



THE RELATIONSHIP BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO WITH THE SEVERITY OF ACUTE CORONARY SYNDROME

Nur Isti Hasanah¹, Jelita Siregar^{2,4}, Anggia Chairuddin Lubis^{3,4}

¹Resident Clinical Pathology, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia

²Department of Clinical Pathology, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia

³Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia

⁴Adam Malik Hospital, Jl. Bunga Lau No.17, Kemenangan Tani, Medan Tuntungan, Medan, Sumatera Utara 20136, Indonesia

*nuristiihasanah@gmail.com

ABSTRACT

Cardiovascular diseases pose a major health problem, representing a significant threat to the global population due to their high mortality rates. According to the World Health Organization (WHO), cardiovascular diseases were the leading cause of death worldwide in 2021. This condition is caused by the accumulation of fatty deposits in the arteries, known as atherosclerosis, which obstructs blood flow and increases the risk of heart attacks. This study aimed to evaluate the relationship between the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) and the severity of acute coronary syndrome at Adam Malik General Hospital. This study was an analytical study with a retrospective design, utilizing secondary data obtained from patients' medical records over a specific period. Patient data were collected from January 2023 to December 2024 from patients hospitalized at Adam Malik Hospital. Sampling was conducted using a total sampling technique, including all 208 patients who met the inclusion criteria during the study period. The collected data were then analyzed using the Kolmogorov–Smirnov test to assess the normality of data distribution. Among 208 patients, 76% were male, with a mean age of 62.2 years (range: 36–81). Most patients had low SYNTAX II scores (74%). The mean NLR and PLR values were 3.58 and 134.35, respectively. A significant positive correlation was observed between NLR and SYNTAX II score ($r = 0.284$; $p < 0.001$) and between PLR and SYNTAX II score ($r = 0.143$; $p = 0.039$). This study demonstrated a significant positive correlation between the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) and the severity of acute coronary syndrome based on the SYNTAX II score. NLR showed a stronger correlation than PLR, highlighting its superior potential as an inflammatory biomarker for assessing disease severity in patients with acute coronary syndrome.

Keywords: acute coronary syndrome; NLR; PLR; syntax II

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INTRODUCTION

Coronary heart disease (CHD) is the most common form of heart disease and is caused by atheromatous changes in the blood vessels supplying the heart. CHD is characterized by inadequate blood and oxygen supply to the myocardium due to obstruction of the coronary arteries, resulting in an imbalance between oxygen demand and supply. The disease typically involves plaque formation within the coronary artery lumen that impairs blood flow. CHD is marked by the progression of atherosclerosis in the coronary arteries, which may remain asymptomatic for a prolonged period. (Farooq et al., 2014). According to data from the Global Burden of Disease (GBD) survey, coronary heart disease (CHD) accounted for 16.2% of all global deaths in 2019. More than 75% of deaths due to cardiovascular diseases occurred in low- and middle-income countries, highlighting a disproportionate

burden in these populations. (Kwon et al., 2020; Lee et al., 2020) Ethnically, South Asian populations exhibit the highest prevalence of CHD (24%), whereas White populations have the lowest prevalence (8%). The incidence of CHD also varies by sex, with men more frequently presenting with typical chest pain, while women more often exhibit atypical symptoms. Modifiable risk factors such as smoking and alcohol consumption are more commonly observed among younger men than younger women. (Lima Dos Santos et al., 2023)

Coronary artery disease has a multifactorial etiology involving both non-modifiable and modifiable risk factors. Non-modifiable risk factors include age, sex, family history, and genetic predisposition, whereas modifiable risk factors comprise hypertension, smoking, obesity, dyslipidemia, and psychosocial factors. In Western countries, increasingly fast-paced lifestyles have promoted higher consumption of fast food and unhealthy diets, contributing to the rising prevalence of ischemic heart disease. Smoking remains a major risk factor and a leading cause of cardiovascular disease. (Shahjehan et al., 2024)

