BRIEF COMMUNICATION

Serum Procalcitonin vs SOFA Score in Predicting Outcome in Sepsis Patients in Medical Intensive Care Unit

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Abstract

Background: Sepsis is a dysregulated host response to infection that leads to acute organ dysfunction. The Sequential Organ Failure Assessment (SOFA) score is one of the gold standard tests in assessing the patient's status during ICU stay and also to predict the clinical outcomes of the patients. Procalcitonin (PCT) is a more specific marker for bacterial infection. In this study, we compared PCT and SOFA scores in predicting morbidity and mortality outcomes in sepsis.

Materials and methods: A prospective cohort study was conducted on 80 patients with suspected sepsis. Patients who were >18 years of age with suspected sepsis presenting to the emergency room within 24–36 hours of illness are included in the study. SOFA score was calculated, and blood was drawn for PCT at the time of admission.

Results: The average SOFA score in survivors was 6.1 ± 1.93, whereas, in nonsurvivors, it was 8.3 ± 2.13. The average PCT level in survivors was 3.7 ± 1.5, whereas, in nonsurvivors, was 6.4 ± 3.13. Area under the curve (AUC) for serum procalcitonin was found to be 0.77 (*p* value = 0.001) with average procalcitonin level of 4.15 ng/mL with sensitivity of 70% and specificity of 60%. AUC of SOFA score was found to be 0.78 (*p* value = 0.001) with an average score of 8, having a sensitivity of 73% and specificity of 74%.

Conclusion: Serum PCT and SOFA scores are significantly elevated in patients with sepsis and septic shock, indicating their utility in predicting the severity and also their ability to assess end-organ damage.

Keywords: Sepsis, Septic shock, Serum procalcitonin, SOFA score.

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Highlights

- In our study, we analyzed and found that in bacterial sepsis, serum procalcitonin is noninferior to SOFA score in predicting the mortality.

Introduction

Sepsis is a dysregulated host response to infection that leads to acute organ dysfunction.[1] Septic shock, which includes an underlying circulatory and cellular/metabolic imbalance that increases mortality, develops in a subgroup of sepsis patients. Despite sufficient volume resuscitation, septic shock is characterized by persistent hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mm Hg or higher and a serum lactate level greater than 2 mmol/L (18 mg/dL).[2]

Early detection and prompt treatment of sepsis have a large mortality benefit. Early detection enables therapeutic intervention to balance oxygen delivery and demand as soon as possible.[3] Sepsis patients experience continuing volume loss and microcirculatory inflammation as a result of delayed diagnosis, which leads to severe and permanent organ failure.

Sequential Organ Failure Assessment score (SOFA) is one of the gold standard tests in assessing the patient's status during ICU stay and also to predict the clinical outcomes of the patients. It is a 24-point measure of organ dysfunctions that uses six organ systems (renal, cardiovascular, pulmonary, hepatic, neurological, and hematologic) where 0–4 points are assigned per organ system, as shown in Table 1.[4]

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The incidence of hospital-acquired infections has similar tendency in patients admitted with sepsis and nonsepsis; however, sepsis patients will develop higher rates of multi-organ failure compared with patients with nonsepsis.[5] Procalcitonin (PCT), along with CRP and ESR, is used as a marker of acute inflammation. Procalcitonin is the precursor of the hormone calcitonin produced

Table 1: Sequential organ failure assessment score

	SOFA score				
Variables	*0*	*1*	*2*	*3*	*4*
Respiratory	PaO_2/FiO_2: >400 SpO_2/FiO_2: >302	PaO_2/FiO_2: <400 SpO_2/FiO_2: <302	PaO_2/FiO_2: <300 SpO_2/FiO_2: <221	PaO_2/FiO_2: <200 SpO_2/FiO_2: <142	PaO_2/FiO_2: <100 SpO_2/FiO_2: <67
Cardiovascular (doses in µg/kg/min)	MAP ≥70 mm Hg	MAP ≥70 mm Hg	Dopamine ≤5 or ANY dobutamine	Dopamine >5 Norepinephrin ≤0.1 Phenylephrine ≤0.8	Dopamine >15 Norepinephrine >0.1 Phenylephrine >0.8
Liver (bilirubin, mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12
Renal (creatinine, mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
Coagulation (platelets × $10^3/mm^3$)	≥150	<150	<100	<50	<20
Neurologic (GCS score)	15	13–14	10–12	6–9	<6

