The effect of on-admission mean platelet volume on TIMI frame count measured after fibrinolytic therapy in patients with acute ST-segment elevation myocardial infarction

ST-Segment yüksekemi akut miyokart enfarktüslü hastalarda başvurdu sırasında ortalama trombosit hacminin fibrinolitik tedavi sonrası TIMI kare sayısı üzerine etkisi

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Objectives: Mean platelet volume has been reported as a predictor of unfavorable prognosis in patients with ST-segment elevation myocardial infarction (MI). We evaluated the relationship between the on-admission mean platelet volume and the response to fibrinolytic therapy using the TIMI frame count in patients with acute ST-segment elevation MI.

Study Design: The study included 87 patients (58 males, 29 females; mean age 55±11 years) who received fibrinolytic therapy within the first 12 hours of symptom onset for acute ST-segment elevation MI. Venous blood samples were obtained to determine the on-admission mean platelet volume and fibrinolytic therapy was administered. Coronary angiography was performed within the first 72 hours and the TIMI frame count was measured for infarct-related artery. TIMI frame count of <40 and ≥40 were defined as complete and incomplete reperfusion, respectively.

Results: Reperfusion was complete in 35 patients (40.2%) and incomplete in 52 patients (59.8%). The mean TIMI frame counts were 31.8±5.9 and 61.2±15.3 in patients with complete and incomplete reperfusion, respectively (p<0.01). Patients with complete reperfusion had a significantly lower mean platelet volume (9.4±0.4 fl vs. 9.7±0.3 fl; p=0.016). There was a highly significant correlation between mean platelet volume and incomplete reperfusion (r=0.742, p<0.0001).

Conclusion: High levels of on-admission mean platelet volume might be associated with insufficient reperfusion response to fibrinolytic therapy in patients with acute ST-segment elevation MI.

Key words: Blood platelets/pathology; coronary angiography; fibrinolytic agents/therapeutic use; myocardial infarction/therapy; myocardial reperfusion; platelet count; risk factors.

Amaç: Ortalama trombosit hacminin ST-segment yükselmeli miyokart enfarktüslü (ME) hastalarda kötü prognozun bir göstergesi olarak bildirilmştir. Bu çalışmada, ST-segment yükselmeli akut ME’li hastalarda başvurdu sonrası ortalama trombosit hacminin fibrinolitik tedavi yanıtını etkileyebileceğini saptanmıştır.

Çalışma planı: Çalışmaya, akut ST-segment yükselmeli ME nedeniyle semptomların ilk 12 saat içinde fibrinolitik tedavi uygulanan 87 hasta (58 erkek, 29 kadın; ort. yaş 55±11) alınmıştır. Hastalardan başvurdu hemen sonra ortalama trombosit hacminin ölçümesi için venöz kan örnekleri alındı ve fibrinolitik tedavi uygulandı. Hastalar ilk 72 saat içinde koroner anjiyografi yapıldı ve enfarktla ilgili arter için TIMI kare sayısı hesaplandı. TIMI kare sayısının ≥40 olması yetersiz reperfüzyon; <40 olması ise tam reperfüzyon olarak tanımlandı.

Bulgular: Otuz beş hastada (%40.2) tam reperfüzyon, 52 hastada (%59.8) ise yetersiz reperfüzyon saptanmıştır. Ortalama TIMI kare sayısı tam reperfüzyon grubunda 31.8±5.9, yetersiz reperfüzyon grubunda 61.2±15 bulundu (p<0.01). Ortalama trombosit hacmi tam reperfüzyon grubunda anlamlı derecede daha düşük idi (9.4±0.4 fl ve 9.7±0.3 fl; p=0.016). Ortalama trombosit hacmi ile yetersiz reperfüzyon yanıtını arasında 2. derecede anlamlı ilişki gözlemdi (r=0.742, p<0.0001).

Sonuç: Fibrinolitik tedavi uygulanan akut ST-segment yükselmeli ME’li hastalarda başvurdu sırasında ortalama trombosit hacminin yüksek olması fibrinolitik tedaviye yetersiz reperfüzyon yanıtıyla ilişkilidir.

Anahtar sözcükler: Trombosit/patoloji; koroner anjiyografi; fibrinolitikaj anjiyografi; risk faktörler.

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Platelet aggregation plays an important role in the pathogenesis of acute myocardial infarction. Mean platelet volume, an indicator of platelet activation, has been reported to be higher in patients with coronary artery disease compared to healthy individuals, and as a possible independent risk factor for myocardial infarction.

