



Does Platelet Distribution Width Correlate with Acute Coronary Syndrome Severity and Coronary Thrombus Burden?

Trombosit Dağılım Genişliği Akut Koroner Sendrom Şiddeti ve Koroner Trombüs Yüğü ile İlişkili mi?

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Abstract

Aim: Platelets play a pivotal role in the pathogenesis of acute coronary syndrome (ACS), and platelet distribution width (PDW) shows the activities of platelets in circulation. The purpose of this study was to determine the association of PDW with the ACS severity and angiographic intracoronary thrombus burden and thrombolysis in myocardial infarction (TIMI) flow grade.

Material and Method: One hundred forty-nine consecutive patients who were diagnosed as having ACS were retrospectively evaluated. Global Registry of Acute Coronary Events (GRACE) scores were calculated from the clinical and laboratory data for ACS severity. TIMI flow grades and thrombus grades of the culprit coronary arteries were calculated for each patient. Patients were grouped into two groups according to their PDW values: high PDW and low PDW. The SPSS 17.0 software was used for statistical analysis.

Results: PDW was found to be correlated with GRACE scores ($p<0.01$). The high PDW group had higher GRACE scores (139 vs. 126, $p<0.05$). Lower TIMI flow grades (0 and 1) were seen in the high PDW group (39 vs. 33, $p<0.05$). No association between intracoronary thrombus load and PDW was found in our study ($p=0.082$).

Conclusion: In our study, patients with higher PDW levels were older and had higher GRACE scores and lower TIMI flow grades. PDW levels correlate with the ACS severity and TIMI flow grade.

Keywords: Platelet distribution width, coronary thrombus, TIMI flow, acute coronary syndrome

Öz

Amaç: Trombositler, akut koroner sendromun (AKS) patogeneğinde önemli bir rol oynar ve trombosit dağılım genişliği (PDW), trombositlerin dolaşımdaki aktivitelerini gösterir. Bu çalışmanın amacı, PDW'nin AKS şiddeti, anjiyografik intrakoronar trombüs yükü ve Miyokard Enfarktüsünde Tromboliz (TIMI) akım derecesi ile ilişkisini belirlemektir.

Gereç ve Yöntem: AKS tanısı alan ardışık 149 hasta geriye dönük olarak değerlendirildi. Akut Koroner Olayların Global Kayıtları (GRACE) skorları, AKS şiddeti için klinik ve laboratuvar verilerinden hesaplanmıştır. Suçlu koroner arterlerin TIMI akım dereceleri ve trombüs dereceleri her hasta için hesaplandı. Hastalar PDW değerlerine göre yüksek PDW ve düşük PDW olmak üzere iki gruba ayrıldı. İstatistiksel analiz için SPSS 17.0 programı kullanıldı.

Bulgular: PDW, GRACE puanları ile korele bulundu ($P<0,01$). Yüksek PDW grubu daha yüksek GRACE skorlarına sahipti (139'a karşı 126, $p<0,05$). Yüksek PDW grubunda daha düşük TIMI akış dereceleri (0 ve 1) görüldü (39'a karşı 33, $p<0,05$). Çalışmamızda intrakoronar trombüs yükü ile PDW arasında ilişki bulunmadı ($p=0,082$).

Sonuç: Çalışmamızda PDW düzeyi daha yüksek olan hastalar daha yaşlıydı ve GRACE skorları daha yüksek ve TIMI akış dereceleri daha düşüktü. PDW seviyeleri, AKS şiddeti ve TIMI akış derecesi ile ilişkilidir.

Anahtar Kelimeler: Trombosit dağılım genişliği, koroner trombüs, TIMI akışı, akut koroner sendrom



INTRODUCTION

Acute coronary syndrome (ACS) includes a spectrum of clinical presentations that result from partial or complete acute obstruction of a coronary vessel. Vulnerable atherosclerotic plaque rupture and resulting thrombus formation is well-known pathophysiology. Clinical presentations vary from unstable angina pectoris (USAP) to sudden cardiac death.^[1] Platelets play a major role in the pathogenesis of ACS. Besides thrombus formation, they are also involved in inflammation and immune system modulation.^[2] Platelets are enlarged after they are activated. Mean platelet volume (MPV) and platelet distribution width (PDW) are the laboratory parameters that show the sizes, in other words, the "activities" of platelets in circulation.^[3] A link between coronary thrombus formation and larger platelet volume in patients with ACS has been shown previously.^[4] In a recent study, an association between PDW and major adverse cardiac events was demonstrated.^[5] In another study, the association between PDW and coronary artery disease (CAD) severity was shown.^[6] The severity of acute coronary events and also intracoronary thrombus load may be related to PDW. In this study, we aimed to determine the association between PDW, ACS severity, angiographic intracoronary thrombus burden, and thrombolysis in myocardial infarction (TIMI) flow grade.

