Original Article

Could Mean Platelet Volume Predicts Impaired Reperfusion and In-Hospital Major Adverse Cardiovascular Event in Patients with Primary Percutaneous Coronary Intervention after ST-Elevation Myocardial Infarction?

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Abstract

Background: *Due to the positive relation between platelet size and platelet reactivity, a high value of the mean platelet volume (MPV) is an independent risk factor to predict acute myocardial infarction (AMI) and its adverse outcome. Few data are available to determinate the prognostic value of MPV in ST-elevation myocardial infarction (STEMI) patients treated with percutaneous coronary intervention (PCI).*

The primary purpose of this study was to evaluate the clinical value of MPV to predict impaired reperfusion and in-hospital major adverse cardiovascular events (MACE) in acute STEMI treated with primary PCI.

Methods: *This study included 203 STEMI patients referring for blood sampling before primary PCI to estimate MPV and determine the thrombolysis in myocardial infarction (TIMI) flow grade, corrected TIMI frame count (CTFC), and in-hospital MACE.*

Results: *The frequency of in-hospital MACE in the group of patients with a high MPV (≥10.3 ng/dl) was significantly more than that of the group with a low MPV (<10.3 ng/dl) (37.8% vs. 4.4%, P<0.001). The no-reflow phenomenon was more frequent in the patients with a high MPV than that of the patients with a low MPV (17.8% vs. 1.9%, P<0.001). The mean MPV in the group of patients with CTFC≥40 was significantly more than that of the group of patients with CTFC<40 (10.9±0.92 vs. 9.45±0.85, P=0.001). After adjustment for baseline characteristics, a high MPV remained a strong independent factor to predict the no-reflow phenomenon (Odds Ratio [OR]=2.263, 95% Confidence Interval [CI]=1.47 to 5.97; P<0.002), in-hospital MACE (OR=2.49, 95% CI=1.34 to 4.61; P<0.004), and CTFC≥40 (OR=2.09, 95% CI=1.22 to 3.39; P<0.003).*

Conclusion: *These findings confirmed that not only could admission MPV predict impaired reperfusion and in-hospital MACE in acute STEMI patients treated with PCI, but also it could be considered a practical way to determine higher-risk patients.*

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Introduction

Atherosclerosis and its complications such as acute myocardial infarction (AMI) are regarded as one of the most important causes of death in industrial societies.[1] Although there are some known risk factors for coronary artery disease such as age, gender, cigarette smoking, hypercholesterolemia, diabetes mellitus, hypertension, and familial history of AMI,[1] the detection of some other factors to determine the true risk of acute coronary syndrome seems necessary.[1] Since platelets play an important role in forming intra coronary vascular thrombosis, they are considered a principal cause of AMI.

An increase in platelet size is concomitant with a rise in platelet reactivity. In addition, the mean platelet volume (MPV) has a direct relation with the indicators of platelet activity such as glycoprotein Ib and glycoprotein IIb/IIIa receptors.[2-9] Previous studies have established that higher amounts of MPV correlate with a poor outcome in AMI patients; nevertheless, only one study has thus far been conducted on the relation between MPV and the outcome of AMI patients treated with primary percutaneous coronary intervention (PCI).[10] The present study sought to determine the value of MPV in AMI patients undergoing primary PCI and its relation with impaired reperfusion and in-hospital adverse outcomes.

Methods

This retrospective, descriptive survey conducted from August 2003 to July 2007 included 214 AMI patients undergoing primary PCI in Modarres Hospital, a university teaching hospital in Tehran, Iran. Eleven patients were excluded subsequently due to a lack of file information and emergency status requiring surgical intervention. Consequently, the population of this study consisted of 203 patients.

AMI was defined as patients with typical chest pain lasting more than 30 minutes and concomitant ECG changes (ST elevation ≥1 mm in at least 2 consecutive precordial or inferior leads) referring within 12 hours from the onset of symptoms. In addition, patients with cardiogenic shock due to AMI within 24 hours from the onset of their symptoms were investigated in this study. The patients were divided into two groups in terms of their MPV: Group 1: MPV<10.2 ng/dl and Group 2: MPV≥10.3 ng/dl (high MPV group).

