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Mean Platelet Volume as a Biomarker for Detection of Reperfusion Abnormalities in STEMI Patients Treated with Primary PCI

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Abstract

Background: ST-Segment Elevation Myocardial Infarction (STEMI) is one a common presentation of cardiovascular diseases. About 40% of patients with (ACS) presented as STEMI. Prevalence of STEMI continues to rise in worldwide [1].

Platelets (PLT) have a central role in pathophysiology of ACS [2]. And a major role in development of no-reflow [6]. Furthermore, increased mean platelet volume (MPV) at admission was associated with long-term mortality in patients with ACS [7].

Aim of Study: We aimed to evaluate the accuracy of MPV as a biomarker for detection of reperfusion abnormalities in STEMI patients treated with primary PCI.

Patients and Methods: This study was conducted at Zagazig University Hospital on 100 consecutive STEMI patients who underwent primary PCI, blood samples obtained on admission, ECG, Echocardiography were done; those patients were divided into two groups; 80 patients who experienced successful reperfusion, and 20 patients who did not.

Results: Post PCI corrected TIMI frame count (CTFC) was correlated with MPV post and pre-PCI as well as MPV; (p=0.005) where patients with high mean platelet volume (MPV) had significant increase in (CTFC).

MPV before and after PCI were significantly higher in unsuccessful reperfusion group compared to successful reperfusion group. MPV showed s gnificant r duction in the successful reperfusion group compared to unsuccessful group (p<0.05).

MPV, systolic wall motion score (SWM score) and door-to-wire time were significant and independent predictors for unsuccessful reperfusion in STEMI patients treated by primary PCI.

Conclusion: Mean platelet volume estimated before, after PCI and MPV are useful biomarkers and showed high accuracy for prediction of unsuccessful reperfusion after primary PCI in STEMI patients.

Key Words: *Mean platelet volume – STEMI – Primary PCI – Unsuccessful reperfusion.*

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Introduction

ST-SEGMENT elevation myocardial infarction (STEMI) is a common presentation of cardiovascular diseases. About 40% of patients with acute coronary syndromes (ACS) are presented as STEMI, and the prevalence of STEMI continues to rise worldwide [1].

Clinical outcome of PCI is determined by several factors including pre-procedural co-morbidities of the patients. Also, other factors have been identified to predict the rates of mortality and morbidity of such patients including gender, previous myocardial infarction, serum creatinine level, procedure urgency, cardiogenic shock, age [2] and lipoprotein levels [3].

Platelets (PLT) play a central role in pathophysiology of ACS [4]. Higher values of mean platelet volume (MPV) characterize patients with unstable angina and myocardial infarction compared to those with stable angina or non-cardiac chest pain; [5]. Also, platelets play a central role in development of no-reflow [6]. Furthermore, increased MPV at admission was linked to longterm mortality in patients with ACS [7].

We aimed to evaluate the accuracy of MPV as a biomarker for detection of reperfusion abnormalities and in hospital outcome in STEMI patients treated with primary PCI.

Patients and Methods

This consecutive observational case-control study was conducted at Zagazig University Hospitals on 100 consecutive patients (72 were men) with age range of 40-73 years admitted to these hospitals within the period from January 2021 till March 2022, presenting with first STEMI within 12 hours of symptoms and undergoing primary PCI.

i- *Patient characteristics:*

The study population consisted of 100 consecutive (72 were men) with age range of 40-73 years admitted to these hospitals within the period from January 2021 till March 2022, presenting with first STEMI within 12 hours of symptoms and undergoing primary PCI. STEMI was defined as typical chest pain lasting for 30min, with ST-segment elevation 1mm in two consecutive precordial or of inferior leads.

Criteria of exclusion:

- Rheumatoid disorders and other autoimmune diseases including vasculitis syndromes.
- Malignancies (including hematologic ones) and/or chemotherapeutic agents.
- Patients on regular renal dialysis.
- Blood dyscrasias including hemolytic anemias and other disorders as well as bone marrow affection disorders.
- Patients undergoing cardiac surgery for emergency coronary revascularization and/or mechanical complications of myocardial infarction.
- Active infection (including COVID19).

