RESEARCH ARTICLE

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Mean Platelet Volume and Platelet Distribution Width in Recurrent Deep Vein Thrombosis

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Objective: The aim of the study is to assess the mean platelet volume (MPV) and platelet distribution width (PDW) in patients with unprovoked recurrent deep vein thrombosis (DVT).

Materials and Methods: Between January 2011-September 2017 patients with recurrent deep vein thrombosis at lower extremity were retrospectively examined and named as Group 1 (n: 30). The MPV and PDW values at the time of first deep vein thrombosis of these patients were compared with MPV and PDW values at recurring phase and also compared with patients' MPV and PDW values in control group (Group 2, n: 30).

Results: The values of mean platelet volume in acute phase group compared with control group, a significant increased in patient group was detected (P= 0.002). MPV values in recurrent period were also higher compared to the control group (P<0.001). When values of MPV in acute and recurrent DVT period were compared, the values in recurrent period were found significanltly high (P<0.001). When PDW values are examined; patient group and control group were compared and it was seen that values in both acute and recurrent period were higher than control group and it was statistically significant (P<0.001).

Conclusion: The increased MPV and PDW values during platelet activation play a role at unprovoked acute and recurrent deep vein thrombosis. PDW is a more specific parameter than MPV; evaluation of MPV and PDW together may provide more effective consideration for venous thrombosis.

***Key Words*:** *Recurrent deep vein thrombosis, mean platelet volume, platelet distribution width*

Tekrarlayan Derin Ven Trombozunda Ortalama Trombosit Hacmi ve Trombosit Dağılım Genişliği

Amaç: Sebebi belli olmayan tekrarlayan derin ven trombozu (DVT) hastalarında ortalama trombosit hacmi (MPV) ve trombosit dağılım genişliğinin (PDW) rolü değerlendirildi.

Gereç ve Yöntem: Ocak 2011-Eylül 2017 arası tekrarlayan alt ekstremite derin ven trombozu olan hastalar retrospektif olarak incelendi. Bunlar hasta grubu (Grup 1, n:30) olarak değerlendirildi. Bu hastaların ilk defa derin ven trombozu geçirdikleri dönemdeki MPV ve PDW değerleri, tekrarladığı dönemdeki MPV ve PDW değerleri ile Kontrol grubu (Grup 2, n:30) olarak kabul edilen komplike olmamış alt ekstremite variköz ven nedeniyle kliniğimize başvuran hastaların MPV ve PDW değerleri ile karşılaştırıldı.

Bulgular: Trombosit hacmi değerlerinde; hasta grubundaki akut dönemdeki veriler ile kontrol grubu karşılaştırıldığında, hasta grubu lehine anlamlı bir artışın olduğu tespit edildi (P=0.002). Yine tekrarlayan dönemdeki MPV değerlerinde de kontrol grubuna göre anlamlı artışın olduğu görüldü (P<0.001). Akut DVT dönemi ile tekrarlayan DVT dönemindeki değerler karşılaştırıldığında; tekrarlayan dönemdeki verilerde anlamlı bir yükseklik olduğu tespit edildi (P<0.001). Trombosit Dağılım Genişliği değerlerinde; hasta grubu ile kontrol grubu karşılaştırıldığında hem akut dönemdeki hem de tekrarlayan dönemdeki değerlerin kontrol grubuna göre yüksek olduğu ve bunun istatistiki olarak anlamlı olduğu görüldü (P<0.001).

Sonuç: Sebebi bilinmeyen akut ve tekrarlayan derin ven trombozunda; trombosit aktivasyonu esnasında yükselen MPV ve PDW değerlerindeki yükseklik rol oynamaktadır. PDW, trombosit aktivasyonunda MPV'ye göre, daha spesifik bir belirteçtir. MPV ve PDW'nin birlikte değerlendirilmesi venöz tromboza yatkınlık açısından daha etkin bir fikir sunabileceği kanaatindeyiz.