The neutrophil-to-lymphocyte ratio (NLR), calculated as the simple ratio of peripheral blood neutrophil count to lymphocyte count, is a biomarker that integrates two components of the immune system: innate immune responses, primarily mediated by neutrophils, and adaptive immune responses, supported by lymphocytes. Neutrophils constitute the first line of defense against invading pathogens through multiple mechanisms, including chemotaxis, phagocytosis, generation of reactive oxygen species (ROS), release of granular proteins, and production and secretion of cytokines. (Bounacera et al., 2022)

Several studies have demonstrated that the neutrophil-to-lymphocyte ratio (NLR) predicts cardiovascular events. In addition, NLR has been shown to predict mortality in the general population. Elevated NLR is significantly associated with increased all-cause mortality (hazard ratio [HR] 1.14, 95% confidence interval [CI] 1.10–1.17 per quartile increase in NLR) as well as cause-specific mortality, including cardiovascular mortality (HR 1.17, 95% CI 1.06–1.29 per quartile increase in NLR). Shah et al. reported that, in a healthy general population, an NLR > 4.5 independently predicted long-term (14-year) coronary heart disease-related mortality. Moreover, the same study demonstrated that NLR improved risk stratification by accurately reclassifying individuals at intermediate risk according to the Framingham Risk Score into lower- or higher-risk categories for cardiovascular mortality. (Bounacera et al., 2022) A study by Bounacera et al. demonstrated that, in a cohort of 324 elderly patients, an NLR greater than 3.68 significantly predicted the presence of carotid atherosclerotic plaque. (Kruger et al., 2015)

The platelet-to-lymphocyte ratio (PLR) represents an integrated reflection of two opposing thrombotic and inflammatory pathways and can be readily calculated from a complete blood count. Initially, PLR was used as a systemic inflammatory biomarker to predict prognosis in neoplastic diseases. In recent years, PLR has increasingly been utilized as a prognostic marker in cardiovascular conditions. (Zhang et al., 2016) Recent studies have indicated that elevated platelet counts and reduced lymphocyte counts play a significant role in adverse cardiovascular outcomes. Azab et al. demonstrated that higher platelet-to-lymphocyte ratio (PLR) values were associated with increased long-term mortality in patients with non-ST-segment elevation myocardial infarction. (Oylumlu et al., 2015). This study aimed to determine the relationship between the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) and the severity of Acute Coronary Syndrome at Adam Malik Hospital, Medan.

METHOD

This study was an analytical study with a retrospective design, utilizing secondary data obtained from patients' medical records over a defined period. The study was conducted at the Sub-Installation of Clinical Pathology, Faculty of Medicine, Universitas Sumatera Utara (FK USU)/Adam Malik Hospital, Medan, in collaboration with the Department of Cardiology and

Vascular Medicine, FK USU/Adam Malik Hospital, from January 2023 to December 2024. Sampling was performed using a total sampling technique, including all patients who met the inclusion criteria and were hospitalized at Adam Malik Hospital.

A total of 208 subjects were included in this study. Subject characteristics were presented in tabular form and described narratively. The association between the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) and the severity of acute coronary syndrome was analyzed using Spearman's correlation test. A p-value of < 0.05 was considered statistically significant. Total sampling was applied to all eligible subjects, namely patients diagnosed with coronary artery disease, specifically those with non-ST-segment elevation myocardial infarction (NSTEMI), as diagnosed by a cardiology specialist, and patients who underwent coronary angiography.

This study was conducted after obtaining ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan (approval number: 822/KEPK/USU/2025).

RESULT

The baseline characteristics of the study subjects are presented in Table 1. The mean age of the participants was 60.18 years with a standard deviation of 9.41 years, while the median age was 62 years, with an age range of 36 to 81 years. Based on sex distribution, the study population consisted of 50 females (24%) and 158 males (76%).

Table 1.

