ORIGINAL ARTICLE

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Predictors of Severity of Coronary Artery Disease in Patients with Acute ST-elevation Myocardial Infarction

Akut ST-elevasyonlu Miyokard Enfarktüsü Olan Hastalarda Koroner Arter Hastalığının Ciddiyetinin Belirleyicileri

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ABSTRACT

Aim: Our study aims to investigate the relationship between platelet-lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and the correlation between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) scores.

Materials and Methods: The patients were divided into three groups according to their SYNTAX score. Group 1 included patients with a SYNTAX score <23, group 2 with a SYNTAX score of 23-32, and group 3 with a SYNTAX score of >33. PLR was calculated as the ratio of platelet count to lymphocyte count.

Results: In multivariate logistic regression analysis, high PLR and NLR ratios and older age were independent predictors of high SYNTAX score II [odds ratio (OR): 1.052; 95% confidence interval (CI): (0.998-1.119), p=0.011; OR: 1.093; 95% CI: (1.016-1.175), p=0.016; OR:1.023; 95% CI: (1.010-1.038), p=0.001, respectively. Patients with high PLR had significantly higher SYNTAX scores [121.7 (114.2-129.3) in group 1; 139.4 (125.9-153.0) in group 2, 187.0 (141.8-232.2) in group 3; p<0.001], and there was a positive correlation between PLR, NLR and SYNTAX scores (r=0.52, p<0.001; r=0.58, p<0.001, respectively).

Conclusion: PLR and NLR were associated with the severity and complexity of coronary artery disease in patients with acute ST-elevation myocardial infarction.

Keywords: Lymphocytes, neutrophils, coronary artery disease, inflammation

ÖZ

Amaç: Trombosit-lenfosit oranı (PLR) ve nötrofil/lenfosit oranı (NLR), olumsuz kardiyovasküler sonuçlarla korelasyon gösteren sistemik enflamatuvar belirteçlerdir. Çalışmamız PLR, NLR ve SYNTAX skoru arasındaki ilişkiyi araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Hastalar SYNTAX skorlarına göre üç gruba ayrıldı. Grup 1'de SYNTAX skoru <23 olan hastalar, grup 2'de SYNTAX skoru 23-32 olan hastalar ve grup 3'te SYNTAX skoru >33 olan hastalar yer aldı. PLR, trombosit sayısının lenfosit sayısına oranı olarak hesaplandı.

Bulgular: Çok değişkenli lojistik regresyon analizinde yüksek PLR ve NLR oranları ve ileri yaş, yüksek SYNTAX skoru 2'nin bağımsız belirleyicileriydi [odds oranı (OR): 1,052; %95 güven aralığı (GA): (0,998-1,119), p=0,011; OR: 1,093; %95 GA: (1,016-1,175), p=0,016, OR: 1,023, %95 GA: (sırasıyla 1,010-1,038), p=0,001]. Yüksek PLO'lu hastaların SYNTAX skorları anlamlı derecede yüksekti [grup 1'de 121,7 (114,2-129,3); grup 2'de 139,4 (125,9-153,0); grup 3'te 187,0 (141,8-232,2); p<0,001] ve PLR, NLR ve SYNTAX puanları arasında pozitif korelasyon vardı (sırasıyla r=0,52, p<0,001; r=0,58, p<0,001).

Sonuç: PLR ve NLR, koroner arter hastalığının ciddiyeti ve karmaşıklığı ile ilişkiliydi.