The mean platelet volume has also been shown to be an independent indicator of inadequate angiographic reperfusion and 6-month mortality in patients with acute myocardial infarction who undergo percutaneous intervention. The effect of the mean platelet volume on reperfusion is still unknown in patients with acute ST-segment elevation myocardial infarction who were given fibrinolytic therapy. Our aim in this study was to determine the effects of the mean platelet volume on reperfusion response to fibrinolytic therapy in patients with acute ST-segment elevation myocardial infarction who were given fibrinolytic therapy.

**PATIENTS AND METHODS**

The study included 87 patients (58 males, 29 females; mean age 55±11) who received fibrinolytic therapy within the first 12 hours of symptom onset for acute ST-segment elevation myocardial infarction. Exclusion criteria included contraindication to fibrinolytic therapy, including (active bleeding, bleeding diathesis, suspicion of aortic dissection, systemic arterial blood pressure of >180 mmHg, history of previous stroke in the past three months, history of serious trauma or surgery in the past one month, age ≥75 years, thrombophilia, anemia and cardiogenic shock. ST-segment elevation myocardial infarction has been defined as ST-segment elevation of >1 mm in two consecutive precordial or inferior derivations on electrocardiogram, presenting with a typical chest pain lasting for more than 30 minutes. The study was approved by the local ethics committee of our hospital and written consents were obtained from all the patients.

Venous blood samples of 3 mL were collected into standard tubes containing dipotassium ethylene-dinitro tetraacetic acid to measure the mean platelet volume and analyzed using a Sysmex SE 9000 analysis device (Roche Diagnostics, Germany) within approximately one hour.

After blood sample collection, all the patients were administered intravenous infusion of 1.5 million IU of streptokinase over 60 minutes and a concomitant treatment with clopidogrel 300 mg loading dose followed by 75 mg/day, unfractionated heparin 0.01 ml/kg and aspirin 100 mg/day was instituted. Coronary angiography with standard projection was performed within the first 72 hours and digital angiograms were assessed by two independent cardiologists. TIMI frame count was measured for the infarct-related artery using the method defined by Gibson et al. The TIMI frame count was calculated as the difference between the value of the first frame showing contrast opacity and the value of the frame showing contrast opacity to predefined final point in the infarct-related coronary artery. The left anterior ascending artery and left circumflex artery were assessed in the left or right anterior oblique position (caudal angle), while the right coronary artery was assessed in the left anterior oblique position (cranial angle). Prespecified final points were the apical bifurcation landmark for the left anterior ascending coronary artery, distal bifurcation landmark furthest from the segment and including the culprit lesion for the left circumflex artery, and the first branch of the posterolateral artery for the right coronary artery. The corrected TIMI frame was measured by dividing the TIMI frame count which was measured for the left anterior ascending coronary artery into 1.7. The TIMI frame count was regarded as 100 in patients without reperfusion. A TIMI frame count of <40 and ≥40 were defined as complete and incomplete reperfusion, respectively. Patients were divided into two groups based on the number of TIMI frame counts (Group 1 included TIMI frame count of ≤40; Group 2 included TIMI frame count of >40).

**Statistical analysis.** Statistical analyses were performed using the SPSS 13.0 program, while the Student t-test was used for comparison of two independent groups. In addition, Mann-Whitney U-test was used for comparison of continuous variables, while the Chi-square test was used for the comparison of categorical variables. Spearman rank correlation test was used to assess the relationship between two continuous variables. The multivariate logistic regression test was also used to analyze the effect of age, sex, and mean platelet volume on TIMI frame count. P value of less than 0.05 was deemed statistically significant.

**RESULTS**

The baseline characteristics of the groups are shown in Table 1. Reperfusion was observed to be complete in 35 patients (40.2%) and incomplete in 52 patients (59.8%) in patients who were administered fibrinolytic therapy due to acute ST-segment elevation myocardial infarction. Patients with incomplete reperfusion response to fibrinolytic therapy were older than patients with complete reperfusion (56.8±10.8 and 52.2±10.4; p=0.040). Pain-injection time was also longer in this patient group (6.3±3.1 hour and 3.5±2.1 hour; p<0.001). Incomplete reperfusion disposition was...
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greater in hypertensive and diabetic patients, whereas no relationship was found between the sex and reperfusion response. In addition, no difference was found between the groups in terms of infarct-related artery or myocardial infarction site.

