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The relationship between platelet indices and residual SYNTAX score in patients with ST-segment elevation myocardial infarction

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ABSTRACT

Objectives: We aimed to investigate the relationship between thrombocyte indices, which have previously been proven to be associated with many cardiovascular diseases and adverse events, and residual SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) score (rSS) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: Our study included 534 patients who underwent primary percutaneous coronary intervention (PCI) for STEMI between January 2018 and June 2021. In our study, only patients who underwent infarct-related coronary artery revascularization in the index procedure were evaluated. First of all, patients were compared into two groups low rSS (rSS ≤ 8) and high rSS (rSS > 8). Our definition of platelet indices includes mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (Pct), MPV to platelet ratio (MPVPR), platelet to lymphocyte ratio (PLR), and MPV to lymphocyte ratio (MPVLR).

Results: The mean age of the study patients was 56.4 ± 10.3 years and 78.8% were male. The high rSS group had higher C-reactive protein, lower lymphocyte count, and significantly higher platelet indices other than PLR and MPV. Among the platelet indices, MPVLR was found to have the best correlation with rSS (r: 0.398, $p < 0.001$). MPVLR (AUC: 0.820, 95% CI: 0.701-0.899) was determined as the best diagnostic power index with 5.08 cut-off value in predicting high rSS with 88% sensitivity and 76% specificity (Youden index: 0.64). Age, right coronary artery involvement as culprit lesion, ejection fraction, diabetes mellitus, and MPVLR (OR: 5.966 [2.489-8.413], $p < 0.001$) and PDW were identified as independent risk factors for predicting high rSS.

Conclusions: In conclusion, increased MPVLR is associated with high rSS in STEMI patients. There is a significant positive correlation between MPVLR and rSS. MPVLR is an independent predictor of high rSS.

Keywords: Coronary artery disease severity, incomplete revascularization, mean platelet volume to lymphocyte ratio, platelet distribution width, residual SYNTAX score

Worldwide, ischemic heart disease is the most common cause of death and its incidence is increasing. Ischemic heart disease is the cause of about 20% of all deaths in Europe, although there is great variation between countries. ST-segment elevation myocardial infarction (STEMI) is a subgroup of ischemic heart disease with a high mortality and morbidity rate, and a clinical and hemodynamic response can be achieved dramatically with primary percutaneous coronary intervention (PCI)-based revascularization [1, 2]. Multi-vessel coronary artery disease occurs in 40–65% of STEMI patients undergoing pri-

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mary PCI and is associated with adverse prognosis [3]. Multi-vessel disease, complex coronary anatomies, and the approach of artery revascularization responsible for isolated infarcts can cause incomplete revascularization.

The extent of coronary artery disease after infarct-related coronary artery PCI, or in other words, incomplete revascularization, can be evaluated with the residual SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) score. The ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) study identified that a high residual SYNTAX score (rSS > 8) is associated with major adverse cardiovascular events (MACE) and poor prognosis in patients with moderate-to-high risk acute coronary syndrome (ACS) [4]. It has also been proven that rSS is an independent predictor of MACE and mortality in STEMI patients [5].

Inflammation and thrombosis are two major mechanisms that play an important role in different stages of atherosclerotic plaque formation, progression, rupture, and thrombosis [6]. Platelet activation plays an important role in the formation and progression of atherosclerosis and thrombus formation on ruptured atherosclerotic plaques [7]. Therefore, it has been suggested that platelet dysfunction is an important factor in the pathogenesis of STEMI [8]. Platelet volume indices; Mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (Pct), and mean platelet volume to platelet ratio (MPVPR) are simple indices that express platelet activity and can be obtained in routine complete blood count tests [9]. The increase in mean platelet volume (MPV) is also an indicator of an increase in platelet activity and aggregation tendency [10]. A relationship between MPV and coronary artery disease has been demonstrated by previous studies [11]. PDW refers to platelet activity as a measure of circulating platelet size variation [12]. Increased PDW values indicate anisocytosis and are associated with increased thrombosis propensity and severity of coronary artery disease in ACS patients [13]. Pct is a measure of total platelet mass. Increased Pct values are associated with major adverse cardiac and cerebrovascular events [14]. Lymphocytes are the earliest cell type involved in the formation of atherosclerotic plaque. A decrease in their number is an indicator of the inflammatory response and contributes to plaque unstabilization. In the inflammatory phase of thrombosis, platelets are accompanied by lymphocytes [6, 15, 16].

Unlike platelet volume indices, platelet to lymphocyte ratio (PLR) and MPV to lymphocyte ratio (MPVLR), which are indices that can evaluate thrombosis and inflammation together, have been shown to have prognostic importance in ACS patients [17, 18]. There is insufficient evidence to show the relationship between rSS, which is a measure of incomplete revascularization, and these platelet indices, which can affect the extent of coronary artery disease. In this study, we aimed to investigate the relationship between rSS and platelet indices and to determine the index with the highest diagnostic power for high rSS prediction.