Anahtar Kelimeler: Lenfosit, nötrofil, koroner arter hastalığı, enflamatuvar

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INTRODUCTION

Platelets significantly influence local inflammation at the site of atherosclerotic plaques. It has been noted that platelets play a significant role in mediating the relationship between the formation of an atherogenic milieu and the local inflammatory response at the vascular wall. When activated, platelets release a range of proinflammatory substances and chemokines to coordinate pro-atherogenic interactions between activated endothelial cells and circulating immune cells. Stromal cell-derived factor-1a and platelet factor 4 are two well-known instances of platelet chemokines. Both have been identified as pro-atherogenic elements that encourage endothelial monocyte adhesion and are found in atherosclerotic plaques[1]. According to recent research, inflammation is a major factor in atherosclerosis. Elevated platelet counts are associated with the long-term incidence of coronary artery disease and accelerate the formation, advancement, and destabilization of atherosclerotic plaques[2]. The development of atherosclerotic plaque is significantly influenced by the immune system. Poor outcomes are associated with inflammation, which is indicated by low lymphocyte levels in individuals with acute coronary syndrome[3]. Patients with acute coronary syndrome who had a high synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score also had a significantly higher platelet-lymphocyte ratio (PLR)[4]. Atherosclerotic plaque contains a large number of neutrophils. Biomarkers such as PLR and neutrophil/lymphocyte ratio (NLR) are correlated with the severity of coronary artery disease in many previous studies[3,4].

The SYNTAX score, which shows the severity of coronary artery disease, not only determines the method of revascularization but also predicts mortality[5]. To predict the complexity of coronary artery disease, simple, practical, non-invasive biomarkers are required. PLR has been reported to correlate with the severity of the SYNTAX score in patients with non-ST-segment elevation myocardial infarction[6]. We, therefore, aimed to investigate the relationship between PLR, NLR, and the SYNTAX score in patients with acute ST-elevation myocardial infarction (STEMI).

MATERIALS AND METHODS

Study Population

Patients with acute STEMI between June 2022 and December 2023 were included in our study. Our study is a retrospective study conducted by scanning hospital data. The written informed consent form was obtained from all patients. The following criteria were used to diagnose STEMI: ST-segment elevation in at least two contiguous leads and typical chest pain lasting longer than 20 minutes, with the cut-off points being ≥0.2 mV in men aged 40 years or older, ≥0.25 mV in men under 40 years, or ≥0.15 mV in women, in leads V2 to V3 and/or ≥0.1 mV in the other leads, as well as posterior (V7-V9) and right derivations (V3R-V4R).

Patients with severe renal failure (creatinine >2 mg/dL) and active infection, being under the age of 18 years, and having an inflammatory disease or cancer were excluded from the study. Blood samples for PLR were contained at the time of arrival at the hospital. The blood was tested using an automated device that measured biochemical levels and performed a full blood count. Hyperlipidemia was defined as receiving treatment for high cholesterol or having a total cholesterol level of more than 220 mg/dL. Blood pressure more than 140/90 mmHg or the usage of antihypertensive drugs was referred to as hypertension. The use of antidiabetic medications, fasting plasma glucose levels of 7.0 mmol/L (126 mg/dL), or glycated hemoglobin A1c readings of 6.5% were all considered the indicators of diabetes mellitus. The study was approved by the Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Clinical Research Ethics Committee (decision no: 60, date: 01.09.2023).

Angiography was carried out utilizing the Judkins method, using multiple projections in all patients. All of the patients had their 300 mg of aspirin loaded with either 180 mg of ticagrelor or 600 mg of clopidogrel before pPCI. Following the decision to do a coronary intervention, bolus heparin at a dosage of 50-70 units/kg was given to each patient. Coronary angiograms were analyzed by two independent cardiologists after the vessel responsible for STEMI was revascularized and SYNTAX II scores were calculated[7]. The patients were divided into three groups, respectively, according to their SYNTAX score; group 1: SYNTAX score <23, group 1: SYNTAX score between 23-32, and group 3: SYNTAX score >33.

