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Mean platelet volume predicts patency of the infarct-related artery before mechanical reperfusion and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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ABSTRACT

Background and aims: Patency of infarct-related artery (IRA) before mechanical reperfusion with primary percutaneous coronary intervention (PPCI) has been associated with better prognosis in patients with ST-Elevation myocardial infarction (STEMI). Mean platelet volume (MPV) increases in STEMI patients and may be associated with increased thrombotic potential. In STEMI patients scheduled for PPCI we sought to assess whether mean platelet volume (MPV), as measured at admission, correlates with "spontaneous" reperfusion of the IRA and short-term clinical outcome.

Methods: Blood samples were obtained on hospital admission in 617 consecutive patients (82% men; age 64 ± 12 years) with STEMI, before PPCI. 372 (61%) patients were treated with the GP IIb/IIIa blocker abciximab. The main study endpoint was mortality at 30 days.

Results: MPV was significantly lower in patients with basal TIMI flow grade 2 -3 compared to patients with TIMI grade 0-1 (median, 9 vs. 8.5 fL, $p<0.0001$). After adjustment, MPV remained an independent predictor of the patency of the IRA (OR 0.63, CI 95% 0.51 – 0.78). A cut off value of 8.95 fL had a predictive negative value of 82% to identify patients with patent IRA. Using this cut point, and after adjusting for confounders, MPV was an independent predictor of 30-day mortality (HR 2.92, CI 95% 1.36 – 6.29). When patients were subdivided according to abciximab use, MPV was a marker of worse outcome but only in patients who did not receive abciximab (HR 3.67, CI 95% 1.13 – 11.49).

Conclusion: An increased MPV is an independent predictor of both a patent IRA (TIMI flow 2 or 3 before PPCI) and 30-day mortality. This marker may be able to identify patients requiring more aggressive antiplatelet therapy.

ST-segment elevation myocardial infarction (STEMI) is a major public health problem and a leading cause of death in developed countries. Early reperfusion of ischemic myocardium is critical for restoring normal heart function. Restoring blood flow in the infarct-related artery (IRA) with Primary Percutaneous Coronary Intervention (PPCI) is currently the therapy of choice in patients with STEMI. Outcomes of patients with STEMI undergoing PPCI are closely related to the initial blood flow in the IRA. Patients with a patent IRA have lower rates of heart failure and cardiogenic shock, improved both early and late ejection fraction and reduced short and long-term mortality [1,2]. Non invasive markers of reperfusion may thus provide important prognostic information. Platelets play a central role in the pathophysiology of acute myocardial infarction contributing to the thrombotic occlusion of the IRA. Circulating platelets are heterogeneous in size, density and reactivity [3,4] and changes in these variables are important for the development of acute coronary syndromes [5]. Coronary artery atheromatous plaque rupture leading to intracoronary thrombus formation is commonly the precipitating event in acute coronary syndromes [6] and, in addition to any prothrombotic changes occurring in the atherosclerotic plaque, the presence of large, more reactive platelets, is also likely to contribute to thrombosis [7]. There is strong evidence indicating than mean platelet volume (MPV) is an important variable and that larger platelets have a higher thrombotic potential. Larger platelets are denser [8], aggregate more rapidly on collagen challenge, produce larger amounts of thromboxane B2 [9], release more serotonin and β-thromboglobulin [10,11] and express more Ib and IIb/IIIa glycoproteins [12]. MPV has been found to be increased in patients with acute myocardial infarction [5,13] and reported to be associated with the no-reflow phenomenon and clinical outcome in patients with STEMI [14]. Little

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is known, however, about the suggested role of MPV as a marker of coronary artery patency in STEMI patients undergoing PPCI. We, therefore, sought to assess whether an association exists between MPV measured at admission, TIMI flow grade before PPCI and patient outcome in STEMI patients referred to a single tertiary centre for PPCI.

Methods

Patients

From June 2005 to March 2007, all patients admitted to our institution with a diagnosis of STEMI and treated with PPCI were included in the study if PPCI was performed within 12 hours from the onset of symptoms. STEMI was defined as typical chest pain >30 minutes with ST-segment elevation >1 mm in two or more contiguous leads (or reciprocal ST depression >1 mm in leads V_1 or V_2), or left bundle branch block. Exclusion criteria were the use of thrombolytic drugs within the previous 24 hours, history of bleeding diathesis, end-stage liver or renal disease, malignancy, systemic inflammatory disease. Patients who presented >12 h from the onset of symptoms were not included. The study was designed and performed in accordance with the regulations of the institutional ethical committee. All patients gave written informed consent prior to study entry.

Laboratory analysis

In all patients, venous peripheral blood samples were drawn on admission for measurement of hematological variables. Samples were obtained at the emergency room or the ambulance before the administration of abciximab, and processed within one hour from collection. All measurements were performed with the ADVIA 120 Haematology System (Bayer Healthcare, Tarrytown, NY, USA), which offers an accurate two-dimensional platelet analysis, determining volume on a cell-by-cell basis by measuring two angles of laser light scatter.

