Journal of Endocrinology, Tropical Medicine, and Infectious Disease (JETROMI)
Journal homepage: https://talenta.usu.ac.id/jetromi

Diagnostic Accuracy of the Systemic Immune-Inflammation Index and Procalcitonin in Patients with Sepsis at Adam Malik Hospital Medan

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ARTICLE INFO
Article history:
Received 11 Agustus 2026
Revised 28 Agustus 2026
Accepted 10 September 2026
Available online 10 September 2026

E-ISSN: 2686-0872
P-ISSN: 2686-0856

How to cite:
NO Parhusip, F Ginting, LE Sihotang. "Diagnostic Accuracy of the Systemic Immune-Inflammation Index and Procalcitonin in Patients with Sepsis at Adam Malik Hospital Medan." Journal of Endocrinology, Tropical Medicine, and Infectious Disease (JETROMI). 8(1): 60-67.

http://doi.org/10.32734/jetromi.v8i1.26805

ABSTRACT

Background: Early diagnosis of sepsis is essential to improve patient outcomes. Procalcitonin (PCT) is a widely used biomarker for sepsis but may be limited by its cost and availability. The Systemic Immune-Inflammation Index (SII), derived from routine hematological parameters, has been proposed as a simple and inexpensive alternative. This study aimed to compare the diagnostic accuracy of SII and PCT in patients with suspected sepsis.
Methods: A cross-sectional diagnostic accuracy study was conducted in the Emergency Department of H. Adam Malik General Hospital, Medan. Fifty-five patients with suspected infection were enrolled, including 32 patients with sepsis and 23 without sepsis based on the Sepsis-3 criteria. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis, including the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Youden index, and comparison of AUCs using the DeLong test.
Results: The optimal cut-off value for SII was 1,752,635, with an AUC of 0.564 (95% CI: 0.42–0.69), sensitivity of 68.8%, and specificity of 56.5%. PCT demonstrated superior diagnostic performance, with an optimal cut-off value of 1.265 ng/mL, an AUC of 0.863 (95% CI: 0.74–0.94), sensitivity of 75.0%, and specificity of 82.6%. The difference in AUC between SII and PCT was statistically significant (p = 0.0007). The combined SII–PCT model yielded an AUC of 0.872.
Conclusion: Procalcitonin demonstrated significantly higher diagnostic accuracy than SII for identifying sepsis. The combined SII–PCT model showed good diagnostic performance and warrants further evaluation in larger studies.
Keyword: sepsis; Systemic Immune-Inflammation Index; procalcitonin; biomarker; diagnostic accuracy.

ABSTRAK

Latar Belakang: Diagnosis dini sepsis sangat penting untuk meningkatkan luaran pasien. Prokalsitonin (PCT) merupakan biomarker yang banyak digunakan untuk diagnosis sepsis, namun biaya dan keterbatasan ketersediaannya dapat membatasi penggunaan rutin. Systemic Immune-Inflammation Index (SII), yang dihitung dari parameter hematologi rutin, diusulkan sebagai biomarker alternatif yang sederhana dan ekonomis. Penelitian ini bertujuan membandingkan akurasi diagnostik SII dan PCT pada pasien dengan kecurigaan sepsis.
Metode: Penelitian uji akurasi diagnostik dengan desain potong lintang ini dilakukan di Instalasi Gawat Darurat RSUP H. Adam Malik Medan. Sebanyak 55 pasien dengan kecurigaan infeksi diikutsertakan, terdiri atas 32 pasien sepsis dan 23 pasien nonsepsis berdasarkan kriteria Sepsis-3. Performa diagnostik dievaluasi