All patients underwent:

i- Thorough history taking and clinical examination.

ii- Laboratory methods: In all cases, venous peripheral blood samples for the MPV measurement were drawn on admission prior to administration of antiplatelet drugs and at 48-72 hours after admission. Mean platelet volume was calculated by automated machine. Change in MPV (defined as MPV) was measured as MPV at 48-72h minus MPV on admission, 12 leads ECGs were done on admission, Echocardiography was performed at bedside on admission and after PCI, Adjunctive pharmacotherapy was used including acetylsalicylic acid and clopidogrel and/or unfractionated heparin during PCI on routine basis.

Angiographic analysis:

Standard views used then analyzed by two independent interventional cardiologists, blinded to laboratory results. Assessment of Thrombolysis in Myocardial Infarction (TIMI) flow scale in infarct-related artery (IRA) at after primary PCI. And corrected TIMI frame count (CTFC) was determined on final angiogram, as described by Gibson et al., CTFC 40 was used to identify patients with unsuccessful reperfusion, as opposed to those with CTFC <40 **[8,9,10]**.

Statistical analysis:

Data were analyzed using SPSS software, to test the normal distribution continuous parametric data are presented as means ± SD. The statistical comparisons of differences in continuous variables between groups were carried out using independent student's *t*-test for parametric data. Categorical variables were represented by frequency and percentage and analyzed using chisquare (X^2) test. Pearson's correlation coefficient was computed to examine the correlation between the values of two continuous variables.

Results

There was no significant difference between both groups regarding the demographic data and risk facors (Age, sex, body mass index, hypertension and diabetes mellitus), clinical presentation, and vital signs. (p>0.05), Also there was no significant difference between both groups regarding troponin-I pre and after PCI and platelets count (p>0.05), (Table1).

There was no significant difference between both groups regarding platelets count, platelet distribution width (PDW) troponin-I pre and after PCI, while there was significant difference between both groups regarding MPV before and after PCI and mean MPV, MPV was significantly increased in unsuccessful reperfusion group compared to successful reperfusion group (p<0.05), (Table 1).

Sensitivity and specificity of MPV before PCI at cut off 10.75 were 90%, 88.7% and 0.94 respectively (Table 2).

There was positive correlation between MPV before PCI and each of MPV, SWM and CTFC while there was negative correlation between MPV before PCI and each of platelet count and post-PCI TIMI flow grade Table (3).

Also there was significant positive correlation between MPV after PCI and each of MPV before PCI, MPV P DW, door to wire time and CFTC while there was significant negative correlation between MPV after PCI and each of platelet count and post PCI TIMI flow grade. Table (3).

Also, there was significant positive correlation between MPV and each of MPV after PCI and CFTC while there was significant negative correlation between MPV and p ost-PCI T IMI f ow grade. Table (3).

Following univariate logistic regression analysis for each independent variable against the unsuccessful reperfusion outcome, we found that the

values for MPV post-PCI, SWM score, and door-to-wire time (in minutes) were significantly and independently associated with unsuccessful reperfusion in patients treated with primary PCI for STEMI, The final logistic regression model proved to be highly significant (p<0.001).

Table (1): Demographic, risk factors & clinical data of the studied groups.

