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Systemic Inflammatory Index and Platelet-to-Lymphocyte Ratio Predict Mortality in Patients with Acute Myocardial Infarction

Serkan Karahan[1*], Ertuğrul Okuyan[1]

[1]*University of Health Sciences, Bağcılar Training and Research Hospital, Department of Cardiology, Istanbul, Turkey.*

Abstract

In this study, we aimed to evaluate the relationship between the laboratory parameters of platelet volume / lymphocyte ratio (PLR) and systemic inflammatory index (SII) with prognosis and mortality in patients with hospitalized GFR (Glomerular filtration rate) <60 ml / min and a diagnosis of acute myocardial infarction (AMI). This study was designed as a retrospective cohort study. 235 myocardial infarction (MI) patients over the age of 18 and with GFR <60 ml / min, hospitalized in our hospital between January 01, 2016 and January 01, 2019, were included in the study. The patients were divided into 2 groups as survival and mortality group. The two groups were compared in terms of demographic characteristics, clinical laboratory data (symptoms, comorbidities, laboratory findings, GFR, coronary angiography, medications and complications). Platelet - lymphocyte ratio (PLR) was obtained by dividing platelet count to lymphocyte count. Systemic inflammatory index (SII) was found by multiplying neutrophil count and PLR value. The mean age of the survival group was 67.1±12,8 years. In the mortality group, the mean age was 69.55±11,1 years. PLR and SII levels were significantly higher in the mortality group compared to the survival group (p=0.002, p=0.029, respectively). According to the results of ROC analysis in mortality group patients, it was found that sensitivity 59.1% and specificity 70.4% for PLR (p=0.002); sensitivity 54.5% and specificity 60.9% for SII (p=0.029). The risk factors were found to be significantly associated with mortality in the regression analysis included PLR (β: 0.007, OR (95% CI): 1.007 (1.001-1.012), p=0.001) and SII (β: 0.001, OR (95% CI): 1.000 (0.999-1.001), p=0.041). PLR and SII were able to predict the mortality from myocardial infarction.

Key words: *Acute myocardial infarction, Mortality, Platelet - lymphocyte ratio, Systemic inflammatory index.*

[*]**Corresponding Author:** Serkan Karahan, Tel: +90 532 159 4401, E-mail: drserkankarahan@gmail.com, ORCID ID: 0000-0003-1203-7615.

Introduction

It is estimated that approximately 17.3 million people worldwide die of coronary heart disease (CHD) and stroke each year, and this figure will be reached to 23.3 million by 2030. CHD is one of the major causes of mortality and morbidity in developing countries (1). The results of the Heart Disease and Risk Factors in Turkish Adults (TEKHARF) study conducted by the Turkish Society of Cardiology between 1990 and 2008 reveal that approximately 2.8 million people in Turkey have CHD and 170 thousand people die from this cause every year (2). Acute coronary syndrome (ACS) is a term used to describe symptoms consistent with acute myocardial ischemia, including myocardial infarction (MI) and unstable angina. One- fourth of all ACSs are ST elevation myocardial infarction (STEMI), the remainder is unstable angina pectoris (USAP) or non-ST elevation myocardial infarction (NSTEMI) (3). In addition to clinical and electrocardiogram (ECG) findings, biochemical markers are important both in the diagnosis of ACS and in evaluating the prognosis (4).

While the peripheral neutrophil count increases in acute myocardial infarction, the lymphocyte count decreases. Considering some other hematological parameters, it has been shown that neutrophil-lymphocyte ratio (NLR) predicts cardiac events in stable coronary syndromes, mortality in ACS, and prosthetic valve thrombosis as an indicator of systemic inflammation. In recent years, it has been shown that the ratio of platelet counts to lymphocyte count (thrombocyte to lymphocyte ratio, TLO) and systemic inflammatory index (SII) can be an indicator of systemic inflammation and are closely related to prognosis in chronic inflammatory diseases and cardiovascular diseases (5-8).

In this study, we aimed to evaluate the relationship between the laboratory parameters of platelet volume / lymphocyte ratio (PLR) and systemic inflammatory index (SII) with prognosis and mortality in patients with hospitalized GFR (Glomerular filtration rate) <60 ml / min and a diagnosis of acute myocardial infarction (AMI).

Materials and methods

This study was designed as a retrospective cohort study. Before the study started, the study protocol was approved by local ethics committee of İstanbul Medipol University Clinical Research (Approval no: 05/04/2021, E-10840098-772.02-1598). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. 235 myocardial infarction (MI) patients over the age of 18 and with GFR <60 ml / min, hospitalized in our hospital between January 01, 2016 and January 01, 2019, were included in the study. The demographic characteristics of the patients, clinical data (symptoms, comorbidities, laboratory findings, GFR, coronary angiography, medications and complications that developed in the patients) were scanned.