menggunakan analisis receiver operating characteristic (ROC), meliputi area under the curve (AUC), sensitivitas, spesifisitas, nilai prediksi positif (PPV), nilai prediksi negatif (NPV), indeks Youden, serta perbandingan nilai AUC menggunakan uji DeLong.
Hasil: Nilai cut-off optimal SII adalah 1.752.635 dengan AUC 0,564 (95% IK: 0,42–0,69), sensitivitas 68,8%, dan spesifisitas 56,5%. Prokalsitonin menunjukkan performa diagnostik yang lebih baik dengan nilai cut-off 1,265 ng/mL, AUC 0,863 (95% IK: 0,74–0,94), sensitivitas 75,0%, dan spesifisitas 82,6%. Perbedaan nilai AUC antara SII dan PCT bermakna secara statistik (p = 0,0007). Model kombinasi SII–PCT menghasilkan AUC sebesar 0,872.
Kesimpulan: Prokalsitonin memiliki akurasi diagnostik yang secara signifikan lebih tinggi dibandingkan SII dalam mengidentifikasi sepsis. Model kombinasi SII–PCT menunjukkan performa diagnostik yang baik dan memerlukan evaluasi lebih lanjut pada penelitian dengan jumlah sampel yang lebih besar.
Keyword: sepsis; Systemic Immune-Inflammation Index; procalcitonin; biomarker; diagnostic accuracy.

1. Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection and remains a major global health problem [1]. According to the Global Burden of Disease (GBD) Study, there were an estimated 48.9 million incident cases of sepsis and 11 million sepsis-related deaths worldwide in 2017, accounting for approximately 19.7% of all global deaths [2]. Although age-standardized mortality has declined substantially over the past three decades owing to advances in infection management, critical care, and healthcare accessibility, sepsis continues to impose a considerable burden, particularly in low- and middle-income countries [3]. Indonesia is among the countries with a high burden of sepsis in Southeast Asia, with hundreds of thousands of cases and deaths reported annually [4].

Early recognition of sepsis remains one of the greatest challenges in emergency care. Sepsis is frequently underdiagnosed because of its nonspecific clinical manifestations and the limited sensitivity of administrative data, whereas overdiagnosis may occur because of variations in clinical awareness, diagnostic criteria, and coding practices [5]. Delayed diagnosis is associated with postponed initiation of antimicrobial therapy and fluid resuscitation, leading to an increased risk of septic shock, multiple organ dysfunction, prolonged hospitalization, and mortality [6]. Moreover, many sepsis survivors experience long-term physical and functional impairments, resulting in substantial socioeconomic consequences [7]. Therefore, accurate and readily available diagnostic biomarkers are essential to facilitate the early identification of sepsis.

Currently, no single gold standard biomarker is available for the diagnosis of sepsis. Although blood culture remains essential for pathogen identification, it is time-consuming and has limited sensitivity. The Sepsis-3 consensus defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, with organ dysfunction identified by an increase of at least two points in the Sequential Organ Failure Assessment (SOFA) score [8]. In addition to clinical assessment, biomarkers have become valuable adjuncts for the diagnosis and severity assessment of sepsis. Procalcitonin (PCT) is one of the most extensively studied biomarkers because its serum concentration increases significantly during systemic bacterial infection and correlates with disease severity. Previous studies have demonstrated that PCT has good diagnostic accuracy for sepsis, with reported area under the receiver operating characteristic curve (AUC) values ranging from 0.86 to 0.94.[11–13] However, routine PCT measurement may be limited by its relatively high cost and restricted availability, particularly in resource-limited healthcare settings.

The Systemic Immune-Inflammation Index (SII), calculated as platelet count × neutrophil count divided by lymphocyte count, has recently emerged as a novel inflammatory biomarker. SII reflects the balance between inflammatory activation and immune status and can be readily derived from routine complete blood count parameters. Previous studies have suggested that SII has promising diagnostic performance in patients with sepsis. Pricop et al. reported an AUC of 0.811 with a sensitivity of 72.7% and specificity of 80.6% for the diagnosis of sepsis.14 Nevertheless, current evidence remains limited, and most studies have focused on

specific infectious conditions or the prognostic value of SII rather than its diagnostic utility. Furthermore, data comparing the diagnostic accuracy of SII with PCT, particularly in Indonesian patients with suspected sepsis, remain scarce.

