be explained by applying new definition of Sepsis-3 instead of systemic inflammatory response syndrome criteria, and performing a statistical analysis method of multivariable regression model unlike previous studies using AUC comparison. The core of this study is to prove that PCT is a statistically significant factor in multivariable logistic regression including other variables just not to compare AUC among biomarkers. We need a careful consideration to interpret this result. This result does not mean that presepsin is not useful for diagnosis of sepsis. In performing test of biomarkers in patient suspected with sepsis at the ED, procalcitonin might be the first choice to distinguish sepsis and septic shock considering the medical circumstances of the institution, and cost-effectiveness.

In this study, optimal cutoff value of PCT for sepsis and septic shock were 0.595 ng/ml (AUC = 0.691, 95% CI: 0.623–0.759, $P < .001$) and 9.1 ng/mL (AUC = 0.734, 95% CI: 0.633–0.836, $P < .001$), respectively. Recent study applying Sepsis-3 definition in patients visiting the ED showed similar result with our study. Kim et al, in 470 sepsis and 109 septic shock of 866 patients, reported that an optimal cutoff value of PCT for sepsis and septic shock were 0.41 ng/dL (AUC: 0.745, sensitivity of 74.8% and specificity of 63.8%) and 4.7 ng/dl (AUC: 0.785, sensitivity of 66.1% and specificity of 79.0%), respectively.[19]

In this study, biomarkers including PCT and presepsin were not independent predictor for mortality. High level of lactate, predisposing chronic pulmonary disease, and high score of SAPS III were associated with higher mortality. Recent study in 250 patients with suspected sepsis at the ED supported the result of our study. Ruangsomboon et al reported that presepsin and PCT is a useful diagnostic biomarker for sepsis in emergency patients, however only SOFA score (HR 1.2, 95% CI: 1.1–1.4) and plasma lactate (HR 1.3, 95% CI: 1.1–1.5) are independent predictors of 30-days mortality in the adjusted model.[20] Zhu et al also reported that The SAPS III model (AUC = 0.812, 95% CI: 0.802–0.822) showed the best crimination ability for predicting mortality in sepsis patients based on Sepsis-3 criteria among clinical scoring system by analyzing the 4th edition of the Medical information Mart for Critical Care database.

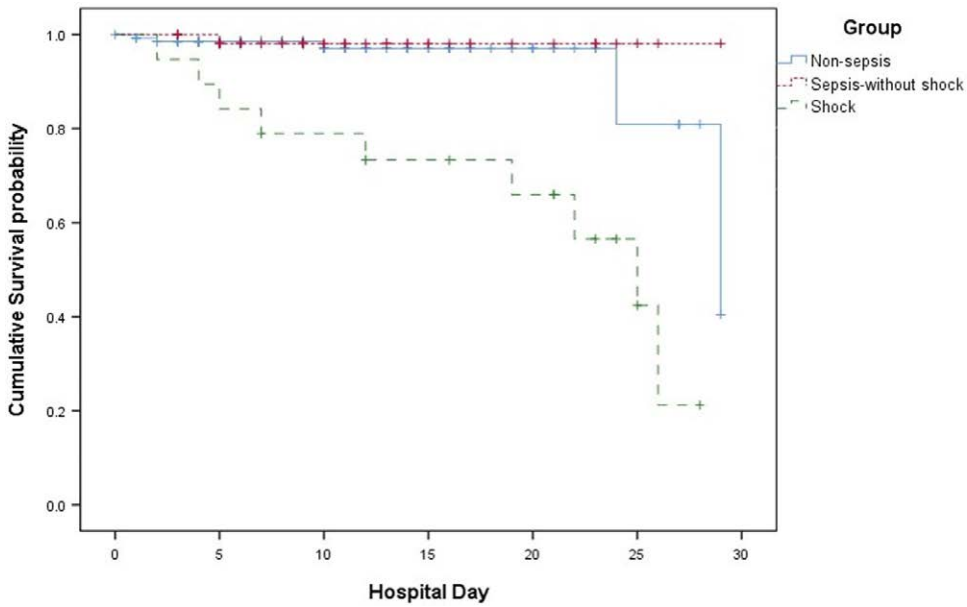


Figure 4. Comparison of survival curves according to non-sepsis, sepsis and septic shock diagnosis.