METHODS

Study Population

In our study, patients who underwent primary PCI for STEMI between January 2018 and June 2021 were retrospectively screened. In the index procedure, only culprit lesion revascularization was our prerequisite, so those who underwent multivessel revascularization in the same procedure, those who were given medical follow-up after their diagnostic angiography, or those who decided to undergo coronary bypass graft surgery (CABG) were excluded from the study. Patients with a previous history of PCI or CABG, those with hematologic/autoimmune/infectious or inflammatory diseases, advanced renal or hepatic disease, a history of malignancy, or those receiving immunosuppressive therapy were excluded from the study. As a result, 534 patients were included in our study. Our study was carried out in accordance with the principles of the Declaration of Helsinki, with the decision of the local ethics committee numbered 2022/126.

The diagnosis of STEMI was determined in accordance with the 2017 European Society of Cardiology (ESC) recommendations, in the presence of characteristic symptoms and signs of myocardial ischemia, by detecting ST segment elevation in at least 2 consecutive electrocardiographic leads consistent with coronary anatomical localization [1]. In patients with multivessel disease who had only culprit lesion revascularization, non-infarct coronary revascularization was planned to be performed before discharge or under elective conditions, depending on the patients'

anginal complaints and hemodynamic status.

Patient Characteristics

Demographic and clinical parameters at admission were recorded from the hospital database. All blood samples were collected before patients underwent coronary angiography. In biochemical analyzes: total cholesterol, low-density lipoprotein cholesterol (LDL-C) (calculated with the Friedewald equation), high-density lipoprotein cholesterol (HDL-C), triglyceride, creatinine, glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP) and albumin results were evaluated. Hematological data included hemoglobin, leukocyte, lymphocyte, thrombocyte, PDW, and MPV measurements. Platelet indices were calculated from these hemogram data. Definition of platelet indices: MPV, PDW, plateletcrit (Pct: platelet count × MPV / 10,000), mean platelet volume to platelet ratio (MPVPR: MPV / platelet count x 100), platelet to lymphocyte ratio (PLR: Platelet count / lymphocyte count) and mean platelet volume to lymphocyte ratio (MPVLR: MPV / lymphocyte count). Echocardiography measurements were performed immediately after performing PCI during hospitalization at the coronary intensive care unit.

Coronary Angiographic Evaluation

Coronary angiography was performed via femoral or radial access for each patient within 90 minutes of admission. Two independent, interventional cardiologists blinded to patient clinical data individually evaluated coronary angiographic images to calculate coronary artery disease severity [19]. Firstly, the SYNTAX score I was calculated using the online SYNTAX score calculator (http://www.syntaxscore.com, version 2.1). for each patient. The rSS was calculated based on the remaining coronary artery lesions after performing PCI for the infarct-related coronary artery. Coronary arteries were evaluated as 16 distinct segments, and segments with luminal stenosis of 50% or more and > 1.5 mm in diameter were evaluated. An rSS >8 was considered a high rSS [4].

Study patients were primarily evaluated as two groups according to the calculated rSS levels: Low rSS (rSS ≤ 8) and high rSS (rSS > 8). According to the MPVLR index cut-off value, which was determined to be the best predictor of incomplete revascularization expressed with high rSS, the study patients were again formed into two groups and compared in terms of their angiographic data: Low MPVLR (MPVLR ≤ 5.08) and high MPVLR (MPVLR > 5.08).

Statistical Analysis

Statistical analyses were performed using SPSS 21 for Windows (SPSS Inc., Chicago, IL). The conformity of the data to the normal distribution was determined by the Kolmogorov-Smirnov test. Continuous data are presented as mean ± standard deviation (SD) for variables with normal distribution and as median (25th-75th percentiles) for variables without normal distribution. The independent sample t-test was used for comparing quantitative variables with normal distribution, while the Mann-Whitney U test was used for comparing the means between groups without normal distribution. Categorical data are presented as "number (%)" and were compared using Pearson's χ^2 test or Fisher's exact test. Spearman analysis was used to evaluate the correlation between rSS and platelet indices. Univariate and multivariate logistic regression analyses were used to evaluate independent risk factors for a high rSS. Receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal platelet indices values to indicate high rSS in terms of both sensitivity and specificity. Intra-observer and inter-observer agreements for 2 cardiologists were calculated using Cohen's kappa coefficient. *P* value < 0.05 was considered statistically significant.

