PLATELET TO LYMPHOCYTE RATIO IS ASSOCIATED WITH PROXIMAL/ MIDDLE SEGMENT OF THE LAD LESIONS IN PATIENTS WITH ACUTE CORONARY SYNDROME

OZLEM ARICAN OZLUK*, MUSTFA YILMAZ*, DURSUN TOPAL**, ERHAN TENEKECIOGLU*, TEZCAN PEKER*, SELCUK KANAT*, KEMAL KARAAGAC*, FAHRIYE VATANSEVER*, PINAR YAGCIIOGLU*

*Department of Cardiology, Bursa Ihtisas Training And Research Hospital, Bursa, Turkey - **Department of Cardiology, Sevket Yilmaz Training And Research Hospital, Bursa, Turkey

ABSTRACT

Aim: Platelet to lymphocyte ratio (PLR) was revealed to have a close relation with major adverse cardiovascular outcomes. The aim of this study was to investigate the association between PLR and lesion localization of left anterior descending artery (LAD) in ST-segment elevation myocardial infarction (STEMI) patients.

Materials and methods: Patients admitted to our hospital with acute anterior STEMI were included. 58 patients who have single-vessel disease at LAD and their hematological parameters were analyzed retrospectively. Proximal segment of LAD lesions were grouped as Group I and mid segment of the LAD lesion grouped as Group II. The groups were compared according to their PLR and other parameters.

Results: Between group I (n = 41, mean age 52.5 ± 12.7) and group II (n = 17, mean ages 52.0 ± 10.8); PLR, was significantly higher in group I (159 ± 99 vs 99.5 ± 37.5 p < 0.05). In group I, left ventricular ejection fraction (LVEF) was significantly lower (P = 0.02). In correlation analyzes, PLR was positively correlated with Troponin I (r = 0.30, P = 0.03) and negatively correlated with LVEF (r = - 0.27 , P = 0.04)

Conclusion: The present study demonstrated that anterior STEMI patients with high PLR had a greater possibility having proximal culprit lesion on the LAD. Therefore PLR can be used as a useful tool to detect not only significant atherosclerosis but also culprit plaque localization in patients with acute STEMI patients.

Key words: Coronary artery disease, platelet to lymphocyte ratio, acute coronary syndrome.

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Introduction

Cardiovascular disease (CVD) including acute myocardial infarction (AMI), remains one of the leading causes of morbidity and mortality in the developed countries. Although CVD mortality rates worldwide declined over the past last decades, it continues to be responsible for about one-third or more of all deaths in individuals over age 35(5). For total coronary events, women lag behind men by 10 years but this gender difference disappears with advancing age(5). Atherosclerosis is the main cause of coronary artery disease (CAD)(5-8). AMI is currently classified as either STEMI or non ST segment elevation (NSTEMI) myocardial infarction. The primary goal in the treatment of STEMI is to open infarct-related artery as soon as possible(8). The best way to achieve this goal is rapid determination and reperfusion of infarct related artery by means of percutaneous coronary intervention (PCI). Culprit lesion localization on the target vessel is one of the significant factor can determine the clinical outcome in STEMI. Proximal LAD lesions require specific and early intervention because of the high risk profile(7,8). In recent years, platelet to lymphocyte ratio (PLR) derived from the
peripheral blood accept as a new prognostic indicator for atherosclerotic CAD\textsuperscript{(9-11)}. It gives an idea about both the aggregation and inflammation pathways, and it is suggested to use in the prediction of coronary atherosclerotic burden. It was also reported that PLR was an independent predictor of no-reflow development in patients presented with acute coronary syndrome and predictor of mortality in patients with STEMI\textsuperscript{(12,13)}.

However, to our knowledge, there are no data about the relationship between PLR and localization of coronary artery lesion yet. Therefore, the aim of this study was to investigate the usefulness of PLR, in predicting the localization of the culprit coronary artery lesion in AMI.

Materials and methods

Fifty-eight patients with anterior STEMI who underwent primary PCI to LAD were enrolled the study. The exclusion criteria included the following: patients who had received fibrinolytic therapy, angiographically any significant stenosis in the right or circumflex coronary artery together with an LAD artery lesion, distal LAD lesions, history of CAD, cancer, chronic inflammatory disorders (rheumatoid arthritis, osteoarthritis, etc.), serum creatinine concentration higher than 2.5 mg/dl. STEMI was diagnosed on the basis of clinical symptoms, blood cardiac injury marker and the presence of ST elevation consistent with AMI in ECG. Patient history, physical examination, 12-lead ECGs, echocardiography, coronary angiography findings, accompanying systemic diseases and medications were recorded. The patients were assessed with respect to cardiovascular risk factors.

