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Original Article

Evaluation of Systemic Immune-Inflammation Index for Predicting Mortality in Sepsis Patients

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ABSTRACT

Introduction: *This study aims to measure the accuracy of Systemic Immune-Inflammation Index (SII) in predicting 28-day mortality in sepsis patients in intensive care unit.* ***Methods:*** *This study was conducted as a retrospective cohort study. The study was conducted in the intensive care unit of Dr. Wahidin Sudirohusodo General Hospital. The study subjects consisted of all sepsis patients admitted to the intensive care unit during the period January 2023 to December 2023 who met the inclusion criteria.* ***Results:*** *Total sample is 147 participants. Systemic Immune-Inflammation Index (SII) showed a significant difference in predicting sepsis mortality. SII has an AUC value of 0.763 with a sensitivity of 69.6% and a specificity of 71.1% at a cut-off of 2003.395.* ***Conclusions****: Systemic Immune-Inflammation Index (SII) scores are associated with increased mortality in sepsis patients in the intensive care unit of Dr. Wahidin Sudirohusodo Hospital. The SII can be a prediction tool in clinical practice in predicting mortality of sepsis patients.*

1. INTRODUCTION

Sepsis is a medical emergency resulting from a systemic inflammatory response to infection that can lead to organ dysfunction and death. Despite advances in the

understanding of pathophysiology, hemodynamic monitoring, and resuscitation strategies, sepsis remains a major cause of morbidity and mortality in the Intensive Care Unit (ICU).[1] Globally, approximately 30 million cases of sepsis occur each year with a mortality rate of 26%.[2] Factors such as advanced age, comorbidities, immunosuppression, and delayed identification and resuscitation contribute to the high mortality rate from sepsis.[3]

Various scoring systems have been developed to evaluates the severity and predict mortality of sepsis patients. One commonly used system is the Acute Physiology and Chronic Health Evaluation II (APACHE II), which asseses the physiologic condition of patients based on 12 clinical variables, chronic health status, and age. The APACHE II score has been shown to have predictive value for patient mortality in the ICU.(4) However, its application in clinical practice requires the measurement of various parameters, which can be an obstacle in some healthcare facilities.

Alternatively, the Systemic Immune-Inflammation Index (SII) was introduced as a simpler parameter, based on neutrophil, lymphocyte, and platelet counts (NxPLT/L), reflecting the balance between the patient's inflammatory and immune processes.(5) Liu et al, found that SII had an AUROC value of 0.840 in predicting sepsis patient mortality within 28 days, with a cutoff SII > 1.7668 indicating a higher mortality risk.[4] A lower SII theoretically indicates the presence of immune compromise or severe inflammation which is often associated with poor prognosis.[5] Therefore, this study aims to evaluate SII scores in predicting mortality of sepsis patients in intensive care settings. The results of the study are expected to provide an overview of alternative scoring systems that are simpler and more applicable in predicting the mortality of sepsis patients.

2. METHODS

This study was an observational study with cohort design conducted retrospectively. The study data were collected from the medical records of patients admitted to the intensive care unit of Dr. Wahidin Sudirohusodo Hospital during the period January 2023 to December 2023. The population in this study were all patients diagnosed with sepsis in the intensive care unit of Dr. Wahidin Sudirohusodo Hospital during that period. The study sample was selected using a total sampling technique, where all patients who met the inclusion criteria were included in the study. Inclusion criteria included patients with a diagnosis of sepsis, aged over 18 years, and had complete medical record data. Patients with incomplete data, chronic liver disease, chronic kidney disease, immunosuppressive diseases, or uncontrolled type II diabetes mellitus were excluded from the study. These exclusion criteria were applied to minimize potential confounding related to immune and metabolic dysfunction. Furthermore, multivariable logistic regression analysis was performed by adjusting for clinically relevant variables associated with sepsis severity, in order to control for confounding factors that may affect 28-day mortality. Data were collected retrospectively by tracing the medical records of sepsis patients admitted to the Intensive Care Unit of Dr. Wahidin Sudirohusodo Hospital. Patients who met the inclusion criteria were recorded sequentially until the required number of samples was met. Total sample is 147 participants. The sample size of 147 patients was sufficient for the planned analyses. There is no sample were excluded. This number exceeds commonly accepted minimum thresholds for ROC curve analysis and fulfilled the recommended events-per-variable