RESULTS

Our study included 534 patients who underwent primary PCI for ST-segment elevation myocardial infarction. The mean age of the patients was 56.4 ± 10.3 years, and 78.8% (n = 421) were men. Our study patients were evaluated into two groups 'low rSS' with rSS ≤ 8 and 'high rSS' with rSS > 8. The mean age of the patients in the high rSS group was significantly higher than that of the low rSS group (58.3 ± 10.3 years vs 55.8 ± 10.2 years, $p = 0.032$). Gender distribution was dominant in terms of the male gender in both groups, but there was no significant difference between the groups. There was no significant difference in terms of BMI, and systolic and diastolic blood

Table 1. Baseline clinical, demographic and laboratory characteristics of the study population

	All patients (n = 534)	Low rSS (n = 397)	High rSS (n = 137)	*p* value
Age (years)	56.4 ± 10.3	55.8 ± 10.2	58.3 ± 10.3	**0.032**
Gender (male), n (%)	421 (78.8)	312 (78.5)	109 (79.5)	0.101
BMI (kg/m^2)	25.6 ± 3.6	25.9 ± 3.8	25.2 ± 4.4	0.233
Heart rate (BPM)	79.2 ± 15.8	78.4 ± 15.1	79.8 ± 14.7	0.101
SBP (mmHg)	121.2 ± 21.4	123.2 ± 21.2	121.3 ± 20.6	0.216
DBP (mmHg)	79.0 ± 12.3	78.7 ± 11.5	78.4 ± 11.4	0.289
Hypertension, n (%)	219 (41)	160 (40.3)	59 (43.1)	0.390
DM, n (%)	91 (17)	67 (16.8)	24 (17.5)	0.603
PAD, n (%)	21 (3.9)	15 (3.7)	6 (4.3)	0.087
Hyperlipidemia, n (%)	379 (70.9)	280 (70.5)	99 (72.2)	0.581
Smoking, n (%)	278 (52)	206 (51.8)	72 (52.5)	0.263
Total cholesterol (mg/dL)	178.7 ± 39.7	178.1 ± 40.8	180.2 ± 40.4	0.408
LDL-C (mg/dL)	105.9 ± 36.1	104.2 ± 36.7	110.2 ± 35.1	**0.009**
HDL-C (mg/dL)	43.2 ± 11.8	42.6 ± 11.6	42.9 ± 11.9	0.355
Triglycerides (mg/dL)	145.1 (95.7 - 245.3)	146.8 (93.1 - 241.2)	142.6 (97.3 - 249.1)	**0.021**
Creatinine (mg/dL)	0.92 ± 0.22	0.91 ± 0.19	0.92 ± 0.21	0.134
Glucose (mg/dL)	117.5 ± 26.1	119.4 ± 25.9	116.5 ± 25.8	0.188
ALT (U/L)	22.1 (17.1 - 31.5)	21.5 (15.5 - 27.2)	22.1 (16.3 - 28.2)	0.097
AST (U/L)	26.4 (20.2 - 32.6)	27.2 (21.8- 32.7)	26.3 (20.1- 33.5)	0.128
CRP (mg/L)	4.4 (1.83 - 9.24)	3.8 (2.45 - 11.8)	6.9 (2.75 - 12.7)	**0.006**
Albumin (g/dL)	3.76 (1.71- 6.76)	3.61 (1.56 - 5.77)	3.87 (1.84 - 6.96)	0.111
Hemoglobin (g/dL)	14.5 (13.5 -15.8)	14.4 (13.3 - 15.4)	14.7 (13.7 - 15.8)	0.094
Leukocytes x10^3/mm^3	11.4 (9.3 - 13.6)	9.8 (8.8 - 11.9)	12.9 (10.1 - 16.6)	**< 0.001**
Lymphocyte x10^9/L	2.56 ± 0.51	3.72 (2.67 - 5.18)	1.72 (1.54 - 2.61)	**0.006**
Platelets x10^3/mm^3	219.5 (174.3 – 261)	218.2 (170 - 254.6)	222.7 (185.6 - 270.2)	0.075
PLR	163.23 ± 35.48	161.44 ± 32.24	165.12 ± 35.48	0.121
MPV (fL)	10.37 ± 1.63	10.23 ± 1.69	10.59 ± 1.59	0.091
MPVLR	3.58 ± 1.52	3.27 ± 1.32	5,66 ± 2.15	**< 0.001**
MPVPR	4.44 ± 1.61	3.21 ± 1.43	5,52 ± 2.06	**< 0.001**
Pct (%)	0.246 ± 0.72	0.217 ± 0.082	0.264 ± 0.064	**0.003**
PDW (%)	14.3 ± 2.9	12.36 ±2.72	17.38 ±2.94	**0.005**
β-blocker	64 (11.9)	47 (11.8)	17 (12.4)	0.096
Calcium channel blocker	85 (15.9)	62 (15.6)	23 (16.7)	0.421
ACEI	59 (11)	45 (11.3)	14 (10.2)	0.313
ARB	74 (13.8)	55 (13.8)	19 (13.8)	0.524
Statin	144 (26.9)	105 (26.4)	39 (28.4)	0.362

