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Original article

Relationship between Mean Platelet Volume and ST Segment Resolution after Reperfusion Therapy in Patients with ST Elevation Myocardial Infarction

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Abstract

Background: ST segment Elevation Myocardial Infarction (STEMI) patients often require reperfusion therapy to restore blood flow to the affected heart muscle. Mean Platelet Volume (MPV) has been proposed as a potential predictor of reperfusion success in STEMI patients. **This study aimed to** show correlation between MPV on admission and ST segment resolution following reperfusion therapy in STEMI patients. **Methods:** This observational, single-center study- was conducted on patients with ACS to assess their clinical outcomes and the predictive role of hematological indices, including; MPV- in determining the effectiveness of reperfusion therapy, encompassing fibrinolytics and primary PCI. Our study comprised 100 STEMI patients, with 50 undergoing PCI and the remaining 50 receiving thrombolytic therapy. Among the PCI group, 42 patients achieved successful treatment, while in the fibrinolytic group, only 32 cases were successful. From all study patients there were 74 experienced ST-elevation resolution (Group A), while 26 cases did not exhibit resolution of their ST abnormalities (Group B). **Results**: ROC curve analysis revealed that MPV-pre at cut-off value of 11.15- could be good predictive test of unsuccessful reperfusion with 76.9% sensitivity and 70.3% specificity (AUC, 0.77 and 95% CI, 0.67-0.87). There is a significant positive correlation between MPV_Pre and MPV_post ($r = 0.254$, $p = 0.011$). **Conclusion:** There is a correlation between MPV on admission and ST segment resolution following reperfusion therapy in STEMI patients. Mean Platelet Volume (MPV) may be utilized as a prognostic predictor of success of thrombolysis following STEMI.

Keywords: STEMI; Mean Platelet Volume; Reperfusion Therapy; Fibrinolysis; pPCI.

Introduction

Acute coronary syndrome (ACS) is one of the most important causes of mortality and morbidity. It is a clinical syndrome that includes unstable angina pectoris (USAP), ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI) (1). Early reperfusion is required for the

myocardium to survive during acute myocardial infarction. Reperfusion of ischemic myocardium tissue with fibrinolysis or percutaneous coronary intervention (PCI) is critical for reducing infarct size and improving outcomes (2).

Resolution of ST elevation reflects both epicardial and myocardial reperfusion. Early and complete resolution of ST segment in the setting of acute myocardial infarction is associated with smaller infarct size, greater ejection fraction and reduced morbidity and mortality (3).

The increase in blood viscosity is one of the mechanisms responsible for the etiopathogenesis of thrombus formation. There are many parameters associated with the increase in viscosity. Platelets release mediators of inflammation, atherosclerosis, coagulation, and thrombosis. platelets contribute to the pathogenesis of STEMI. Reactivity of Platelets correlate with the platelet size that measured by Mean platelet volume (4).

Increased MPV indicates a higher number of large platelets with greater prothrombotic activity. In patients with acute thrombotic events, it predicts the occurrence of subsequent adverse cardiovascular events (5).

The role of hematologic indices- including MPV- in evaluating the adequacy of reperfusion therapy especially in association with occurrence of ST resolution- is still unclear for the researchers (6).

The purpose of this study was to show correlation between MPV on admission and ST segment resolution following reperfusion therapy- including fibrinolysis or PCI-, in patients with STEMI.

Patients and methods

This observational, Cross-Sectional single center study included; all patients with ACS and diagnosed as ST segment Elevation Myocardial Infarction (STEMI)- who were admitted at coronary care unit at "Benha University Hospital" in the period from June 2022 to December 2022. We aimed to study the clinical outcome in this category of patients and to evaluate the role of hematological indices- including MPV- to predict adequacy of reperfusion therapy (fibrinolytics & primary PCI).

STEMI (ST segment Elevation Myocardial Infarction) is defined by symptoms of myocardial ischemia accompanied by a persistent elevation of the ST segment on the electrocardiogram (ECG) and the subsequent release of biomarkers of myocardial necrosis (7).