According to sepsis-3, a new (or presumed new) increase in SOFA score above baseline in the presence of infection makes the diagnosis of sepsis. Increasing SOFA scores are associated with incremental increases in mortality. FiO_2, fraction of inspired oxygen; GCS, Glasgow coma scale; MAP, mean arterial pressure; PaO_2, arterial oxygen pressure; SOFA, sequential organ failure assessment (score); SpO_2, oxygen saturation

Table 2: Baseline characteristics of the study

Serial number	*Characteristics*	*Survivors (n)*	*Non-survivors (n)*	*p-value*
1.	Age	59.8 ± 11.6	56.9 ± 12.1	0.3
2.	Sex			
	Males	27 (33.7%)	20 (25%)	
	Females	23 (28.8%)	10 (12.5%)	
3.	Duration of complaints	5.04 ± 4.01	5.03 ± 3.91	0.9
4.	Complaints at presentation			
	Fever	35 (43.7%)	45 (56.3%)	
	Altered sensorium	15 (18.7%)	25 (31.2%)	
	Cough	8 (10%)	13 (16.2%)	
	Dysuria	5 (6.2%)	9 (11.2%)	
	Abdominal pain	3 (3.7%)	7 (8.7%)	
5.	Comorbidities			
	Diabetes mellitus	30 (37.5%)	30 (37.5%)	
	Hypertension	10 (8%)	16 (20%)	
	Chronic kidney disease	5 (6.2%)	9 (11.2%)	
	Obstructive airway disease	4 (5%)	6 (7.5%)	
	Coronary artery disease	4 (5%)	7 (8.7%)	
6.	Blood parameters			
	Haemoglobin	10.08 ± 2.27	9.74 ± 0.09	0.5
	Total counts	17148 ± 7452	19619 ± 6023	0.1
	Platelets	2.43 ± 1.28	2.67 ± 1.72	0.4
7.	SOFA score	6.1 ± 1.93	8.3 ± 2.13	0.0001
8.	Serum procalcitonin	3.7 ± 1.5	6.4 ± 3.13	0.0001

by the thyroid gland. Extra thyroidal tissues release PCT when exposed to bacterial infections in response to bacterial endotoxins and inflammatory cytokines.[6] Procalcitonin is an effective marker for diagnosis of sepsis and to predict disease severity as well as mortality.[7] Procalcitonin is a more specific marker for bacterial infection, but it is also increased in viral infections and noninfectious inflammatory conditions. Unlike C-reactive protein (CRP), which peaks after 2–3 days, PCT is detectable 3–4 hours after an infection, peaks at 6–12 hours, and has a half-life of roughly 24 hours.[8]

Materials and Methods

In this study, we compare PCT and SOFA scores in predicting morbidity and mortality outcomes in sepsis. After obtaining approval from Institutional Ethical Committee, a prospective cohort study was conducted on 80 patients with suspected sepsis from the Emergency Department and Medical Intensive Care Unit in SRM Medical College and Research Centre from May 2019 to November 2020 for a period of 18 months. Patients who were >18 years of age with suspected sepsis presenting to the emergency room within 24–36 hours of illness are included in the study. Patients who are pregnant, had multiple trauma, with a history of malignancy, severe burns, heatstroke, mesenteric embolism, and recent surgery within the last 1 month are excluded from the study.

The following details were recorded – presenting symptoms and signs, co-morbidity, vitals, lab parameters, and SOFA score at the time of admission. The patients were followed up till discharge from hospital or in-hospital death. About 5 mL of the patient's blood was collected at the time of admission and stored at –80°C till all data collection was complete, and serum was analyzed with the XPRESSBIO ELISA KIT (Sandwich ELISA) to measure PCT. Based on the final outcome, all the 80 patients were divided into survivors (50) and nonsurvivors (30).