The patients were divided into 2 groups as survival and mortality. The two groups were compared in terms of demographic characteristics, clinical data. Platelet - lymphocyte ratio (PLR) was found by dividing platelet count to lymphocyte count. Systemic inflammatory index (SII) was found by multiplying neutrophil count and PLR value.

Statistical Analysis

The data obtained in this study were

analyzed using SPSS v.25 (SPSS, Chicago, USA) statistical program. Descriptive statistics such as frequency distribution, mean and standard deviation were used to evaluate the data. The difference between the means of two independent groups was compared with the student's t test, and the differences between more than two groups were compared with the analysis of variance with the parametric test. Mann-Whitney U and Kruskal-Wallis tests, which are nonparametric alternatives of these tests, were used in cases where parametric test assumptions were not met. Categorical data were analyzed using the Chi-square or Fisher's Exact test. Values of $p < 0.05$ were considered statistically significant at 95% confidence interval.

Results

Comparison of laboratory and socio-demographic findings between the groups of patient and control was shown in table 1. The mean age of the survival group was 67.1±12,8 years. In the mortality group, the mean age was 69.55 ± 11.1 years. PLR and SII levels were significantly higher in the mortality group compared to the survival group (p=0.002, p=0.029, respectively). There wasn't any statistical significance between the groups in terms of gender, hospitalization duration, coronary artery disease, heart failure, STEMI, Non-STEMI, hypertension, hyperlipidemia, diabetes mellitus, smoking, nephropathy, medications (acetyl salicylic acid, beta blocker, statins, ACE inhibitors, clopidogrel, ticagrelor, GFR (ml / min), hemoglobin (g/dL), creatinine (mg/dL), neutrophils (109/L), lymphocytes (109/L), and platelet count (109/L) (Table 1).

ROC analysis results in patients with mortality are shown in Table 2. According to the results of ROC analysis in patients with mortality, sensitivity and specificity have been found 59.1% 70.4% respectively for PLR (p=0.002); sensitivity and specificity have been found 54.5% 60.9% respectively for SII (p=0.029) (Table 2, Fig. 1).

Multiple logistic regression analysis of factors associated with mortality is shown in table 3. The risk factors found to be significantly associated with mortality in the regression analysis included PLR (β: 0.007, OR (95% CI): 1.007 (1.001-1.012), p=0.001) and SII (β: 0.001, OR (95% CI): 1.000 (0.999-1.001), p=0.041) (Table 3).

Table 1: Socio-demographic features and clinical and laboratory parameters of the patients.

Parameters	**Survival (N=169, 71.9%)** Mean ± SD (min-max), n (%)	**Mortality (N=66, 28.1%)** Mean ± SD (min-max), n (%)	**p**
Age (year)	67.1 ± 12.8 (32-101)	69.55 ± 11.1 (46-100)	0.187
Gender			
Male	99 (58.6%)	40 (40.4%)	0.778
Female	70 (41.4%)	26 (59.6)	
Number of Days of Hospitalization	3.14 ± 1.8 (1.0-15.0)	3.11 ± 2.2 (1.0-13.0)	0.918
Coronary artery disease	57 (33.7%)	23 (34.8%)	0.872
Heart failure	24 (14.4%)	10 (15.2%)	0.880
STEMI	99 (58.6%)	33 (50.0%)	0.235
Non-STEMI	70 (41.4%)	33 (50.0%)	0.235
Hypertension	132 (78.1%)	47 (71.2%)	0.267
Hyperlipidemia	29 (17.2%)	11 (17.2%)	0.996*
Diabetes mellitus	63 (37.3%)	27 (40.9%)	0.609
Cigarette	32 (18.9%)	11 (16.7%)	0.682
Nephropathy	50 (29.6%)	16 (30.8%)	0.075*
Acetyl salicylic acid	167 (98.8%)	66 (100.0%))	0.377
Beta blocker	121 (71.6%)	47 (71.2%)	0.953*
Statins	137 (81.1%)	59 (89.4%)	0.124*
ACE inhibitors	81 (47.9%)	24 (36.4%)	0.110*
Clopidogrel	115 (68.0%)	46 (69.7%)	0.808
Ticagrelor	48 (28.4%)	20 (30.3%)	0.774
GFR (ml / min)	47.81 ± 14.3 (5.0-60.0)	46.47 ± 15.9 (5.0-60.0)	0.531
Hemoglobin (g/dL)	12.00 ± 2.4 (1.6-18.4)	11.63 ± 2.0 (6.9-16.7)	0.255
Creatinine (mg/dL)	1.55 ± 1.1 (0.8-10.0)	1.68 ± 1.3 (0.8-9.7)	0.434
Neutrophils (10^9/L)	7.89 ± 4.2 (0.2-24.0)	7.58 ± 3.0 (2.6-18.0)	0.600
Lymphocytes (10^9/L)	2.55 ± 2.8 (0.2-31.8)	2.00 ± 4.8 (0.3-12.3)	0.146
Platelet (10^9/L)	253.13 ± 76.7 (72.0-658.0)	267.83 ± 74.5 (133.0-490.0)	0.181*
PLR	144.33 ± 112.6 (9.7 ± 979.4)	216.61 ± 213.3 (25.0 ± 1531.0)	0.002*****
Systemic inflammatory index (SII)	1243.3 ± 1659.9 (4.20-17218.0)	1919.3 ± 2966.0 (200.20-22111.2)	0.029*****