Hyperlipidemia was diagnosed as low-density cholesterol (LDL) was greater than 100 mg/dl or lipid-lowering medication was used. Blood pressure of all patients was measured. Systolic blood pressure (SBP) equal or greater than 140 mmHg and/or diastolic blood pressure equal or greater than 90 mmHg or under control by using blood pressure-lowering medications were defined as hypertension. Patients with a fasting glucose level equal or greater than 126 mg/dl on two separate occasions or using oral antidiabetic drugs or insulin were defined as diabetes mellitus.

Acute anterior STEMI was identified by new ST elevation at the J point in two contiguous leads with the cut-points: 0.1 mV in anterior leads other than leads V2–V3 where the following cut points apply $\leq 0.2$ mV in men and $\geq 0.15$ mV in women and typical chest pain lasting 20 minutes or longer. In all patients, the culprit lesion was shown by coronary angiography for confirming the diagnosis of acute anterior myocardial infarction.

Analysis of blood samples

Complete blood count and basic biochemical parameters were evaluated retrospectively from blood samples obtained by antecubital vein puncture upon admission to the emergency department. Peripheral venous blood samples were drawn into Ethylenediamine tetraacetic acid (EDTA) containing biochemistry tubes. Whole blood cell count and volume analyses were performed using Beckmann Coulter LH 780 Hematology Analyzer device. Other biochemical measurements were determined by standard laboratory methods.

Echocardiography

All patients underwent a complete transthoracic echocardiography (TTE) and Doppler study using multiple views in left lateral decubitus position. Echocardiographic examination was performed within 24 hours of admission. TTE study was performed using a 3.5 MHz transducer on a GE Vivid 7 Pro device. Echocardiographic measurements were made according to the criteria recommended by American Society of Echocardiography\textsuperscript{(14)}. Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and ejection fraction (LVEF) were measured from the apical 4-chamber view using the modified Simpson method.

Angiography

All patients underwent coronary angiography to determine the infarct-related artery and revascularization. Determination of infarct-related artery was accomplished by observing a thrombosed critical stenosis of LAD in certain locations. The proximal to and including first major septal branch is classified as the proximal LAD, while the segment just below the first major septal branch is the mid LAD. The distal segment of the LAD is the terminal third of the artery. A narrowing of $\geq 70\%$ in other vessels were defined as additional vessel disease.

Statistical analysis

The study data analyzed using the SPSS (Statistical Package for the Social Sciences) version
16.0 software package (SPSS Inc, Chicago, Illinois, USA). The study population was divided into two groups based on the localization of the LAD lesions. Descriptive statistics are given in the mean ± standard deviation while the categorical variables were expressed as number and percentage (%).

In order to investigate the distribution of data, Kolmogorov Smirnov test was used. Normally distributed variables compared across groups by means of student t test. The nonparametric variables compared using the Mann-Whitney U test. Relationships between variables were examined by the Spearman’s rho correlation. A p value less than 0.05 was considered statistically significant for all the statistical assessments.

Results

The study population was classified according to their localization of the LAD lesions. Forty-one patients with proximal LAD lesion were defined as Group I, seventeen patients with mid LAD lesion were defined as Group II. The demographic, biochemical and echocardiographic characteristics are shown in Table 1 and Table 2.

The two groups did not significantly differ with respect to the major cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, and heredity. Both groups were similar with regard to mean age and gender distribution.

Comparison of the groups with respect to the laboratory data revealed that Group I had significantly higher cardiac injury marker: CK-MB (P < 0.05). PLR and Platelet distribution width (PDW) were significantly higher in the Group I compared to Group II (P < 0.05 and P < 0.05, respectively). Lymphocyte count was significantly lower in group I (P < 0.05). No significant differences were noted between the routine biochemical data of both groups.

In group I, left ventricular ejection fraction was significantly lower (P < 0.05), left ventricular end-systolic volume were significantly higher (P = 0.02).

