Could mean platelet volume be a predictive marker for mechanical valve thrombosis?

Ortalama trombosit hacmi mekanik kapak trombozuna işaret eden bir belirteç olabilir mi?

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Background: In this study, we investigated the clinical importance and possibility of mean platelet volume to be a predictive marker for acute mechanical valve thrombosis.

Methods: Mean platelet volume was measured in 28 consecutive patients (mean age 47.3±12.8 years) with mechanical valve thrombosis and 91 control subjects (mean age 46.1±5.8 years). In the study group, blood samples were collected at the first admission (group 1, first measurement) and in the postoperative routine control after discharge (group 1, second measurement). The first control group (group 2) was defined by having a mechanical valve with no history of thrombosis of the mechanical valve. The second control group (group 3) was selected in a consecutive manner from the catheterized cardiac patients who proved to have normal coronary angiograms. Diagnosis of mechanical valve obstruction was based on clinical examination, echocardiography, and cinefluoroscopy.

Results: Mean platelet volume was significantly higher in group 1 (first measurement) patients than in group 1 (second measurement), group 2 and group 3 patients ($p<0.05$). There were slightly higher mean platelet volume values in group 1 (second measurement) than in group 2 and group 3, although they were not statistical significance ($p>0.05$).

Conclusion: It was shown for the first time that patients with mechanical valve thrombosis have higher mean platelet volumes than control subjects. Therefore, mean platelet volume might be used as a follow-up marker of thrombosis in patients with mechanical valve thrombosis.

Key words: Mean platelet volume; mechanical valve; mechanical valve thrombosis.

Amaç: Bu çalışmada ortalama trombosit hacminin mekanik kapak trombozundaki klinik önemi ve akut mekanik kapak trombozuna işaret eden bir belirteç olma olasılığı araştırıldı.

Çalışma planı: Ortalama trombosit hacmi mekanik kapak trombozu olan ardışık 28 hastada (ort. yaş 47.3±12.8 yıl) ve 91 kontrol olgusunda (ort. yaş 46.1±5.8 yıl) ölçüldü. Çalışma grubunda kan örnekleri ilk başvuruda (grup 1, ilk ölçüm) ve taburcu olduktan sonraki ameliyat sonrası rutin kontrolde (grup 1, ikinci ölçüm) toplandı. İlk kontrol grubu (grup 2) mekanik kapağı olan, mekanik kapak trombozu öyküsü olmayanlar olarak tanımlandı. İkinci kontrol grubu (grup 3) kateterizasyon yapılan ve normal koroner anjiyogramları olan kardiyak hastalar arasından ardışık bir şekilde seçildi. Mekanik kapak obstrüksiyonu tanısı klinik inceleme, ekokardiyografi ve sinefloroskopi temel alınarak konuldu.

Bulgular: Ortalama trombosit hacmi grup 1'deki (ilk ölçüm) hastalarda diğer grup 1 (ikinci ölçüm), grup 2 ve grup 3'deki hastalardan anlamlı olarak yüksek idi ($p<0.05$). Grup 1'deki (ikinci ölçüm) ortalama trombosit hacmi değeri grup 2 ve grup 3'den hafif yüksek olduğu halde istatistiksel olarak anlamlı değildi ($p>0.05$).

Sonuç: Mekanik kapak trombozu olan hastalarda ortalama trombosit hacminin kontrol grubuna göre daha yüksek olduğu ilk defa gösterildi. Bu nedenle ortalama trombosit hacmi, mekanik kapak trombozu olan hastalarda trombozun takip belirteci olarak kullanılabilir.

Anahtar sözcükler: Ortalama trombosit hacmi; mekanik kapak; mekanik kapak trombozu.

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Platelet activation plays a crucial role in the prothrombotic events leading to mechanical valve obstruction (MVO). Increased platelet reactivity, as well as shortened bleeding time, is associated with increased platelet volume.[1,2] Higher mean platelet volume (MPV) values have been observed in more patients with stroke and acute myocardial infarction, unstable angina pectoris (USAP), coronary artery ectasia, preeclampsia, and renal artery stenosis than in control subjects.[3-7] However, so far no studies have assessed the relationship between MPV and mechanical valve thrombosis.

Thus, this study examines for the first time the spontaneous MPV variability during the acute phase of a thrombosed mechanical valve in 28 consecutive patients.