Major adverse cardiovascular events (MACE), comprising death, cardiogenic shock, MI, cerebrovascular accident (CVA), and mechanical complications leading to urgent revascularization, were investigated in all the patients.

The CBC of all the patients was sampled on admission in test tubes containing ethylenedinitro tetra acetic acid (EDTA) as an anticoagulant substance. The beginning of sampling to the end of sample analysis took less than 2 hours. All the measurements were done using just one Aoutoanalysor-104 Hitachi hematology system. No patient received clopidogrel, heparin, or integrilin before sampling. All the patients underwent coronary angiography in standard projection for different coronary arteries (Siemens Company) using the Judkins 7F and guiding catheter. The thrombolysis in myocardial infarction (TIMI) flow of the infarct-related arteries was determined before and after PCI. Subsequently, corrected TIMI frame count (CTFC) was measured by two cardiologists not aware of the MPV results in order to have a more quantitative study. The TIMI of the involved vessels was determined before and after PCI. CTFC, defined as an impaired reperfusion, was measured to have a more quantitative study. The no-reflow phenomenon was defined as TIMI<3 after PCI in spite of residual stenosis <50%, absence of significant dissection, or visible thrombosis or spasm. Further more, all the patents were checked as regards having any kind of in-hospital MACE.

All the patients received 325 mg ASA and at least 300 mg Plavix before PCI and received 100 u/kg heparin to achieve Active clotting time (ACT)>300 s or 70 u/kg integrilin and heparin to achieve activated clotting time (ACT)=200-250 during the procedure of PCI. All the collected data were analyzed using SPSS 13 software.

Results

This study recruited 203 patients, comprised of 160 (78.8%) men and 43 (21.2%) women, with a mean age of 56±11.2 years. Of the total study population, 95 (46.8%) patients had three-vessel involvement, 59 (29.1%) had small vessel disease, and only 1 (0.5%) had left main coronary artery disease. Stenting was done for 179 (88.2%) cases. Conventional PCI was performed for 13 (6.4%) patients, and the procedure was unsuccessful in 11 (5.4%) patients. For 35 (17.2%) patients, drug-eluting stents; and for 144 (70.9%) patients, non-drug stents were inserted.

A total of 189 (91.6%) patients had a stable hemodynamic, and 17 (8.4%) had systolic blood pressure≤90 mmHg on admission. The mean systolic blood pressure (SBP) of the patients was 119.7±27.04 mmHg, and their mean MPV was 9.55±0.88 ng/dl. The patients were divided into two groups on the basis of their MPV: Group 1: 158 (77.8%) cases with a low MPV (MPV <10.3 ng/dl) and Group 2: 45 (22.2%) cases with a high MPV (MPV≥10.3 ng/dl).

In-hospital MACE was detected in 39 (19.2%) cases, comprised of mortality in 15 (7.4%) cases and other in-hospital major events in 24 (11.8%) other cases consisting of 8 (3.9%) cases of MI, 2 (1%) cases of CVA , 12 (5.9%) cases of shock, and 2 (1%) cases of mechanical complications.

The demographic, clinical, and procedural characteristics

of the patients in the MPV groups are summarized in Table 1. There was no difference between the patients in the high MPV group and low MPV group with respect to having such factors as age, gender, hypercholesterolemia, diabetes mellitus, hypertension, and prior AMI. Although cigarette smoking was slightly more frequent in the low MPV group, the high MPV group had more patients with a higher Killip class on admission and longer time of hospitalization.

In addition, the number of cases with anterior wall MI and left anterior descending coronary artery involvement in the high MPV group was significantly more than that of the low MPV group, as demonstrated by Table 1.