Successful reperfusion was defined as disappearance or improvement of chest pain combined with resolution of ST-segment elevation by ≥50% in the single lead with maximum elevation on baseline ECG 90 min of starting SK infusion or shortly after PPCI that restores TIMI-II to III flow without intra-procedural complications.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University; Approval code: MS 26.3.2022.

This study included 100 patients in two groups: The first group: 50 patients will be treated with fibrinolysis.

The second group: 50 patients underwent primary percutaneous coronary intervention.

Inclusion criteria were; aged 18 years or older, both male and female, who have been admitted with ST segment elevation myocardial infarction and are treated with either streptokinase or primary percutaneous coronary intervention, provided they have no contraindications for thrombolysis and no contraindication to pPCI.

Exclusion criteria were patients with a prior history of coronary artery heart disease, a known bleeding diathesis, abnormal platelet counts, end-stage liver disease, renal failure, or those currently receiving oral anticoagulation medication, coronary artery bypass graft surgery, complex interventional procedures.

According to current guidelines, pPCI is the preferred strategy for patients within 12 h of symptom onset (8). When PCI is not available or when the delay between presentation to a hospital and primary PCI is anticipated to be in excess of 90 minutes, fibrinolytic therapy should be considered in patients who can be treated within 2 to 3 hours of symptom onset and who are not at high risk for intracranial hemorrhage (9).

Methods:

Patients were subjected to I) **History taking:** Including **A)** The personal history, risk factors as hypertension, diabetes mellitus, obesity, drug intake, smoking and comorbid diseases including renal, hepatic diseases or collagenic disorders…. etc. **B)** Cardiovascular history: Including history of previous cardiovascular disease, history of medication used and any cardiovascular related operation. **C)** History of conditions that interfere with fibrinolytic therapy as previous ischemic stroke, intracranial hemorrhage, cancer or pervious major operation……. etc.

II) Physical examination: General examination: Including Vital signs (Blood pressure, Temperature, Heart rate, Respiratory rate). Cardiovascular examination.

III) Laboratory examination including Complete blood count (CBC)performed by an automated hematology analyzer showing platelet, MPV, PDW, red blood cells and white blood cells indices., cardiac biomarker (troponins, CK-MB), renal function tests (urea, creatinine) …. etc.

IV) Electrocardiography: Standard 12-lead ECG were recorded using electrocardiographic device at 25 mm/s speed and 10 mV/mm scale at time of admission, then re-evaluation after reperfusion therapy (including fibrinolysis or primary percutaneous coronary intervention (pPCI).

V) Transthoracic Echocardiography: All patients evaluated at admission by transthoracic echocardiography for the assessment of regional wall abnormalities and overall left ventricular systolic function and for exclusion of mechanical complication. Systolic function was assessed using the biplane Simpson's method, which involves tracing the endocardial borders in the end diastolic and end systolic apical four-chamber and two-chamber views for calculation of left ventricular ejection fraction (LVEF). The LVEF measurement provides a quantitative assessment of left ventricular systolic function, with values less than 50% indicating impaired systolic function.

VI) Treatment by Reperfusion therapy: (including fibrinolysis and primary percutaneous coronary intervention (pPCI).

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test and ANOVA (F) test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Results

Regarding the demographic data in our study, there was no significant difference between the two study groups regarding age, gender, BMI, smoking status, and prevalence of medical comorbidities- as diabetes, hypertension, and dyslipidemia- however vital signs were comparable between the two groups, **Table (1).**

Analysis of CK-MB and serum creatinine among our patients showed no significant difference between the two groups. However, serum troponin, platelet count and platelet distribution width showed a significant elevation in patients with non-ST segment resolution, **Table (2).**

For patients who underwent PCI, 84% of those in the "Successful" group- had a positive outcome, while only 16% experienced an unsuccessful result. On the other hand, in the "Unsuccessful" group, 64% received PCI successfully, while 36% did not achieve the desired outcome. Similarly, for patients who received Thrombolytic therapy, 64% in the "Successful" group benefited from the treatment, whereas 36% did not. In contrast, in the "Unsuccessful" group, 36% had a successful outcome, while 64% did not. There was a statistically significant difference in treatment outcomes between the two groups, **Table (3).**