MATERIAL AND METHOD

The clinical, angiographic, and laboratory data of 149 consecutive patients who were diagnosed as having ACS [11.4% USAP, 56.4% ST-elevation myocardial infarction (36.3% anterior myocardial infarction, 20.1% inferior myocardial infarction), 32.2% non-ST elevation myocardial infarction (NSTEMI)] were evaluated in this study. The Global Registry of Acute Coronary Events (GRACE) score for in-hospital mortality was calculated.^[7] GRACE scoring estimates the probability of in-hospital death in patients with ACS. All patients' angiographic records were evaluated by an interventional cardiologist who was blinded to their clinical and demographic data. TIMI flow grades and thrombus grades of the culprit coronary arteries were calculated for each patient.^[8-10] TIMI flow grades were defined as TIMI 0 Flow=No penetration of contrast beyond stenosis (100% stenosis, occlusion); TIMI 1 Flow=Penetration of contrast beyond stenosis but no perfusion of distal vessels (99% stenosis, sub-total occlusion); TIMI 2 Flow=Contrast reaches distal vessels but either at a decreased rate of filling or clearing when compared with the other coronary arteries (partial perfusion); TIMI 3 Flow=Contrast reaches the distal bed and clears at the same rate when compared with the other coronary arteries (complete perfusion). TIMI thrombus grades were defined as Grade 0: No visible thrombus; Grade 1: Angiographic features suggesting the presence of thrombus; Grade 2: Definite thrombus in angiographic views with the greatest dimension of <1/2 vessel diameters;

Grade 3: Definite thrombus in angiographic views with the greatest dimension from >1/2 to <2 vessel diameters; Grade 4: Definite thrombus in angiographic views with the greatest dimension of >2 vessel diameters; Grade 5: Complete thrombotic occlusion of a vessel. Thrombus grades of patients with a TIMI thrombus grade 5 were reclassified from angiographic views after the removal of total occlusion after a guidewire advancement of balloon angioplasty.^[11] The patients were divided into two groups according to the 50% percentile of PDW values, patients with high PDW and patients with low PDW. Patients with malignant disease, renal or hepatic failure, acute or chronic infection, inflammatory disease, and any hematologic disease including anemia, were excluded from the study. Immediately after emergency department admission, venous blood samples were drawn for blood chemistry analysis and complete blood counts, which were performed using a Sysmex counter XT 1800i (Sysmex). The study was carried out with the permission of KTO Karatay University NonInterventional Clinical Researches Ethics Committee (Date: 20.12.2021, Decision No: 2021-0199). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Statistical analysis

The SPSS 17.0 software was used for statistical analysis. Spearman's rank correlation test was performed to determine the association between PDW and GRACE risk score. The Kruskal-Wallis test was used to determine any difference between the PDW values of each TIMI flow grade and each thrombus grade subclass. The t-test and Mann-Whitney test were used to test the difference between continuous variables of the high-PDW and low-PDW groups. The Chi-square test was used to test the difference between categorical variables of the high and low-PDW groups.

RESULTS

The demographic, clinical, laboratory, and angiographic data of the patients are presented in **Table 1**. Our study group consisted of mostly male patients. Most of the patients were aged around the sixth decade. Acute anterior myocardial infarction was the most frequently seen presentation.

We found that PDW ($r=0.304$, $p<0.001$) was significantly positively correlated with GRACE scores. When the analysis was performed among each TIMI thrombus grade alone, PDW values showed no differences ($p=0.187$). Patients were grouped into two groups according to their angiographic thrombus size: low thrombus burden (TIMI thrombus grade 0 and TIMI thrombus grade 1) and high thrombus burden (TIMI thrombus grade 2, 3, and 4) and PDW values did not differ between these groups [11.6 (8.9-19.9) vs. 11.9 (9.3-22.0), $p=0.40$].

Table 1. Demographic, clinical, laboratory, and angiographic data of the patients.

Variable		
Age		60.1±12.4
Sex (Male %)		117 (78.5%)
Diabetes mellitus		28 (18.8%)
Hypertension		61 (40.1%)
Hyperlipidemia		65 (43.6%)
Current smokers		50 (33.5%)
Creatinin (mg/dL)		0.9 (0.4-3.0)
PDW (fL)		11.8 (8.9-22.0)
Presentation		
USAP		17 (11.4%)
NSTEMI		48 (32.2%)
Anterior MI		54 (36.3%)
Inferior MI		30 (20.1%)
GRACE score		134.4 (68-334)
TIMI thrombus grade	Number of patients	Median PDW
0	36 (24.2%)	11.45 (8.9-15.2)
1	27 (18.1%)	11.8 (9.4-19.9)
2	37 (24.8%)	12.5 (9.6-22.0)
3	40 (26.8%)	11.5 (9.3-16.3)
4	9 (6%)	12.4 (9.7-16.2)
TIMI Flow Grade	Number of patients	Median RDW
0	52 (34.9%)	11.75 (9.3-22.0)
1	13 (8.7%)	12.7 (9.7-18.8)
2	37 (24.8%)	13.5 (9.4-20.1)
3	47 (31.5%)	11.4 (8.9-19.9)

PDW values according to angiographic TIMI flow grades were different between the groups ($p<0.01$). It was seen that patients with TIMI-3 flow grade had lower PDW values than other patients. A comparison of demographic, clinical, laboratory, and angiographic characteristics of the high-PDW and low-PDW patient groups is given in **Table 2**. Patients in the high PDW group were older. Female sex predominance was present in the high PDW group. Patients in the high PDW group had higher GRACE scores. Lower TIMI flow grades (0 and 1) were seen in patients in the high PDW group. The coronary thrombus burden of the high-PDW and low-PDW groups was not different.