	Successful reperfusion (n=80)	Unsuccessful reperfusion (n=20)	Statistical analysis	p-value
Age (y)	56.7±9.03 (40-73)	59.1±6.2 (47-70)	t=1.38	0.17
Gender:				
Male	58 (72.5%)	14 (60%)	X^2=0.05	0.82
Female	22 (27.5%)	6 (40%)		
Weight (Kg)	76.7±15.2 (55-107)	76.8±10.5 (56-97)	t=0.05	0.96
Height (cm)	166.1±6.5 (149-187)	167.8±6.2 (155-179)	t=1.03	0.31
BMI (Kg/m^2)	27.7±5.1 (20.4±39)	27.3±3.8 (22.1-35.2)	t=0.41	0.69
Diabetes mellitus	24 (30%)	8 (40%)	X^2=0.73	0.39
Hypertension	45 (56.3%)	10 (50%)	X^2=0.25	0.62
Dyslipidemia	34 (42.5%)	1 (55%)	X^2=1.10	0.32
Current smoking	40 (50%)	8 (40%)	X^2=0.64	0.42
CAD family history	28 (35%)	5 (25%)	X^2=0.72	0.39
SBP (mmHg)	142.9±22.1 (95-180)	143.5±20.4 (105-175)	t=0.11	0.92
DBP (mmHg)	88.2±16.7 (55-120)	91±14.4 (65-110)	t=0.67	0.51
Heart rate (beat/min)	85.6±14.1 (55-125)	87.1±15.9 (60-124)	t=0.42	0.68
Troponin-I (ng/L)	10.9±1.06 (0.15-43.65)	13.04±2.05 (0.2-27.8)	t=0.89	0.37
Platelet count (x 10^3/ml)	264.6±80.6 (123-455)	237.8±64.2 (123-340)	t=1.32	0.17
PDW (%)	11.09±1.7 (6.9-16.2)	11.5±1.5 (8-15.3)	t=1.12	0.25
MPV pre-PCI (fL)	9.4±1.03 (7.9-12.6)	11.6±0.8 (10.1-13)	t=9.13	<0.001*
MPV post-PCI (fL)	8.8±0.94 (7.3-11.6)	12.1±1.09 (9.8-13.3)	t=13.3	<0.001*
MPV (fL)	–0.52±0.09 (–2.3 to 1.8)	0.47±0.24 (–2.4 to 2.1)	t=4.52	<0.001*

Abbreviations: BMI: Body mass index; CAD: coronary artery disease. PCI: Percutaneous coronary intervention; SBP: Systolic blood pressure; DBP: Diastolic blood pressure. PCI: Percutaneous coronary intervention; MPV: Mean platelet volume; PDW; Platelet distribution width.

Data are represented as mean ± SD or Number (%). Data are analyzed using independent student t-test or chi-square (X^2) test.

Table (2): Diagnostic performance of MPV in predicting unsuccessful reperfusion.

Variables	Area under ROC curve	p-value	95% CI	Cut-off value	Sensitivity	Specificity
MPV post-PCI (fL)	0.98	<0.001**	0.94-0.99	10.25	90%	92.5%
MPV pre-PCI (fL)	0.94	<0.001**	0.90-0.98	10.75	90%	88.7%
MPV (fL)	0.82	<0.001**	0.68-0.95	0.05	75%	83%
SWM score	0.69	0.01**	0.55-0.83	24.5	60%	56%
Door-to-wire time (min.)	0.66	0.026*	0.52-0.81	77.5	55%	59%

Abbreviations: PCI: Percutaneous coronary intervention; MPV: Mean platelet volume; SWM: Segmental wall motion (by Echo).

Data are represented as mean ± SD or Number (%). Data are analyzed using independent student t-test or chisquare (X^2) test.

Table (3): Pearson correlation between MPV pre-PCI, MPV post-PCI and MPV with the o her variables.

		MPV pre-PCI	MPV post-PCI	MPV
Age (y)	*r*	0.135	0.094	–0.031
	p	0.181	0.355	0.758
Weight (Kg)	*r*	–0.098	0.003	0.146
	p	0.331	0.977	0.148
Height (cm)	*r*	0.122	0.151	0.087
	p	0.226	0.133	0.390
Body mass index (Kg/m^2)	*r*	–0.157	–0.057	0.126
	p	0.118	0.571	0.211
Systolic blood pressure (mmHg)	*r*	0.156	0.032	–0.169
	p	0.121	0.755	0.093
Diastolic blood pressure (mmHg)	*r*	0.149	0.092	–0.152
	p	0.143	0.365	0.130
Heart rate (beat/min)	*r*	–0.043	0.045	0.140
	p	0.673	0.654	0.165
Troponin-I (ng/L)	*r*	0.042	0.068	0.058
	p	0.678	0.499	0.566
MPV pre-PCI (fL)	*r*	–	0.616	–0.020
	p	–	<0.001**	0.843
MPV post-PCI (fL)	*r*	0.616	–	0.561
	p	<0.001**	–	<0.001**
MPV (fL)	*r*	–0.020	0.561	–
	p	0.843	<0.001**	–
Platelet count (x10^3/ml)	*r*	–0.230	–0.204*	–0.024
	p	0.021*	0.041*	0.814
PDW (%)	*r*	0.189	0.232	0.131
	p	0.060	0.020*	0.192
SWM score	*r*	0.235	0.185	–0.009
	p	0.019*	0.065	0.933
Door-to-wire time (min)	*r*	0.144	0.211	0.158
	p	0.152	0.035*	0.116
Number of diseased vessels	*r*	–0.081	–0.056	0.018
	p	0.424	0.577	0.858
Number of stents	*r*	–0.115	–0.094	0.001
	p	0.257	0.351	0.991
Post-PCI TIMI flow grade	*r*	–0.561	–0.639	–0.301
	p	<0.001**	<0.001**	0.002**
CTFC	*r*	0.559	0.659	0.341
	p	<0.001**	<0.001**	<0.001**