In correlation analyzes, PLR was not significantly correlated to age, creatinine and MPV. On the other hand, PLR was positively correlated with CK-MB (r = 0.27, P = 0.03), troponin I (r = 0.03, P = 0.03) and LVESV (r = 0.29, P < 0.05). Also There was a negative correlation between PLR and LVEF (r= -0.27, P = 0.04). Correlations analyzes between the PLR and the patient variables were shown in Table 3.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I (n=41)</th>
<th>Group II (n=17)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.5 ± 12.7</td>
<td>52.0 ± 10.8</td>
<td>0.87</td>
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<tr>
<td>Male, n (%)</td>
<td>37 (90.2%)</td>
<td>13 (76.5%)</td>
<td>0.16</td>
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</table>

### Coronary Risk Factors

| Smoking (n, %)             | 23 (56%)       | 11 (65%)        | 0.54    |
| Hypertension (n, %)        | 7 (17%)        | 3 (17%)         | 0.95    |
| Diabetes mellitus (n, %)   | 2 (4.9%)       | 2 (11.8%)       | 0.34    |
| Family History (n, %)      | 2 (4.9%)       | 2 (11.8%)       | 0.34    |

### Biochemical parameters

| Glucose (mg/dl)            | 129 ± 36.1     | 121 ± 34        | 0.47    |
| Urea (mg/dl)               | 15.0 ± 4.1     | 14.8 ± 3.6      | 0.74    |
| Creatinin (mg/dl)          | 0.81 ± 0.2     | 0.75 ± 0.2      | 0.28    |
| HDL-cholesterol (mg/dl)    | 38.1 ± 11.2    | 39.4 ± 10.7     | 0.74    |
| LDL-cholesterol (mg/dl)    | 114 ± 29       | 117.3 ± 44.4    | 0.76    |
| Triglycerid (mg/dl)        | 122 ± 85       | 126.9 ± 94      | 0.72    |
| CK-MB(U/L)                 | 248 ± 200      | 152 ± 140       | 0.04    |
| Troponin I (ng/ml)         | 186.9 ± 118    | 123.1 ± 110     | 0.03    |

### Hematologic parameters

| WBC count (10^3/mm^3)      | 12.65 ± 3.32   | 11.95 ± 2.89    | 0.45    |
| Lymphocyte count (10^3/mm^3)| 1.5 ± 1.3     | 2.1 ± 1.6       | 0.03    |
| Platelet count (10^3/mm^3) | 231.02 ± 60.9 | 243.88 ± 60.9  | 0.19    |
| PLR                        | 159 ± 99       | 195.5 ± 37.5    | 0.02    |
| MPV (fL)                   | 8.6 ± 0.8      | 8.8 ± 1.1       | 0.41    |
| PDW (%)                    | 16.7 ± 0.4     | 16.3 ± 0.5      | 0.02    |

### Table 1: Demographic and biochemical characteristics of study groups.

Data are presented as means ± SD. P value of < 0.05 was considered statistically significant. LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein, CK-MB: Creatine Kinase Myocardial Band, WBC: White Blood Cell, PLR: Platelet to Lymphocyte Ratio, MPV: Mean Platelet volume, PDW: Platelet Distribution Width.

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<th>Group II (n=17)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>LVEDV (ml)</td>
<td>98.8 ± 27.3</td>
<td>83.4 ± 14.1</td>
<td>0.06</td>
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<tr>
<td>LVESV (ml)</td>
<td>53.1 ± 21.6</td>
<td>38.9 ± 9.8</td>
<td>0.02</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>37.8 ± 9.2</td>
<td>46.3 ± 8.2</td>
<td>0.02</td>
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</table>

### Table 2: Echocardiographic parameters in study groups.

Data are presented as means ± SD. P value of < 0.05 was considered statistically significant. LVEDV: Left Ventricular End-Diastolic Volume, LVESV: Left Ventricular End-Systolic Volume, LVEF: Left Ventricular Ejection Fraction.
Unfortunately, at this point noninvasive methods those patients with proximal occlusion. From noninvasive methods is based on identifying coronary lesion in anterior myocardial infarction clinical usefulness of detecting the level of LAD incidence of adverse outcomes in STEMI with malignant ventricular arrhythmias and higher proximal culprit LAD lesions have been associated early intervention. Previous studies showed that large, this segment stenosis require specific and given the high-risk profile the LAD constitute a special subgroup of CAD, Atherosclerotic stenosis of the proximal segment of occlusion and plaque rupture tended to cluster with patients with STEMI have reported that sites of myocardial ischemia results in life-threatening complications including electrical instability, heart failure, left ventricular remodeling, and valvular dysfunction. Epidemiological studies of patients with STEMI have reported that sites of occlusion and plaque rupture tended to cluster within the proximal segments of these vessels. Atherosclerotic stenosis of the proximal segment of the LAD constitute a special subgroup of CAD, given the high-risk profile.

Because of the myocardium at risk is relatively large, this segment stenosis require specific and early intervention. Previous studies showed that proximal culprit LAD lesions have been associated with malignant ventricular arrhythmias and higher incidence of adverse outcomes in STEMI. The clinical usefulness of detecting the level of LAD coronary lesion in anterior myocardial infarction from noninvasive methods is based on identifying those patients with proximal occlusion. Unfortunately, at this point noninvasive methods give limited data about the location of the LAD lesions. Even electrocardiography, which is most used test, may remain insufficient to predict the level of coronary obstruction in anterior STEMI.

