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Association of Neutrophil-lymphocyte ratio and platelet lymphocyte ratio with GRACE risk score and high-sensitivity Troponin T in acute coronary syndrome patient



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ABSTRACT

Background: Inflammatory indicators such as alterations in neutrophils, platelets, and lymphocytes are linked to the acute coronary syndrome. This research seeks to understand the association of the Platelet Lymphocyte Ratio (PLR) and Neutrophil-Lymphocyte Ratio (NLR) with the Grace score as well as the association between NLR and PLR with High Sensitivity Troponin T (hs-cTnT) as a serum biomarker that aids in ACS diagnosis.

Methods: The 99 patients who met the inclusion criteria for this study were the subject of an analytical investigation with a retrospective cross-sectional design. Based on the ratio of lymphocytes to neutrophils, NLR is determined. Based on the ratio of platelets to lymphocytes, PLR is determined. hs-cTnT laboratory samples were collected more than three hours after the ischemia complaint first manifested,

using the Grace risk score as a predictor of mortality. Using SPSS program 25.0, data were examined.

Results: Bivariate analysis using the Spearman correlation test. There is a correlation between NLR and GRACE risk scores ($r=0.348$; $p<0.001$), PLR and GRACE risk scores ($r=0.434$; $p<0.001$), NLR and hs-cTnT ($r=0.343$; $p=0.001$), PLR and hs-cTnT ($r=0.284$; $p=0.004$). ROC curve analysis, NLR cut-off value 4.45 (sensitivity 73.3%; specificity 72.6%), and PLR cut-off value 139.77 (sensitivity 66.7%; specificity 59.5 %) to detect High grace score. NLR cut-off value 2.17 (sensitivity 62.9%; specificity 60 %), and PLR cut-off value 108.38 (sensitivity 60.7%; specificity 60 %) to detect High hs-cTnT.

Conclusion: In this study, there was a relationship between NLR and PLR with the Grace risk score as well as a relationship between NLR and PLR with hs-cTnT.

Keywords: Acute Coronary Syndrome, High Sensitivity Troponin T, Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio, Grace Risk Score.

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INTRODUCTION

ACS is an emergency in the Cardiology field due to an imbalance of the supply and demand of oxygen in the coronary artery as a result of atherosclerosis and spasm processes that block or narrow the coronary artery.¹⁻³ ACS raises mortality and morbidity rates.⁴ Based on the classification, Three categories of ACS exist: unstable angina pectoris, ST-elevation myocardial infarction, and non-ST elevation myocardial infarction.⁴⁻⁶ In Indonesia, the prevalence of ACS in 2015 was 32.314 instances in men and 18.846 cases in women. The age group with the highest prevalence in hospitals is those between 45 and 64 years old, with 29,074

cases, followed by those over 65, with 14,733 cases.⁷

The incidence of ACS is related to systemic inflammation, where an increase in neutrophils has an atheroinflammation effect which contributes to thrombus formation and coronary plaque rupture, increased platelets also increase the inflammatory response because they can produce thromboxane and other inflammatory mediators, besides megakaryocyte proliferation from increased platelets can cause a thrombocytosis process. which can weaken stability and promote atherosclerosis. On the other hand, lymphocytes have the opposite effect on neutrophils and

platelets, whereas lymphocytes have an anti-atherosclerotic effect, so a decrease in lymphocytes is related to the incidence of ACS, and vice versa.⁸⁻¹¹ The inflammatory biomarkers neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) can be easily and affordably measured from a complete blood count.

Numerous studies have demonstrated that NLR and PLR are related to ACS.^{12,13} The goal of this study is to find an association between NLR and PLR with the Global Registry of Acute Coronary Event (GRACE) Score, a score that can predict ACS patients' mortality within six months, and the High Sensitivity Troponin T (hs-cTnT), a serum biomarker with high

sensitivity to establish the diagnosis in ACS patients at Kanujoso Djatiwibowo General Hospital, Balikpapan, in 2022.

METHODS

The sample used in this study is a sample of patients who were diagnosed with ACS based on medical records at Kanujoso Djatiwibowo Hospital in Balikpapan from January 2022 to December 2022. This study is an analytical study with a retrospective cross-sectional design. The research ethics committee of the Kanujoso Djatiwibowo Hospital in Balikpapan granted permission for this study with Etichal Clearance No. 02/I/KEPK-RSKD/2023.