Abbreviations: MI: Myocardial infarction; PCI: Percutaneous coronary intervention; MPV: Mean platelet volume; PDW: Platelet distribution width; SWM: Segmental wall motion (by Echo); TIMI: Thrombolysis in myocardial infarction; CTFC: Corrected TIMI frame count.

Table (4): Results of final multivariate logistic regression model used to test the independent association of the input variables with the unsuccessful reperfusion outcome.

	β-coefficient	Odds ratio	95% confidence interval for odds ratio	*p*-value
Age (y)	0.022	1.022	0.975-1.071	0.361
Gender	0.111	1.117	0.793-1.302	0.216
BMI (Kg/m^2)	0.087	1.091	0.897-1.186	0.543
Platelet count (x 10^3/ml)	–0.003	0.997	0.998-1.005	0.445
PDW (%)	0.037	1.037	0.943-1.112	0.709
MPV pre-PCI (fL)	0.096	1.101	0.802-1.241	0.476
MPV post-PCI (fL)	1.341	3.823	2.166-6.798	<0.001**
SWM score	1.235	3.438	1.639-5.932	<0.001**
Door-to-wire time (min)	0.242	1.275	1.102-1.748	0.028*
ST-segment resolution	–0.016	0.984	0.961-1.008	0.188

Abbreviations: BMI: Body mass index; PCI: Percutaneous coronary intervention; MPV: Mean platelet volume; PDW: Platelet distribution width; SWM: Segmental wall motion (by Echo).

Discussion

Cardiovascular diseases are the leading cause of mortality globally, and ST-segment elevation myocardial infarction (STEMI) is one of the most common manifestations of cardiovascular diseases. Up to 40% of patients with acute coronary syndromes are presented as STEMI. The prevalence of STEMI continues to rise in many parts of the world; although the advances in the treatment of STEMI [1].

STEMI is an emergency that requires a quick identification, stratification and management to ensure good outcome [11,12]. The standard management for myocardial infarction patients involves reperfusion therapy [13,14].

Platelets (PLT) have a central role in pathophysiology of acute coronary syndromes [4]. Platelet size measured by mean platelet volume (MPV) is an indicator for the activity of platelets [15]; more active platelets have higher thrombotic potential compared to small platelets [4]. Moreover, higher values of MPV characterize patients with unstable angina and myocardial infarction compared to those with stable angina or non-cardiac chest pain; high levels of MPV have been identified as an independent risk factor for stroke and myocardial infarction [16].

Furthermore, it has been shown that increased MPV at admission was associated with long-term mortality in patients with acute coronary syndrome [17,18].

The current study aimed to evaluate the accuracy of mean platelet volume as a biomarker for detection of reperfusion abnormalities in STEMI patients treated with primary PCI.

This study was conducted at Zagazig University Hospital on 100 consecutive STEMI patients who underwent PCI; those patients were divided into two groups, 80 patients who experienced successful reperfusion and 20 patients who experienced suboptimal reperfusion.

The patients of the two groups showed match regarding age, gender distribution, body mass index, smoking status and clinical comorbidities, including diabetes mellitus, hypertension, dyslipidemia, and family history of CAD.