PATIENTS AND METHODS

This study was performed during the recovery process of the patients and included the file recording system and operation notes. Permission for the study was obtained from the local ethics committee. Exclusion criteria were prior myocardial infarction, coronary artery disease, cerebrovascular events, hematological disorders, and acute or chronic infection. Between 2006 and 2009, 47 patients with MVO were surgically treated at Türkiye Yüksek İhtisas Hospital. Follow-up data was available for 39 patients (82%) with a mean follow-up of 6.4±1.3 months. In seven patients, there was only pannus in the mechanical valves. Four of them were excluded by MVO with a history of cerebrovascular or cardiovascular events. In 28 patients (the study group), there was MVO due to thrombosis. Ninety-one age and gender-matched patients were determined for two control groups.

The diagnosis of mechanical valve obstruction was based on clinical examinations and diagnostic procedures. The main clinical signs of obstruction were dyspnea, congestive heart failure, and embolism. Diagnosis was established in all patients by echocardiography and cinefluoroscopy.

In the study group, blood samples were collected upon admission before the operation (group 1 first measurement) and in postoperative routine control after discharge (mean 6.4 month) (group 1 second measurement). The first control group (group 2) was defined by having a mechanical valve with no history of thrombosed mechanical valve (TMV). The second control group (group 3) consisted of 59 subjects who were selected in a consecutive manner from the catheterized patients during the same study period and who proved to have normal coronary angiograms. In group 1 (second measurement) and group 2, the patient's international normalized ratio (INR) was between 2.5-3.5 when the blood samples were collected.

Blood samples were taken in the supine position from the antecubital vein with a 20-gauge needle by applying minimal tourniquet force. The blood sample, which was used for the full blood count and MPV values, was drawn into a Vacutainer tube (BD Vacutainer Systems, Belliver Industrial Estate, Plymouth, UK) containing 0.04 ml of the 7.5% K3 salt of ethylenediaminetetraacetic acid (EDTA). These blood samples were analyzed after two hours of venipuncture by a Beckman Coulter LH 750 Analyzer (Miami, Florida, USA).

Statistical analysis

Continuous variables were given as the median ± standard deviation; categorical variables were defined as percentages. A chi-square test was used to compare differences of frequencies in patient characteristics. The other statistical differences of continuous variables between groups were determined using the one-way ANOVA and Tukey tests. Statistical significance was defined as $p<0.05$.

RESULTS

One hundred and nineteen consecutive patients were included in this controlled clinical study. The average age of the patients was 46.4±12 years and 82.36% were women. Baseline demographic and operative data, INR, platelet counts, white blood cell count (WBC-C), and red blood cell count (RBC-C) are summarized in tables 1 and 2.

Female gender had a significant frequency in all of these groups ($p<0.01$). Mitral valve replacement was found to be significantly elevated in groups 1 and 2 ($p<0.05$). In addition, 71.42% of patients had additional pannus in group 1 (1st measurement).

There were no significant differences in red blood cell and platelet count between the groups ($p>0.05$). White blood cell count was higher in group 1 (1st measurement) than in the others ($p<0.05$).

In group 1 (1st measurement), 82.15% of patients were receiving subtherapeutic doses of anticoagulants (INR <2) at the time of diagnosis.

Mean platelet volume was found to be significantly elevated in patients in group 1 (1st measurement) (11.8±1.1 fl) compared with group 1 (2nd measurement) ($p<0.05$), group 2 ($p<0.05$), and group 3 ($p<0.05$). There were higher MPV values in group 1 (2nd measurement) than in group 2 and group 3, although they were not statistically significant ($p>0.05$).

Table 1. Demographic and operative characteristics of the study population

	Age Mean±SD	Men/Women	AVR	MVR	AVR+MVR	TVR	Pannus+thrombus	Thrombus	n
Group 1 (1st measurement)	47.30±12.8	5/23	1	23	3	1	20	8	28
Group 1 (2nd measurement)	47.30±12.8	5/23	1	23	3	1	20	8	28
Group 2	46.63±7.1	6/26	12	18	2	0	0	0	32
Group 3	45.35±13.7	10/49	0	0	0	0	0	0	59

SD: Standard deviation; AVR: Aortic valve replacement; MVR: Mitral valve replacement; TVR: Tricuspid valve replacement.