ratio for multivariable logistic regression. After all study subjects were enrolled, clinical and laboratory data were collected to calculate APACHE II score and Systemic Immune-Inflammation Index (SII). The APACHE II score was calculated based on acute physiologic parameters, chronic health status, and patient age obtained from laboratory examinations and vital signs at the time of ICU admission. The SII was measured based on blood test results on the first day of ICU admission, which included neutrophils, platelets, and lymphocytes. The collected data will be processed and presented in the form of narratives, tables, or graphs, including mean values, standard deviations, frequencies, and percentages, using SPSS 27 for Windows.

All steps and procedures in this study were carried out after providing explanations to the participants and obtaining their consent through signing the informed consent form. This study has also been approved by the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University, with protocol number UH24100867, which ensures that this study meets ethical standards and protection of research subjects.

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off values, sensitivity, and specificity for SII and APACHE II. The area under the curve (AUC) with 95% confidence intervals (CI) was calculated to assess discriminatory performance. Logistic regression analysis was conducted to evaluate the association between SII, APACHE II, and 28-day mortality. Both univariable and multivariable models were constructed, and odds ratios (OR) with 95% CI were reported. Variables included in the multivariable model were selected based on clinical relevance and prior literature.

3. RESULTS

The total sample in this study consisted of 147 patients diagnosed with sepsis and admitted to the intensive care unit of Dr. Wahidin Sudirohusodo Hospital during the period from January 2023 to December 2023. Of these, 102 patients experienced mortality within 28 days, while the other 45 patients survived.

Table 1 presents the sample characteristics based on the incidence of mortality 28 days after sepsis diagnosis. Analysis showed that there were no significant differences between the groups of patients who died and those who survived in terms of age, gender, BMI, and comorbidities with p values > 0.05. This suggests that the characteristics of patients in both groups were relatively homogeneous.

Table 1. Sample characteristics of the research subjects

Characteristics		28-day mortality		p-value
		Yes (n = 102)	No (n = 45)	
		Mean ± SD / n (%)	Mean ± SD / n (%)	
Age (year)		51.40 ± 17.09	52.47 ± 15.17	0.630[a]
Gender	Male	52 (51)	30 (66.7)	0,078[b]
	Female	50 (49)	15 (33.3)	
BMI (kg/m^2)		23.38 ± 4.31	22.68 ± 3.59	0.371a
Comorbid	There is	63 (61.8)	25 (55.6)	0.479[b]
	None	39 (38.2)	20 (44.4)	

Analysis of the relationship between APACHE II score and mortality showed that patients with higher APACHE II scores had a greater risk of mortality within 28 days after sepsis diagnosis ($p < 0.05$). In addition, the Systemic Immune-Inflammation Index (SII) was also significantly higher in patients who did not survive compared to those who did ($p < 0.05$). These results indicate that both APACHE II and SII scores can be significant independent predictors of sepsis patient mortality at Dr. Wahidin Sudirohusodo Hospital (Table 2).

Comparison between APACHE II and Systemic Immune-Inflammation (SII) scores showed significant differences in the context of sepsis mortality. This study found that APACHE II and SII scores were higher in patients who died within 28 days, suggesting a strong association between these two parameters and mortality.

Table 2. Relationship between APACHE II Score and Systemic Immune-Inflammation Index (SII) to Mortality

Parameters	28-day mortality		p-value
	Yes (n = 102)	No (n = 45)	
	Mean ± SD	Mean ± SD	
APACHE II Score	24.26 ± 5.83	18.53 ± 4.91	< 0.001
SII	5362.48 ± 5463.07	1538.79 ± 874.41	< 0.001

The ROC curve presented in Figure 1 shows that the APACHE II score yields an area under the curve (AUC) value 0.784, indicating a good ability to predict mortality in sepsis patients. This value indicates that the APACHE II score is able to distinguish well between patients who die and those who survive within 28 days. Meanwhile, the SII showed an AUC value of 0.763, which also showed good accuracy, but slightly lower than the APACHE II score.