Patients with ACS who entered the Emergency Room with complete medical record data and were diagnosed with STEMI, NSTEMI, or UAP, which was confirmed by electrocardiographic data, available serum biomarkers like high sensitivity troponin T (hs-cTnT), and full blood laboratory results from data, were included in the samples. Exclusion criteria were incomplete medical record data, patients with active infections, malignancies, sufferers of hematological diseases, blood transfusions, liver disease, kidney disease, autoimmune diseases, use of steroids, and chemotherapy.

Electrocardiographic examinations, the presence of ischemia symptoms, and serum biomarker test results are used to make the diagnosis of ACS. Based on the ratio of lymphocytes to neutrophils, NLR is determined. Based on the ratio of platelets to lymphocytes, PLR is determined. The Grace score, which is based on details like age, heart rate, systolic blood pressure, creatinine, the cardiac arrest upon admission, ST-segment deviation, abnormal cardiac enzymes, and Killip class, is used to predict mortality. The scores 109 (low risk), 109-140 (Intermediate risk), and >140 (High risk) are the three risk categories according to the Grace Risk Score. The hs-cTnT test was taken more than three hours after the ischemia complaint first manifested.

The 25.0 version of SPSS software was used to analyze the data. The Kolmogorov-Smirnov test is used to determine the normality test of the data. The Mean is used to present numerical variables (Standard Deviation). NLR, PLR, and hs-

cTnT are shown as Median (Minimum-maximum). thereafter percentages are shown for categorical variables. Bivariate analysis using the Spearman correlation test. The cut-off values for NLR and PLR, as well as the sensitivity and specificity of the High GRACE Risk Score and hs-cTnT with levels > 14 pg/ml, were determined using ROC analysis.

RESULT

The inclusion criteria for this study included 99 medical record data with ACS patients in total. The subjects of this study's characteristics include age, gender, BMI, ACS type, Grace Risk Score, NLR, and PLR (Table 1). Age was found to be an average of 57.82 ± 9.80 , sex was more in males with a total of 74 (74.7%) BMI with an average of 25.74 ± 3.95 , more ACS types in the NSTEMI category with a total of 54 (54.5%), Grace Risk Score was higher in Low risk 48 patients (48.5%), median (min-max) of NLR 3.13 (0.46 - 16.33), median (min-max) of PLR 129.55 (54.8 - 291.8), and median (min-max) of hs-cTnT 47.1 (2.0 - 9202.0).

There is a positive correlation between NLR and PLR with GRACE Risk Score and hs-cTnT. Table 3 shows the results of the sensitivity and specificity of NLR and PLR to the Grace Risk Score with an NLR cut-off value of 4.45 with a sensitivity of 73.3% and a specificity of 72.6%. while the PLR

cut-off value was 139.77 with a sensitivity of 66.7% and a specificity of 59.5%. Table 4 shows the results of the sensitivity and specificity of NLR and PLR to hs-cTnT with an NLR cut-off value of 2.17 with a sensitivity of 62.9% and a specificity of 60.0%. while the PLR cut-off value was 108.38 with a sensitivity of 60.7% and a specificity of 60.0%.

DISCUSSION

Endothelial dysfunction is related to the Inflammatory process as the initial process of acute coronary syndrome. Inflammatory cells have an important role in plaque rupture and thrombosis in ACS. When the body is experiencing an inflammatory process there is an increase in the level of cortisol and catecholamines, the high level of cortisol makes the apoptotic process of lymphocytes high, this explains the evolutionary development of coronary disease causing low levels of lymphocytes.^{8,9} On the other hand, in the development of atherosclerosis, neutrophils aid in the event of an inflammatory process, neutrophils activate macrophages in the context of lipid mediation functions, and macrophages express atherogenic factors like interleukin 6 (IL-6), CD40, and CD80 for foam cell formation. When myocardial tissue damage occurs, the emergence of metabolites such as arachidonic acid, chemokines, reactive

Table 1. Study characteristic

Variable	Frequency (N=99)
Age (mean \pm SD)	57.82 \pm 9.80
Sex, n (%)	
Male	74 (74.7%)
Female	25 (25.3%)
BMI (mean \pm SD)	25.74 \pm 3.95
ACS, n (%)	
STEMI	35 (35.4%)
NSTEMI	54 (54.5%)
UAP	10 (10.1%)
GRACE Risk Score, n (%)	
Low Risk	48 (48.5%)
Intermediate Risk	36 (36.4%)
High Risk	15 (15.2%)
NLR (Median (min-max))	3.13 (0.46 - 16.33)
PLR (Median (min-max))	129.55 (54.8 - 291.8)
Hs cTnT (Median (min-max))	47.1 (2.0 - 9202.0)