Mean TIMI frame count was 3.8±5.9 and 61.2±15.3 in patients with complete (Group 1) and incomplete reperfusion (Group 2), respectively. The on-admission mean platelet volume was found to be highly significantly related to incomplete reperfusion (r=0.742, p<0.0001). Multivariate logistic regression analysis demonstrated that increased mean platelet volume (OR=3.8, 95% CI 1.8-8.5; p<0.0001), age (OR=5.3, 95% CI 2.6-16.1; p<0.0001) and multivessel disease (OR 3.8, 95% CI 1.9-6.8; p=0.0008) were independent predictors for incomplete reperfusion response. Correlation analysis also showed a relationship between mean platelet volume and platelet count (r=0.241, p<0.0001), whereas there was no relationship between platelet count and perfusion response (r=0.046, p=0.58).

DISCUSSION

The purpose of fibrinolytic therapy in cases with acute ST-segment elevation myocardial infarction is to preserve myocardial viability and function, by providing early reperfusion. However, complete reperfusion response is obtained in only 50-60% of the patients. There are several factors which affect reperfusion response to fibrinolytic therapy and which result in incomplete reperfusion. These include hemodynamic factors, local arterial anatomy, thrombus formation and cellular factors. In our study we demonstrated that age, presence of hypertension or diabetes mellitus, multivessel disease, pain-injection time and mean platelet volume were determining factors of reperfusion response to fibrinolytic therapy. Reperfusion response was found to be better in younger patients, non-hypertensives or non-diabetics, patients without multivessel disease and those with a low level of mean platelet volume. Prolonged pain-injection time was found to be associated with incomplete reperfusion.

Response to thrombolytic therapy can be assessed by both invasive and non-invasive approaches. Non-invasive approaches include pain relief or resolution, ≥50% decrease in ST-segment based on the electrocardiography performed 90 minutes after the onset of fibrinolytic therapy, and decreased cardiac enzyme level. On the other hand, invasive approaches include measurement of TIMI flow or TIMI frame count in the infarct-related artery by coronary angiography. At present, no consensus has been reached on practicability and standardization of noninvasive approaches.

TIMI frame count is a valuable method in the assessment of reperfusion. A TIMI frame count of ≥40 is considered as incomplete perfusion. TIMI frame count of ≥40 following fibrinolytic therapy has been reported as being associated with a poor clinical
outcomes. In-hospital mortality and severe cardiac events were more common in patients with higher TIMI frame count. TIMI frame count is also valuable in the detection of coronary reperfusion. However, being an invasive approach restricts its use in current practice. As a result, there is a need for easy to use and inexpensive biochemical markers consistent with TIMI frame count.

Aggregation, subendothelial collagen adhesion and activation of platelets following plaque detachment are the pivotal step in the pathogenesis of acute coronary syndrome. The process is maintain by mediators released from activated platelets. The remarkable role of platelets in the pathogenesis of acute coronary syndrome has been a matter of interest. Measurement of the mean platelet volume is an easy and simple approach to assess platelet function. Mean platelet volume is known to be increased in patients with risk factors for coronary artery disease compared to healthy individuals. Pizzulli et al. reported a higher mean platelet volume in patients with unstable angina pectoris compared to those with stable angina pectoris. Mean platelet volume is also known to be associated with mortality and prognosis in patients with acute myocardial infarction. Rapid depletion of platelets in cases with acute coronary syndrome leads to the release of immature plateletes from the bone marrow into the circulation, and as a consequence platelets with an increased mean platelet volume compared to matured platelets. Platelets with increased mean platelet volume are more hemostatically active. This is due to the presence of more active stored mediators in platelets with a large volume. As a result, these platelets play a primary role in the process of thrombosis. It is also important in terms of the efficacy of fibrinolytic therapy. Increased platelet activation adversely affects thrombolytic process, thereby leading to incomplete reperfusion response to fibrinolytic therapy.

In our study, we observed that mean platelet volume was higher in the patients with incomplete reperfusion (TIMI frame count of ≥40) compared to those with complete reperfusion (TIMI frame count of <40). We found a linear relationship between on-admission mean platelet volume and incomplete reperfusion response, whereas there was no significant relationship between platelet count and reperfusion response.

Early detection of reperfusion response to fibrinolytic therapy may allow immediate and effective administration of advanced treatment options. Mean platelet volume, a biochemical marker, may be helpful to assess the response to fibrinolytic therapy owing to its easy to use and measurable nature. High on-admission mean platelet volume may suggest incomplete reperfusion response to fibrinolytic therapy.

In conclusion, platelets play a critical role in the process of acute myocardial infarction. Complete reperfusion response to fibrinolytic therapy is not achieved in patients with increased mean platelet volume. Measurement of mean platelet volume in patients monitored for acute myocardial infarction may be helpful in determining patients at risk for incomplete reperfusion response to fibrinolytic therapy.

REFERENCES
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