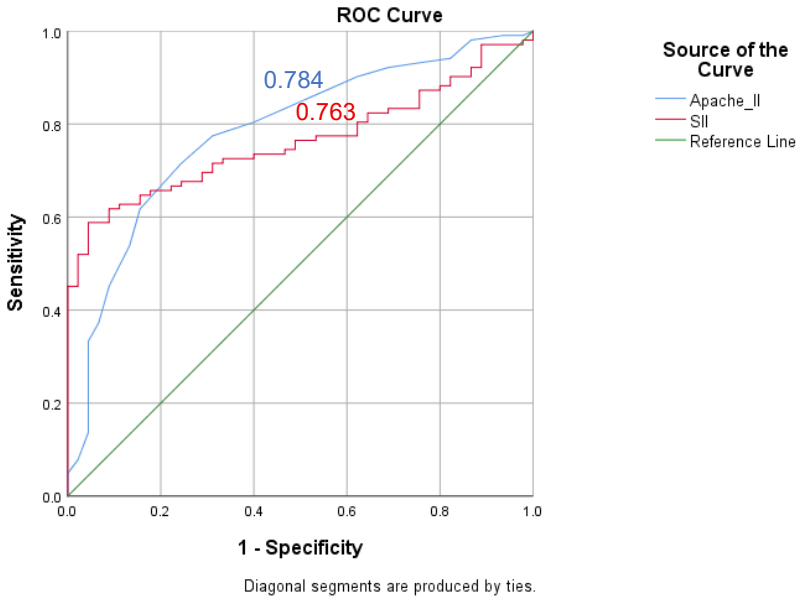

Figure 1. AUC Curve between APACHE II Score and Systemic Immune-Inflammation Index (SII) on Mortality

Table 3. Diagnostic Test Comparison between APACHE II Score and Systemic Immune-Inflammation Index (SII)

Description	APACHE II Score	SII
AUC (ROC)	0.784	0.763
Cut-off	21.50	2003.395
Sensitivity	71.6%	69.6%
Specificity	75.6%	71.1%

Table 3 presents the cut-off value for APACHE II score of 21.50 with a sensitivity of 71.6% and specificity of 75.6%. Meanwhile, the cut-off value for SII was determined at 2003.395 with a sensitivity of 69.6% and specificity of 71.1%. Although both tools showed significant ability in predicting mortality, the APACHE II score showed better results based on the higher AUC value and balance between sensitivity and specificity.

Table 4. Comparison of Accuracy of APACHE II Score and Systemic Immune-Inflammation Index (SII) in Predicting Sepsis Mortality

Measurement tool	28-day mortality						p-value	OR	Accuracy (%)	PPV (%)	*NPV (%)*
	Yes		No		Total						
	n	%	n	%	n	%					
APACHE II Score											
≥ 21,50	73	71.6	11	24.4	84	57.1	<0.001	7.781	72.79	83.9%	51.7%
< 21,50	29	28.4	34	75.6	63	42.9					
SII											
≥ 2003,395	71	68.9	13	29.5	84	57.1	0.001	5.291	69.39	85.7%	55.4%
< 2003,395	32	31.1	31	70.5	63	42.9					

Comparison between APACHE II score and Systemic Immune-Inflammation Index (SII) showed a significant difference in predicting sepsis mortality. The results showed that patients with an APACHE II score ≥ 21.50 had a higher probability of 28-day mortality compared to patients with lower scores (OR = 7.781, $p < 0.001$). SII also showed a significant association with mortality, with an OR of 5.291 ($p = 0.001$), although this value was lower compared to APACHE II. The highest diagnostic accuracy in predicting mortality was found in the APACHE II score with a value of 72.79%, followed by SII with an accuracy of 69.39% (Table 4).