Table1. Patient's demographic, clinical, and procedural characteristics in MPV groups*

	Low MPV (n=158)	High MPV (n=45)	P value
Male	79.1	77.8	0.85
Age (y)	55.27±10.6	58.67±13.29	0.12
SBP (mmHg)	120.98±24.7	115.22±33.84	0.29
Hypertension	31.6	31.1	0.95
Diabetes mellitus	20.3	31.1	0.13
Cigarette smoking	51.3	35.6	0.06
Hyperlipidemia	36.7	37.8	0.90
Prior MI	11.4	15.6	0.45
Ant wall MI	60.8	80	0.02
Killip class			
I	91.2	68.9	<0.01
II	4.4	6.7	0.54
III	0	2.2	0.06
IV	4.4	22.2	<0.01
IRA (%)			
RCA	27.2	13.3	0.05
LCX	8.9	4.4	0.34
LAD	63.9	82.3	
3VD	44.3	55.6	0.02
Base line	81.1	86.7	0.18
TIMI Flow 0/1			0.43
Integrilin	10.8	11.1	0.95
Duration of hospitalization (d)	6.52± 3.12	9.91±5.23	0.01

*Data are presented as the mean±SD (P value for Mann-Whitney test) or percentage of patients (P value for chi-square test)
MPV, Mean platelet volume; SBP, Systolic blood pressure; MI, Myocardial infarction; Ant, Anterior, IRA, Infarct-related artery; RCA, Right coronary artery; LCx, Left circumflex artery; LAD, Left anterior descending artery; 3VD, Three vessels disease, TIMI, Thrombolysis in myocardial infarction

The mean MPV in the group of patients with the no-reflow phenomenon (11 cases: 5.4%) was 9.98±1.08 ng/dl and in the group without it was 9.35±0.87 ng/dl; there was no significant difference in the mean MPV between these two groups (P=0.17). Nonetheless, the frequency of the no-reflow phenomenon in the high MPV group was significantly higher than that of the low MPV group (P<0.0001, 17.8 % vs. 1.9%).

After adjustment for basic characteristics, MPV remained a strong independent factor to predict the no-reflow phenomenon (Odds Ratio [OR]=2.263, 95% Confidence Interval [CI]=1.47 to 5.97; P<0.002), which indicated that the no-reflow group was 3 times more likely to have MPV≥10.3 ng/dl (Table 2).

The prognostic significance of MPV to cause the no-reflow phenomenon with a cut-off value of 10.3 ng/dl was determined via the receiver operating characteristics (ROC). The area under the ROC curve showed that the prognostic significance of MPV for the no-reflow phenomenon was 83% (95% CI=.76 to .91). Also, an MPV of 10.3 ng/dl had a sensitivity of 60.1% and specificity of 83.9% to cause the no-reflow phenomenon (Figure 1) (ROC curve).

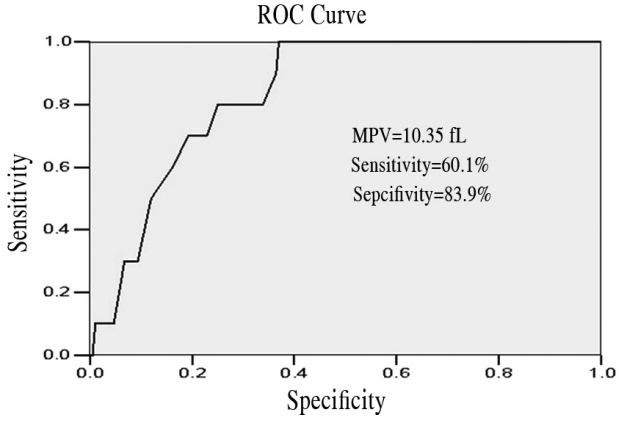

Figure 1. Sensitivity and specificity of mean platelet volume (MPV) to predict the no-reflow phenomenon

This study showed that 143 (70.4%) patients had TIMI=0, 25 (12.3%) had TIMI=1, 26 (12.8%) had TIMI=2, and 9 (4.4%) had TIMI=3 before PCI. Additionally, 11 (5.4%) patients had TIMI=0, 7 (3.4%) had TIMI=1, 28 (13.8%) had TIMI=2, and 157 (77.3%) had TIMI=3 after PCI.

Ignoring the amount of MPV, diabetes mellitus was not a risk for the no-reflow phenomenon (P=0.72, 22.9% vs. 18.2%). Also, the prevalence of multi-vessel disease had no significant difference between the group of patients with the no-reflow phenomenon and the group without it (OR=0.72, 95 % CI=0.213 to 2.44; P=0.6).