Also, the two groups of patients showed no significant differences regarding chest pain, and dyspnoea pre and post-PCI, reperfusion arrhythmias, systolic blood pressure, diastolic blood pressure and heart rate. (p>0.05).

In this study, the angiographic findings between the two groups were evaluated. There were significant differences between the two groups regarding ST-segment resolution, SWM score, door to-wire time, post PCI TIMI flow grade, ST-segment resolution rate was significantly higher among patients in the successful reperfusion group compared to those in the suboptimal reperfusion group. Patients with successful reperfusion significantly showed lower SWM score, and door-to wire time. On the other hand, significant higher mean of post PCI TIMI flow grade was found for successful reperfusion patients.

Regarding the laboratory tests, each of troponin-I pre-PCI, 12h after PCI and 24h after PCI wasn't different between the two groups. The same was found regarding the platelet count and PDW. (p>0.05).

However, MPV significantly varied between the two groups: Pre-PCI, post PCI and MPV MPV before and after PCI were significantly higher in unsuccessful suboptimal reperfusion group compared to successful reperfusion group.

The change of mean platelet volume (MPV) showed significant reduction in the successful reperfusion group compared to suboptimal reperfusion group.

In our study, MPV pre-and post PCI as well as MPV showed h gh (Area under ROC curve) AUC with a significant value and high sensitivity and high specificity. MPV post PCI showed an AUC of 0.98 with a sensitivity of 90% and specificity of 92.5%. Also, MPV post PCI showed high AUC of 0.94 with sensitivity and specificity of 90%, and 88.7%, respectively. MPV also showed h gh AUC of 0.82, sensitivity of 75%, and specificity of 83%; these values were lower compared to MPV pre-and post PCI. SWM score and door-to wire time were significantly varied between the two groups; however, MVP before and after PCI as well as MPV showed higher AUC, sensitivity and specificity compared to SWM score, and door-to wire time. Therefore, MVP is better and more accurate biomarker for the predicting successful reperfusion compared to SWM score, and door-to wire time.

It was suggested that MPV monitoring after PCI might aid risk stratification. MPV cutoffs for predicting poor clinical outcomes among patients treated with PCI range between 8-9.25 [19-21].

In our study, the cutoff of MPV for predicting poor clinical outcomes was higher than 9.25 and

it was 10.25 for MPV post PCI, and 10.75 for MPV pre-PCI.

Similar to our findings, it was reported that MPV can predict immediate angiographic perfusion and short term major adverse cardiac events for STEMI patients underwent primary PCI, with a cutoff 1095 that could predict major adverse cardiac events with an AUC of 0.79, sensitivity and specificity of 76%, and 75%, respectively (22). However, our study focused on the success of reperfusion with higher sensitivity and specificity values and higher AUC.

Dugu et al., suggested that MPV has a role as a useful hematological marker for early and simple identification of patients with stable coronary artery disease at high risk for post PCI low reflow **[23]**.

Multivariate logistic regression model in this study showed that MPV post PCI, SWM score and door-to-wire time were significant and independent predictors for unsuccessful reperfusion in STEMI patients treated by primary PCI.

Similar to our findings, Huczek et al., showed that high MPV was a strong independent predictor of impaired angiographic reperfusion among STEMI patients treated with primary PCI with an odd of 4.7 **[24]** which was higher than the odd of our findings (OR of MPV post PCI=3.823).

High MPV was also a significant predictor for six-month mortality among such patients **[24]**.

Additionally Huczek et al., revealed that CTFC 40 was a significant predictor with an OR of 10.1 **[24]**. In this study, although we found that CTFC was significantly lower among patients with successful reperfusion, CTFC was significantly and positively associated with MPV pre and post PCI as well as MPV

Avci et al., showed that rising MPV during hospitalization of STEMI patients was associated with long-term mortality, high MPV was an independent predictor of all cause mortality **[2]**.