4. DISCUSSIONS

This study used medical record data from 147 sepsis patients who were admitted to the intensive care unit of Dr. Wahidin Sudirohusodo Hospital and met the inclusion criteria. The results showed that the mortality rate within 28 days reached 102 patients (69,39%). A previous study in Palembang reported a mortality rate of 54.9% in the same period.[6] Meanwhile, a study in China reported a mortality rate of 20.52% in 833 sepsis patients in the ICU.[7] Another study in Makassar by Gusriadi recorded a mortality rate of 66.7% in sepsis patients in the ICU.[8] Thus, the mortality rate in this study was higher compared to several previous studies.

The mean age of sepsis patients who died within 28 days was 51.40 ± 17.09 years, while patients who survived had a mean age of 52.47 ± 15.17 years. This difference was not significant in determining patient mortality ($p > 0.05$). Data from Brazil including 15,189 patients showed that the mean age of sepsis patients was 50 years, with a range of 18 to 106 years.[9] A study in India with 150 sepsis patients reported a mean age of 57.07 ± 14.4 years, which is in line with the findings of this study.[10]

Most of the patients in this study were male, had a normal body mass index (BMI), and had comorbidities. A study by Chae et al. reported that out of 770 sepsis patients, 63.5% had normal BMI.[11] Another study also showed that 97.4% of sepsis patients had at least one comorbidity.[12] Male gender is a known risk factor for sepsis and septic shock. The annual relative risk of sepsis in males is 1.3 times higher than in females, as androgen hormones suppress cell-mediated immune responses, whereas female sex hormones are protective. Sex hormones may modulate inflammatory responses in sepsis, potentially influencing neutrophil, lymphocyte, and platelet counts, which are components of the SII. However, further studies are needed to clarify this relationship.[13,14]

Systemic Immune-Inflammation (SII) is also associated with sepsis mortality. Results showed that higher SII was significantly associated with an increased risk of short-term mortality in sepsis patients. SII can be a prediction tool in clinical practice. Tang et al. reported that SII can predict 39- and 909-day mortality and the risk of adverse cardiovascular events in critically ill patients with heart failure.[20] A meta-analysis by Liang et al. also found that high SII at hospital admission increased the risk of mortality in sepsis patients[21].

These results can be explained because SII reflects the patient's inflammatory, immune, and thrombotic pathways. [5] Elevated SII indicates an exaggerated inflammatory response due to neutrophil activation that can lead to tissue damage and organ failure, while lymphopenia at high SII reflects immune suppression that increases the risk of secondary infection and delayed recovery. In addition, the interaction of platelets and neutrophils in the formation of neutrophil extracellular traps (NETs) contributes to microvascular thrombosis and organ dysfunction in sepsis.[21] The results showed that SII has a good predictive value of 28-day mortality with AUC 0.763, cut-off 1878.66, sensitivity 67.2% and specificity 63.9%. The optimal SII cut-off identified in this study differs from values reported in previous studies, such as Zhang et al. and Nurulita et al. This variability may be attributed to differences in patient populations, disease severity, baseline inflammatory status, timing of laboratory measurements, and clinical management strategies. Such heterogeneity underscores the need for population-specific validation before applying a universal SII cut-off in sepsis prognostication. The study of Nurulita et al. reported a cut-off of 1131.26 with a sensitivity of 83% and specificity of 25%.[22] Zhang et al. also reported a cut-off of 3910 with an AUC of 0.867, sensitivity of 71.9% and specificity of 85.2%.[23] Thus, SII can be a good predictive tool for mortality of sepsis patients.

Overall, both diagnostic accuracy and diagnostic odds ratio showed that the APACHE II score had the higher accuracy in predicting 28-day sepsis mortality compared to the SII. Although the APACHE II more accurated, SII can be a simpler predictive tool in predicting mortality. The SII only need blood count, while the APACHE II used more data.

Limitations of this study include the retrospective design that limited the collection of additional data and the absence of control for factors such as treatment variation and sepsis severity.

5. CONCLUSION

Systemic Immune-Inflammation Index (SII) scores are associated with increased mortality in sepsis patients in the intensive care unit of Dr. Wahidin Sudirohusodo Hospital. The SII demonstrated an AUC of 0.763 (95% CI) with a sensitivity of 69.6% and a specificity of 71.1% at a cut-off of 2003.395. The SII can be a simple prediction tool in clinical practice in predicting mortality of sepsis patients.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.