Table 4

Prognostic factors for mortality in patients with sepsis.

	Univariate analysis		Multivariate analysis	
Variable	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Age, yr	1.003 (0.971–1.036)	.877		
Male	1.384 (0.489–3.916)	.540		
Underlying diseases				
Cardiovascular	2.465 (0.851–7.134)	.096		
Cerebrovascular	0.429 (0.056–3.292)	.416		
Chronic pulmonary	3.396 (1.100–10.485)	.034	7.035 (1.687–29.341)	.007
Chronic kidney	0.911 (0.296–2.806)	.871		
Chronic liver	3.268 (0.895–11.938)	.073		
Malignancy	1.130 (0.358–3.573)	.835		
Bacteremia	1.348 (0.473–3.839)	.576		
AKI	1.379 (0.424–4.488)	.594		
Laboratory				
WBC (10^3/μL)	0.964 (0.889–1.045)	.377		
Total bilirubin (mg/dL)	1.160 (0.808–1.664)	.421		
BUN (mg/dL)	0.972 (0.925–1.020)	.244		
Creatinine (mg/dL)	1.234 (0.874–1.742)	.232		
LDH (U/L)	1.001 (1.000–1.003)	.135		
Lactate (mmol/L)	1.218 (1.025–1.446)	.025	1.328 (1.061–1.663)	.013
PaO_2 (mm Hg)	0.995 (0.984–1.006)	.394		
Presepsin (pg/mL)	1.000 (1.000–1.001)	.077		
CRP (mg/dL)	1.027 (0.982–1.074)	.252		
Procalcitonin (ng/mL)	1.002 (0.987–1.018)	.762		
APACHE II	1.057 (0.998–1.119)	.057		
SAPS III	1.046 (1.018–1.075)	.001	1.046 (1.015–1.078)	.003

Values are presented as mean ± standard deviation or number (%).

AKI = acute kidney injury, APACHE II = acute physiology and chronic health evaluationII, BUN = blood urea nitrogen, CI = confidence interval, CRP = C-reactive protein, HR = hazzard ratio, LDH = lactate dehydrogenase, PaO_2 = partial pressure of oxygen, SAPS III = simplified acute physiology score III, WBC = white blood cell.

Serum lactate has been well known and world-widely accepted as an important biomarker of tissue hypoxia and dysfunction in sepsis and septic shock.[21–23] These result of our study suggest that it is important to evaluate the initial level of lactate and track the lactate clearance as a target of resuscitation in early phase of sepsis and septic shock, and consistent with the international guidelines of Surviving Sepsis Campaign.[24] Regarding prediction for prognosis in sepsis and septic shock, monitoring of lactate level and clinical scoring system including the SAPS III might be helpful.

5. Study limitations

First, this was a retrospective single center study, which may limit the generalizability of this study. Further multicenter researches in diverse setting and populations might be needed to support our study. Second, patients who were suspected sepsis and performed many biomarkers by the subjective judgement of the emergent medicine physician were enrolled in this study without a formal protocol. Therefore, there may be a selection bias for enrolled patients including sepsis and non-sepsis group. Third, the diagnosis time after visiting the ED and the therapeutic method may vary according to each condition of patients, because the classification of diagnosis was made retrospectively. The differences of duration from the ED visiting to diagnosis, and inconsistent therapeutic strategy might have affected outcomes.

6. Conclusion

In conclusion, PCT was most useful biomarker for predicting sepsis and septic shock among biomarkers in patients at the ED. Regarding prognosis, a high level of lactate, predisposing chronic pulmonary disease, and high score of SAPS III at the ED were an independent prognostic factors for mortality.

Author contributions

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