Therefore, this study aimed to evaluate and compare the diagnostic accuracy of SII and PCT in patients with suspected sepsis presenting to the Emergency Department of H. Adam Malik General Hospital, Medan.

2. Method

This cross-sectional diagnostic accuracy study was conducted in the Emergency Department of H. Adam Malik General Hospital, Medan, Indonesia, from March to May 2026. The minimum sample size was calculated using the receiver operating characteristic (ROC) curve approach based on the method described by Hanley and McNeil. Assuming an expected area under the curve (AUC) of 0.75, a significance level (α) of 0.05, and a statistical power of 80%, the minimum required sample size was 55 participants. Eligible patients were recruited using a consecutive sampling method.

Adult patients (≥18 years) presenting with suspected or confirmed infection were enrolled. Patients were classified into sepsis and non-sepsis groups according to the Sepsis-3 criteria. Sepsis was defined as suspected or documented infection accompanied by an increase of at least two points in the Sequential Organ Failure Assessment (SOFA) score from baseline which was recorded in the medical record. Patients with hematological disorders, active malignancy, those receiving chemotherapy or high-dose immunosuppressive therapy, active autoimmune disease, isolated viral infection without evidence of bacterial infection, chronic kidney disease, liver cirrhosis, or incomplete clinical and laboratory data were excluded.

Demographic and clinical characteristics, including age, sex, source of infection, and SOFA score, were obtained from medical records. Blood samples were collected at admission before definitive treatment. Complete blood count parameters, including neutrophil, lymphocyte, and platelet counts, and serum procalcitonin (PCT) levels were routinely tested in most sepsis patient. The Systemic Immune-Inflammation Index (SII) was calculated using the following formula: SII = platelet count × neutrophil count / lymphocyte count.

The diagnostic performance of SII and PCT for identifying sepsis was evaluated using receiver operating characteristic (ROC) curve analysis. The optimal cut-off values were determined using the Youden index. Diagnostic accuracy was assessed by calculating the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CI). The AUCs of SII and PCT were compared using the DeLong test, and the diagnostic performance of the combined SII–PCT model was also evaluated.

Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software version 23.0 (MedCalc Software Ltd., Ostend, Belgium). Continuous variables were expressed as mean ± standard deviation or median (interquartile range), depending on data distribution, and were compared using the independent t-test or Mann–Whitney U test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. A two-sided p value <0.05 was considered statistically significant.

The study protocol was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara/H. Adam Malik General Hospital. Written informed consent was obtained from all participants or their legal representatives before enrollment.

3. Results and Discussion

3.1. Characteristics of the Study Population

A total of 157 patients with suspected infection presented to the Emergency Department during the study period. Among them, 86 underwent complete blood count, serum procalcitonin (PCT), and Sequential

Organ Failure Assessment (SOFA) evaluation. After applying the inclusion and exclusion criteria, 55 patients were included in the final analysis, comprising 32 patients with sepsis and 23 patients without sepsis.

Patients with sepsis were older than those without sepsis (59.22 ± 13.40 vs. 51.30 ± 11.56 years). The median SOFA score was also markedly higher in the sepsis group (4.5 [IQR 6] vs. 1 [IQR 1]), indicating more severe organ dysfunction. Hematological parameters differed between the two groups, with patients with sepsis demonstrating a higher median neutrophil percentage (86.8% vs. 78.0%), a lower mean lymphocyte percentage (7.25 ± 4.17% vs. 16.43 ± 10.79%), and a lower median platelet count (157,000/µL vs. 280,000/µL). Consequently, the median Systemic Immune-Inflammation Index (SII) was higher in the sepsis group than in the non-sepsis group (2,303,262 vs. 1,530,622). The mean of serum PCT concentrations were also substantially higher in patients with sepsis (4.94 ng/mL vs. 0.20 ng/mL). The overall study population consisted of 30 females (54.5%) and 25 males (45.5%), with a comparable sex distribution between the two groups. Pneumonia was the most common source of infection overall (36.4%) and among patients with sepsis (43.8%), whereas urinary tract infection predominated in the non-sepsis group (39.1%) (Table 1).