rSS = Residual SYNTAX score, BMI = Body mass index, BPM = Beats per minute, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, DM = Diabetes mellitus, PAD = Peripheral arterial disease, LDL-C = Low-density lipoprotein cholesterol, HDL-C = High-density lipoprotein cholesterol, ALT = Alanine aminotransferase, AST = Aspartate aminotransferase, CRP = C-reactive protein, PLR = Platelet to lymphocyte ratio, MPV = Mean platelet volume, MPVLR = Mean platelet volume to lymphocyte ratio, MPVPR = Mean platelet volume to platelet ratio, Pct = Plateletcrit, PDW = Platelet distribution width, ACEI = Angiotensin-converting enzyme inhibitor; ARB = Angiotensin receptor blocker

pressures. Risk factors such as hypertension, diabetes mellitus (DM), peripheral arterial disease (PAD), hyperlipidemia, and smoking did not differ significantly between the groups. While no difference was found in total cholesterol and HDL cholesterol, it was found that LDL cholesterol was significantly higher in the high rSS group (110.2 ± 35.1 mg/dL vs 104.2 ± 36.7 mg/dL, $p = 0.009$) and triglyceride level was significantly higher in the low rSS group [146.8 (93.1 - 241.2) mg/dL vs 142.6 (97.3 - 249.1) mg/dL, $p = 0.021$]. While there was no significant difference between the groups in other biochemical parameters, it was observed that the CRP level was higher in the high rSS group [6.9 (2.75 - 12.7) mg/L vs 3.8 (2.45 - 111.8) mg/L, $p = 0.006$]. From the hemogram data, hemoglobin and platelet counts did not differ significantly between the groups, and the leukocyte counts in the high rSS group [12.9 (10.1-16.6) ×103/mm3 vs 9.8 (8.8 - 11.9) ×103/mm3, $p < 0.001$] and the lymphocyte count in the low rSS group [3.72 (2.67 - 5.18) ×109/L vs 1.72 (1.54 - 2.61) ×109/L, $p = 0.006$] were found to be significantly higher. There was no significant difference in the medical treatments of the study patients before the index procedure. Baseline clinical, demographic, and laboratory data of our study patients and rSS groups are presented in Table 1.

The distribution of hemogram data and rates, which we define as platelet indices, between the groups is as follows: (i) Although numerical superiority in PLR and MPV is observed in the High rSS group, the difference between the groups is not statistically significant. (ii) MPVLR ($p < 0.001$), MPVPR ($p < 0.001$), Pct ($p = 0.003$) and PDW ($p = 0.005$) were observed to be significantly higher in the high rSS group. Platelet indices data distribution is presented numerically in Table 1 and graphically in Fig. 1.

MPVLR, MPVPR, Pct, and PDW seem to be ahead of other platelet indices in our search for the most appropriate platelet index for the prediction of the high level of rSS (> 8), due to their different distributions among the rSS groups and the correlation relationships detected with rSS. The diagnostic power of thrombocyte indices in predicting high rSS was tested by ROC analysis. According to the analysis results, it was found that the platelet indices MPVLR [Area under the curve (AUC): 0.820], Pct (AUC: 0.712), and PDW (AUC: 0.754) had a significant diagnostic value for the prediction of high rSS (for each $p < 0.001$). MPVLR was determined as the index with the best diagnostic power in predicting high rSS with a cut-off value of 5.08, sensitivity of 88% and specificity of 76% (Youden index: 0.64). Platelet indices