Baseline Characteristics of the Study Subjects

Characteristics	Category / Parameter	Value
Sex	Male, n (%)	158 (76%)
	Female, n (%)	50 (24%)
Age (Year)	Mean (SD)	60,18 ± 9,41
	Median (Min - Max)	62,00 (36 - 81)
SYNTAX 2 Score	Mean (SD)	21,69 (14,07)
	Median (Min - Max)	22,65 ((-2,5) - 48,70)
SYNTAX 2 Score Category, %	Low	154 (74 %)
	High	54 (26%)

Regarding the SYNTAX II score, the mean score was 21.69 with a standard deviation of 14.07, and the median score was 22.65, with values ranging from -2.5 to 48.70. Based on SYNTAX II score categorization, 154 subjects (74%) were classified into the low-score group, while 54 subjects (26%) were classified into the high-score group. Table 2 presents the distribution of platelet count, absolute neutrophil count, absolute lymphocyte count, NLR, and PLR in patients with acute coronary syndrome. Prior to descriptive analysis, data normality was assessed using the Kolmogorov–Smirnov test, and all parameters showed p-values < 0.05 , indicating non-normal distributions. Accordingly, all parameters are presented as median values with minimum and maximum ranges.

Table 2.

Platelet Count, Absolute Neutrophil Count, Absolute Lymphocyte Count, NLR, and PLR in Patients with Acute Coronary Syndrome

Parameter	Subject (n=208)
Trombosit, (μL)	
Median (Min – Max)	248.500 (59.000 – 543.000)
Absolute Neutrophil, ($\times 10^3/\mu\text{L}$) Median (Min – Max)	6,7 (1,87 – 38,28)
Absolute Lymphocyte, ($\times 10^3/\mu\text{L}$) Median (Min – Max)	1,89 (0,32 – 13,00)
NLR	
Median (Min – Max)	3,58 (0,50 – 35,55)
PLR	
Median (Min – Max)	134,35 (19,38 – 1066,7)

Table 3 presents the differences in platelet count, absolute neutrophil count, absolute lymphocyte count, NLR, and PLR among patients with acute coronary syndrome categorized according to SYNTAX II score (low and high). Based on the prior normality assessment, all variables were non-normally distributed; therefore, between-group comparisons were performed using the Mann-Whitney U test.

Table 3.

Differences in Platelet Count, Absolute Neutrophil Count, Absolute Lymphocyte Count, NLR, and PLR in Patients with Acute Coronary Syndrome According to SYNTAX II Score Categories (Low and High)

Parameter	SYNTAX 2 Score		<i>p</i>
	Low	High	
Trombosit, (/μL) Median (Min-Max)	249,500 (59.000-543.000)	244,500 (103.000 – 472.000)	0,611
Absolute Neutrophil, (x 10 ³ /μL) Median (Min-Maks)	6,51 (1,87 – 17,85)	8,06 (1,87 – 38,28)	<0,001
Absolute Lymphocyte, (x 10 ³ /μL) Median (Min-Max)	2,03 (0,32 – 13,00)	1,48 (0,39 – 3,72)	0,002
NLR Median (Min-Max)	3,30 (0,50 – 22,44)	5,9 (0,83 – 35,55)	<0,001
PLR Median (Min-Max)	129,57 (19,38 – 762,50)	163,20 (59,95 - 1066,67)	0.040

Mann-Whitney Test

Table 4.

Correlation Analysis between NLR and PLR and the Severity of Acute Coronary Syndrome Based on SYNTAX II Score Categories

Variabel	<i>r</i>	<i>P</i>
NLR	0,284	<0.001
PLR	0,143	0,039

Spearman's correlation test

Spearman's rank correlation analysis was used to assess the association between NLR and PLR and the severity of acute coronary syndrome based on SYNTAX II score categories. The correlation analysis showed that NLR had a correlation coefficient of $r = 0.284$ with a significance value of $p < 0.001$. Meanwhile, PLR demonstrated a correlation coefficient of $r = 0.143$ with a p -value of 0.039.