Note. BMI: Body Mass Index; GRACE: Global Registry of Acute Coronary Event Score; NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; hs-cTnT: High Sensitivity Troponin T.

oxygen species, intracellular adhesion molecules-1 (ICAM-1), platelet factor, and Myeloperoxidase (MPO) is highlighted. MPO also encourages the formation of low-density lipoprotein (LDL), which is then oxidized and phagocytosed by macrophages to form folate.^{10,14}

The inflammatory process also affects the production of platelets; the proinflammatory state that results from the release of inflammatory factors like

IL-1 and IL-3 promotes the proliferation of megakaryocytes and an increase in the number of circulating platelets. The pathophysiology of ACS may involve platelet-fibrin formation and platelet activation being increased by a high platelet count.^{11,15}

According to Liu et al. an increase in NLR (> 3.17), as well as an increase in PLR (> 169.8), is related to an increase in the Grace Risk Score, In addition, it

can lower survival rates and raise the frequency of major adverse cardiovascular and cerebrovascular events (MACCE).¹⁶ The GRACE Risk Score and NLR and PLR are correlated in this study. Siregar et al. demonstrated the relationship among NLR and GRACE scores in coronary disease ($r=0.570$, $P0.001$), as well as PLR and GRACE scores in coronary disease ($r=0.485$, $P0.001$).¹⁷ According to Intan et al. there is a strong association ($r=0.27$, $P=0.004$) between PLR and Grace Risk Score.¹⁸

In addition to increasing and correlating with atherosclerotic levels in ACS patients and being able to predict long-term bad prognosis, hs-cTnT is superior to standard hs-cTnT in the ability to predict severe lesions in NSTEMI patients.¹⁹ This study discovered an association between NLR to hs-cTnT and PLR to hs-cTnT ($r=0.343$, $p=0.001$) and both ($r=0.284$, $p=0.004$). According to Korkmaz et al. there is a significant association between NLR and troponin result. For positive troponin, the average NLR was 5.49 ± 4.01 , and for negative troponin, it was 2.40 ± 1.36 ($p<0.001$).²⁰ In addition, Altun et al. discovered that NLR and hs-cTnT had a correlation in NSTEMI patients ($r=0.449$, $p0.001$).¹⁹

the ROC curve for the Grace Risk score, whose NLR cut-off value is 4.45 and has a sensitivity of 73.3% and a specificity of 72.6%, is examined in this study. A sensitivity of 66.7% and a specificity of 59.5% were associated with the PLR cut-off value of 139.77. In addition, the ROC curve for hs-cTnT will be examined. The ROC curve's cut-off value for NLR is 2.17, with a sensitivity of 62.9% and a specificity of 60.0%. A sensitivity of 60.7% and a specificity of 60% were associated with the PLR cut-off value of 139.77.

This study is a single-center study and cross-sectional design thus additional research with big samples with diverse samples, and multicenter research is needed. This study measures the laboratory of complete blood count and high sensitivity troponin T just one time in the emergency department so laboratory evaluation after the first laboratory to assess prognosis and changes in the laboratory as well as to assess changes in troponin results are all necessary.

Table 2. NLR and PLR correlation to GRACE Risk Score and Hs-cTnT

Spearman Correlation	GRACE Score		Hs-cTnT	
	<i>r</i>	<i>p</i> -value	<i>r</i>	<i>p</i> -value
NLR	0.348	<0.001	0.343	0.001
PLR	0.434	<0.001	0.284	0.004

Note. GRACE: Global Registry of Acute Coronary Event Score; NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; hs-cTnT: High Sensitivity Troponin T.

Table 3. Cut-off Value, AUC, Sensitivity and Specificity of NLR and PLR on Grace Risk Score

Variable	Cut-off value	AUC	Sensitivity	Specificity
NLR	4.45	0.736	73.3%	72.6%
PLR	139.77	0.754	66.7%	59.5 %

Note. NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; AUC: Area Under Curve.

Table 4. Cut-off Value, AUC, Sensitivity and Specificity of NLR and PLR on Hs-cTnT

Variable	Cut-off value	AUC	Sensitivity	Specificity
NLR	2.17	0.645	62.9%	60%
PLR	108.38	0.580	60.7%	60%

Note. NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; AUC: Area Under Curve.