Statistical Analysis

For statistical analysis, SPSS 22.0 (SPSS Inc., Chicago, IL) was utilized. The median or mean ± standard deviation was used to express continuous variables. The chi-square or Fisher's exact tests were employed to compare categorical variables that were given as percentages. To determine the normality of data distributions, the Kolmogorov-Smirnov test was used. The one-way ANOVA was used for continuously distributed data with a normal distribution. Non-normally distributed data were examined with the Kruskal-Wallis test. The Mann-Whitney U test was applied in post-hoc analysis of non-parametric data. To evaluate data conforming to normal distribution, the Tukey or Tamhane's test was used in post-hoc analysis, depending on the equality of variances. The PLR cut-off value was calculated using receiver-operating characteristic analysis to predict the severity and complexity of coronary artery disease in STEMI patients. For determining the appropriate cut-off value, Youden's J statistic was performed. For independent

characteristics predicting the high SYNTAX score in patients with STEMI, univariate and multivariate regression analyses were used. The Spearman correlation test was used to investigate the relationship between the PLR and the severity of the coronary arteries. Statistics with p values <0.05 were considered significant.

RESULTS

This study consisted of 613 patients who underwent coronary angiography for STEMI. Group 1 included patients with a SYNTAX score of <23, group 2 included patients with a SYNTAX score between ≥23-32, and group 3 included those with a SYNTAX score of >33. Table 1 summarizes the basic characteristics and laboratory findings. Group 3 had higher rates of multivessel disease and chronic total occlusion, and left ventricular ejection fraction was lower in this group compared to other groups. Patients in group 3 were older and had a higher rate of diabetes mellitus. There was no difference between the two groups in terms of other demographic characteristics. When we examined the biochemical and hematological measurements Table 2, neutrophil levels were detected to be significantly higher in group 3, whereas lymphocyte rates were lower in this group. PLR and NLR were significantly higher in group 3 [PLR, group 1: 121.7 (114.2-129.3), group 2: 139.4 (125.9-153.0), group 3: 187.0 (141.8-232.2), p<0.001; NLR, group 1: 4.1 (3.8-4.5), group 2: 5.4 (4.7-6.2), group 3: 6.8 (5.0-8.7), p<0.001, respectively].

Table 1. Baseline clinical and angiographic characteristics of the study population according to the severity of coronary artery disease

Variables	Group 1 (n=406)	Group 2 (n=173)	Group 3 (n=34)	p value
Male	306 (75.4%)	124 (71.7%)	24 (70.6%)	0.581
Age (years)	57±12	60±13	66±11	**<0.001**
Hypertension	145 (35.7%)	67 (38.7%)	19 (55.9%)	0.062
Diabetes mellitus	109 (26.8%)	47 (27.2%)	18 (52.9%)	**0.005**
Hypercholesterolemia	100 (24.6%)	36 (20.8%)	8 (23.5%)	0.082
Smoking	225 (55.4%)	88 (50.9%)	17 (50%)	0.432
Body mass index (kg/m^2)	28.2±4.6	27.6±3.8	26.7±4.6	0.102
Systolic blood pressure (mmHg)	129.6±24.0	127.6±24.3	126.8±27.4	0.07
Diastolic blood pressure (mmHg)	78.9±14.0	77.3±14.3	76.9±15.8	0.09
Left ventricular ejection fraction (%)	48±9	41±9	37±11	**<0.001**
Multi-vessel disease	154 (37.9%)	119 (68.8%)	33 (97.1%)	**<0.001**
Chronic total occlusion	19 (4.7%)	33 (19.1%)	20 (58.8%)	**<0.001**