The higher mean age observed in patients with sepsis is consistent with previous studies identifying advanced age as an important risk factor for sepsis. Aging is associated with immunosenescence, characterized by impaired innate and adaptive immune responses, which increases susceptibility to severe infections and organ dysfunction[8]. In the present study, sex distribution was comparable between the sepsis and non-sepsis groups, suggesting that sex was not a major determinant of sepsis occurrence in this population.

Pneumonia was the predominant source of infection among patients with sepsis. This finding is consistent with epidemiological reports indicating that pneumonia is the leading infectious cause of sepsis worldwide. Pulmonary infections may trigger an exaggerated systemic inflammatory response, ultimately resulting in organ dysfunction and the development of sepsis[9].

Table 1. Characteristics of Patients with Infection at RS Adam Malik

Variable	Non-Sepsis (n=23)	Sepsis (n=32)
Age (years)	51,30 ± 11,56	59,22 ± 13,40
Neutrophil (%)	78 (65,5-85,7)	86,80 (80,8-92,1)
Lymphocyte (%)	16,43 ± 10,79	7,25 ± 4,17
Platelet (/uL)	280.000 (294.500-335.000)	157.000 (128.500-310.500)
SII	1.531 (703-3.997)	2.303 (1.196-3.879)
PCT (ng/mL)	0,2 (0,89)	4,94 (13,60)
Sex, n (%)		
Male	10 (43,5)	15 (46,9)
Female	13 (56,5)	17 (53,1)
Source of Infection, n (%)		
Intra-abdominal infection (IAI)	2 (8,7)	7 (21,9)
Skin and Soft Tissue Infection (SSTI)	6 (26,1)	7 (21,9)
Pneumonia	6 (26,1)	14 (43,8)
Urinary tract infection	9 (39,1)	4 (12,5)

3.2. Diagnostic Performance of SII and PCT

Receiver operating characteristic (ROC) curve analysis demonstrated that the optimal cut-off value for SII was 1,752,635, yielding an area under the curve (AUC) of 0.564 (95% CI: 0.42–0.69) [see Fig. 1], with a sensitivity of 68.8%, specificity of 56.5%, positive predictive value (PPV) of 68.8%, and negative predictive

value (NPV) of 56.5%. In contrast, PCT showed superior diagnostic performance, with an optimal cut-off value of 1.265 ng/mL, an AUC of 0.863 (95% CI: 0.74–0.94), sensitivity of 75.0%, specificity of 82.6%, PPV of 85.7%, and NPV of 70.4% (Table 2).

Table 2. Diagnostic Performace of SII and PCT

Parameter	SII	PCT	*p-value*
Cut-Off	1.753	1,2650	
AUC ROC	0,564 (95% CI 0,42-0,69)	0,863 (95% CI 0,74-0,94)	
Sensitivity (%)	68,8 (95% CI 50-83,9)	75 (95% CI 56,6-88,5)	
Specificity (%)	56,5 (95% CI 34,5-76,8)	82,6 (95% CI 61,2-95,0)	
PPV (%)	68,8	85,7	*0.0007*
NPV (%)	56,5	70,4	
Youden Index	0,3	0,58	