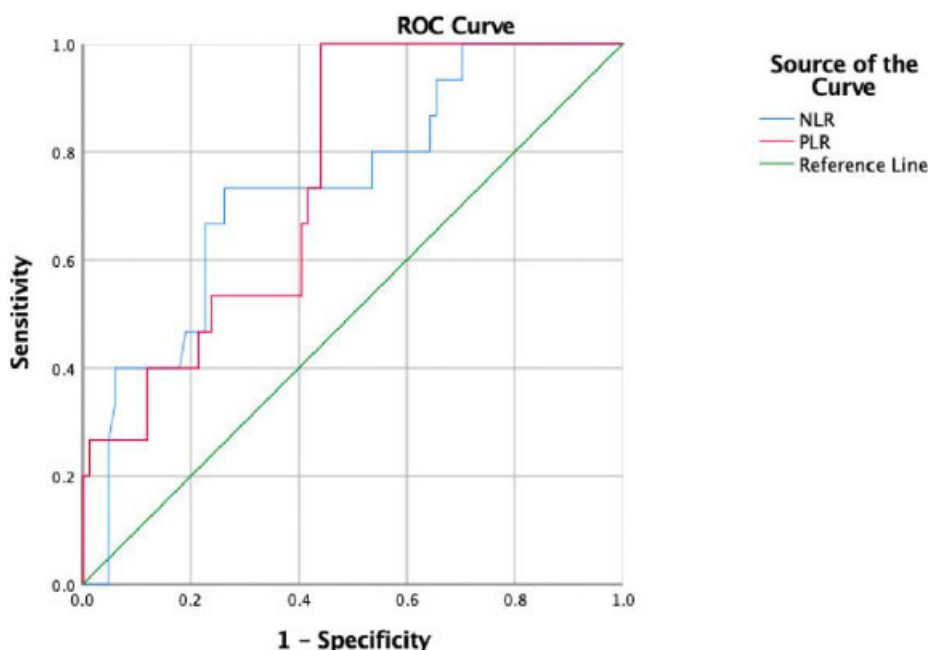


Figure 1. ROC Curve Analysis for NLR and PLR with GRACE Score.

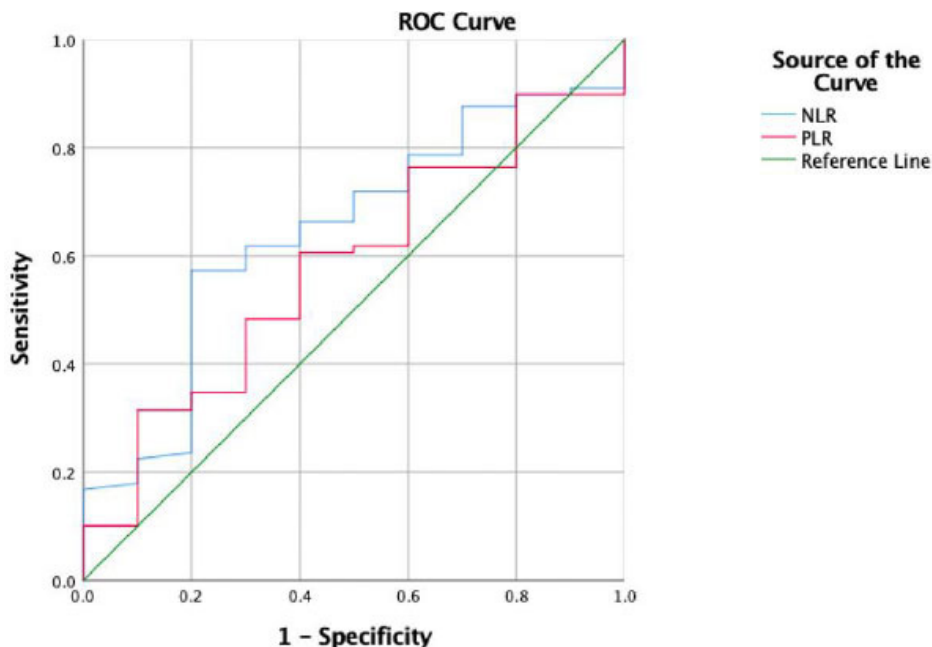


Figure 2. ROC Curve Analysis for NLR and PLR with hs-cTnT.

CONCLUSION

During the transition from atherosclerosis to plaque rupture, inflammation plays a significant role in the development of ACS. Both the Grace risk score, which serves as a predictor of death, and high sensitivity troponin T, a serum biomarker that aids in the diagnosis of patients with the acute coronary syndrome, have a substantial association with NLR and PLR as quick, simple, and affordable measures of inflammation.

CONFLICT OF INTEREST

There isn't a conflict of interest at the moment making this manuscript.

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AUTHOR CONTRIBUTION

All author have a contribution to making this manuscript.

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