ARAŞTIRMA/RESEARCH

Changes in mean platelet volume values in patients with pulmonary thromboembolism

Pulmoner tromboemboli hastalarında ortalama trombosit hacmindeki değişiklikler

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Abstract

Purpose: This clinical study aimed at determining whether mean platelet volume values were useful in predicting embolic load by comparing the values of patients diagnosed with pulmonary thromboembolism with pulmonary arterial computed tomography obstruction index.

Material and Methods: This retrospective study enrolled 120 inpatients with pulmonary thromboembolism diagnosis in emergency service. Patients' mean platelet volume, Troponin-I, D-dimer values, arterial blood gases, chest radiographs, electrocardiograms, echocardiograms and venous doppler ultrasound findings were recorded. Moreover, pulmonary arterial computed tomography obstruction index for each case was calculated by extracting data from patients' computed tomography angiographies.

Results: There was a statistically significant difference particularly between pulmonary arterial computed tomography obstruction index values of the cases having mean platelet volume value < 8.5fl and mean platelet volume value > 8.5fl (25.0 and 45.0). Pulmonary arterial pressure of the group with mean platelet volume level > 8.5 was found significantly higher compared to the group with mean platelet volume level < 8.5fl.

Conclusions: Usefulness of correlation between mean platelet volume and pulmonary arterial computed tomography obstruction index in assessing the severity of embolism is unclear.

Key words: Pulmonary embolism, mean platelet volume, computed tomography angiography

Öz

Amaç: Bu klinik çalışmada amaç pulmoner tromboemboli tanısı alan hastalarda ortalama trombosit hacmi ile emboli yükünün ilişkisini ortaya koymaktır.

Gereç ve Yöntem: Bu retrospektif çalışmaya pulmoner emboli tanısı alan 120 hasta dahil edildi. Hastaların ortalama trombosit hacmi, Troponin-I, D-dimer değerleri, arter kan gazları, göğüs radyografisi, elektrokardiyografi, ekokardiyografi ve venöz doppler ultrason bulguları kaydedildi. Ayrıca bilgisayarlı tomografi anjiyografi kullanılarak pulmoner arteriyel obstrüksiyon indeksi hesaplandı.

Bulgular: Ortalama trombosit hacmi ile pulmoner arter basıncı arasında ve pulmoner arteriyel obstrüksiyon indeksi arasında pozitif korelasyon tespit edildi. Ortalama trombosit hacmi < 8.5fl olan ve > 8.5fl olan gruplar arasında pulmoner arter obstrüksiyon indeksi açısından istatistiksel anlamlı bir fark tespit edildi (25.0 and 45.0). Ortalama trombosit hacmi > 8.5fl olan olan grupta pulmoner arter basıncı < 8.5fl olan gruptan istatistiksel anlamlı olarak yüksek bulundu.

Sonuç: Pulmoner arteriyel bilgisayarlı tomografi obstrüksiyon indeksi ile ortalama trombosit hacmi arasındaki korelasyonun pulmoner embolizm şiddetini belirlemedeki değeri net değildir.

Anahtar kelimeler: Pulmoner embolizm, ortalama trombosit hacmi, bilgisayarlı tomografi anjiyografi

INTRODUCTION

Pulmonary thromboembolism (PTE) is a blockage of blood flow to a particular site due to an obstruction of the pulmonary artery and its branches by a thrombus that originates in the venous system[1]. Generally, it is considered a high mortality and morbidity disease[2]. In spite of the advances in diagnosis and treatment of pulmonary thromboembolism, there still exist several challenges in clinical management of patients. Since precise diagnosis cannot be provided by laboratory tests, it becomes difficult to diagnose PTE and therefore often delays treatment, which results in increased mortality. Radiological methods have primarily been used today for diagnostic purposes[3,4].

Mean Platelet Volume (MPV) has been determined in automated blood count profiles since the 1980s and it does not require any additional costs[5]. In clinical hematology laboratories, MPV is measured by using ethylenediamine tetraacetic acid (EDTA) as an anticoagulant. Normal value is accepted, on average, as 7.4-12 fl (femtoliter, $\mu m3$). It is observed higher in young adults and children[6]. Increased MPV is related to megakaryocytic increase as a response to thrombopoietic stress. Large thrombocytes can be defined as stress thrombocytes[7]. Thrombocyte volume parameters are objective parameters in evaluating the size of the thrombocyte. Thrombocyte volume is an indicator of thrombocyte function and activation[6].

In thrombotic and prethrombotic incidences, changes in thrombocyte volume parameters are observed[8]. In former studies, it has been revealed that larger thrombocytes are more active thrombocytes. Large thrombocytes are more easily impaired by thrombocyte aggregation agonists such as ADP, collagen and epinephrine. These large thrombocytes produce more prothrombotic and vasoactive factors such as arachidonic acid metabolites, serotonin and ATP, and they have more dense granules[7,9,10].