Table 2. Biochemical and hematological measurements of the study population

Variables	Group 1 (n=406)	Group 2 (n=173)	Group 3 (n=34)	p value
Hemoglobin (g/dL)	14.3±1.7	14.2±1.9	13.4±1.9	0.008
WBC (X10^9/L)	11.4±3.2	12.1±3.5	11.9±4.2	0.066
Neutrophil (X10^9/L)	7.8±2.9	8.7±3.6	9.0±4.2	**0.002**
Lymphocyte (X10^9/L)	2.6±1.3	2.3±1.3	1.8±1.2	**0.002**
Monocyte (X10^9/L)	0.7±0.3	0.7±0.3	0.7±0.3	0.95
Platelet (X10^9/L)	249±74	243±59	248±65	0.60
NLR	4.1 (3.8-4.5)	5.4 (4.7-6.2)	6.8 (5.0-8.7)	**<0.001**
PLR	121.7 (114.2-129.3)	139.4 (125.9-153.0)	187.0 (141.8-232.2)	**<0.001**
Glucose (mg/dL)	114 (110-140)	122 (116-152)	128 (122-164)	0.06
Creatinine (mg/dL)	1.1±0.2	1.2±0.2	1.2±0.4	0.74
Total cholesterol (mg/dL)	193±45	190±48	192±68	0.81
Triglycerides (mg/dL)	154 (146-163)	159 (143-175)	134 (108-160)	0.37
LDL-C (mg/dL)	124±38	121±44	128±52	0.64
HDL-C (mg/dL)	40±8	40±9	42±11	0.38
Hs-CRP (mg/L)	6.5 (6.0-7.1)	8.5 (7.0-10.0)	8.8 (4.8-12.7)	0.006

NLR: Neutrophil/lymphocyte ratio, PLR: Platelet-lymphocyte ratio, Hs-CRP: High-sensitivity C-reactive protein, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, WBC: White blood cell

The following receiver operating characteristic analysis of PLR and NLR values was used to predict the SYNTAX >33 [NLR cut-off ≥3.28, area under the curve (AUC): 0.605; 95% confidence interval (CI): (0.557-0.653) with 61.4% sensitivity and 55.4% specificity, p<0.001, and PLR cut-off ≥100.8, AUC: 0.587; 95% CI: (0.538-0.635) with 62.8% sensitivity and 50.2% specificity, p<0.001] Figure 1. A positive correlation between PLR, NLR, and SYNTAX score II was found (r=0.52, p<0.001 and r=0.58, p<0.001, respectively). High PLR and NLR ratios and older age were independent predictors of high SYNTAX score II [odds ratio (OR): 1.052; 95% CI: (0.998-1.119), p=0.011; OR: 1.093;95% CI: (1.016-1.175), p=0.016; OR: 1.023; 95% CI: (1.010-1.038), p=0.001, respectively] Table 3.

DISCUSSION

This is the first study to investigate the relationship between NLR, PLR, and SYNTAX scores in patients with STEMI. We found that NLR, PLR, and age were associated with high SYNTAX scores. These practical markers may be capable of predicting the high SYNTAX score. Platelets have an important role in the atherosclerosis. They produce anti-inflammatory and immunomodulatory chemicals during the rupture of plaque[8,9]. Neutrophils secrete pro-inflammatory mediators. Extracellular neutrophil traps may contribute to the formation of atherosclerotic plaque. The role of neutrophils has been examined in many studies of myocardial ischemia-reperfusion and absence of myocardial reflow.

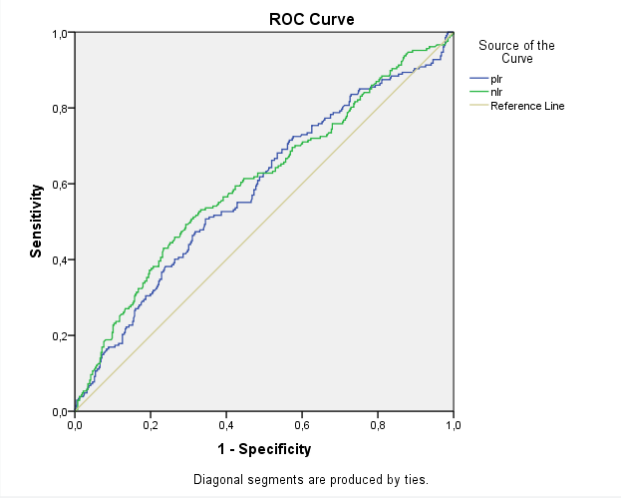

Figure 1. The receiver operating characteristic (ROC) curve analysis for cut-off values of plr and nlr for predicting predicting a high SYNTAX score II