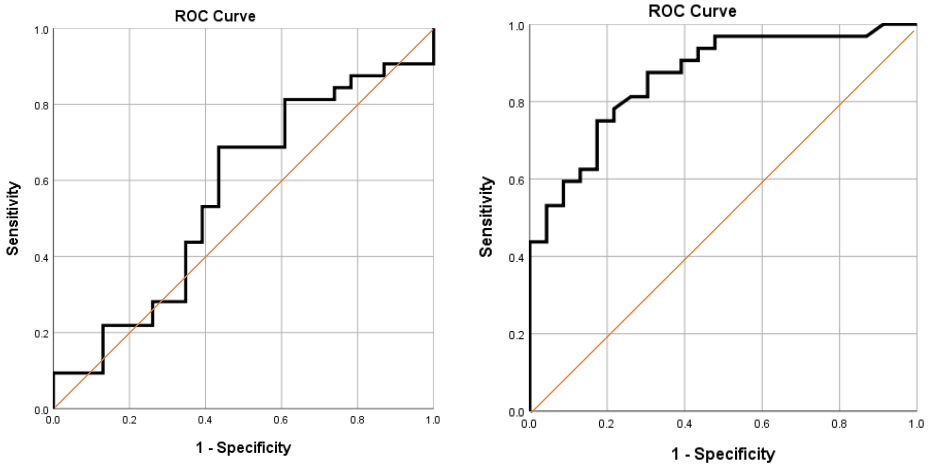

Figure 1. (a) ROC curve of SII, (b) PCT

Comparison of the ROC curves using the DeLong test demonstrated a statistically significant difference between SII and PCT (ΔAUC = 0.299, $z = 3.408$, $p = 0.0007$), indicating that PCT had significantly better diagnostic accuracy than SII for differentiating patients with sepsis from those without sepsis (Table 3).

Table 3. Comparisan of AUC score between SII and PCTI using DeLong Test

Variable	*Difference between AUC*	*Standard Error*	z	95% CI	*p-value*
SII vs Procalcitonin	0,299	0,0877	3,408	0,127–0,471	0,0007

The present study demonstrated that SII had limited diagnostic performance for identifying sepsis. With an AUC of 0.564, SII exhibited poor discriminatory ability, only slightly better than chance. Although SII is biologically plausible because it integrates neutrophil, lymphocyte, and platelet counts to reflect the balance between systemic inflammation and immune status, alterations in these hematological parameters are not specific to sepsis and may occur in various inflammatory conditions. Consequently, the diagnostic specificity of SII may be reduced when applied to a heterogeneous emergency department population [10,11].

Our findings differ from those reported by Pricop et al., who demonstrated good diagnostic performance of SII for sepsis, with an AUC of 0.811, sensitivity of 72.7%, and specificity of 80.6% [12]. This discrepancy may be explained by differences in study populations, sample size, disease severity, and diagnostic criteria. Unlike the relatively homogeneous population included in the study by Pricop et al., our study enrolled patients with diverse sources of infection, including pneumonia, intra-abdominal infection, urinary tract infection, and skin and soft tissue infection, each of which may elicit distinct inflammatory responses.

Furthermore, the relatively small sample size and variations in disease severity at presentation may have contributed to the lower discriminatory performance observed in our study.

Taken together, these findings indicate that SII has limited diagnostic ability in distinguishing sepsis from non-sepsis patients according to the Sepsis-3 criteria. Although it has a strong biological rationale and potential as an adjunct biomarker, SII cannot yet replace more specific biomarkers for sepsis diagnosis. Further studies with larger sample sizes, multicenter designs, and serial evaluation of SII values are needed to clarify its diagnostic role in patients with sepsis.

In contrast, PCT demonstrated good diagnostic accuracy, with an AUC of 0.863, sensitivity of 75.0%, and specificity of 82.6%. These findings are consistent with previous studies reporting good diagnostic performance of PCT in patients with sepsis. Wacker et al. reported a pooled sensitivity of 77%, specificity of 79%, and an AUC of approximately 0.85, while Gupta et al. reported AUC values ranging from 0.86 to 0.96 depending on blood culture status. Similarly, a study conducted at Dr. Sardjito General Hospital reported an AUC of 0.941 with sensitivity and specificity of 89% and 90%, respectively [13-15]. Although the diagnostic performance of PCT in the present study was slightly lower than that reported in some previous studies, this difference may reflect variations in patient characteristics, infection sources, disease severity, and study settings. Unlike studies conducted exclusively in intensive care units, the present study included a broader emergency department population with varying clinical presentations.