Patient treatment

All patients received 250 mg aspirin at the time of diagnosis and before arrival to the catheterization laboratory. Abciximab (a loading dose of 0.25 mg/kg followed by a continuous infusion of 0.125 μg/Kg/min during 12 hours) was administered in 372 patients (61%) as prescribed by the treating physician in the emergency department of the local hospital or during patient transfer to our institution. Non-fractionated heparin was given during the procedure to achieve an activated clotting time of 250 to 300 seconds. In every patient a loading dose of clopidogrel (300 mg) was administered in the emergency department, during transportation or immediately on arrival to the catheterization laboratory, and before PPCI. "Early" administration of clopidogrel was defined as administration of clopidogrel before arrival to the catheterization laboratory. Aspirin (100 to 150 mg/day) was continued indefinitely, and clopidogrel (75 mg/day) was prescribed for one month if bare metal stents were implanted and for at least 6 months if drug-eluting stents were used.

Coronary angiography and intervention

Coronary angiography was performed using standard techniques. Multiple projections of the coronary arteries were recorded digitally. Angiograms were reviewed by two independent expert interventional cardiologists and a third reviewer was involved when discrepancies emerged. The IRA Thrombolysis In Myocardial Infarction (TIMI) flow was assessed in every patient. A "patent" IRA was that with a TIMI flow grade 2 or 3, and an "occluded" artery that with an initial TIMI flow grade 0 or 1. PCI was performed according to standard techniques. The use of stents and the type of stent (bare metal or drug-eluting stent) was left to the operator's discretion. Left ventricular ejection fraction (LVEF) was calculated from tracing contours of the LV in right anterior oblique sequences using the area-length method with correction for the right oblique projection [15]. Angiographic "success" was defined as the achievement of a minimum stenosis diameter reduction to less than 20% in the IRA with TIMI flow grade 3 [16]. Severe coronary thrombosis was defined as the presence of a luminal defect >10 mm and visible from multiple projections. Time to treatment was defined as the time from the onset of symptoms to balloon inflation. Door-to-balloon time was defined as the time from the first contact with the medical system to balloon inflation.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), or as median (interquartile range, IQR), and compared with the Student's T or Mann-Whitney U-tests, as appropriate. Categorical variables are presented as percentages and compared by means of chi-square or Fisher's exact tests. Analysis of normality was performed with the Kolmogorov–Smirnov test. Optimal cutoff point of MPV to predict patency of the IRA was calculated with receiving operating characteristics (ROC) analysis. Multivariate logistic regression models adjusted by age, gender, cardiovascular risk factors, antiplatelet therapy administered, time to treatment and hematological variables were used to identify predictors of patency of the IRA. Cox-regression analysis adjusted by age, gender, cardiovascular risk factors, patency of IRA, time to treatment, cardiogenic shock and LVEF was performed to identify independent predictors of 30-day mortality. Survival curves were generated by means of the Kaplan-Meier method. All tests are two-tailed, and a p value of 0.05 or less was considered significant. All analyses were performed with SPSS 15.0 statistical package for Windows (SPSS Inc., Chicago, Ill.).

Results

Baseline characteristics

During the study period, 617 patients were included in the study. At baseline coronary angiography the IRA showed a TIMI flow grade 0 or 1 in 426 patients (69%), and grade 2 or 3 in 191 (31%) patients. Baseline characteristics in all patients and those in the two TIMI flow groups are shown in Table 1. Angiographic success was achieved in

Table 1
Baseline characteristics of the study patients.

	All patients (n = 617)	TIMI flow grade 0 – 1 (n = 426)	TIMI flow grade 2 – 3 (n = 191)	P value
Age (years)	63 ± 12	63 ± 12	63 ± 12	0.890
Male sex	81%	82%	80%	0.501
Family history	6.5%	6%	7%	0.479
Hypertension	37.5%	38%	37%	0.858
Diabetes	17.5%	16%	19%	0.424
Current smokers	35%	32%	38%	0.143
Dyslipemia	33.5%	29%	38%	0.026
Location				
Anterior	41%	42%	40%	0.990
Inferior	51%	52%	50%	0.741
Posterolateral	4.5%	4%	5%	0.568
Undetermined	2.6%	2%	3%	0.398
Cardiogenic shock	4.5%	4.9%	3%	0.397
Multivessel disease	48%	44%	52%	0.055
Early clopidogrel use	32%	32%	32%	1.000
Abciximab use	61%	60%	62%	0.478
LVEF (%)	57 ± 14	56 ± 14	58 ± 14	0.187
Complete revascularization	55%	57%	53%	0.335
Procedural (PPCI) success	89%	86%	94%	0.002
Time to treatment (min)	245 [159-378]	260 [170-385]	229 [145-333]	0.017
Door to balloon time (min)	125 [90-170]	122 [86-170]	131 [96-170]	0.310

Data are expressed as mean ± standard deviation for normally distributed data, median (interquartile range) for non-normally distributed data, and percentage (%) for categorical variables. LVEF: left ventricular ejection fraction.