MPV pre-and post PCI and MPV weren't affected by any of the demographics of patients, laboratory findings or blood pressure. But they are correlated with each other and correlated with platelet count as well as PDW, SWM score and door-to-wire time. MPV was positively and significantly associated with MPV post PCI, CTFC and negatively associated with post-PCI TIMI flow grade.

In this study, we estimated MPV pre- and post PCI and also estimated MPV In agreement with the previous study **[24]**, both MPV pre and post PCI were negatively and significantly associated with platelet count, whereas the correlation between MPV and platelet count was insignificant; however, the previous study didn't report MPV **[24]**.

A previous study revealed that MPV was correlated with age, longer time to reperfusion, and hypertension, but it provided prognostic information that was independent of such variables **[24]**.

In contrast to the previous findings, we found that MPV wasn't affected by any of demographics, blood pressure, or the heart rate.

In our study, Post PCI TIMI flow was negatively associated with MPV post and pre-PCI as well as MPV; this negative correlation was in agreement with Frrag et al., who reported that there was a negative correlation between MPV and TIMI flow (p=0.006) where patients with high MPV had significant reduction in their TIMI flow **[22]**.

Conclusion:

The mean platelet volume pre-PCI, post PCI and MPV showed significant and h gh accuracy for the prediction of unsuccessful reperfusion among STEMI patients treated with PCI.

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متوسط حجم الصفائح الدموية كمؤشر لتتبع عن إختلال إعادة التروية فى مرضى احتشاء عشلة ارتفاع مقطع الاس تى المعالجين بالتلدخل الأولى بالدعامة

احتشاء عضلة القلب إرتفاع مقطع الإس تى هو أحد الأعراض الشائعة لمتلازمة الشريان التاجى الحادة ويزداد معدلة فى جميع أنحاء العالم.

الصفائح الدموية لها دور مركزى فى الفيزيولوجيا المرضية لمتلازمة الشريان التاجى الحادة وارتبط زيادة متوسط حجم الصفائح الدموية بالوفيات طويلة الأمد فى المرضى المصابين بمتلازمة الشريان التاجى الحادة.

الهدف من الدراسة : لقد هدفنا إلى تقييم دقة متوسط حجم الصفائح الدموية كعلامة حيوية إعادة التروية فى مرضى احتشاء عضلة القلب إرتفاع مقطع الإس تى المعالجين بالتدخل الأولى بالدعامة.

المرضى والطرق : أجريت هذه الدراسة فى مستشفى جامعة الزقازيق على ١٠٠ مريض متتالى من مرضى احتشاء عضلة القلب إرتفاع مقطع الإس تى المعالجين بالتدخل الأولى بالدعامة.

وتم الحصول على عينات الدم عند الدخول، وتخطيط القلب، وتخطيط صدى القلب. تم تقسيم هؤلاء المرضى إلى مجموعتين. ٨٠ مريضاً تم إعادة التروية بنجاح بالتدخل الأولى بالدعامة ، و ٢٠ مريضاً عانوا من إختلال إعادة التروية.

النتائج : كان متوسط حجم الصفائح الدموية قبل وبعد إعادة التروية فى مرضى احتشاء عضلة القلب إرتفاع مقطع الإس تى المعالجين بالتدخل الأولى بالدعامة أعلى بشكل ملحوظ فى مجموعة المرضى الذين عانوا من إختلال إعادة التروية مقارنة بالمجموعة الأخرى أ ($p<0.05$).

قياس متوسط حجم الصفائح الد موية قبل وبعد إعادة التروية ومؤشر درجة حركة البطين الأيسر أثناء الانقباض والوقت المستنفد من وصول المريض لحين فتح الشريان بالسلك، أظهروا تنبئاً مهماً ومستقلاً لإختلال إعادة التروية فى مرضى احتشاء عضلة القلب ارتفاع مقطع الإس تى المعالجين بالتدخل الأولى بالدعامة الخلاصة قياس متوسط حجم الصفائح الدموية قبل وبعد إعادة التروية فى مرضى احتشاء عضلة القلب إرتفاع مقطع الإس تى المعالجين بالتدخل الأولى بالدعامة هى مؤشرات حيوية مفيدة وإظهرت دقة عالية للتنبؤ بإختلال التروية.