AUC: Area under the curve, plr: Platelet-to lymphocyte ratio, NLR: Neutrophil/lymphocyte ratio, ROC: Receiver operating characteristic

It was concluded that neutrophils have a detrimental effect on the myocardium where ischemia-reperfusion is forced. Acute stress and inflammation with coronary disease can raise plasma cortisol levels, leading to more neutrophils and fewer lymphocytes in circulation. In studies conducted on patients with acute coronary syndrome, a higher number of active neutrophils was observed in blood samples taken from the plaque-ruptured area compared to samples taken from the peripheral arterial region[10].

The SYNTAX score is an angiographic risk stratification score used to measure coronary involvement and choose the best revascularization strategy for each patient depending on their clinical setting. The effect on mortality may be related to the SYNTAX score.

In our study, we found a correlation between increased PLR and NLR and high SYNTAX scores. A high PLR ratio was found in patients with coronary artery disease as a prognostic factor in numerous previous studies[11]. PLR has also been used to predict the prognosis of coronary slow flow[12] and it has also been found to be an indicator of plaque burden[13]. In addition, high levels of PLR ratio have been reported to be related to in-stent restenosis, saphenous vein graft disease, atrial fibrillation, heart failure, and poor coronary collateral circulation[13]. Sari et al.[14] found that the NLR and PLR may be used to predict the high SYNTAX score before coronary angiography. Systemic immune-inflammation index, which comprises NLR and PLR, has been reported to be associated with coronary artery disease in many studies[15]. By managing hyperlipidemia and thrombosis, atherosclerosis can be slowed down and cardiovascular events can be reduced by lowering the inflammatory response. Examining these biomarkers in patients with acute coronary

Table 3. Univariate and multivariate regression analysis of independent variables in predicting a high SYNTAX score

	Univariate analysis			Multivariate analysis		
Variables	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Age	1.027	1.014-1.041	**0.001**	1.023	1.010-1.038	**0.001**
Hypertension	1.279	0.908-1.803	0.159	-	-	-
Diabetes mellitus	1.247	0.865-1.799	0.237	-	-	-
PLR	1.003	1.001-1.005	**0.001**	1.052	0.998-1.119	**0.011**
NLR	1.087	1.043-1.132	**<0.001**	1.093	1.016-1.175	**0.016**

NLR: Neutrophil/lymphocyte ratio, PLR: Platelet-lymphocyte ratio, OR: Odds ratio, CI: Confidence interval

syndrome will aid in both diagnosing high SYNTAX scores and predicting the patient's prognosis. The high SYNTAX score was indicated by higher PLR and NLR levels, as we observed. Before invasive angiography, PLR and NLR, which are readily obtained from routine blood tests, can be computed rapidly.

Study Limitations

The present investigation has various constraints. First of all, the PLR and NLR were assessed as potential predictors of the high SYNTAX score in our small, single-center retrospective study. By drawing additional blood samples from the patients who were part of our study, an average calculation for biomarkers could be made. Finally, there are significant confounders that we do not know, like medication previously taken by patients, which can affect the inflammatory process. Larger, multi-center prospective studies are needed.

CONCLUSION

The strategy to be followed for subsequent coronary lesions is as important as a primary percutaneous intervention in the early period of STEMI. New biomarkers and scoring systems are parameters that can help in the treatment and prediction of prognosis. PLR and NLR may help classify high-risk patients with STEMI as they are practical, cost-effective biomarkers.

Ethics

Ethics Committee Approval: This study was conducted according to the guidelines of the Declaration of Helsinki and approved by Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Clinical Research Ethics Committee (decision no: 60, date: 01.09.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: M.K., Ç.A., Concept: C.A., A.D., Design: C.A., Data Collection or Processing: M.K., Ç.A., Analysis or Interpretation: A.D., Literature Search: C.A., Writing: C.A., A.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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