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Serial changes of mean platelet volume in relation to Killip Class in patients with acute myocardial infarction and primary percutaneous coronary intervention

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ABSTRACT

Introduction: Mean platelet volume (MPV) is related to the reactivity of platelets. Among survivors of acute myocardial infarction (MI), greater MPV is known to be associated with impaired reperfusion and higher mortality. The aims of the study is to investigate the dynamic changes of MPV and the relation between MPV and cardiac function in patients with acute MI and received primary percutaneous coronary intervention (PCI).
Materials and Methods: This retrospective cohort study included patients presented during January 2008 to March 2011 to Peking University Third Hospital with ST-segment elevation MI. All patients received successful PCI. MPV was measured serially, using a Sysmex XE2100 haematology analyser, from admission to day-7 after MI.
Results: In 375 patients, MPV was at its highest value (10.2 ± 1.0 fL) and correlated well with platelet distribution width (PDW, $r = 0.833$, $p < 0.0001$) at the admission, and then reduced by 16% within the 24 hours, together with marked weakening of its correlation with PDW. Patients with poorer ventricular function, estimated by high Killip Class (≥2, n = 96), had higher MPV values at all-time points. By logistic regression model and after adjusting for related confounders, high MPV remained as an independent predictor of Killip Class ≥2 (OR 1.873, CI 95% 1.373 − 2.673, $p = 0.001$). Clopidogrel pre-usage resulted in significant MPV reduction on admission.
Conclusions: MPV undergoes rapid and dynamic changes during the acute phase of MI, and was higher in patients with high Killip Class, suggesting a predictive value of MPV in ventricular dysfunction and clinical outcome of acute phase of MI.

Introduction

Platelets play an important role in plaque rupture and thrombus formation leading to acute coronary syndrome (ACS) and myocardial infarction (MI). It has been shown that platelet size, measured as mean platelet volume (MPV), relates to their reactivity [1]. MPV is readily available with routine blood counts and is therefore an attractive index to investigate in clinical settings. Larger platelets are metabolically and enzymatically more active than smaller ones [2], and have greater prothombotic potential [3]. MPV is positively correlated with indicators of platelet activity including aggregation, release of thromboxane A2 or β-thromboglobulin and expression of glycoproteins Ib or IIb/IIIa [1,2,4,5]. A recent systematic review and meta-analysis showed that MPV was higher in patients with acute MI than in those without acute MI [6]. Elevated MPV has been regarded as an independent risk factor for MI [6]. Among survivors of MI, greater MPV is also associated with impaired reperfusion [2,7,8] and higher morbidity and mortality [2,6,7,9,10]. In patients with metabolic syndrome and ST-segment elevation MI (STEMI), increased MPV at the admission may be associated with the degree of left ventricular (LV) systolic dysfunction [11].

A majority of these studies on patients with MI only measured MPV from admission blood samples prior to drug administration. There are few reports on dynamic changes of MPV in patients with MI receiving

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primary percutaneous coronary intervention (PCI) [6]. Furthermore, despite the well-recognized association between MPV and clinical or angiographic outcomes in patients with MI, the relation between MPV and LV systolic dysfunction after PCI remains unclear. The aims of this study were to define the dynamic changes of MPV following MI and to determine the relationship between platelet indices and cardiac function, estimated by the Killip Class.

Methods

Patients

We conducted a retrospective study on patients who presented with STEMI during January 2008 to March 2011 to the Department of Cardiology, Peking University Third Hospital. Permission for the study was obtained by a local ethics committee. STEMI was diagnosed according to the American College of Cardiology/American Heart Association guidelines in 2004 [12]. Digital angiograms were analyzed by two experienced interventional cardiologists, blind of MPV results. In order to assess coronary blood flow as a continuous variable, the corrected TIMI frame count (CTFC) was determined on the final angiogram, as previously described by Gibson et al. [13]. All patients received successful PCI (defined as coronary angiography with optimized flow of TIMI grade 3). Of consecutive patients with STEMI, those who had one of the following conditions were excluded: 1) major kidney or hepatic disease; 2) malignancy; 3) infectious disease; 4) usage of clopidogrel prior to the onset; and 5) other causes of acute MI including embolism due to cardiac valvular disease, autoimmune disease and massive gastrointestinal hemorrhage.

Killip Classification

Killip Class was evaluated by three clinicians during day-1 after acute MI according to the classic article [14]. Class 1: no evidence of heart failure; Class 2: signs indicating mild to moderate degree of heart failure (e.g. S3 gallop, rales < half-way up lung fields or elevated jugular venous pressure); Class 3: pulmonary edema, and Class 4: cardiogenic shock or hypotension. Patients were re-grouped according to assigned Killip Class.