ROC curve analysis revealed that MPV-pre at cut-off value of 11.15- could be good predictive test of unsuccessful reperfusion with 76.9% sensitivity and 70.3% specificity (AUC, 0.77 and 95% CI, 0.67-0.87). MPV-post at cut-off value of 10.35 could be excellent predictive test of unsuccessful reperfusion with 80.8% sensitivity and 70.3% specificity (AUC, 0.89 and 95% CI, 0.82-0.96), **Table (4)** and **Figure (1).**

There is a statistically significant positive correlation between MPV_Pre and MPV_post ($r = 0.254$, $p = 0.011$). Age is weakly positively correlated with MPV_Pre ($r = 0.108$), while BMI shows a weak negative correlation with MPV_Pre ($r = -0.173$) and a weak positive correlation with MPV_post ($r = 0.059$). Ejection Fraction (EF) has a significant negative correlation with MPV_post ($r = -0.223$, $p = 0.026$). Other variables exhibit weak correlations with both MPV-Pre and MPV-post, **Table (5).**

Significant findings include a significant positive association with age (OR = 1.44, p = 0.011*), a significant negative association with sex (OR = 0.01, p = 0.018*), and significant positive associations with both MPV_Pre (OR = 3.94, p = 0.017*) and MPV_post (OR = 7.9, p = 0.006)- indicating that higher age and mean platelet volume measurements are associated with increased odds of

unsuccessful reperfusion. Platelet count also demonstrates a modest positive association (OR = 1.04, p = 0.012). Other variables such as BMI, smoking, family history, DM, HTN, dyslipidemia, and PDW- do not show statistically significant associations with the outcome, **Table (6).**

Table 1: Comparison of study groups regarding Demographic, risk factors & clinical data.

	Successful (n=74)		Unsuccessful (n=26)		Test of sig.	p-value
Age (mean ± SD)	58.43	7.98	61.92	9.62	1.8	0.1
Sex Female	19	25.7%	7	26.9%	0.1	0.9
No. &% Male	55	74.3%	19	73.1%		
BMI (mean ± SD)	26.82	2.17	27.04	3.34	0.3	0.8
Smoking No. &%	27	36.5	11	42.3	0.3	0.6
Family history No. &%	57	77	19	73.1	0.2	0.9
DM No. &%	27	36.5	11	42.3	0.3	0.6
HTN No. &%	30	40.5	15	57.7	2.3	0.1
Dyslipidaemia No. &%	27	36.5	13	50	1.5	0.2
SBP (mean ± SD)	138.58	26.11	134.04	17.66	0.8	0.4
DBP (mean ± SD)	93.78	17.45	94.23	12.94	0.1	0.9
Heart rate (mean ± SD)	87.03	9.87	91.04	13.19	1.6	0.1

BMI: Body Mass Index, DBP: Diastolic Blood Pressure, DM: Diabetes Mellitus, HTN: Hypertension, SBP: Systolic Blood Pressure.

Table 2: Comparison of study groups regarding laboratory data.

	Successful (n=74)		Unsuccessful (n=26)		T/U	p-value
	Mean	**± SD**	**Mean**	**± SD**		
CK_MB(U/L)	88.36	65.22	91.69	40.41	1.2	0.3
Troponin(ng/L)	20.98	11.17	29.56	11.05	3.4	0.001*
Creatinine (mg/dL)	1.11	0.26	1.14	0.34	0.5	0.6
EF(%)	48.80	6.34	44.54	6.87	2.9	0.005*
Platelet count(10^9/L)	284.69	93.82	361.69	65.35	4.6	<0.001*
PDW(fL)	11.92	2.84	12.23	1.77	0.7	0.5
MPV_Pre(fL)	10.28	1.40	11.65	1.05	5.2	<0.001*
MPV_post(fL)	9.49	1.22	11.59	1.07	7.8	<0.001*

CK_MB: Creatinine Kinase_MB, EF: Ejection Fraction, PDW: Platelet Distribution Width, MPV_Pre**:** Mean Platelet Volume Pre-perfusion therapy, MPV_post: Mean Platelet Volume Post- perfusion therapy.