*: Mann Whitney-U test used. STEMI: ST elevation myocardial infarction, ACE: Angiotensin converting enzyme, GFR: Glomerular filtration Rate, PLR: Platelet - lymphocyte ratio.

Table 2: ROC analysis results in patients with mortality

	Cut-off	**Sensitivity**	**Specifity**	**AUC (95% CI)**	**p**
PLR	>141.2	59.1%	70.4%	0.632 (0.549-0.716)	0.002
SII	>943.8	54.5%	60.9%	0.592 (0.508-0.676)	0.029

AUC: Area under the curve; PLR: Platelet- lymphocyte ratio; SII: Systemic inflammatory index.

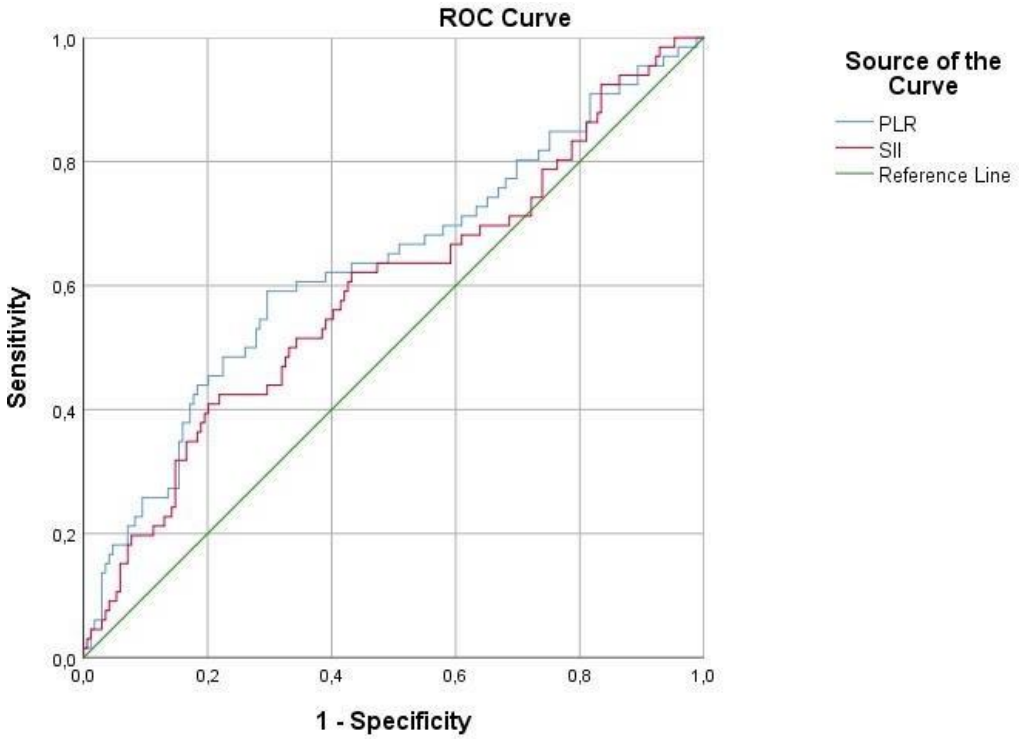

Figure 1: ROC analysis of PLR and SII.

Table 3: Multiple logistic regression analysis of factors used for mortality

	β	OR (95% CI)	p
PLR	0.007	1.007 (1.001-1.012)	**0.001**
SII	0.001	1.000 (0.999-1.001)	**0.041**

PLR: Platelet- lymphocyte ratio; SII: Systemic inflammatory index.

Discussion

In this study, the effects of retrospective clinical and laboratory data on mortality were evaluated in 235 myocardial infarction (MI) patients over 18 years of age and with GFR <60 ml / min, hospitalized in coronary intensive care unit. There was a significant relationship between the laboratory markers obtained, especially PLR and SII, and those who died from myocardial infarction. Myocardial infarction is a disease with significant morbidity and mortality. While 169 (71.9%) patients survived in our study, 66 (28.1%) patients died in the hospital. PLR and SII levels were statistically significantly higher in the mortality group compared to the survive group. The risk factors found to be significantly associated with mortality in the regression analysis included PLR and SII.