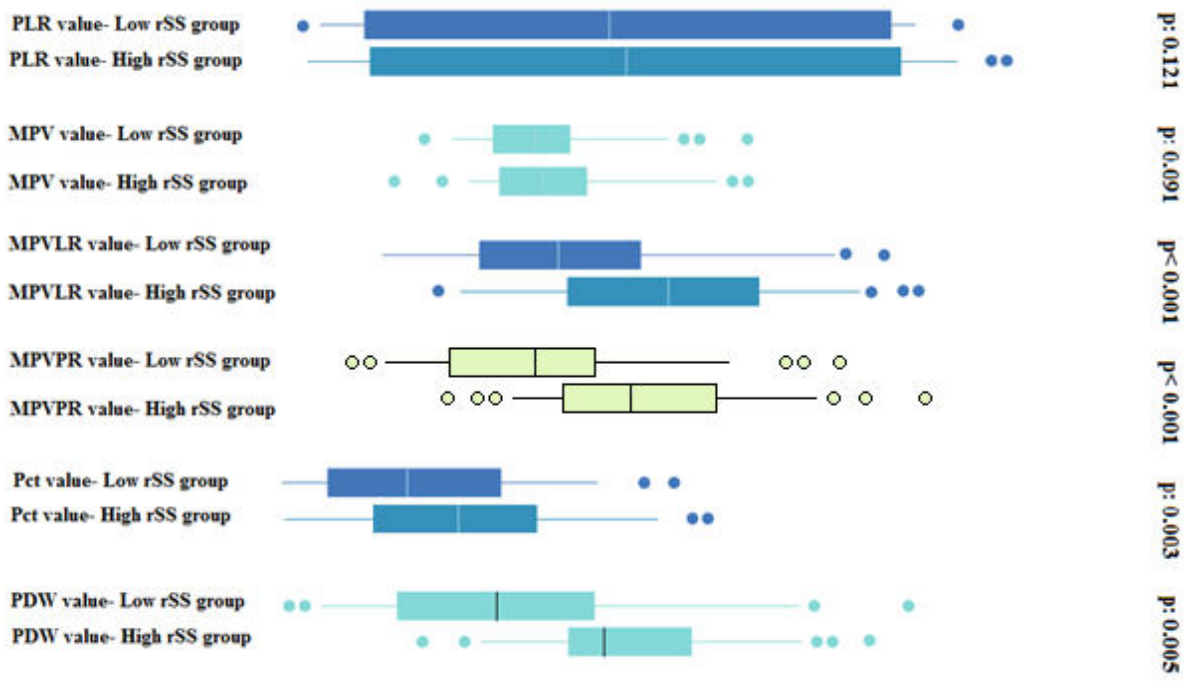
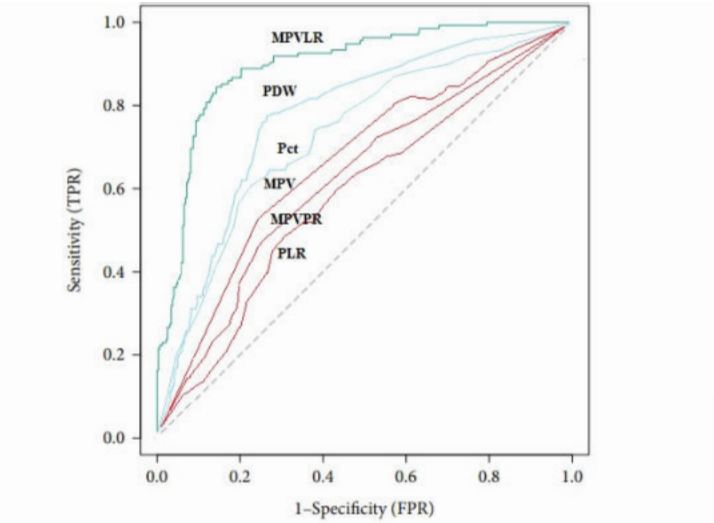


Fig. 1. Platelet indices values of patients with low and high rSS. PLR = Platelet to lymphocyte ratio, MPV = Mean platelet volume, MPVLR = Mean platelet volume to lymphocyte ratio, MPVPR = Mean platelet volume to platelet ratio, Pct = Plateletcrit, PDW = Platelet distribution width.

Table 2. Baseline echocardiographic and angiographic characteristics of the study population

	All patients (n = 534)	Low MPVLR (n = 321)	High MPVLR (n = 213)	*p* value
LVEF (%)	53.4 ± 6.9	54.8 ± 6.1	53.6 ± 6.5	0.129
Culprit vessel, n (%)				
LAD	254 (47.6)	170 (52.9)	84 (39.4)	**< 0.001**
CXA	164 (30.7)	94 (29.3)	70 (32.9)	
RCA	116 (21.7)	57 (17.8)	59 (27.7)	
Coronary artery lesions, n (%)				
SVD	231 (43.2)	154 (48)	77 (36.2)	**< 0.001**
DVD	175 (32.8)	103 (32.1)	72 (33.8)	
TVD	128 (24)	64 (19.9)	64 (30)	
SYNTAX score	16.1 (10.6 - 21.6)	15.5 (10.1- 22.2)	17.1 (11.1 - 24)	**0.003**
SYNTAX score group, n (%)				
Low (≤ 22)	360 (67.4)	250 (77.9)	110 (51.6)	**< 0.001**
Moderate-High (> 22)	174 (32.6)	71 (22.1)	103 (48.4)	
rSS	3.4 (0 - 7.9)	4.4 (2.6 - 8.1)	6.15 (3.6 - 9.6)	**< 0.001**

MPVLR = Mean platelet volume to lymphocyte ratio, LVEF = Left ventricular ejection fraction, LAD = Left anterior descending, CXA = Circumflex artery, RCA = Right coronary artery, SVD = Single-vessel disease, DVD = Double-vessel disease, TVD = Triple-vessel disease, SYNTAX = SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery, rSS = Residual SYNTAX score