Table 3: Comparison of study groups regarding type of treatment

	Successful (n=74)		Unsuccessful (n=26)		Total	X^2	p-value
	No.	%	No.	%			
PCI	42	84%	8	16%	50	5.2	0.02*
Thrombolytic therapy	32	64%	18	36%	50		

PCI: Percutaneous Coronary Intervention.

Table 4: Diagnostic performance of MPV in predicting unsuccessful reperfusion.

	AUC	p-value	95% CI	Cut-off value	Sensitivity	Specificity
MPV_Pre	0.77	<0.001*	0.67-0.87	11.15	76.9	70.3
MPV_post	0.89	<0.001*	0.82-0.96	10.35	80.8	70.3

AUC: Area Under Curve, CI: Confidence Interval

Table 5: Correlation between MPV pre- and MPV post- MPV with other variables.

	MPV_Pre		**MPV_post**	
	R	**p-value**	**R**	**p-value**
MPV_Pre	---	---	0.254	0.011*
MPV_post	0.254	0.011*	---	---
Age	0.108	0.283	-0.036	0.720
BMI	-0.173	0.085	0.059	0.558
CK_MB	0.132	0.190	-0.035	0.728
Troponin	0.180	0.072	0.157	0.120
Creatinine	0.011	0.911	-0.090	0.373
SBP	-0.054	0.597	-0.159	0.114
DBP	-0.035	0.729	-0.052	0.609
Heart rate	0.024	0.816	0.177	0.077
EF	-0.100	0.323	-0.223	0.026*
Platelets count	0.182	0.069	0.189	0.059
PDW	-0.011	0.912	-0.083	0.410

BMI: Body Mass Index, DBP: Diastolic Blood Pressure, SBP: Systolic Blood Pressure, CK_MB: Creatinine Kinase_MB, EF: Ejection Fraction, PDW: Platelet Distribution Width, MPV_Pre**:** Mean Platelet Volume Pre-perfusion therapy, MPV_post: Mean Platelet Volume Post- perfusion therapy.

Table 6: multivariate logistic regression model used to test the independent association of the input variables with the unsuccessful reperfusion outcome.

	coefficient	OR	95% of OR		P-value
Age	0.361	1.44	1.08	1.90	0.011*
BMI	0.300	1.35	0.73	2.49	0.337
Sex	-5.031	0.01	0.00	.42	0.018*
Smoking	1.093	2.98	0.20	45.18	0.431
Family History	2.130	8.42	0.29	242.14	0.214
DM	-2.668	0.07	0.00	2.34	0.137
HTN	0.814	2.26	0.27	18.57	0.449
Dyslipidemia	-2.515	0.08	0.00	1.87	0.117
Platelets_count	0.042	1.04	1.01	1.08	0.012*
PDW	0.542	1.72	0.98	3.02	0.059
MPV_Pre	1.372	3.94	1.28	12.18	0.017*
MPV_post	5.188	7.9	4.52	10.31	0.006*

BMI: Body Mass Index, DM: Diabetes Mellitus, HTN: Hypertension, PDW: Platelet Distribution Width, MPV_Pre**:** Mean Platelet Volume Pre-perfusion therapy, MPV_post: Mean Platelet Volume Post- perfusion therapy, OR: Odds Ratio.