Although PCT showed significantly better diagnostic performance than SII, its Youden index of 0.58 indicates that an optimal balance between sensitivity and specificity has not yet been achieved. Therefore, PCT should be considered a valuable adjunctive biomarker rather than a stand-alone diagnostic test for sepsis, and its interpretation should always be integrated with clinical assessment and established diagnostic criteria.

3.3. Diagnostic Performance of the Combined SII-PCT Model

Receiver operating characteristic (ROC) curve analysis demonstrated that the combined SII–PCT model achieved good diagnostic performance for differentiating patients with sepsis from those without sepsis. The combined model yielded an AUC of 0.872 (95% CI: 0.755–0.947; $p < 0.0001$), with a sensitivity of 81.25% and a specificity of 78.26% (Table 4).

Table 4. Diagnostic Performance of SII and PCT Combination in Sepsis

Parameter	Nilai	*p-value*
AUC ROC	0,872 (0,755-0,947)	<0,0001
Sensitivity (%)	81,25	
Specificity (%)	78,26	
Youden Index	0,59	

Compared with the individual biomarkers, the combined SII–PCT model demonstrated the highest AUC. However, the improvement over PCT alone was modest (AUC 0.872 vs. 0.863), while the Youden index increased only slightly from 0.58 to 0.59. These findings indicate that although combining SII with PCT provided good overall diagnostic performance, the additional contribution of SII beyond PCT alone was limited in the present study.

A previous study by Li et al. reported that the combination of SII and PCT demonstrated superior predictive performance for short-term adverse outcomes in patients with septic shock, with an AUC of 0.893.45 This finding supports the concept that biomarkers reflecting different aspects of sepsis pathophysiology may provide complementary clinical information [16]. Nevertheless, unlike the study by Li

et al., which focused on patients with septic shock and prognostic outcomes, the present study evaluated the diagnostic performance of the combined biomarkers in a heterogeneous population of patients with suspected sepsis presenting to the emergency department.

The relatively small incremental benefit observed in the present study may be explained by the limited discriminatory ability of SII as an individual biomarker, the heterogeneous sources of infection, variations in disease severity at presentation, and the relatively small sample size. Therefore, although the combined SII–PCT model demonstrated good diagnostic performance, the findings suggest that PCT remains the principal contributor to the overall diagnostic accuracy, while SII provides only a modest additional benefit.

4. Conclusion

Patients with sepsis in this study were characterized by older age, higher SOFA scores, higher neutrophil percentages, higher serum procalcitonin (PCT) levels, lower lymphocyte percentages, and lower platelet counts than patients without sepsis, with pneumonia being the most common source of infection. Procalcitonin demonstrated significantly better diagnostic accuracy than the Systemic Immune-Inflammation Index (SII) for distinguishing patients with sepsis from those without sepsis. Although the combined SII–PCT model achieved good diagnostic performance, its improvement over PCT alone was modest, indicating that SII provided only limited additional diagnostic value. These findings suggest that PCT remains a more reliable biomarker for the diagnosis of sepsis in the emergency department, while SII may serve as an adjunctive biomarker because of its low cost and wide availability. Further multicenter studies with larger sample sizes are warranted to validate the diagnostic role of SII and to determine whether combining SII with established biomarkers provides meaningful clinical benefits.

Acknowledgements

The authors would like to express their sincere gratitude to the Faculty of Medicine, Universitas Sumatera Utara, and H. Adam Malik General Hospital, Medan, for their support and facilitation of this study. We also thank the staff of the Emergency Department and the Clinical Pathology Laboratory for their assistance with patient recruitment and laboratory examinations. Finally, we are grateful to all participants who willingly took part in this study.

Conflict of Interest

The authors declare no conflict of interest.

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