There was a significant difference between the mean MPV in the group of patients with CTFC≥40 and patients with CTFC<40 (P=0.001, 10.9±0.92 vs. 9.45±0.85). The frequency of the patients with CTFC≥40 after PCI in the high MPV group was significantly more than that of the low MPV group (P<0.0001, 7.8% vs. 37.5%), and also the mean CTFC in the high MPV group was more than that of the low MPV group (P<0.0001, 33.98±18.8 vs. 22.05±9.84). After adjustment for basic characteristics, a high MPV was corroborated as an independent predictor of CTFC≥40 after PCI in both univariate and multivariate analyses (Table 2 & Figure 2).

Table 2. Prognostic significance of MPV ≥10.3 ng/dl

	Unadjusted OR (CI: 95%)	P value	Adjusted OR* (CI: 95%)	P value
No Reflow	2.96 (1.47-5.97)	0.002	2.96 (1.47-5.97)	0.002
TIFC≥ 40	2.16 (1.32-3.55)	0.002	2.09 (1.29-3.39)	0.003
MACE	2.82 (1.64-4.85)	0.001	2.49 (1.34-4.61)	0.004

*Adjusted for age, gender, systolic blood pressure, hypertension, diabetes, hyperlipidemia, smoking, previous myocardial infarction, anterior wall myocardial infarction, Killip≥2, infarct- related artery, multi-vessel disease, baseline TIMI flow grade 0/1 and stent utilization
MPV, Mean platelet volume; TIFC, Thrombolysis in myocardial infarction frame count; MACE, Major adverse cardiovascular events

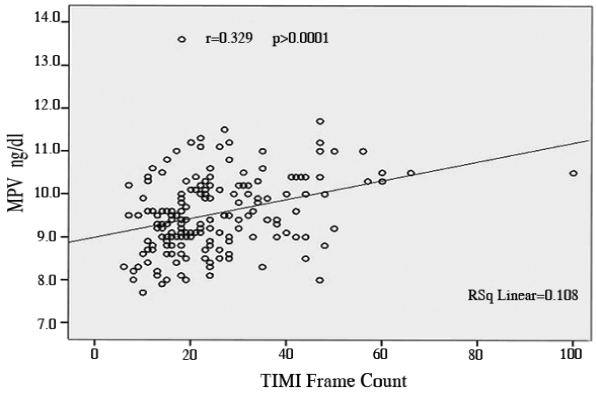

Figure 2. The correlation between corrected thrombolysis in myocardial infarction frame count (CTFC) and Mean platelet volume (MPV)
TIMI, Thrombolysis in myocardial infarction

The mean MPV in the group of patients with EF ≤30% was higher than that of the group of patients with EF ≥50 % (P=0.004, 9.33±0.89 ng/dl vs. 9.88±0.99 ng/dl). Also, the number of patients with EF ≤30% in the high MPV group was more than that of the low MPV group (P=0.001, 12% ng/dl vs. 33.3%); however, there was a negligible relation between the decrease in EF and the increase in CTFC as a negative correlation index (r=0.19, P<0.009) (Figure 3).

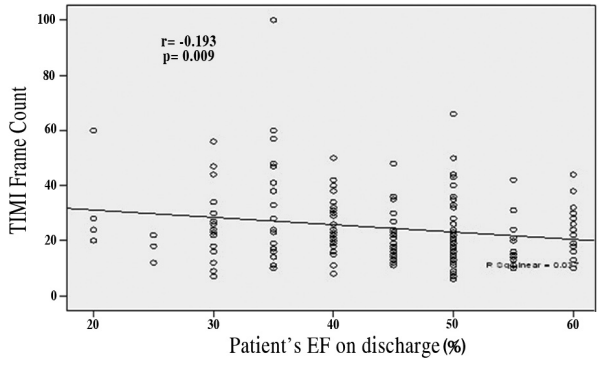

Figure 3. The correlation between Corrected TIMI Frame Count (CTFC) and patients' ejection fraction
TIMI, Thrombolysis in myocardial infarction; EF, Ejection fraction

Table 3. The correlation between TIMI, Corrected TIMI Frame Count (CTFC); and MACE, mortality, shock and MI