Echocardiography

Echocardiography was performed in the first or second day after admission using a GE-Vivid 7 system with a 3.3-MHz multiphase array probe. LV fractional shortening (FS) was measured from 2-D short-axis view and ejection fraction (LVEF) was determined using a modified Simpson's method biplane version with apical two- and four-chamber views. Image acquisition and analyses were performed by experienced cardiologists.

Blood Sampling and Haemotological Analyses

In all cases, peripheral blood was drawn at the admission prior to administration of anti-platelet drugs or PCI, and then in the morning of the first, third and seventh day after hospitalization. Blood samples were collected into standardized tubes (INSEPACK ST serials, Beijing, China) containing dipotassium ethylenediaminetetraacetate (EDTA-K2) powder as anticoagulant and stored at room temperature. All measurements were performed within 30 min after collection at the hospital clinical chemistry using a Sysmex XE2100 Haematology System (Sysmex Corporation, Kobe, Japan) with the impedance resistance method. The 95% reference ranges are 9 − 13 fL for MPV, 9 − 17 fL for platelet distribution width (PDW), and 101 − 320 × 10^9/L and 125 − 350 × 10^9/L for platelet counts of women and men, respectively. PDW is defined as the width of the size distribution curve at the 20% level of the peak [15].

Biochemical Analyses

Serum samples were obtained at admission and then every 6 hours within the first 48 hours for assay of creatine kinase (CK) and CK-MB to determine peak values. Blood samples were taken between 24 − 48 h after admission for analysis of high-sensitive C-reactive protein (hs-CRP), creatinine and blood lipids, and 8–48 h for N-terminal pro B-type natriuretic peptide (NT-pro-BNP). Levels of CK, CK-MB, creatinine, hs-CRP and blood lipids were analyzed using Beckman Coulter AU5400 automatic chemical analyzer (California, USA). NT-pro-BNP was measured using Roche E601 immunoassay analyzer (Mannheim, Germany). All the tests were done at the department of clinical biochemistry, Peking University Third Hospital.

Adjunctive Pharmacotherapy

All patients received routine medication that included aspirin at 300 mg before intervention, unfractioned heparin (in bolus at 70–100 U/kg or 50–70 U/kg, respectively, for patients without and with the use of glycoprotein IIb/IIIa inhibitor (abciximab) followed by 1000 U per hour during the PCI procedure). Clopidogrel was given at a loading dose of 300 to 600 mg and a maintenance dose of 75 mg daily during hospitalization. Abciximab was administered during PCI at 0.25 mg/kg in bolus followed by a 0.125 μg/kg/min 12-24 h infusion, at the discretion of the operator. Other drugs commonly prescribed were angiotensin-converting enzyme inhibitors or angiotensin II receptor blocker, β-blockers, statins and isonitrate.

Statistical Analysis

Results were presented as mean ± standard deviation (SD) or as percentages. Baseline clinical parameters between sub-groups were compared using Student's unpaired t-tests, One-way ANOVA, Chi-squared tests or Mann-Whitney Test. To test the normal distribution, the Kolmogorov-Smirnov test was used. One-way ANOVA followed by post-hoc analysis was used for comparison of hematological indices at various time-points. Repeated-measures ANOVA followed by post-hoc analysis was used for comparison of MPV values among different Killip Class groups and at various time-points or influence of abciximab use on MPV values. Spearman or Pearson correlation was used to identify the bivariate correlations. To assess the value of MPV in predicting the admission Killip Class score, logistic regression was performed to obtain odds ratio (OR) and 95% confidence interval (CI) with all confounders (including age, sex, fasting blood glucose, diabetes mellitus, hypertension, pre-infarction angina, time from onset to admission, serum creatinine, anterior MI, ST-segment resolution after PCI, and CTFC) entered in the selection procedure with a p level <0.05 staying in the model. Statistical significance was defined as $p < 0.05$. All analyses were performed with SPSS for Windows version 15.0 (SPSS, Chicago, IL).

Results

Baseline Characteristics of All Study Population

Of a total of 474 consecutive patients with STEMI and successful PCI, 69 patients were excluded for the following reasons: infectious disease (n = 44), major renal or hepatic disease (n = 17), other causes of acute MI (n = 6) or malignancy (n = 2). Another 30 patients, who had taken clopidogrel (75 mg daily continuously at least for one week) formed a separate group for testing potential influence of clopidogrel usage on haemotological parameters (this group had the same inclusion criteria except clopidogrel pre-usage). Thus, 375 patients were enrolled in the study. Baseline patient characteristics and medication are shown in Table 1. The mean interval from onset of the symptom to hospital arrival was 4.8 ± 4.0 h and the door to PCI time was 95 ± 26 min. Of them, 279