Results

A total of 80 patients with a diagnosis of sepsis were included in the study, out of which 47 (59%) subjects were male and 33 (41%) were females as shown in Table 2. The mean age of the

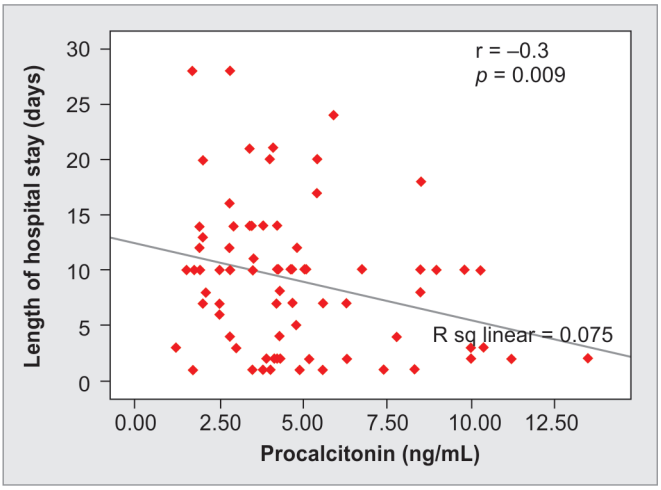
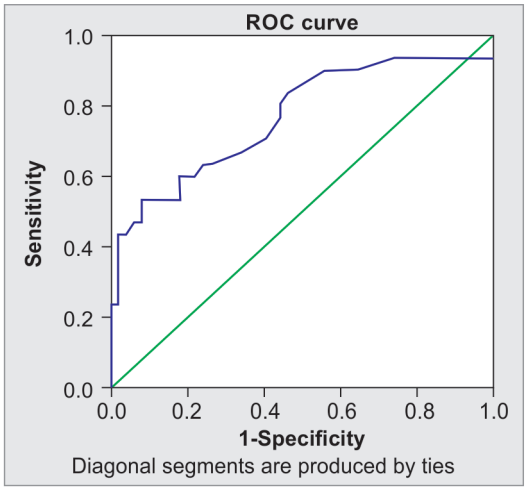


Fig. 1: Association of PCT with length of hospital stay



Area under the curve

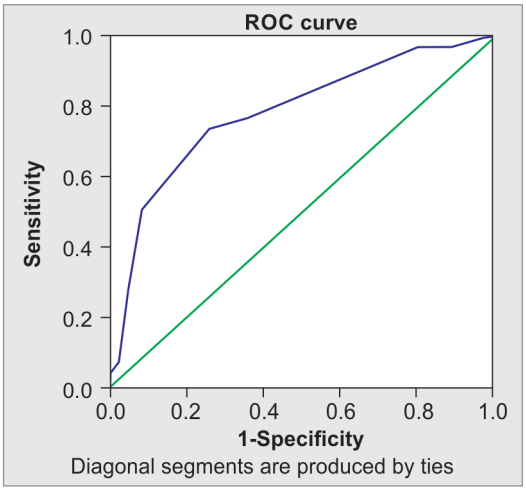
Test result variable(s): PCT

Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.766	0.059	0.000	0.651	0.881

Fig. 2: Receiver operating curve of PCT

study participants was 58 ± 12 years. About 50 patients (63%) survived (survivors group) and 30 patients (37%) did not survive (nonsurvivors' group). About 66% of the nonsurvivors were males. Fever (87.5%), altered sensorium (51%), and cough (27%) were the predominant presenting complaints. The common comorbidities associated were diabetes mellitus (75%), hypertension (32.5%), chronic kidney disease (17.5%), obstructive airway disease (16%), and coronary artery disease (15%). The total WBC counts were higher in the nonsurvivors' group.

The most common etiology for sepsis in our study population was urosepsis (25%), followed by acute exacerbations of chronic obstructive pulmonary airway disease with pulmonary infection (12.5%), meningitis (12.5%), and skin and soft-tissue infections (6%). Common organisms isolated in our subjects were Pseudomonas



Area under the curve

Test result variable(s) SOFA score

Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.782	0.055	0.000	0.674	0.890

The test result variable(s): SOFA score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

Fig. 3: Receiver operating curve of SOFA

(28%), Klebsiella (28%), *E. coli* (21%), and others (23%). The average SOFA score in survivors was 6.1 ± 1.93, whereas, in nonsurvivors, it was 8.3 ± 2.13. The average PCT level in survivors was 3.7 ± 1.5, whereas in nonsurvivors, was 6.4 ± 3.13. In our study, 30 patients succumbed to illness, the cause of death being multiple organ dysfunction syndrome (50%), acute respiratory distress syndrome (27%), and septic shock (23%). It was observed that patients who required interventions such as dialysis (40%) and assist control mode ventilation (45%) had a worse outcome.