	CTFC<40	CTFC≥40	P value	TIMI=3	TIMI≤ 2	P value
MACE	13(8.1%)	6(25%)	0.0100	12(7.6%)	12(26.1%)	0.0010
Mortality	5(3.1%)	6(25%)	<0.0001	5(3.2%)	10(27.7%)	<0.0001
Shock	4(2.5%)	4(16.7%)	<0.0001	4(2.6%)	8(17.4%)	<0.0001
MI	7(4.4%)	0	0.5600	7(4.5%)	1(2.2%)	0.4800

TIMI, Thrombolysis in myocardial infarction; CTFC, Corrected TIMI frame count; MACE, Major adverse cardiovascular events; MI, Myocardial infarction

The mean MPV in the group with mortality was significantly higher than that of the group without mortality (P<0.0001, 9.49±0.86 ng/dl vs. 10.41±0.81ng/dl). Also, there was a significant difference between the mean MPV between the group of patients with in-hospital MACE and the group without in-hospital MACE (P<0.0001, 10.29±0.95 ng/dl vs. 9.46±0.83 ng/dl).

The mean MPV in the group of patients referring with shock was significantly higher than that of the group without shock (P=0.001, 9.5±0.86 ng/dl vs. 10.39±0.92 ng/dl). In addition, the frequency of shock in the high MPV group was more than that of the low MPV group (P<0.0001, 20.5% vs. 1.5%).

The frequency of the recurrence of MI in the high MPV group was higher than that of the low MPV group (P<0.0001, 11.4% vs. 1.9%).

After adjustment for basic characteristics, MPV remained a strong independent predictor to cause in-hospital MACE in patients with STEMI after primary PCI (OR=2.49, 95% CI=1.34 to 4.61; P=0.004) (Table 2).

Discussion

This study recruited 203 patients with a mean age of 56±11.2 years, which was five years less than the mean age of the patients in the Huczek study[10] but was approximately similar to the mean age of the patients in other studies on MPV.[11] In addition, 78.8% of our patients were men; this percentage was similar to that in other studies on the relation between MPV and acute coronary syndrome insofar as men accounted for 70-80% of their study populations.[10-14]

The present study compared the demographic, clinical, and procedural factors between high MPV and low MPV patients and found no significant differences between these two groups. This finding was similar to that in another study conducted specifically on the correlation between the risk factors of acute coronary syndrome patients and MPV. The Kilicli-Camur study demonstrated that apart from such known risk factors as age, cigarette smoking, diabetes mellitus, and hypertension, a high MPV was an independent risk factor for acute coronary syndrome and patients' survival.[11] Unlike the present study, in the Huczek study on the relation between MPV and demographic characteristics

of patients with primary PCI, the frequency of hypertension, as a risk factor, in the high MPV group was lower than that in the low MPV group.[10] This difference is probably due to the fact that patients in the said study were older than our subjects.

Chiming in with the Huczek study, the odds ratio of vessel involvements in our study had no significant difference between the high and low MPV groups. Be that as it may, compared with the Huczeck study, we observed a higher rate of anterior wall MI and left anterior descending artery involvement in our high MPV group.[10] There is no logical explanation to justify the high value of MPV as an independent risk factor for anterior wall MI.

The use of different methods for the detection of the no-reflow phenomenon has led to a different prevalence for it in various studies. The no-reflow prevalence with a definition of TIMI≤2 with the absence of macro-vascular obstruction has been reported to be approximately 12-15%.[12-14] The no-reflow prevalence with a perfusion grade method has been reported at 29%[15] and with contrast echocardiography at 34-39%.[16,17]

The no-reflow phenomenon and CTFC≥40 associates with a poor patient outcome such as increased mortality, 30-day mortality, in-hospital MACE, and left ventricular remodeling as well as MI recurrence and heart failure.[18-23] The rate of the no-reflow phenomenon was 5.4% in our study, which was less than that in other studies; e.g. 10.8% in the Huczeck study.[10] This difference may be because the other studies chose older patients, more patients with killip IV class, more patients with a low EF on admission, and higher-risk patients with a positive past history of MI. Furthermore, unlike the present study, PCI procedures were conducted on graft vessels in other studies.

We found that a high value of MPV was an independent hematological marker for the easier detection of patients in whom the no-reflow, slow-flow (CTFC≥40), and consequently in-hospital MACE might happen after primary PCI.