Variables	Cut-off value	AUC	95% CI	Youden Index	*p* value
PLR	162.12	0.602	0.524 - 0.706	0.52	0.164
MPV	10.41	0.644	0.542 - 0.714	0.54	0.244
MPVLR	5.08	0.820	0.701 - 0.899	0.64	**< 0.001**
MPVPR	4.64	0.628	0.520 - 0.726	0.52	0.256
Pct	0.236	0.712	0.623 - 0.807	0.59	**< 0.001**
PDW	15.6	0.754	0.601 - 0.812	0.58	**< 0.001**

Fig. 2. Receiver operating characteristic curve showing the optimal values of platelet indices for a high rSS prediction. AUC = Area under the curve, CI = Confidence interval, PLR = Platelet to lymphocyte ratio, MPV = Mean platelet volume, MPVLR = Mean platelet volume to lymphocyte ratio, MPVPR = Mean platelet volume to platelet ratio, Pct = Plateletcrit, PDW = Platelet distribution width.

Table 3. Correlation between rSS and clinical variables

	Correlation coefficient	*p* value
Age	0.204	**0.012**
LDL-C	0.096	0.356
Triglycerides	-0.124	0.402
CRP	0.234	**0.009**
Leukocytes	0.145	0.224
Lymphocyte	-0.201	0.102
Platelets	0.087	0.508
PLR	0.230	0.078
MPV	0.198	0.184
MPVLR	0.398	**< 0.001**
MPVPR	0.240	**0.024**
Pct	0.286	**0.008**
PDW	0.292	**< 0.001**

LDL-C = Low-density lipoprotein cholesterol, CRP = C-reactive protein, PLR = Platelet to lymphocyte ratio, MPV = Mean platelet volume, MPVLR = Mean platelet volume to lymphocyte ratio, MPVPR = Mean platelet volume to platelet ratio, Pct = Plateletcrit, PDW = Platelet distribution width

ROC analysis details are presented in Fig. 2.

Study patients were divided into two subgroups according to the determined MPVLR cut-off value: 'low MPVLR' with MPVLR ≤ 5.08 and 'high MPVLR' with MPVLR > 5.08. Baseline echocardiographic and angiographic measurements of study patients were evaluated comparatively between MPVLR subgroups (Table 2). The mean ejection fraction (EF) of the study patients was 53.4 ± 6.9 %, and there was no significant difference between the 'low' and 'high MPVLR' groups. It was observed that LAD was involved at a rate of 47.6% as the culprit coronary artery. LAD involvement was found to be higher in the low MPVLR subgroup. It was found that RCA involvement was 21.7%, and the high MPVLR subgroup had a significantly higher rate of involvement. While single-vessel involvement was observed more frequently in the low MPVLR subgroup, three-vessel involvement was observed more frequently in the high MPVLR subgroup ($p < 0.001$). The SYNTAX score was found to be 17.1 (11.1 - 24) in the high MPVLR group and 15.5 (10.1 - 22.2) in the low MPVLR group ($p = 0.003$). When SYNTAX score ≤ 22 was grouped as low SYNTAX and SYNTAX score >22 as moderate-high SYNTAX: It was found that 67.4% of the study patients were in the low SYNTAX group and patients in the low MPVLR group were significantly higher in the low SYNTAX group ($p < 0.001$). It was determined that the patients in the high MPVLR group had a higher rate in the moderate-high SYNTAX group ($p < 0.001$). rSS was found to be significantly higher in the high MPVLR subgroup compared to the low MPVLR group [6.15 (3.6 - 9.6) vs 4.4 (2.6 - 8.1), $p < 0.001$]. The residual SYNTAX score and correlation analysis of clinical variables are presented in Table 3. It was observed that age and CRP had a significant positive correlation with rSS. Although they were significantly different between the residual SS groups, LDL, triglyceride, leukocyte, and lymphocyte levels were not found to be significantly correlated with rSS. The correlation between hemogram data and rates, which we define as platelet indices, and rSS is as follows: (i) PLR and MPV did not make a significant difference between the rSS groups, nor did it show a significant correlation with rSS. (ii) MPVLR (r: 0.398, $p < 0.001$), MPVPR (r: 0.240, $p = 0.008$), Pct (r: 0.286, $p = 0.008$) and PDW (r: 0.292, $p < 0.001$) had a significant positive correlation with rSS.

