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RESEARCH ARTICLE

Evaluating the Prognostic Impact of the Systemic Immune-Inflammation Index On One-Year Survival in Non-Small Cell Lung Cancer Patients Receiving Platinum-Based Chemotherapy: Initial Findings From West Sumatra, Indonesia

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ABSTRACT

Background and objective: The Systemic Immune-Inflammation Index (SII) is a noninvasive biomarker derived from platelet, neutrophil, and lymphocyte counts. It functions as an objective predictor in assessing immune response and inflammation in patients with Non-Small Cell Lung Cancer (NSCLC). Despite its potential clinical value, SII remains relatively underutilized in Indonesia, particularly in West Sumatra. This study seeks to investigate the prognostic role of SII in patients with advanced-stage NSCLC. Methods: This retrospective cohort study included 65 patients diagnosed with advanced-stage NSCLC who had undergone at least three chemotherapy cycles between January 2020 and December 2022 at Dr. M Djamil Hospital, Padang. Survival duration was recorded in months, starting from the commencement of therapy until either the patient's passing or the conclusion of the observation period, with the last follow-up conducted in December 2023. Patients were categorized into two survival groups: those who lived for less than a year and those who survived for at least a year. The optimal SII cutoff value for predicting one-year survival was determined through receiver operating characteristic (ROC) curve analysis. Results: The mean SII value in the group with a survival period of less than one year was higher compared to the other group (3,414.95 × 10^9/L vs. 1,517.95 × 10^9/L). ROC analysis yielded an Area Under the Curve (AUC) value of 0.745 (95% CI: 0.62–0.87). The optimal SII threshold for predicting one-year survival was identified as 1760.00 × 10^9/L, with a sensitivity of 74% and a specificity of 81%. Conclusion:. The SII serves as a promising prognostic advanced-stage NSCLC patients.

INTRODUCTION

Lung cancer remains the leading cause of cancer-related mortality worldwide, with an estimated 1,796,144 deaths reported in GLOBOCAN 2020.[1] Non-Small Cell Lung Cancer (NSCLC) constitutes the Majority of lung cancer cases, with clinical outcomes that are not significantly better than other solid organ malignancies. A study conducted by Ermayanti et al. in 2021 in West Sumatra found that adenocarcinoma and squamous cell carcinoma were the most common subtypes of lung cancer.[2]

Despite advancements in systemic therapy, targeted therapy, and immunotherapy, the prognosis for NSCLC patients remains unfavorable.[3]

Cancer is recognized as a systemic disease, primarily due to prolonged inflammation, which is a defining characteristic of tumor progression. Traditionally, tumor immunology has concentrated on local immune responses within the tumor microenvironment. However, an effective anti-tumor response requires continuous interaction between the immune system and peripheral tissues. To mount an adequate immune defense, all immune cell lineages must be involved, not only within the tumor site but also throughout the broader immune system.[4]

Various inflammatory biomarkers derived from systemic immune cells, including the platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and neutrophil-to-lymphocyte ratio (NLR), have been identified as prognostic indicators in different cancer types, including lung cancer.[3] While these biomarkers primarily assess two types of inflammatory cells, the Systemic Immune-Inflammation Index (SII) offers a more comprehensive evaluation by incorporating three peripheral blood parameters: platelet, neutrophil, and lymphocyte counts. This novel noninvasive biomarker provides a broader reflection of immune balance and systemic inflammation. Studies suggest that SII serves as a more objective prognostic indicator with superior predictive value in assessing patient outcomes.[5]

Hu et al. were the first to report the prognostic significance of SII, identifying it as a strong predictor of poor outcomes in a cohort of 133 hepatocellular carcinoma patients.[6] SII levels reflect the balance of lymphocytes, neutrophils, and platelets, making it a potentially reliable marker of the host's immune response.[3] A meta-analysis by Zhang et al., which encompassed seven studies with a total of 2,786 cases investigating the association between SII and Overall Survival (OS) in lung cancer, demonstrated that elevated SII levels were significantly linked to poorer OS. Patients with high SII exhibited shorter survival durations compared to those with lower SII, highlighting its potential role as a prognostic biomarker in lung cancer management.[5]