In this context, PLR derived from routine complete blood count test is an inexpensive, easily available inflammatory indicator. It is known that inflammation plays an integral role in atherosclerosis. Previous studies reported that high circulating platelet count and low blood lymphocyte count have been shown that to be related with major cardiovascular outcomes in patients with CAD. In acute setting, lymphopenia is a common finding during stress response, resulting from increased levels of corticosteroids and has good discriminative ability for the diagnosis of AMI. In recent years, PLR accepted as a new prognostic indicator for atherosclerotic CAD. It gives an idea about both the aggregation and inflammation pathways. Previous studies found that PLR is useful in predicting the CAD severity, no-reflow in primary PCI and complexity of coronary atherosclerosis in patients with acute coronary syndrome.

We found higher PLR levels in proximal LAD lesions compared to those who have mid LAD lesions in anterior STEMI patients. There is no study in the literature investigating the relationship between PLR and the level of culprit lesion in anterior STEMI patients. Therefore, present study gains importance as it is the first study in this field.

Azab et al reported that PLR plays a role as a marker of long term mortality in NSTEMI. Recent study by Temiz et al. showed that PLR can be used as a predictor early cardiovascular mortality in STEMI. In accordance with the literature, in the present study, patients with high PLR values have lower LVEF and higher cardiac injury marker; CK-MB and troponin.

In our population, most of the patients had proximal lesion, similar to epidemiologic studies results. Also we found that PLR is significantly higher in patients with proximal LAD lesions. In addition we detected a significant relationship between the level of LAD lesions and PDW, an established indicator of platelet activity. These simple markers, especially PLR, are easily available parameter and inexpensive in routine clinical measurement. It may be useful during admissions to hospital for detecting the high risk profile patients in anterior myocardial infarction.

<table>
<thead>
<tr>
<th>Parameters</th>
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<th>p value</th>
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<tbody>
<tr>
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<tr>
<td>Creatinin</td>
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<td>0.8</td>
</tr>
<tr>
<td>CK-MB</td>
<td>0.27</td>
<td>0.03</td>
</tr>
<tr>
<td>Troponin I</td>
<td>0.3</td>
<td>0.03</td>
</tr>
<tr>
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<td>-0.27</td>
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<td>0.29</td>
<td>0.04</td>
</tr>
<tr>
<td>MPV</td>
<td>-0.2</td>
<td>0.73</td>
</tr>
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Table 3: Correlations between the platelet to lymphocyte ratio and the patient variables. P value of < 0.05 was considered statistically significant. CK-MB: Creatine Kinase Myocardial Band, LVEF: Left Ventricular Ejection Fraction, LVEDV: Left Ventricular End-Diastolic Volume, LVESV: Left Ventricular End-Systolic Volume, MPV: Mean Platelet Volume

Discussion

In the present study, we have shown that PLR at admission was significantly increased in the proximal left anterior descending lesion than to mid segment lesion in acute anterior AMI patients. In addition we also showed that LVEF levels were significantly lower and cardiac enzyme were significantly higher in patients with proximal LAD lesion. STEMI is still common cause of mortality and morbidity in developed countries. STEMI characterized by an acute occlusion of blood flow to the myocardial territory supplied by the infarct-related artery (IRA). Myocardial ischemia results in life-threatening complications including electrical instability, heart failure, left ventricular remodeling, and valvular dysfunction. Epidemiological studies of patients with STEMI have reported that sites of occlusion and plaque rupture tended to cluster within the proximal segments of these vessels. Atherosclerotic stenosis of the proximal segment of the LAD constitute a special subgroup of CAD, given the high-risk profile.

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There are some limitations of our study. The basic limitations of our study are the small sample size and lack of long-term follow-up data. Other limitations may include the enrollment of acute coronary syndrome patients only anterior STEMI. Therefore, there is a need for future studies with larger sample size underwent primary PCI that will explore the relationship between PLR levels and the level of culprit lesions in AMI and evaluate the long-term outcomes of that relationship.

In conclusion, the present study demonstrated that anterior STEMI patients with high PLR had a greater possibility having proximal culprit lesion on the LAD. Therefore PLR can be used as a useful tool to detect not only significant atherosclerosis but also culprit plaque localization in patients with acute STEMI patients.

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Corresponding author
OZLEM ARICAN OZLUK
Kardiyojolo Klinigi, Bursa Yuksek Ihtisas Egitim ve Arastirma Hastanesi, Yildirim Bursa
(Turkey)