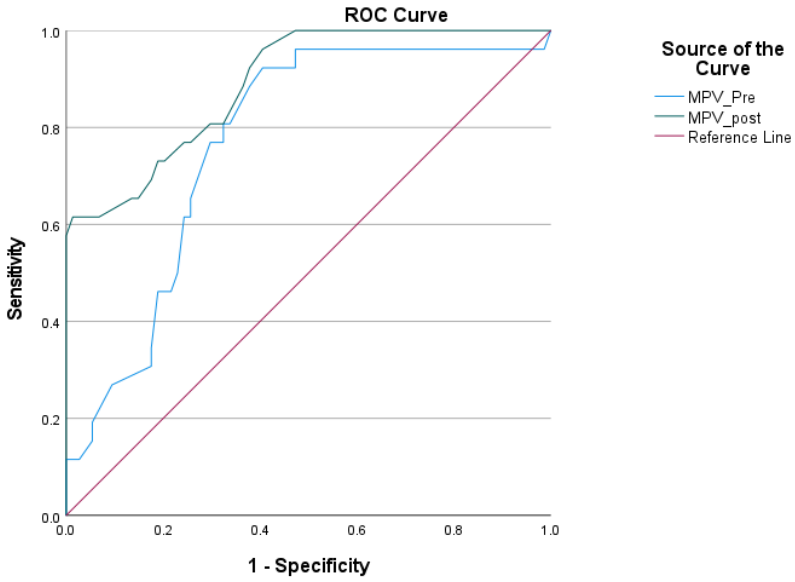

Fig. 1: Receiver Operating Characteristic (ROC) curve analysis of the cut-off values of MPV for prediction of unsuccessful reperfusion

Discussion

One of the leading causes of death and morbidity is acute coronary syndrome (ACS), encompassing unstable angina pectoris (USAP), STEMI, and NSTEMI. Early reperfusion via percutaneous coronary intervention (PCI) or fibrinolysis is crucial for myocardial survival post-acute myocardial infarction (10), with ST segment resolution serving as an indicator for better outcomes. Platelet size, indicated by Mean Platelet Volume (MPV), is a key factor in thrombus formation, and variations in MPV can impact clot dissolution during acute coronary syndromes. Elevated MPV has been associated with adverse cardiovascular events in thrombotic patients, emphasizing its potential relevance in assessing reperfusion therapy effectiveness, particularly in relation to ST resolution (11).

In our observational, single-center study conducted at "Benha University Hospital" between June 2022 and December 2022, we examined patients with ACS admitted to the coronary care unit to assess their clinical outcomes and the predictive role of hematological indices- including MPV- in determining the effectiveness of reperfusion therapy, encompassing fibrinolytics and primary PCI. Our study comprised 100 STEMI patients, with 50 undergoing PCI and the remaining 50 receiving thrombolytic therapy. Among the PCI group, forty two (42) patients achieved successful treatment, while in the fibrinolytic group; only thirty two (32) cases were successful. Seventy four (74) patients experienced ST-elevation resolution (Group A), while twenty six (26) cases did not exhibit resolution of their ST abnormalities (Group B).

Regarding the demographic data in our study, there was no significant difference between the two study groups regarding age, gender, BMI, smoking status, and prevalence of medical comorbidities- as

diabetes, hypertension, and dyslipidemia- however, vital signs were comparable between the two groups.

In a similar study in agreement with us, there was no significant difference between their studied groups regarding gender, smoking status, and prevalence of medical comorbidities- as hypertension and dyslipidemia- however, against our findings, age and diabetes were significantly comparable between their groups (12).

In accordance with our results, a study found that there was no significant difference between the study groups regarding sex, smoking status, and prevalence of medical comorbidities- as diabetes, hypertension, and dyslipidemia- however, there was no significant difference between the studied groups regarding age (13).

Analysis of CK-MB and serum creatinine among our patients showed no significant difference between the two groups. However, serum troponin, platelet count and platelet distribution width- showed a significant elevation in patients with non-ST segment resolution.

Contrary to our results, a study found that serum troponin, serum creatinine, and platelet count- showed no significant difference between the two groups. However, CK-MB showed a significant elevation in patients with ST segment resolution (12).

Comparing the two groups studied a study revealed that the group with lower resolution of ST segment enjoyed higher PDW, MPV and WBC values- which were statistically significant (13).

In addition, a study reported that MPV is not associated with post-intervention reperfusion in patients with STEMI treated with fibrinolysis. They suggested that MPV cannot be a marker of impaired reperfusion (14). There variation may be due to different sample sizes.