In former studies, MPV increase has been shown in diseases such as deep venous thromboembolism, acute coronary syndrome, stroke, preeclampsia and renal artery stenosis[5,11]. One hypothesis in this study was in the form of changes in platelet volume may be valuable for assessing the severity of pulmonary thromboembolism. Embolic load of pulmonary embolism is often used to assess the risk of adverse

events. PACTOI formula has been developed to predict embolic load and it has been confirmed in various studies to be compatible with clinical data[12,13].

While calculating PACTOI developed by Qanadli et al. 0, 1 or 2 points are given for each segmental artery depending on segmental pulmonary artery branches being entirely open, partially obstructed or entirely obstructed. Given that there is proximal obstruction to segmental artery, scoring is similarly done according to the total segments nurturing the obstructed vein. The score based on a total of 20 segmental branches being entirely open or entirely obstructed varies from 0 to 40. Obstruction index ratio is obtained by dividing this score by 40, which will be provided when all veins are obstructed. In the PACTOI formula, 'n' indicates segmental artery number in thrombus distal (a value between 0 - 20) and 'd' indicates degreee of obstruction (a value between 0 - 2). PACTOI can be calculated with the formula as follows[14]:

$$PACTOI = \Sigma\ (n \times d) \times 100\ /\ 40$$

This study was designed to determine the relationship between PACTOI that shows thrombus load and MPV volume in patients diagnosed with PTE and examine the role of MPV in indicating embolic load.

MATERIAL AND METHODS

This retrospective study included patients who presented to the emergency unit of Yıldırım Beyazıt University, Faculty of Medicine, Ankara Atatürk Training and Research Hospital and who were diagnosed with pulmonary thromboembolism upon their thoracic computed angiographies. PACTOI was measured by radiologists on thoracic computed tomography angiographies of 120 patients enrolled in the study. The study was made with the approval from Atatürk Education and Research Hospital of the Ethics Committee.

Demographic data

Demographic data such as age and gender were recorded. Patients with diseases that may affect MPV (such as hemorrhage, iron deficiency anemia, myeloproliferative disorders, myelodisplastic syndrome, kongenital platelet function abnormalities, idiopathic thrombocytopenic

purpura, hypersplenism) were recorded and excluded from the study.

Blood tests

Information that can be found in patient files such as arterial blood gases (ABG), complete blood count, international normalized ratio (INR), lactate, troponin-I and D-dimer levels of all patients were also recorded. Blood tests of patients had been obtained in the first minutes of the admission to the emergency room. "Sysmex KX-21N Automated Hematology Analyzer" was used for blood count and MPV through the use of automatic floating discriminators. 8.5 threshold values was used for MPV inspired by the work of the Braekkan et al[15] and some comparisons were made accordingly.

Radiology

Pulmonary arterial pressure (PAP), ejection fraction (EF), right ventricular width, which were detected by Transthoracic Echocardiography, were measured. Patients diagnosed with acute lower and upper extremity deep venous thrombosis (DVT) on venous doppler ultrasonography (USG) were recorded.

PTE diagnosis was determined regarding the presence of filling defect within lumen at a lobar, segmental and, if possible, subsegmental level in the main pulmonary artery, right and left pulmonary artery via spiral computed tomography pulmonary angiography (SCTPA) images. Patients were recorded by being classified as acute massive emboli, submassive emboli, non-massive emboli upon evaluating their clinical and SCTPA.

Massive emboli are defined as obstruction of over 50% of pulmonary vascular field or two or more lobar arteries. Submassive emboli is defined as filling defect on at least one segmental pulmonary artery on condition that less than massive PTE with echocardiographic findings as acute dilatation of the right atrium and right ventricle, paradoxical septal motion and increased systolic PAP. Other cases of PTE was defined as a non-massive PTE. Cross-sectional images of spiral SCTPA of PTE patients were provided from the image archiving system. Using these images, computed tomographic pulmonary angiography obstruction index was calculated via mediastinal window for each patient, upon common views of two radiologists, one of whom was a specialist on thorax.

Patients of massive and submassive pulmonary embolism with shock or hypotension of at least 15 minutes were selected as candidates for thrombolytic therapy. Thrombolytic therapy was given to the patients without contraindications.

Statistical analysis

Data analysis was done via Statistical Package for the Social Sciences (SPSS) for Windows 11.5 software package program. In order to test whether the distribution of continuous variables was close to a normal distribution, Kolmogorov–Smirnov test was used. Descriptive statistics for continuous variables was defined as mean ± standard deviation or median (the lowest-the highest), for categorical variables it was defined as number of cases and percentages (%). When the number of independent groups was 2 in terms of the significance of the difference regarding median values, Mann Whitney-U test was applied; whereas when more than two groups were involved, the significance of the difference was subjected to Kruskal-Wallis test. Spearman's correlation test was used to find whether there was a significant relationship between continuous variables. For the data obtained, P < 0,05 was considered statistically significant.