Increased inflammatory marker levels in the blood are associated with poor outcome in heart failure as in many chronic diseases. An increased inflammatory stimulus causes the secretion of many inflammatory cytokines. These inflammatory cytokines show detrimental effects on the myocardium, leading to decreased left ventricular function and thus heart failure (1, 4, 5, 7, 9). White blood cells and their subgroups are important

inflammatory markers in cardiovascular disease. High neutrophil levels indicate increased inflammatory response, while low lymphocyte count indicates poor general health and high physiological stress. Both low lymphocyte count and high neutrophil count are important risk factors in predicting reduced survival in patients with heart failure (1, 4, 6). In a study by Oylumlu et al., they reported that PLR was significantly higher in patients admitted with a diagnosis of acute ST-elevation myocardial infarction when compared with those who did not develop stent thrombosis. However, they also stated that PLR is an important and independent predictor of stent thrombosis in patients with acute STEMI (6).

There is a relationship between low lymphocyte counts and adverse outcomes in patients with chest pain, stable CAD, unstable angina, and congestive heart failure (26-28). The histological basis of this relative lymphopenia is due to the release of cortisol in response to the stress of myocardial ischemia (4, 10, 11). Similarly, ST has been associated with low lymphocyte counts in our study as well. The advantage of PLR is that it reflects both activated coagulation and inflammatory pathways, and so it may be superior to platelet or lymphocyte counts alone in predicting adverse outcomes such as ST. In a study by Luke et al. in 191 patients with cute Coronary Syndrom (ACS) and SCAD (Stable Coronary Artery Disease), PLR values were significantly higher in ACS than SCAD (12). In a study by Azab et al. in 619 patients with NSTEMI, higher PLR values were associated with increased long-term mortality in patients with non-ST segment elevation myocardial infarctions (13).

The roles of PLR and other complex markers of systemic inflammatory response have been primarily described in relation to the prognosis of ACS. It has been shown that PLR correlates with a greater overall mortality in patients with NSTEMI (13). In a study by Sun et al. in 5886 patients with STEMI, Higher PLR was associated with recurrent myocardial infarction, heart failure, ischemic stroke, and all-cause mortality in patients with STEMI (14). In our study, PLR levels were statistically significantly higher in the mortality group compared to the survive group. According to the results of ROC analysis in patients with mortality, sensitivity and specificity have been found 59.1% 70.4% respectively for PLR. However, the risk factors found to be significantly associated with mortality in the regression analysis included PLR (β: 0.007, OR (95% CI): 1.007 (1.001-1.012), p=0.001).

Chronic inflammation has been considered to have major contributions to several important diseases, including cancer, cardiovascular disease, diabetes and metabolic syndrome (4, 15-17). Hu et al. first reported on the use of the SII in hepatocellular carcinoma, and the index had significant associations with prognostic clinical outcomes, including vascular invasion, tumor size and early recurrence (18). Seo et al. first reported the predictive value of SII in patients with chronic heart failure and further extended the importance of SII to cardiovascular disease (19). In a study by Yang et al, the addition of SII to the clinical model was improved the predictive power for major cardiovascular events including AMI, chronic heart failure and cardiovascular death in patients with coronary artery disease. However, high SII is an independent prognostic marker of future

adverse events and increases the predictive value for adverse events among patients with coronary artery Disease (7). In our study, SII levels were statistically significantly higher in the mortality group compared to the survive group. According to the results of ROC analysis, in patients with mortality, sensitivity 54.5% and specificity 60.9% for SII. However, the risk factors found to be significantly associated with mortality in the regression analysis included SII (β: 0.001, OR (95% CI): 1.000 (0.999-1.001), p=0.041).

Limitations of Study

The study has some limitations. Our study was designed as an observational, retrospective and single center study. In addition, periodic repetition of PLR and SII measurements will likely affect results. We did not compare PLR and SII with other markers used in myocardial infarction. Moreover, multi-center and prospective studies should be planned to support these preliminary results. Compared to other studies in the literature, the strengths of our study, our sample was larger and our results were supported by logistic regression analysis.

Conclusion

As inexpensive and easily available new inflammatory markers, PLR and SII were significantly higher in patients with GFR <60 ml / min and died from myocardial infarction (MI). In addition, PLR and SII were able to predict the mortality from myocardial infarction. However, PLR levels can predict hemodynamically severe coronary obstruction better than SII. The utility of this new marker warrants to be investigated in various cardiac situations. Large-scale, prospective, and multicenter studies will be necessary to clarify the relationship between PLR, SII and Myocardial infarction.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgment

Authorship Contributions: Idea/Concept and design; SK, EO, control/supervision; SK, EO, data collection and/or processing; SK, EO, analysis and/or interpretation; SK, literature review; SK, EO, writing the article; SK, EO, critical reviewing; SK, EO. There are no funding sources.

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