This study aims to evaluate the prognostic significance of the Systemic Immune-Inflammation Index (SII) in patients with advanced-stage NSCLC undergoing platinum-based chemotherapy. Notably, this research represents the first application of SII in Indonesia, particularly among the population of West Sumatra

2. Materials and Methods

This study utilized an analytical observational design with a retrospective cohort approach. It included patients diagnosed with advanced-stage NSCLC who had undergone at least three cycles of chemotherapy between January 2020 and December 2022 at Dr. M Djamil Hospital, Padang. Patients with a history of radiotherapy or targeted therapy, malignancies in other organs, or chronic systemic inflammatory conditions—such as autoimmune diseases, hematological disorders, congestive heart failure, prior hemodialysis, cardiopulmonary bypass, corticosteroid use, and metabolic disorders (including uremia, acidosis, and gout)—were excluded from the study.

Relevant patient data, including age, sex, smoking history, pathology, TNM staging, chemotherapy regimen, and one-year survival status, were collected from medical records. The SII was determined using the formula: platelet count × neutrophil count/lymphocyte count. Survival duration was measured in months, beginning from the initiation of therapy until either the patient's death or the completion of the observation period, with the final follow-up conducted in December 2023.

Patients were classified into two survival categories: those with a survival duration of less than one year and those who survived for at least one year. The optimal SII cutoff value for predicting one-

year survival was established through receiver operating characteristic (ROC) curve analysis. The study protocol was approved by our institution's medical ethics committee.

3. RESULTS

This study enrolled a total of 65 participants, comprising 53 males (81.53%) and 12 females (18.47%). Table 1 presents the comprehensive characteristics of advanced-stage non-small cell lung cancer patients in each survival group from 2020 to 2022. The Median age of the participants was 58 years, ranging from 25 to 74 years, with the most patients in the group <60 years (64.61%). The Majority of patients were smokers/ former smokers (81.54%). According to histopathological findings, squamous cell carcinoma is the most predominant type (47.69%). Stage distribution was as follows: Stage IIIb included 5 patients (7.69%), stage IIIc had 2 patients (3.08%), stage IVa had 40 patients (61.54%), and Stage IVb involved 18 patients (27.69%). Most patients in this study received a carboplatin + paclitaxel chemotherapy regimen (89.24%). This study demonstrated that chemotherapy regimens were associated with one-year survival ($p<0.05$).

Table 1. Characteristics of Patients in Survival Group.

Characteristic		Patients (n,%)	Survival		*p*
			<1 Year n=43	≥1 Year n=22	
Age					
	<60	42 (64.61%)	27	15	0.66
	≥60	23 (35.39%)	16	7	
Sex					
	Male	53 (81.53%)	36	17	0.52
Smoking status					
	Never smoker	12 (18.46%)	7	5	0.52
	Smoker/ Former Smoker	53 (81.54%)	36	17	
Histopathology					
	Adenocarcinoma	25 (38.46%)	15	10	0.68
	Squamous cell	31 (47.69%)	22	9	
	Adenosquamous	9 (13.84%)	6	3	
TNM Staging					
	IIIb	5 (7.69%)	4	1	0.68
	IIIc	2 (3.08%)	0	2	
	IVa	40 (61.54%)	27	13	
	IVb	18 (27.69%)	12	6	
Chemotherapy regimen					
	Carboplatin + paclitaxel	4 (6.15%)	0	4	0.001
	Cisplatin + paclitaxel	58 (89.24%)	40	18	
	Carboplatin + gemcitabine	3 (4.61%)	3	0	

Table 2. The Mean SII for One Year Survival

		Mean SII (±SD)	*p* (95% CI)
Survival	**<1 Year**	3414.95 (±3300.18)	0.01 (455.63-3338.36)

The average Systemic Immune-Inflammation Index (SII) in the group with less than one-year survival

is higher compared to other groups (3,414.95 x 109/L vs 1,517.95 x 109/L). The data suggests that individuals with higher SII values are more likely to experience a survival duration of less than one year. The statistical analysis underscores a meaningful relationship between the Systemic Immune-Inflammation Index and the one-year survival rate (p: 0.01; 95%CI: 455.63-3338.36), highlighting the potential utility of SII as a prognostic indicator in this context. The results emphasize the strength of the predictive model, with a remarkable Area Under the Curve (AUC) value of 0.745 (95% CI 0.62-0.87). According to the ROC analysis, the ideal cutoff for SII to forecast one-year survival was determined to be 1760.00 x 109/L with a sensitivity of 74% and specificity of 81%.