According to what previous studies have proved, platelet size has a positive relation with platelet reactivity and its aggregation. Also, a higher value of MPV predisposes patients to acute coronary syndrome and in-hospital MACE after acute coronary syndrome.[24-30]

We showed that the respective sensitivity and specificity of MPV with a cut-off value of 10.3 to cause the no-reflow phenomenon was 60.1% and 83.9%, while in the Huczeck study, the sensitivity and specificity of MPV with the same cut-off point were 61.9% and 74.3%, respectively.[10]

Although in the present study, a high value of MPV, regardless of adjustment for basic characteristics, was an independent risk factor for CTFC≥40, the Pierson correlation test showed a lower correlation index between MPV and CTFC in this study than that in the Huczeck study (P<0.0001, r=0.698 vs. P<.0.0001, r=0.329). These differences were related to our smaller study population. Moreover in the Huczech study, CTFC=100 was defined conventionally as TIMI=0.1 after PCI; however, this study only chose cases whose CTFC was possible to calculate.[10]

We demonstrated that a measurement of MPV could be helpful to detect patients with MPV≥10.3 and consequently higher-risk patients for in-hospital MACE. Martin et al. showed that a higher value of MPV, up to six months after MI, was accompanied by an increase in the risk of MI recurrence and 2-year mortality.[31] In addition, Huzceck et al. measured MPV on admission and reported that a high MPV was an independent risk factor for 6 months' MACE.[10] In our group of patients with mortality, any type of in-hospital MACE and cardiogenic shock had a higher mean MPV by comparison with the other group with none of those complications. With respect to hospital MI, there was no significant difference in mean MPV between the two groups; however, the frequency of MI, like other causes of mortality and shock, was far higher in the high MPV group. As a result, after the multivariate analysis and adjustment for basic factors, a high MPV remained an independent risk factor for in-hospital MACE. This finding is acceptable inasmuch as MPV is a risk factor for the no-reflow phenomenon and CTFC≥40. The findings of Pabon et al., whose study showed a direct relation between in-hospital mortality and a high MPV on admission, support our findings.[32]

We showed that mortality and in-hospital MACE rate were 1.36 times more for every 10 frames of increase in CTFC.

In spite of a significantly higher frequency of EF≤30 in the group of patients with TIMI≤2 after PCI, we observed a negligible relation between a decrease in EF and increase in CTFC with r=0.19 as a negative correlation index. It may have been in consequence of the fact that we neither utilized a quantitative index to determine EF and nor did we employ a more sensitive index for the left ventricular function. As was expected, mean MPV in group of EF≤30% was more than that in the group of patients with EF≥50%. Moreover, the frequency of patients with EF≤30% in the high MPV group was higher than that of the low MPV group, which indicated that the left ventricular function could strongly predict the long-term mortality of patients with MI.

Limitations of study

Whereas numerous similar studies have used Absiximab during PCI, we made use of integrilin. However, only 22 out of the 203 patients in our study received integrilin, which is much fewer than the subjects in other studies. Therefore, the findings are not suitable for comparison or generalization. On the other hand, because the patients' characteristics for the prescription of integrilin and the specified protocol were not determined beforehand, the

results which had no significant differences in different groups of MPV, CTFC, and MACE were not discussable.

Unlike the Huczeck study, we made no intervention on graft vessels. Another weak point in the present study is that time constraints, a lack of facilities for long-term follow-up, and the intention to augment the reliability of the results prompted us to only report in-hospital mortality, compared with several studies on MPV, which had followed 6-month mortality of patients.

Although, EDTA, an anticoagulant of complete blood count samples, can raise the size of the platelet, it was not considered a disturbance in our study because if measurement is done within 60 to120 minutes after sampling, volume change will be about 3.4%;[32,33] and if it is done over a 30-minute period after sampling, the rate of increase will be less than 0.5 ng/dl.[34]

Like other studies, heterotypic platelets were not excluded in our study due to the need for flow-cytometry, which is not only expensive and time consuming but also requires special devices, to which we had no access.

Conclusion

Admission MPV in AMI patients is a strong and independent factor to show impaired reperfusion and its related mortality. Also, MPV measurement is a simple and feasible way to detect high-risk patients requiring different approaches and treatments.

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