RESULTS

Mean age of 120 patients enrolled in the study was 61.36 ± 15.74 (23 - 90). 59 (49.2%) of them were male and 61 (50.8%) were female. 11 (9.1%) patients were 40 years old and below; 109 (90.9%) patients were over 40 years old. 56 cases were 65 years old and over (46.6%).

Clinical findings

Acute deep vein thrombosis was found in 61 (50.8%) patients detected via venous doppler USG on patients' presentation; whereas in 59 (49.2%) of them there was no indication of acute deep vein thrombosis. On echocardiography, enlargement in right ventricles was detected in 81 (67.5%) patients. In 35 (29.1%) patients, pulmonary arterial pressure was measured over 35. Number of patients, whose EF was lower than 50%, was 15 (12.5%).

PACTOI and MPV

In the evaluation of 120 cases regarding their clinical data and PACTOI, 61 (50.8%) of them were

considered non-massive emboli, 53 (44.2%) were considered submassive emboli, and 6 (5.0%) were considered massive emboli. While 90 (75.0%) patients received only anticoagulant therapy, remaining 30 (25.0%) patients received anticoagulant therapy together with thrombolytic therapy. Mean values of patients' numeric data, MPV, PACTOI, D-dimer, troponin-I, PAP, platelet, INR calculation are provided in Table 1.A concurrent (positive) correlation was found between MPV and PACTOI (r=0.181; p<0.05). A concurrent (positive) correlation of MPV was indicated between D-Dimer and troponin-I, respectively (r=0.203, r=0.257, p<0.05). Moreover,

on echocardiography, a concurrent (positive) correlation was also determined between MPV and PAP, which acts as a right ventricular load indicator (r = 0.215; p < 0.05). It was indicated that PACTOI had a concurrent (positive) correlation with D-dimer and troponin-I, respectively (r = 0.365 and r = 0.284, p < 0.05).In addition, a concurrent (positive) correlation of PACTOI was also determined between lactate and PAP, respectively (r = 0.203; r = 0.493, p < 0.05) (As shown in Table 2). MPV median value was found higher in sub-massive/massive emboli group compared to non-massive emboli group and there was a statistically significant difference between groups (p=0.041).

Table 1. Mean values of laboratory findings of patients with pulmonary thromboembolism.

Data (Units)	Mean value	Std. deviation	Min-Max
MPV (fL)	8.37	0.93	$6.20 - 10.90$
PACTOI (%)	33.54	18.14	$2.50 - 70$
D-DIMER (ng/mL)	4560.16	2938.71	$268 - 10000$
TROPONIN-I (ng/mL)	0.26	0.65	$0.00 - 3.96$
PAP (mmHg)	49.08	17.19	20.0 - 100
PLT (/mm^3)	239316	83049.03	93000-504000
INR	1.22	0.92	$0.80 - 11.00$

MPV: mean platelet volume; PACTOI: pulmonary arterial computed tomography obstruction index; PAP: pulmonary arterial pressure; PLT: platelet count; INR: international normalized ratio.

Table 2. Correlation coefficients and significance levels of MPV and PACTOI levels with each other and with age, d-dimer, troponin, lactate and PAP

	MPV		PACTOI	
	r	p*	r	p*
MPV (fL)	1.000	.	0.181	0.048
PACTOI (%)	0.181	0.048	1.000	.
AGE	0.164	0.073	0.196	0.032
D-DIMER (ng/mL)	0.203	0.026	0.365	< 0.001
TROPONIN-I (ng/mL)	0.257	0.005	0.284	0.002
PAP (mmHg)	0.215	0.019	0.493	< 0.001

* Spearman's correlation test; MPV: mean platelet volume; PACTOI: pulmonary arterial computed tomography obstruction index; PAP: pulmonary arterial pressure

PACTOI median value was significantly higher in sub-massive/massive emboli group compared to non-massive emboli group (p < 0.001).

MPV and PACTOI median values of the patients receiving thrombolytic therapy were found statistically higher than those who did not receive thrombolytic therapy (p = 0.048 and p < 0.001) (As shown in Table 3).PACTOI, PAP and Troponin-I median levels of the group with MPV level of 8.5 and higher were found statistically higher than the group with MPV level below 8.5 (p = 0.018; p = 0.030 and p = 0.011) (As shown in Table 4).