The duration of hospital stay was higher among survivors than nonsurvivors (11 vs 4 days, $p = 0.001$). There was a significant difference [$p = 0.0001$] in SOFA and serum PCT levels between survivors and nonsurvivors groups. There was no significant difference in clinical presentation and risk factors between survivors and nonsurvivors. There was no significant difference in total count, platelet count, and hemoglobin in the two groups.

In our study of 80 patients, there was a negative correlation between the procalcitonin levels and duration of hospital stay ($r = -0.3$, $p = 0.009$) as shown in Figure 1.

Figure 2 indicates that the AUC for serum procalcitonin to be 0.77 (p-value = 0.001) with average procalcitonin level of 4.15 ng/mL with sensitivity of 70% and specificity of 60%.

The AUC of SOFA was found to be 0.78 (p-value = 0.001) with an average value of 8, having a sensitivity of 73% and specificity of 74%, which is shown in Figure 3. Area under the curve of PCT and SOFA are comparable and this indicates PCT is a valuable biomarker for sepsis.

Discussion

With a mortality rate of 30%, sepsis is one of the primary causes of death despite the availability of improved resuscitation techniques.

Therefore, early diagnosis in determining the degree of sepsis increases the likelihood of starting prompt and targeted treatment. Different biomarkers can be used to gauge the severity of sepsis, direct antibiotic therapy, gauge a patient's reaction to treatment, and forecast sepsis consequences. A more accurate biomarker of SIRS, sepsis, and septic shock caused by bacterial infections has been thought to be PCT. However, the exact role of PCT in various stages of sepsis remains undefined.

The most common etiology in our study was urinary tract infection, whereas, in the study done by Mayr et al.[9] in the United States, the most common presentation was respiratory infections that could be because of referral bias. His study also concluded that male gender and the presence of comorbidities are associated with severe sepsis and worse outcome. This is similar to our study, where 66% of the nonsurvivors with severe sepsis were males with comorbidities. In the Indian scenario research done by Chatterjee et al.,[10] it was shown that respiratory infections followed by intra-abdominal and blood-borne infections were common causes, whereas, in our study, we found that high incidence of urosepsis followed respiratory tract infections, which could be due to referral bias. Diabetes was found to be an independent risk factor in the development of sepsis and septic shock, and patients with uncontrolled sugars had worse outcomes, as discussed by Koch et al.[11] In our study, 75% of the patients had diabetes.

A study done by Assicot et al.[12] concluded that high-serum PCT was associated with septic shock due to bacterial infections and increased mortality among adults and children. Our study also agrees with the same where the PCT in nonsurvivors was double the values found in survivors.

Our results were comparable to the study done by Vamseedar et al.[13] who suggested serum procalcitonin and SOFA score can be used to assess the severity of sepsis that can aid in early intervention and prevent bad outcomes. In his study, SOFA score and PCT were high in all the sepsis patients similar to our study. Procalcitonin was found to be elevated more than the cutoff of 0.57 ng/mL in all the patients (100%), making it an ideal marker for bacterial infection, as suggested by Ashitha et al.[14] The average PCT value in our study is 5.05 ng/mL. Procalcitonin was an independent predictor of mortality, and also the levels of PCT could differentiate between survivors and nonsurvivors.

In our study, we found out that serum procalcitonin is noninferior to SOFA score in predicting the mortality in sepsis and combining SOFA score with serum procalcitonin increases the sensitivity in prognosticating the outcome of sepsis.

Conclusion

Serum PCT and SOFA scores are significantly elevated in patients with sepsis and septic shock, indicating their utility in predicting the severity and also their ability to assess end-organ damage. Therefore, PCT levels with SOFA scores may be helpful in assessing the severity of sepsis and its complications. Procalcitonin monitoring is a fast and reliable approach to assessment of patients with septic shock with few limitations. SOFA score is a simple and effective method to describe organ failure in critically ill, and thus the combination of these two might enable accurate prediction of outcome assessment.

This was a single-center-based study, so the results cannot be generalized. Some of the study population received the antibiotics early, hence, their procalcitonin would have been low even though having a high SOFA score. Some of the patients had chronic kidney disease as a comorbidity, which could have influenced elevated serum procalcitonin. Procalcitonin sample and SOFA score were only used as single observation rather than serial reports.

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