***Anahtar Kelimeler*:** *Tekrarlayan derin ven trombozu, ortalama trombosit hacmi, trombosit dağılım genişliği*

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Introduction

Venous thromboembolism (VTE), deep vein thrombosis (DVT) and pulmonary embolism are the clinical conditions with high mortality and morbidity. The stasis, endothelial damage and hypercoagulability are involved in the pathogenesis of venous thromboembolism (1). Prolonged immobilization, various malignancies, advanced age, cardiopulmonary and other organ failure, acquired or genetic hematologic disorders can be listed as risk factors for deep vein thrombosis (2).

Patients with venous thromboembolism; are confronted with the risk of recurrence inversely proportional to the time since the first episode, ranging from 5 to 7% per year

(3). It is crucial to distinguish venous thromboembolism as provoked and unprovoked. The provoked venous thromboembolies may depend on risk factors such as; major surgery, pregnancy or permanent factors such as cancer. The venous thromboembolies which are not identified with any clinical risk factors are named as unprovoked. Unprovoked venous thromboembolies have a higher risk of recurrence than other (4, 5).

Platelets play an important role in the pathogenesis of venous thromboembolism and atherosclerosis (6, 7). Platelets volume indices; low-cost tests that are measured as a part of complete blood count and accurately demonstrate platelet activation and function (8). Mean platelet volume (MPV) and platelet distribution width (PDW) are valid, important, and interesting parameters used in the investigation of clinical conditions due to their wide usage. Platelets dimensions measured with these parameters; aggregation correlates with thromboxane A2 or β-thromboglobulin release and platelets activation related with the expression of glycoprotein 1b and IIb / IIIa receptors (9).

Besides there are few studies indicating a relation between unprovoked venous thrombosis and MPV and PDW, there has been no study of these parameters in recurrent venous thromboembolism. The purpose of this study is to evaluate the role of MPV and PDW in patients with recurrent deep vein thrombosis.

Material and Methods

Patients with recurrent lower extremity deep vein thrombosis (17 female, 13 male, average age 52.37±13.61) who were diagnosed clinically and radiological in our hospital between January 2011 and September 2017 were retrospectively examined. These were evaluated as the patient group (Group 1 (n: 30)). The MPV and PDW values at the time of the first deep vein thrombosis of these patients were compared with the MPV and PDW values at the recurring phase and also compared with the patients MPV and PDW values who have uncomplicated lower extremity varicose veins considered as the control group (Group 2, n: 30)) (14 female, 16 male). Left ventricular systolic dysfunction (EF <50), coronary artery disease, recent trauma, recent surgical operation, acute or chronic infection, stroke, antilipid and antiplatelet treatment, atrial fibrillation, obesity, known malignancy, peripheral arterial disease, chronic renal and hepatic diseases, diabetes mellitus, oral anticoagulant usage, oral contraceptive usage and pregnant patients were not included in the study.

Demographic data of patients in groups; age, sex, hypertension, smoking, hyperlipidemia and as hematologically; hemoglobin (Hb), white blood cell (WBC), platelet count (Plt), MPV and PDW values were examined. Antihypertensive drug use or systolic blood pressure >140 mmHg, diastolic blood pressure> 90 mmHg was defined as hypertension. Total serum cholesterol level ≥200 mg/dL, low-density lipoprotein (LDL) cholesterol ≥130 mg/dL, or lipid-lowering drug use was described as hyperlipidemia.

Statistical Analaysis: While repeated measures were evaluated between groups, variance analysis was used for repeated measures within and between groups. Data were presented with average and standard deviation in number and percentage; chi-square test was used for categorical variables. Analyses were performed using SPSS 19 software (IBM SPSS Statistics 19; SPSS Inc., an IBM Company, Somers, NY). A P-value <0.05 was considered significant.

Results

Characteristic and demographic datas of the patients in the groups are given in Table 1. There was no significantly difference among age, gender, hypertension, diabetes, hyperlipidemia and smoking cigarette between groups.