Logistic regression analysis was performed to identify independent risk factors in the prediction of high rSS and to compare these effects of platelet indices (Table 4). From clinical and demographic factors: Age [OR: 1.298, 95% CI: 1.013 - 1.796, $p = 0.002$], Culprit vessel: RCA involvement [OR: 2.210, 95% CI: 1.594 - 4.223, $p < 0.001$], EF [OR: 1.066, 95% CI: 0.903 -1.190, $p = 0.015$] and DM [OR: 1.640, 95% CI: 1.138 - 3.136, $p = 0.009$] were defined as independent risk factors for high rSS. Among the platelet indices: MPVLR [OR: 5.966, 95% CI: 2.489 - 8.413, $p < 0.001$] and PDW [OR: 2.540, 95% CI: 1.318 - 3.236, $p = 0.009$] were detected as independent risk factors for high rSS.

Intra-observer and inter-observer agreements for SYNTAX score (SS) and rSS measurements were calculated [Intra-observer agreement: kappa coefficient ($\varkappa$) for SS measurement: 0.85 ($p = 0.013$) (for ZYG) and 0.87 ($p = 0.024$) (for AK) and $\varkappa$ for rSS measurement: 0.82 ($p = 0.005$) (for ZYG) and 0.85 ($p = 0.011$)

Table 4. Univariate and multivariate logistic regression analyses for independent predictors of high residual SYNTAX score

	Univariate analysis			Multivariate analysis		
	Odds ratio	**95% CI**	***p* value**	**Odds ratio**	**95% CI**	***p* value**
Gender (male)	1.513	1.027 - 2.785	0.042	1.107	0.692 - 2.011	0.484
Age	1.068	1.012 - 1.126	0.008	1.298	1.013 - 1.796	**0.002**
Culprit vessel: RCA	2.161	1.344 - 3.162	< 0.001	2.210	1.594 - 4.223	**< 0.001**
EF	0.997	0.857 - 1.498	0.022	1.066	0.903 - 1.190	**0.015**
Smoking	1.566	1.112 - 2.282	0.004	1.056	0.756 - 1.583	0.447
Hypertension	1.898	1.388 - 2.841	0.021	1.377	0.873 - 2.422	0.076
DM	2.124	1.418 - 3.586	< 0.001	1.640	1.138 - 3.136	**0.009**
Albumin	0.984	0.802 - 1.309	0.365			
Hemoglobin	0.962	0.753 - 0.998	0.031	1.098	0.862 - 1.438	0.863
Leukocytes	0.998	0.844 - 1.303	0.208			
Platelets	1.043	0.894 - 1.172	0.182			
Platelet indices						
MPVLR	4.102	2.428 - 6.552	< 0.001	5.966	2.489 - 8.413	**< 0.001**
PDW	3.214	1.148 - 3.856	< 0.001	2.540	1.318 - 3.236	**0.009**
Pct	2.142	1.481 - 3.568	< 0.001	1.340	1.183 - 3.163	0.079
MPV	0.989	0.831 - 1.330	0.282			
MPVPR	0.976	0.735 - 0.989	0.013	1.089	0.826 - 1.484	0.836
PLR	0.968	0.824 - 1.283	0.249			

CI = Confidence interval, RCA = Right coronary artery, EF = Ejection fraction, DM: Diabetes mellitus, MPVLR = Mean platelet volume to lymphocyte ratio, PDW = Platelet distribution width, Pct = Plateletcrit, MPV = Mean platelet volume, MPVPR = Mean platelet volume to platelet ratio, PLR = Platelet to lymphocyte ratio

(for AK); Inter-observer agreement (between ZYG and AK): ϰ for SS measurement: 0.84 ($p = 0.021$) and ϰ for rSS measurement: 0.79 ($p = 0.017$)].

DISCUSSION

In this study, in which we examined the relationship between platelet indices and rSS, MPVLR and PDW were defined as independent predictors of high rSS. We found that MPVLR was the index with the best correlation with rSS and the best diagnostic power for rSS prediction.

Platelet activation plays an important role in the formation and progression of atherosclerotic plaques and thrombus formation when these plaques rupture [7, 20]. An increase in MPV is one of the indicators of increased activation and aggregation of platelets [10]. In a well-designed study conducted at the cellular level, larger platelets were shown to be more metabolically and enzymatically active [21]. Platelets with increased size and metabolic activity can accelerate the thrombosis and inflammatory response. The formation of ACS is facilitated and its course is adversely affected due to more active platelets. Previous studies have shown that MPV is associated with mortality and MACE in patients with myocardial infarction with and without ST-segment elevation [8, 22]. Inflammation and thrombosis mechanisms are involved in the formation and destabilization of atherosclerotic plaque, its rupture, and finally thrombosis [6, 23]. Platelets are accompanied by lymphocytes in thrombosis formation [15]. Lymphocytes are one of the most important cell types that play a role in the formation of atherosclerotic lesions, and their number decreases as a result of the increased inflammatory response [16]. Inflamma-

