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Regular Article

Mean platelet volume is a predictor of ST resolution following thrombolysis in acute ST elevation myocardial infarction

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ABSTRACT

Background: Larger mean platelets volumes (MPV) are thrombogenic and frequently seen after ST-segment elevation myocardial infarction (STEMI). This study aimed to examine the association of MPV and resolution of ST-segment after thrombolysis in STEMI patients as and its impact on clinical outcome.
Methods: Patients presenting to the emergency department with the diagnosis of first STEMI and were referred to thrombolysis were screened. Patients with ≥50% ST-segment resolution (STR) 90 minutes after thrombolysis were assigned as "Responder" and those with <50% STR were assigned as "Non-Responders". Demographic, clinical comorbidities and risk factor were recorded along with and angiographic data. In-hospital occurrence of major adverse cardiac events (MACE), including acute heart failure (AHF), reinfarction and death were investigated. Additionally, the patients were followed for 6 additional months after their discharge from the hospital.
Results: STR ≥ 50% was seen in 60.2% of patients after thrombolysis. Responders had significantly lower MPV ($P = 0.001$) and the critical MPV values were 8.0 femtoliter (fL) and 8.2 fL in predicting STR and MACE. Patients with MPV ≥8.2 fL had lower probability of STR and higher rates of AHF ($P < 0.001$), and MACE ($P = 0.001$) compared to the patients with lower platelet volume. In multivariate regression, MPV was an independent predictor of STR ($P < 0.001$) as well as MACE (HR = 4.8, 95% CI of 1.8-12.4; $P = 0.001$). Triple vessel disease was another independent factor that predicted MACE.
Conclusion: Higher MPV's at admission were associated with lower STR and higher occurrence of major adverse cardiac events in patients receiving thrombolytic therapy for first time STEMI.

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Introduction

Circulating platelets are heterogeneous in size, density and reactivity [1,2], and changes in these variables are important for the development of acute coronary syndromes [3]. There is strong evidence indicating that the corpuscular volume of the platelets, also know as mean platelet volume (MPV), is an important variable in predicting systemic inflammation and the thrombotic potential of the blood [4]. Larger platelets are denser and they are associated with increased thrombogenesis [5]. Larger size platelets are frequently seen in females and those > 75 years old [6]. The proportion of larger size platelets increases in patients with acute myocardial infarction [7,8] and the MPV is associated with the no-reflow phenomenon in patients with ST elevation myocardial infarction (STEMI) and thereby it may adversely alter the clinical outcome [9].

The elevation of the ST segment in electrocardiography is generally associated with a significant injury to the myocardium compared to those with no elevation of the ST segment. Early revascularization of the myocardium is the mainstay of therapeutic strategy for an acute coronary syndrome [10]. Myocardial revascularization is achieved with either primary coronary intervention or pharmacologic thrombolysis. Electrocardiographic resolution of a ST elevation can be used as measure of reversal in the ischemic injury to the myocardium [11–13]. Responders refer to the group of patients in whom the degree of ST elevation drops to less than 50% of their original level.

We sought to examine the relationship between MPV and ST resolution in a cohort of patients admitted with first myocardial infarction after receiving thrombolytic therapy and to further evaluate its clinical impact. We hypothesized that there was no correlation between the volume of the platelets and the degree of ST resolution.

Patients and Methods

Study design and protocol was reviewed and approved by the Institutional Review Board at Tabriz University of Medical Sciences.

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The design of the study was prospective and observational examining the mean platelet volume of the patients with STEMI treated with streptokinase at the time of their admission. Subject number was calculated with G Power and determined to include 173 patients to attain a power 0.80 with 95% confidence interval. Power calculation was performed based on the findings reported by Yasar et al [14].

Inclusion Criteria

All patients admitted to the emergency department with the diagnosis of first STEMI who were referred to thrombolysis from September 2012 through December 2013 were included. These patients had to be ineligible for primary percutaneous coronary intervention (PCI). Patients were initially screened and only those with symptoms starting < 12 hours prior to their admissions were included in this study.

Exclusion Criteria

Patients with any contraindication to the use of thrombolytic medications, such as aortic dissection, systolic blood pressure > 180 mmHg, history of head trauma or any surgical procedure within past 90 days, history of cerebrovascular accident within the past 90 days, were excluded. Additionally patients who reported adverse hypersensitivity reaction to streptokinase, thrombocytopenia, anemia with a hemoglobin < 10 gm/dL, presence of cardiogenic shock at the time of admission, old MI and current use any combination of antiplatelet agents, were excluded.

Definitions

STEMI was defined as a typical chest pain lasting longer than 30 minutes accompanied by greater than 1 mm ST segment elevation in the inferior leads or greater than 2 mm in two consecutive precordial leads. Myocardial reperfusion was assessed by ST segment resolution in 12-lead ECG. The extent of ST segment elevation in all involved leads (V1-V6, I, aVL for the anterior wall and II, III and aVF for the inferior wall) was measured and recorded at the time of admission and 90 minutes after receiving thrombolytic treatment. ST segment recovery was quantified and grouped based on ST segment resolution. If it was resolved ≥ 50%, the patients were assigned to the "Responders" and if the ST segment resolution was < 50%, they were assigned to "non-Responders" [15].