The general averages of the laboratory parameters, the mean values in the groups and the statistical differences between them are given in Table 2. There was no significant difference in hemoglobin values between the two groups and within the group of patients. There was a significant difference between the acute and recurrent period of the patients' MPV values (P= 0.005). There was no significantly difference between the two groups in platelet values; but between

Table 1. Distribution of characteristic and demographic datas according to groups

Variables		Group		P
		Control (n=30)	Patient (n=30)	
Age		47.67±12.96	52.37±13.61	
Gender	Female	14 (46.7)	17 (56,7)	0.438
	Male	16 (53.3)	13 (43.3)	
Hypertansion	+	22 (73.3)	19 (63.3)	0.405
	-	8 (26.7)	11 (36.7)	
Smoking	+	23 (76.7)	21 (70)	0.559
	-	7 (23.3)	9 (30)	
Hyperlipidemia	+	25 (83.3)	23 (76.7)	0.519
	-	5 (16.7)	7 (23.3)	

Chi-square test were used

Table 2. Distributions of laboratuary parameters according to groups

	Average values	Group		p_1
		Control (n=30)	Patient (n=30)	
Hb1 (g/dL)	13.44±1.68	13.94±1.7	12.94±1.53	0.019
Hb2 (g/dL)	13.62±1.63	13.94±1.7	13.3±1.52	0.131
p_2		1.000	0.069	
Plt1 (10^3)	262±78	256±78	268±80	0.565
Plt2 (10^3)	252±82	256±78	249±87	0.745
p_2		1.000	0.041	
MPV1 (fL)	9.63±1.59	9.03±1.02	10.24±1.83	0.002
MPV2 (fL)	9.98±1.57	9.03±1.02	10.93±1.44	<0.001
p_2		1.000	<0.001	
PDW1 (fL)	13.44±3.86	10.34±1.02	16.54±3.07	<0.001
PDW2 (fL)	13.04±3.69	10.34±1.02	15.75±3.39	<0.001
p_2		1.000	0.079	
WBC1 (10^3/mL)	7.3±1.9	7.7±1.5	6.9±2.3	0.110
WBC2 (10^3/mL)	7.7±2.1	7.7±1.5	7.7±2.7	0.895
p_2		1.000	0.005	

p_1: Comparison between groups
p_2: Comparison in group.
Hb1, Plt 1, MPV 1, PDW1,WBC1:The values at acute dvt period
Hb2, Plt 2, MPV 2, PDW2,WBC2: The values at acute recurrent dvt period
one way variance analysis test were used for recurrent measures

acute and recurrent period of DVT in patient group, there was a significantly difference in platelets counts (P= 0.041). The values of mean platelet volume (MPV1); in the acute phase group compared with the control group, it was found that there was a significant increased in patient group (P= 0.002). MPV values in the recurrent period (MPV2) were also significantly increased compared to the control group (P<0.001). When the values of MPV in acute DVT period (MPV1) and recurrent DVT period (MPV2) were compared, MPV2 values were found significantly high (P<0.001). When the platelets distribution width (PDW) values are examined; when the patient group and the control group were compared, it was seen that the values in both the acute and recurrent period were higher than the control group and it was statistically significant (P<0.001). There was no significantly difference in PDW data between acute and recurrent periods in the patient group (P= 0.079).

Discussion

Platelets play a central role in the pathogenesis of thrombo-embolic diseases. Platelet size reflects platelet activation. Large platelets are more metabolic and enzymatically active than small ones and produce greater amounts of thromboxane A2 and express more glycoprotein Ib and IIb / IIIa receptors. MPV and PDW are indicators of platelet activation. While MPV is a measure of mean platelets size, PDW measures platelets size variability and may be an indicator of active platelets release (10).

MPV is one of the platelet volume indicators and is a simple and reliable parameter showing platelets activation and function. There are studies showing increased MPV levels in patients with coronary artery disease (11, 12). MPV has been defined as an independent risk factor for myocardial infarction and stroke (13, 14). In a hospital-based cohort study (n: 206,554), the relationship between MPV quintiles and vascular mortality was assessed. In patients with MPV ≥11.01 fL (highest quintile), vascular mortality was shown to be at the highest level in patients with MPV below 8.7 fL. This increased risk is beginning to become evident in the values above the MPV of 9.61 fL. (15). Also in a study performed by Berger and colleagues in 6354 patients (16), a positive correlation was found between MPV and peripheral artery disease. The above data pertain purely to arterial thromboembolism. There are limited such data concerning venous thromboembolism.