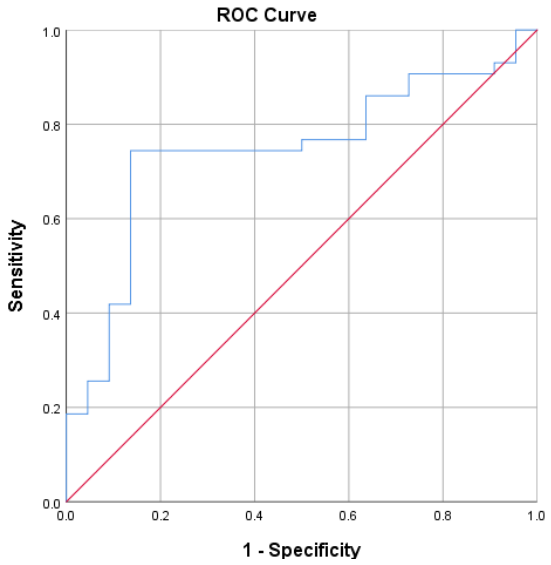

Figure 1. The ROC curve of SII for One Year Survival

4. DISCUSSION

Our study specifically investigated the prognostic value of the one-year survival of SII in NSCLC patients treated with platinum-based chemotherapy. The Majority of our patients were male, aged 25-74 years, with a significant proportion under 60 years. In contrast, a study by Ermayanti et al. in West Sumatra found that while the Majority of lung cancer patients were also male (77.8%), females tended to be younger and pre-dominantly non-smokers, with distinct histopathological profiles and disease characteristics.[2] Supporting our findings, Marco Galvez-Nino's research in Lima, Peru, highlighted that lung cancer in patients aged 40 or younger exhibited different clinical and pathological features compared to older patients, with a higher incidence in females and a predominant histological type of adenocarcinoma. Both studies corroborate our observation of a significant number of younger patients with advanced stages of NSCLC.[7] These findings collectively emphasize the critical importance of considering age and gender in the epidemiological and prognostic assessment of lung cancer.

Findings revealed that among the subtypes of NSCLC, squamous cell carcinoma was the most common, occurring in 31 patients (47.70%), followed by adenocarcinoma in 25 patients (38.50%). This differs from other studies in West Sumatra, which found a higher prevalence of adenocarcinoma (55.0%) in females and squamous cell carcinoma (41.1%) in males, and AlQudah et al. in Jordan, where adenocarcinoma accounted for over half of the cases across both sexes.[2,8] These discrepancies can be attributed to the exclusion of some adenocarcinoma patients in our study who had previously received targeted therapy or radiotherapy. This exclusion likely skewed our histological distribution towards squamous cell carcinoma, highlighting the impact of prior treatment on histo-pathological reporting in lung cancer research.

In our study, the Majority of patients with advanced-stage NSCLC have diagnosed at stage IVa, representing 61.5% of the study, which underscores the prevalent issue of late-stage diagnosis. This finding aligns with R. Soo's review, which reports a similar trend, with 71.3% of NSCLC patients being diagnosed with metastatic stage IV across Southeast Asia. Several factors contribute to this delayed diagnosis, including limited access to healthcare facilities, lack of early screening programs, and the often asymptomatic nature of early-stage lung cancer. Furthermore, socioeconomic barriers and the limited availability of molecular testing and targeted therapies in certain regions exacerbate this issue, delaying the initiation of appropriate treatment. Both studies highlight the critical need for improved early detection strategies and equitable access to advanced diagnostic and therapeutic modalities to enhance survival outcomes for NSCLC patients in Southeast Asia.[9]