DISCUSSION

A global study by Maas and Appelman (2010) demonstrated that men have a 2–3 times higher risk of developing acute coronary syndrome compared with premenopausal women, with this gap narrowing after menopause due to the loss of the protective effects of estrogen. (Appelman et al., 2015) According to the Global Burden of Disease Study 2023, the incidence of acute coronary syndrome increases significantly from the age of 55 years onward due to degenerative changes in the arterial wall, increased vascular stiffness, and chronic low-grade inflammation ('inflammaging'), which enhances the vulnerability of atherosclerotic plaques to rupture. (GBD 2023). This finding is consistent with data from the American Heart Association, which report that although the risk of coronary heart disease increases with advancing age, its incidence among younger populations has also been rising, particularly in developing countries. (Virani et al., 2020) The Framingham Heart Study demonstrated that each 10-year increase in age is associated with a 2–3-fold higher risk of cardiovascular events in men and a 3–4 fold higher risk in women. (Gulati et al., 2020).

The study results showed that the majority of patients (74%) were classified into the moderate SYNTAX II score category, while 26% were categorized as high risk. This distribution reflects the anatomical complexity of coronary lesions in patients with acute coronary syndrome undergoing coronary angiography in Indonesia. A study by Kawashima et al. in an Asian population reported a similar distribution, with approximately 70–75% of patients falling into the low-to-moderate SYNTAX score categories. (Kawashima et al., 2023) The relatively high proportion of patients in the moderate category observed in this study may be explained by several factors. First, the study population encompassed a broad spectrum of acute coronary syndrome, including non-ST-segment elevation myocardial infarction (NSTEMI), which may be associated with lower anatomical complexity compared with ST-segment elevation myocardial infarction involving multivessel disease. (Byrne., 2023) Second, the demographic characteristics of the study subjects, with a mean age of approximately 60 years, may not yet reflect the maximal accumulation of atherosclerotic burden typically observed in older populations. (Kawashima et al., 2021) Third, sociodemographic factors and access to healthcare services in Indonesia may influence the timing of patient presentation, whereby patients with very high SYNTAX scores may have experienced pre-hospital mortality or opted for medical therapy without revascularization. (Amsterdam et al., 2014)

Increased platelet activity is a risk factor of thrombotic events, including myocardial infarction and unstable angina (acute coronary syndrome, ACS), being associated with low sensitivity to antiplatelet drugs [4,5,6,7]. Platelet activity can be affected by platelet phenotypic features such as their size [8,9,10] and the content of “young” reticulated forms. (Bodrova et al., 2024) This variability is consistent with the findings of Zhou et al. (2022), who reported that platelet activation is significantly increased in acute coronary syndrome due to acute inflammatory processes, release of thrombogenic mediators, and activation of platelet–leukocyte aggregates, which promote coronary thrombus formation. (Pluta et al., 2022) In this study, the median absolute neutrophil count was $6.7 \times 10^3/\mu\text{L}$, indicating increased inflammatory activity during the acute phase of coronary artery disease. These findings are consistent with the study by Buonacera et al. (2022), which reported that neutrophils are innate immune cells that are among the first to be recruited to the site of myocardial injury and play an important role in amplifying the inflammatory response through the release of pro-inflammatory cytokines, proteolytic enzymes, and the formation of neutrophil extracellular traps (NETs), which can accelerate thrombosis in the coronary arteries. Therefore, an increased neutrophil count during the acute phase of coronary artery disease may reflect the degree of systemic inflammation and is associated with disease severity. Neutrophil activation is recognized as a key component in the processes of inflammation and thrombosis in various cardiovascular diseases, including acute coronary syndrome. (Buonacera et al., 2022)

A study by Hongyun et al. (2025) reported that lymphocytes, as a component of the adaptive immune response, can infiltrate blood vessels and trigger inflammatory signal transduction. A reduction in lymphocyte counts during inflammatory regulation may exacerbate the progression of atherosclerosis. (Kannappalli et al., 2025) Furthermore, a study by Li et al. (2022) demonstrated that lymphopenia has strong prognostic value in relation to mortality and the risk of complications in patients with acute coronary syndrome. (Gao et al., 2022)