Thrombolytic Treatment

Patients were infused intravenously with streptokinase 1,500,000 I.U for duration of 20 to 30 minutes. The efficacy and safety of this regimen has been previously shown [16]. Additionally, they received acetyl salicylic acid 300 mg, clopidogrel 300 mg to 600 mg orally, unfractionated or low molecular weight heparin, and statins. Mean Platelet volume was measured prior to receiving the loading dose of antiplatelet agents.

Peripheral blood samples were collected in citrate tubes at the time of admission and were stored until they were analyzed within 24 hours of collection. Biochemical analyses were performed to measure serial and peak creatine kinase (CK) with MB fraction, cardiac troponin (cTNI), triglycerides, cholesterol, serum glucose and creatinine. Mean platelet volume was measured as a part of complete blood cell count (CBC). We enrolled angiographic data of patients in whom a coronary angiogram was performed within the first 72 hours following admission at the discretion of the treating cardiologist. An interventional cardiologist who was blinded to the hematological and electrocardiographic results performed coronary angiograms. Coronary anatomy and the number of the involved vessels with > 50% stenosis were reported and recorded.

Additionally the degree of the patency in the involved artery was assessed by Thrombolysis in Myocardial Infarction (TIMI) flow grading as defined elsewhere [17]:

- TIMI 0 flow (no perfusion) refers to the absence of any antegrade flow beyond a coronary occlusion.
- TIMI 1 flow (penetration without perfusion) is faint antegrade coronary flow beyond the occlusion, with incomplete filling of the distal coronary bed.
- TIMI 2 flow (partial reperfusion) is delayed or sluggish antegrade flow with complete filling of the distal territory.
- TIMI 3 flow is normal which fills the distal coronary bed completely.

Major adverse cardiac events (MACE) was a composite variable defined as either the individual or combined occurrence of acute heart failure (cardiogenic shock/pulmonary edema), reinfarction, stroke or death.

Statistical Analysis

All data points were entered in a excel datasheet and analyzed by SPSS ver. 18.0 (Chicago, IL). The primary endpoint for this study was ST segment resolution on ECG. ST segment resolution greater or equal to 50% was considered as "Responders". Secondary endpoints included TIMI flow grade, heart failure and/or cardiogenic shock, in-hospital mortality and MACE. Main independent variable was mean platelet volume. The mean platelet volume was also assessed as a categorical variable of high volume (greater than or equal to 8.0 fL) or low volume (<8.0 fL) based on the critical point assessment for STR. Data were presented as value (percentage) for categorical variables and means ± STD for numerical values with normal distribution. Pearson analysis was used to correlate ST segment resolution and mean platelet volume and Spearman analysis was used to correlate TIMI flow grades and MPV. Receiver operator characteristic curves were plotted to examine the predictive value of MPV on MACE and ST segment resolution. Area under the curve and the cutoff values were calculated and values > 0.65 were considered reasonable models for prediction. Multivariate regression models were constructed to identify the role of several independent variables on ST segment resolution; logistic regression analyses were used to examine the association between MACE and models with combination of contributing risk factors. Null hypotheses were rejected where P values were < 0.05.

Results

Two hundred patients with STEMI receiving thrombolytic therapy were admitted in the aforementioned period. Four patients due to concurrent use of acetyl salicylic acid, two patients due to the presence of an old MI and three patients because of incomplete laboratory data were excluded. With these exclusions, 191 patients (157 males and 34 females) were enrolled in this study. Demographic, clinical data are shown in Table 1. One hundred and fifteen patients (60.2%) were responders and 76 patients (39.8%) were non-responders. Twenty-one (18.3%) of responders and 13 (17.1%) of non-responders were female (P = 0.83). Responders were older (62 ± 13 vs. 59 ± 11; P = 0.032) and less frequently diabetic (16.5% vs. 30.3%; P = 0.021). Mean MPV was significantly higher in non-responders (7.7 ± 1.6 fL vs. 8.9 ± 1.8 fL; P = 0.001). From the onset of symptoms, responders presented to the emergency care units approximated 1.5 hours earlier than non-responders (P = 0.001). Two groups were not significantly different in terms of other traditional coronary risk factors (Table 1).

Angiographic data (Table 2) were available for 150 patients (91 responders and 59 non-responders) during the index hospitalization. Responders more frequently had single vessel involvement than non-responders (P = 0.03). In addition, the LAD artery was significantly diseased in 88.1% of responders while its involvement was observed in 74.7% of non-responders (P = 0.04).

Clinical, electrocardiographic and biochemical outcome of the patients were shown in Table 3 based on their STR response. Mean left