This study demonstrated that the Majority of patients (89.20%) received the carboplatin + paclitaxel chemotherapy regimen, with statistical analysis revealing a significant relationship between the chemotherapy regimen and one-year survival ($p = 0.021$). In comparison, the first study by V. Georgoulias et al. assessed the efficacy of docetaxel/cisplatin versus gemcitabine/docetaxel, finding similar objective response rates between the two groups but noting that gemcitabine/docetaxel had a more favorable toxicity profile.[10] The second study by Giannicola D'Addario et al. conducted a meta-analysis comparing platinum-based versus non-platinum-based chemotherapy, concluding that platinum-based regimens significantly increased response rates and 1-year survival, albeit with higher toxicity.[11] Together, these findings underscore that while different chemotherapy regimens, including those based on platinum agents, can influence overall survival rates and response, they also vary considerably in their toxicity profiles.

The Majority of patients had a survival of less than one year (22 out of 65 patients), highlighting a poor prognosis for advanced-stage NSCLC patients receiving plati-num-based chemotherapy. This finding aligns with Agus Setyawan U et al., where one-year survival rates were very low among 54 wild-type adenocarcinoma lung cancer patients undergoing chemotherapy, with only 12.5% of patients receiving carboplatin/pemetrexed and 6.7% of patients receiving carboplatin/paclitaxel surviving one year.[12] In contrast, Soeroso NN et al. emphasize the importance of genetic mutations in survival rates. Patients with EGFR mutations had a median overall survival of 15 months compared to 8 months for those without the mutations, while TP53 mutations were associated with a lower overall survival of 7 months compared to 9 months for non-mutations.[13] This comparison underscores the critical need for improving early detection, diagnosis, and treatment strategies to enhance survival outcomes in advanced NSCLC patients.

This study demonstrated that the average SII in patients with less than one-year survival was significantly higher compared to other groups (3,414.95 x 109/L vs 1,517.95 x 109/L), indicating that elevated SII values are associated with shorter survival durations. This finding is consistent with results from other studies investigating the prognostic value of SII in NSCLC. For instance, a study on stage III NSCLC patients undergoing curative intent chemoradiotherapy (CRT) found that a low SII (<1,266) at diagnosis was independently associated with improved OS, disease-specific survival (DSS), and pro-gression-free survival (PFS), highlighting the potential of SII as an effective prognostic indicator.[14] Similarly, research on resected NSCLC patients demonstrated that pre-operative inflammatory status, including high SII values (≥808.9), strongly influences long-term prognosis, with higher SII correlating with more invasive disease stages and poorer survival outcomes.[15] These studies collectively emphasize the importance of SII as a valuable biomarker for predicting survival in NSCLC patients, underscoring the need for its integration into clinical practice to enhance patient stratification and treatment planning.

The Systemic Immune-Inflammation Index (SII) was found to have a statistically significant Area Under the Curve (AUC) of 0.866 (95% CI: 0.782–0.950). The optimal SII threshold for predicting chemotherapy response was identified as 1931.50×10^9/L, with sensitivity and specificity values of

76.7% and 74.3%, respectively. Among the study participants, 36 (55.38%) exhibited elevated SII levels (≥1931.50), while 29 patients had lower SII values.

This result aligns with the meta-analysis by Wang et al., which demonstrated that higher pretreatment SII levels correlate with poorer overall survival (OS), reduced progression-free survival (PFS), and lower cancer-specific survival (CSS) in NSCLC patients.[16] Similarly, findings by Wei Guo et al. reinforce this conclusion, showing that SII, when combined with the neutrophil-to-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), is significantly linked to OS in NSCLC cases. More importantly, SII emerged as an independent prognostic indicator for OS, demonstrating a stronger predictive capability compared to NLR and PLR. Furthermore, its prognostic significance remained evident even in the lung adenocarcinoma subgroup.[17]

Collectively, these findings reinforce the importance of SII as a reliable prognostic biomarker for NSCLC patients.

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