DISCUSSION

In our study group, we determined admission MPV, a marker of platelet reactivity, and WBC, a marker of inflammation, to be independent predictors of thrombosed mechanical valve patients. To our knowledge, this study has examined for the first time the relationship between MPV and thrombosed mechanical valves. We found that patients with thrombosed mechanical valves had significantly higher MPV values than control subjects.

Mean platelet volume is an indicator of platelet activation, which has an important role in the pathophysiology of thrombosis. Large platelets that contain more dense granules are metabolically and enzymatically more active than small platelets and have higher thrombotic potential. They express higher levels of prothrombotic substances, thromboxane A2, serotonin, b-thromboglobulin, and procoagulatory surface proteins, such as P-selectin and glycoprotein IIIa.[7-12] Previously, it was suggested that an elevated WBC-C might be a marker of a hypercoagulable state.[13] The induction of monocyte procoagulant activity with either interleukin 6 (IL-6) or interleukin 8 (IL-8), which were shown to be overexpressed in leucocytes in acute myocardial infarction (MI) patients, has been proposed as a possible link between inflammation and thrombosis in developing intravascular thrombus.[13] Furthermore, it was shown that on the surface of monocytes, IL-6 and IL-8 caused an increase in tissue factor expression, which with factor Vlla initiates the extrinsic pathway of the coagulation cascade.[14-16] In our study, MPV and WBC-C were found to be significantly elevated in patients in Group 1 (1st measurement) compared with the other groups. There was thrombosis in only Group 1 (1st measurement) patients.

In previous studies, increased MPV was found to be associated with unstable angina pectoris, acute MI, coronary artery ectasia, and congestive heart failure.[1,5,7,9,12,17] In addition, several reports have demonstrated that there is a close relationship between MPV and cerebrovascular disease.[4,5] However, no previous study has examined the relationship between MPV and mechanical valves; hence, we determined to investigate MPV values in patients with thrombosed mechanical valves. We demonstrated that MPV values were more elevated in Group 1(1st measurement) than in the other groups.

It is a known fact that increased platelet activation and aggregation are closely related to mechanic valve thrombosis. In previous reports, different methods were used to analyze the platelet activation: optical aggregometry, a platelet function analyzer (PFA-100), a platelet reactivity test or platelet aggregate ratio, flow cytometry, and thromboxane B(2) generation. All tests have limitations in their use due to complex preanalytical factors, reduced specificity, and poor reproducibility. However, MPV is a simple marker not requiring an advanced or expensive technology.[18]

Table 2. Laboratory data and characteristics of the study population

	Group 1 (1st measurement)	Group 1 (2nd measurement)	Group 2	Group 3
Platelet (x10^3/mm^3)	242±32	237±40	228±69	221±48
White blood cell (x10^3/mm^3)	11.68±2.81*	7.14±1.50	7.30±1.64	7.37±1.74
Red blood cell (x106/mm^3)	4.45±0.49	4.11±0.33	4.27±0.72	4.62±0.59
International normalized ratio	1.54±0.56*	2.71±0.82	2.85±0.22	1.18±0.46
Mean platelet volume (fl)	8.90±0.85*	8.50±0.87	8.40±0.95	8.06±0.88

INR, WBC and MPV count had significant differences (*) in group 1 (1st measurement), ($p<0.01$, $p<0.001$, and $p<0.001$, respectively). There was no significant difference between groups and the other variables.

Our study shows that MPV has clinical importance. Higher MPV seems to be an independent risk factor for TMV. Pizzulli et al.[9] suggest that because platelets stay in the circulation for 7-11 days, they might be detected days before symptoms appear. Similarly, Martin et al.[8] have indicated a correlation between higher MPV and recurrence or death after the first MI in their prospective study.[8] In our study group, MPV values were more elevated on admission before the operation than six months after discharge. We believe the same correlation might exist between MPV and TMV. In routine control, days before MVO symptoms, elevated MPV might be a suspect for TMV. However, to show a possible predictive value for TMV, more prospective studies with higher patient groups should be performed. We can only suggest that MPV and WBC-C might be a valuable and advantageous sign.

In closing, our study is the first to display a significant increase in MPV and WBC-C in patients with MVT. We believe that MPV and WBC-C might be valuable in the prediction of TMV and in planning the need for additional therapy to improve outcomes in patients who have mechanical valves.

Declaration of conflicting interests

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