tory responses cause lymphopenia due to increased lymphocyte apoptosis as a result of stress-induced cortisol secretion associated with ACS [24, 25]. This reduction is one of the indicators of growth, destabilization, and rupture of atherosclerotic plaques. The lower the lymphocyte count, the more unstable the plaque [26]. In other words, the increase in MPV and the decrease in the number of lymphocytes indicate that a suitable environment is ready for the formation of atherosclerotic lesions. MPV and lymphocyte count are included in routine hemogram data. MPVLR, which shows the MPV / lymphocyte count, is an index that can be easily calculated from routine hemogram data and can show the thrombosis and inflammation responses alone [27]. In a study by Hudzik *et al*. [28]; MPVLR was found to be an independent predictor of mortality, no-reflow, and MACE in ST-segment elevation myocardial infarction patients.

The prevalence of multivessel coronary artery disease in STEMI patients undergoing PCI is approximately 40-65%. As the number of diseased vessels increases, the risk of cardiac death and MACE also increases [3, 29]. The optimal management of residual stenoses after infarct-related artery reperfusion in STEMI patients remains a matter of debate [30]. rSS indicates residual coronary atherosclerotic load after PCI. The prognostic value of rSS was investigated for the first time in the ACUITY study, and high rSS (> 8) was found to be a strong predictor of 1-year mortality, cardiac mortality, unplanned revascularization, and MACE [4]. Loutfi *et al*. [31] showed significant reductions in 1-year MACE in STEMI patients with lower rSS. Burgess *et al*. [5] reported the rates of cardiac death and myocardial infarction (MI) at follow-up as 5%, 15%, and 26% for MVD and STEMI patients with rSS of 0, 1-8, and > 8, respectively. Significantly higher rates of cardiac mortality and MI were found in the group with rSS > 8. Braga *et al*. [32] found that rSS was positively correlated with all-cause mortality and MACE in patients who underwent primary PCI for STEMI and were found to have MVD. rSS has also been identified as an independent predictor of these outcomes during follow-up.

PDW refers to platelet activity as a measure of circulating platelet size variation [12]. Elevated PDW values indicate anisocytosis, indicating increased platelet activity, which is associated with an increased propensity for thrombosis and severity of coronary artery disease in ACS patients [13]. In our study, PDW was higher in the high rSS group and was found to be an independent predictor of high rSS.

DM is closely associated with cardiovascular diseases, and it has been shown that the risk of coronary artery disease increases 2 to 4 times in patients with DM [33]. The addition of DM to existing risk factors leads to increased severity of coronary artery disease and the number of diseased vessels is high in these patients [34]. Our results support this situation and rSS was found to be higher in patients with DM.

The first variable that comes to mind when atherosclerosis is mentioned is advanced age. As age increases, the presence and prevalence of atherosclerotic disease increases. In addition, the frequency of diabetes, hypertension, and hyperlipidemia increases with age. The most common cause of death in the elderly is cardiovascular diseases caused by atherosclerotic changes. As expected, the mean age was higher in the high rSS group, as seen in our study [4, 35].

Ischemic heart disease is one of the most important causes of EF decrease, and as the number of diseased vessels increases, EF is expected to decrease [36]. As previously shown [37], low EF is one of the independent predictors of high rSS in our study as well.

To the best of our knowledge, this is the first study to examine the relationship between MPVLR and rSS. In our study, we demonstrated a positive correlation between MPVLR and the degree and complexity of residual coronary stenosis in patients with STEMI after PCI. We found that higher MPVLR levels were more common in STEMI patients with high rSS and that increased MPVLR levels independently predicted high rSS.

Limitations

In this retrospective study, the relatively small sample size and absence of a control group are our main limitations. In addition, it is difficult to make a causal inference, since we examined the relationship between platelet indices and rSS cross-sectionally. The effect of increased MPVLR on short- and long-term cardiovascular events has not been evaluated; therefore, we cannot comment on the prognostic effects of our results. This was a retrospective single-center analysis with no potential to avoid selection bias. Even

after the adjusted analysis, some confounding factors may have affected the results.

CONCLUSION

In conclusion, increased MPVLR is associated with higher rSS in STEMI patients. There is a significant positive correlation between MPVLR and rSS. MPVLR is an independent predictor of high rSS. With our results, we can suggest that MPVLR may be a valuable and easily applicable biomarker that can provide additional information in the risk stratification of patients with STEMI after PCI.

Authors' Contribution

Study Conception: EY, SÇ; Study Design: EY, SÇ; Supervision: EY, SÇ; Funding: N/A; Materials: N/A; Data Collection and/or Processing: EY, SÇ; Statistical Analysis and/or Data Interpretation: EY, SÇ; Literature Review: EY, SÇ; Manuscript Preparation: EY, SÇ and Critical Review: EY, SÇ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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