The study results showed that NLR values were significantly higher in the high SYNTAX II score group compared with the moderate score group ($p < 0.001$). This finding confirms the superiority of NLR as an integrative inflammatory biomarker that reflects two distinct immunological pathways: innate immune responses mediated by neutrophils and adaptive immune responses mediated by lymphocytes. A study by Tamhane et al. demonstrated that NLR provides superior prognostic information compared with absolute neutrophil or lymphocyte counts alone in patients with acute coronary syndrome. (Shu et al., 2025) The findings of this study, which demonstrate the inferior performance of PLR compared with NLR, are consistent with several previous studies. A meta-analysis by Li et al., which analyzed 12 studies involving a total of 5,517 patients, reported that

although elevated PLR was associated with an increased risk of mortality in acute coronary syndrome, substantial interstudy heterogeneity was observed and the strength of the association was weaker than that of NLR.²⁵

A study by Bilgin et al. (2024) demonstrated that, among patients with NSTEMI, the median neutrophil-to-lymphocyte ratio (NLR) in the high SYNTAX II score group ranged from 4.8 to 5.5 and was significantly higher than that in the low SYNTAX II score group, which ranged from 2.6 to 3.0 ($p < 0.001$). These findings are consistent with the results of the present study, in which the high SYNTAX II score group also exhibited a significantly elevated NLR. This consistency further confirms the superiority of NLR as an integrative inflammatory biomarker that reflects two distinct immunological pathways: innate immune responses mediated by neutrophils and adaptive immune responses mediated by lymphocytes. (Bilgin et al., 2024) The positive correlation analysis showed that NLR was significantly associated with disease severity ($r = 0.284$, $p < 0.001$). This finding is consistent with the study by Li et al., which reported that the neutrophil-to-lymphocyte ratio (NLR) was positively and linearly correlated with the SYNTAX score ($r = 0.270$; $p < 0.001$) and was an independent predictor of long-term cardiovascular mortality in patients with unstable angina pectoris (UAP). (Li et al., 2022)

In this study, the median platelet-to-lymphocyte ratio (PLR) was higher in the group with a high SYNTAX II score compared to the low-score group (163.20 vs. 129.57; $p = 0.040$). This finding suggests that an elevated PLR tends to be associated with greater coronary lesion complexity, as PLR reflects the interplay between platelet activity and immune response, both of which play a role in atherosclerotic inflammation. Several studies have reported an association between PLR and the severity of coronary artery disease, although the angiographic scoring systems, patient populations, and assessment models vary across studies. However, the correlation between PLR and the SYNTAX II score in this study was weak ($r = 0.143$; $p = 0.039$), indicating that the utility of PLR as a single marker for assessing the anatomical complexity of the coronary arteries remains limited. Other correlational studies evaluating the relationship between hematological ratios and coronary artery disease complexity using scoring systems such as SYNTAX or Gensini have similarly reported variable associations, ranging from weak to moderate. These findings suggest that PLR does not consistently provide strong individual predictive value for the severity of coronary lesions. The limited predictive value of PLR can partly be explained by the fact that platelet counts are strongly influenced by external factors such as acute or chronic infection, anemia, physiological stress, and the use of antiplatelet therapy. These factors may affect PLR values without directly reflecting the degree of vascular inflammation or atherosclerotic burden, thereby weakening the correlation between PLR and angiographic scores such as SYNTAX II. This is consistent with observations that other inflammatory markers (e.g., NLR, SII) often demonstrate a stronger association with the severity of CAD compared with PLR alone. (Pruc et al., 2023)

CONCLUSION

This study demonstrates a significant positive association between inflammatory biomarkers and the severity of acute coronary syndrome as assessed by the SYNTAX II score. The neutrophil-to-lymphocyte ratio (NLR) showed a stronger and more consistent correlation with disease severity compared with the platelet-to-lymphocyte ratio (PLR), highlighting the superior clinical utility of NLR as an integrative inflammatory biomarker. Elevated NLR values were significantly associated with higher SYNTAX II scores, reflecting greater anatomical complexity and multivessel coronary artery disease.

Although PLR differed significantly between SYNTAX II score categories, its correlation with disease severity was weak, suggesting limited prognostic value compared with NLR. These findings are consistent with previous studies and meta-analyses indicating that NLR outperforms PLR in predicting coronary artery disease complexity and adverse outcomes. Overall, NLR represents a

simple, cost-effective, and readily available biomarker that may aid in risk stratification and assessment of disease severity in patients with acute coronary syndrome.

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