In Tromsø study conducted by Braekkan et al. (17) on 25923 patients, it was shown that there was a correlation between acute unprovoked venous thromboembolism and increased MPV (≥9.5fL) values. In a study on platelets indices on 2013 patients with acute deep vein thrombosis; Cay et al. (18) found that MPV values were higher than the control group and they stated that the presence of DVT may be closely related to increased platelet activation. Similarly Gulcan et al. (19) found that MPV values in newly diagnosed acute DVT patients were significantly higher than in the control group. In a study, including 147 patients, examining the relationship between acute deep vein thrombosis and mean platelet volume in patients staying hospital, MPV values were found as high in these patients and it was suggested that this was an independent predictor (20). In another study examining the relationship between recurrent pulmonary embolism and platelet indices, the MPV and PDW values in recurrent cases were detected significantly higher than in non-recurrent cases. In addition, recurrent pulmonary

embolism cases after treatment showed that MPV was still higher than those who did not recur. As a result, it has been determined that MPV may be an indicator for recurrent pulmonary embolism and may be useful for predicting recurrence (21).

As it can be seen in these studies, there is a positive relationship between acute deep vein thrombosis and MPV values. However, in our examination of the literature, no study was found related to the relationship between MPV and recurrent deep vein thrombosis. Mean platelet volume values in this study; the MPV value in the acute phase (MPV1) in the patient group was measured as 10.24±1.83 fL on average and it was found to be significantly higher than the control group (mean value: 9.03±1.02) (P= 0.002) The mean platelet values in the recurrent periods of the patients (MPV2) were measured as 10.93±1.44 fL, which was higher in the mean level than the control group (P<0.001). MPV2 values were found to be significantly higher than MPV1 values in patients with acute and recurrent DVT (P<0.001).

PDW; measures the size of platelets and is another indicator of platelet activation at the same time (22). Increased PDW levels have been reported in myeloproliferative diseases, diabetes mellitus, and coronary artery disease (23).

Some authors have indicated that high PDW is associated with platelet anisocytosis and have suggested that this anisocytosis may be related to the formation of pseudopodia. Khandekar et al. (23) have found that the PDW is higher in patients with acute ST-segment elevation than in those with stable coronary artery disease. Celik et al. (24) have suggested that the PDW is an independent correlate of in-hospital major adverse cardiovascular events. In addition, Rechkinski et al. (25) have reported that the PDW is an independent risk factor for cardiac mortality and either death, recurrent MI or the need for an additional revascularization procedure. Further, Jindal et al. (26) have reported that the PDW is significantly increased in diabetic patients, and these authors have stressed that it may be even higher in patients who have developed microvascular complications.

There are few studies showing the relationship between platelet distribution width and venous thromboembolism. In a study of Kamisli and et al. (27) it was demonstrated that elevated MPV and PDW values in patients with cerebral sinus venosus thrombosis at early phase and this was related with the severity of the disease and the extent of parenchymal lesions.

In a study completed by Sevuk and et al. (28), they found that MPV and PDW values in acute DVT patients were higher than the control group. They also showed that MPV and PDW values were significantly higher in patients with acute DVT and pulmonary embolism compared to patients with DVT alone, and the serial MPV and PDW measurements and percent changes in these parameters may be a useful marker for pulmonary embolism after acute DVT.

As it was mentioned before, in a study fulfilled by Araz et al. (21), MPV and PDW values in recurrent pulmonary embolism cases were found significantly higher than non-recurrent cases.

In this study platelets distribution volume values in the acute phase in the patient group (PDW1) was measured as 16.54±3.07fL on average and it was found to be significantly higher than the control group (average value: 10.34±1.02 fL) (P<0.001). However, the mean PDW values (PDW2) of the patients in the recurrent period were measured as 15.75±3.39 fL, which was found to be higher in the average level than the control group (P<0.001). There was no meaningful difference found in PDW data between acute and recurrent periods in the patient group (P= 0.079).

In the light of literature and our study findings; the increased mean platelet volume and platelet distribution width values during platelet activation play a role at the development of unprovoked acute and recurrent deep vein thrombosis. Beside the platelet distribution width is more specific parameter than mean platelet volume; the evaluation of MPV and PDW together may provide a more effective idea for venous thrombosis predisposition. We consider that the antiagregan treatment as continuous therapy after the end of anticoagulant treatment of deep vein thrombosis may be useful in the prevention of recurrence.

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