Table 2. Comparison of demographic, clinical, laboratory, and angiographic characteristics of the high-PDW and low-PDW patient groups.

	Low-PDW (n=78)	High-PDW (n=71)	P-value
Age	57.5±12.4	62±11.8	<0.01
Sex (Male %)	68 (87.2%)	49 (69%)	<0.01
Diabetes mellitus	13 (16.6%)	15 (21.1%)	0.05
Presentation			
USAP	8 (10.2%)	9 (12.7%)	
Anterior MI	26 (33.3%)	28 (39.4%)	
Inferior MI	19 (24.4%)	11 (15.5%)	
NSTEMI	25 (32.1%)	23 (32.4%)	
Creatinin (mg/dL)	0.7 (0.4 – 0.9)	1 (0.9 – 3.0)	0.93
GRACE score	126 (68 – 192)	139 (75 – 334)	<0.05
Thrombus grade			
0 and 1	36 (46.1%)	27 (38.0%)	
2, 3, and 4	42 (53.8%)	44 (61.9%)	0.08
TIMI flow grade			
0 and 1	33 (42.3%)	39 (54.9%)	
2 and 3	45 (57.6%)	32 (45.9%)	<0.05

DISCUSSION

In our study, PDW was found to be higher, especially in women and the elderly. High PDW may be one of the reasons why cardiovascular adverse events are more frequent in these special groups. PDW can be used as an important parameter to indicate adverse cardiac events in these patient groups. In our study, we also found a significant relationship between PDW levels and GRACE scores, and TIMI flow grade in patients with ACS. The GRACE risk scoring system has been shown to accurately predict mortality for patients with ACS, including ST-elevation MI, non-ST-elevation MI, and unstable angina pectoris.^[12] In other words, GRACE scores indicate the severity of ACS. In addition to thrombus formation, platelets also play a role in inflammation and the immune system. During acute myocardial infarction, they activate leukocytes by secreting inflammatory mediators and form aggregates with leukocytes.^[13,14]

Platelets are heterogeneous in size. When they pass from the bone marrow to the peripheral circulation, they are in large volume and this is suitable for their reactivity.^[15,16] During the time that platelets are in circulation, their volume gradually decreases.^[17] In the case of stress, platelet production is stimulated and large platelets are released into the circulation.^[18] PDW is a reflection of this. Increased megakaryocyte heterogeneity as a result of increased thrombopoietic activity in the bone marrow results in an increase in PDW in peripheral blood count.^[19] The growth of platelets in ACS indicates increased thrombopoietic activity in the bone marrow.^[20] PDW is also a reflection of this. Increased megakaryocyte heterogeneity as a result of increased thrombopoietic activity in the bone marrow results in an increase in PDW in peripheral blood counts.^[19] The growth of platelets in ACS indicates increased thrombopoietic activity in the bone marrow.^[20] Thus, increased PDW in patients with ACS may be a marker of increased thrombopoietic activity driven by increased cytokines.

In our study, the relationship between GRACE risk scores and PDW can be explained by the increased thrombopoietic activity caused by increased cytokines, and it can be said that the cause of ACS severity is correlated with increased stress. In addition, we aimed to evaluate the relationship between coronary thrombus and PDW according to the degree of TIMI thrombus in our study. We could not find a similar study in the literature. A study in which only the presence of thrombi was evaluated was found, and a relationship was shown between the presence of thrombi and PDW.^[22] However, in our study, no correlation was found between coronary thrombi and PDW according to the TIMI thrombus grade.

In our study, the mean PDW value was also found to be associated with TIMI flow grade. There was an inverse correlation between TIMI flow grade and PDW. It was thought that this result might be a reflection of the relationship between low TIMI flow grades and the severity of ACS. In a study performed on patients with ST-elevation MI^[12] after

primary PCI, when no-reflow was defined as group 1 (TIMI flow grade 0, 1, or 2) and angiographic success was defined as group 2 (TIMI flow grade 3), PDW was found to be higher in patients without reflow, similar to our study. As a result, PDW, a laboratory marker of "stress platelets," was thought to be related to the severity of ACS and TIMI flow grades. In addition, PDW was found to be higher, especially in women and the elderly, and could be used as an important parameter to show adverse cardiac events in these groups.

Limitations

The main limitation of this study was its single-center and retrospective design. We demonstrated an association between PDW levels and ACS severity but found no association between intracoronary thrombus load and PDW in our study.

CONCLUSION

The reason for this result could be the small study population. Nevertheless, this study can provide a basis for clinical studies with larger study populations. In addition, our study population consisted of patients with acute coronary syndrome, including those with ST-elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina pectoris, and these subgroups were not evaluated in detail due to the low number of patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of KTO Karatay University NonInterventional Clinical Researches Ethics Committee (Date: 20.12.2021, Decision No: 2021-0199).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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