A study indicated that higher MPV may correlate with thrombolysis failure in patients with STEMI. MPV can be utilized as an available factor for evaluating thrombolysis outcome (15).

Furthermore, in a study, the STEMI patients were divided in two groups on the basis of having or not having TIMI flow III and their MPV and WBC were compared. Their study demonstrated that occluded infarct-related artery group, compared with patent infarct-related artery group, and had higher MPV & WBC values (16).

Our results revealed that MPV- measured before and after the intervention- showed a significant elevation in association with non-resolution of the ST segment elevation. On looking at each individual group, the post-intervention MPV showed a significant drop compared to the corresponding preintervention value. Using a cut-off value of 11.95 fL, pre intervention MPV had sensitivity and specificity of 76.9% and 70.3% respectively for predicting cases with no ST-resolution.

In the same direction, a study demonstrated that MPV values of 8.0 fL was determined to be the critical point for prediction of STR. Using this cut-off point, AUC was 0.69 ± 0.04. Specificity and sensitivity of the test was 72% and 38%, respectively (12).

A study showed that in patients with CAD, higher level of immature platelets was associated with higher rate of MACE- defined as a composite of all-cause mortality, myocardial infarction, unplanned revascularization, or hospitalization for angina- in 31 months follow up (17).

According to another study, immature platelets have large number of dense granules with higher MPV and have higher thrombogenicity potential resulting in a high metabolic and enzymatic activity. On the other hand, in a cohort of 3,750 patients undergoing coronary angiogram, a study demonstrated that the size of platelets is larger among those older than 75 years old and there was a direct correlation between the size of the platelets and age. However, these investigators failed to show any correlation to the incidence of coronary atherosclerosis and severity of CAD linked to the larger size of platelets (18).

In a meta-analysis of 16 cross-sectional studies, they showed that in patients with stable coronaries MPV was approximately 0.92 fL larger in patients with AMI than those without AMI. Such a difference was not observed in patients who had unstable angina (5).

Several studies proved that in patients with STEMI undergoing primary PCI, higher MPV was associated with higher frequency of no reflow, higher corrected TIMI frame count and higher mortality or even with a longer follow up mortality. The rate of stent restenosis was higher in patients with larger size platelets. Additionally, there is an association between higher MPV and impaired function of the left ventricle after percutaneous revascularization of the coronaries (19-21).

Only a few studies have assessed the association of MPV with outcome of STEMI following thrombolytic therapy. In a study of 122 patients with STEMI, a study showed that larger platelet volumes were associated with higher rate of thrombolytic failure defined as constellation of various endpoints including need for rescue PCI, in-hospital mortality, unplanned PCI during hospitalization or complete occlusion of the IRA in the follow-up angiography (15).

Recently a study had evaluated the association of MPV with reperfusion at tissue level based on electrocardiographic STR and simultaneously has evaluated its impact on enzymatically determined infarct size and in-hospital mortality and heart failure following thrombolytic therapy in STEMI. In agreement with us, MPV showed a significant elevation in association with non-resolution of the ST segment elevation (21).

In determining the desire cut off point of MPV in predicting non-resolution of ST segment, a study revealed 0.05 FL with 71.8% sensitivity and 80.9% specificity on the basis of ROC curve with AUC 0.76 (13).

In another study attempting to the detect the desired cut off point for predicting occlusion of coronary artery 8.55 FL had a sensitivity of 74% and specificity of 60% with AUC 0.71 (16).

In another study by Huczek et al., the desired cutoff point of MPV in predicting no-reflow after performing PCI, 10.3 FL was found to have sensitivity of 61.9 and specificity of 74.3% with AUC 0.8 (22).

Conclusion

There is a correlation between mean platelet volume (MPV) on admission and ST segment resolution following reperfusion therapy including; fibrinolysis or percutaneous coronary intervention (PCI) in patients with STEMI. MPV may be utilized as a prognostic predictor of success of revascularization following STEMI and may favor using pPCI over fibrinolysis in resuming blood flow to an obstructed coronary vessel.

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