DISCUSSION

In this particular study, it was found that MPV values were higher both in massive/sub-massive emboli group than non-massive emboli group, and in patients receiving thrombolytic therapy than the ones who did not receive thrombolytic therapy. PACTOI values of patients with MPV level higher than 8.5 fL were also observed significantly higher than patients with MPV level below 8.5 fL. MPV is a parameter that can be obtained through routine complete blood count and is a rather simple and easy method that does not require any additional

costs in evaluating platelet functions[5]. Even though it is hard to acquire accurate epidemiological data due to difficulty in its diagnosis, general incidence of PTE is thought to be 117 / 100.000 according to

the data in the United States of America (USA). It is estimated that 600.000 new PTE cases have been developing in the USA every year and that 60.000 of them result in mortality[16].

Table 3. MPV and PACTOI levels of cases regarding emboli type and thrombolytic therapy

Variables	MPV (fL)	PACTOI (%)
Emboli Type		
Non-Massive	8.1 (7.6 - 8.8))	15.0 (2.5 - 35.0)
Sub-Massive/Massive	8.5 (8.0 9.0)	50.0 (37.5 - 70.0)
P - value	0.041*	< 0.001*
Thrombolytic Therapy		
Not receiving	8.3 (6,2 - 10,6)	25.0 (2.5 - 57.5)
Receiving	8.6 (6.5 - 10.9)	50.0 (20.0 - 70.0)
P - value	0.048*	< 0.001*

* Mann Whitney-U test; PACTOI: pulmonary arterial computed tomography obstruction index; MPV: mean platelet volume

Table 4. PACTOI, PAP and troponin levels of cases in terms of the MPV level

Variables	MPV < 8.5 fL (n = 65)	MPV ≥ 8.5 fL (n = 55)	P - value
PACTOI (%)	25.0 (2.5 - 62.6)	45.0 (5.0 - 70.0)	0.018
PAP (mmHg)	45 (25 - 100)	50 (20 - 90)	0.030
Troponin-I (ng/mL)	0.015 (0.0 - 3.96)	0.059 (0.0 - 2.99)	0.011

PACTOI:pulmonary arterial computed tomography obstruction index; MPV:(mean platelet volüme; PAP:pulmonary arterial pressure

In one study, it was revealed that the risk of deep vein thrombosis and pulmonary thromboembolism increases for those aged over 50 and the most common ages to encounter pulmonary embolism are in the ages of 50 - 65[17]. In fact, anatomic changes that occur particularly in lower extremity veins with increased age facilitate the formation of deep vein thrombosis by slowing down the blood flow. Compared to other studies in the literature, in our clinical study we had 11 (9.1%) patients who were 40 and under 40 years old, and 109 (90. 9%) who were over 40 years old. There were also 56 cases who were over 65 (46.6%).

In this study, we evaluated the relationship of PAP with MPV and PACTOI values of the patients. We found that there was a weak positive correlation between MPV and PAP (r = 0.215, P < 0.05). On the other hand we indicated a correlation regarding PACTOI and PAP (r = 0.493, P < 0.05). This finding makes us think that PAP value develops in parallel with PTE load.

Former studies have demonstrated that the sensitivity and specificity of SCTPA are over 90% in predicting PTE[18,19]. In addition to the success of spiral computed tomography pulmonary angiography in diagnosing PTE, since Qanadli et al had defined PACTOI, it became possible to evaluate embolic load objectively in PTE cases.

PACTOI accounts for poor prognosis and acts as an independent, strong risk factor for early death in acute PTE[12,13].

In a study, it was reported that the frequency of venous thromboembolism was higher in patients with MPV value > 9.5 fl compared to the ones with MPV value < 8.5 fl[15]. In our study, we also found a statistically significant difference between PACTOI mean values (25.0) of the cases having MPV value < 8.5fl and PACTOI mean values (45.0) of the cases having MPV value > 8,5fl. Similarly, when we compared the group having MPV level > 8.5 with the group having MPV < 8.5, PAP and troponin-I median levels were indicated statistically high (P = 0.018; P = 0.030 and P = 0.011, respectively).

Moreover, in this study, we determined a weak positive correlation between MPV and D-dimer (P < 0.05)and a positive correlation between PACTOI and D-dimer was available. These findings we gathered are comparable to the similar studies in the literature[20]. However, between similar groups in the study by Hilal et al it did not observe significant differences in terms of MPV, which conflict with our work[21]. Retrospective design and the small number of cases are the main limitations of this study. Due to the retrospective design MPV values after PTE treatment couldn't be included to the study; also mortality data could not be obtained,

because the majority of patients could not be reached. In addition, the study does not include a control group consisting of normal subjects. The sensitivity of CT angiography in the diagnosis of pulmonary embolism is not 100%; this may also affect the results cause an inability to detect small obstructions.

In conclusion, MPV increased in acute PTE patients and and has a weak correlation with PAP and PACTOI. Hence, relationship between MPV and embolic load is unclear in PTE patients. These findings should be investigated by more inclusive, well-designed prospective studies.

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