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Association of Mean Platelet Volume with Angiographic Thrombus Burden and Short-term Outcome in Patients with ST-segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Mean platelet volume (MPV), is an indicator of platelet reactivity and could be a biomarker of the risk and prognosis of patients with ST-segment elevation myocardial infarction (STEMI).

Objectives: Testing the predictive value of MPV for angiographic thrombus burden and short-term outcomes in patients with STEMI undergoing primary percutaneous coronary intervention (PPCI).

Patients and Methods: Seventy-two patients presented with acute STEMI to the Cardiology Department of Ain Shams University Hospitals for PPCI. MPV was measured on admission. Angiographic thrombus burden and post-interventional thrombolysis in myocardial infarction (TIMI) flow grade and myocardial blush grade (MBG) were recorded. Patients were followed up for 3 to 6 months. **Results:** The patients' ages ranged between 33 and 73 (mean age 53.22 ± 9.96 years). This study included 62 males and 10 females. The MPV of the studied cases was 9.97 ± 1.31 fl. MPV was higher among patients with high thrombus burden (HTB) (11.42±1.007 vs. 9.53±1.039. p< 0.001) and patients with MBG (0-1) and TIMI flow<3 (10.59±1.839 vs 9.81±1.092, p 0.04 and 11.77±0.74 vs 9.87±1.26, p 0.004 respectively). The primary composite endpoint occurred in 12 patients with a higher MPV (10.95 ± 1.14 vs. 9.73 ± 1.29, p 0.01). In univariate regression analysis for the predictors of MBG (0/1), the MPV was an independent predictor of MBG (odds ratio 0.487, and p <0.006), CI (0.292- 0.811).

Conclusion: MPV may be a useful biomarker to help identify higher-risk patients with large intracoronary thrombus burden, who might require more potent antiplatelet therapy.

Keywords: Mean platelet volume; Coronary artery disease; Angiographic thrombus burden; Thrombolysis in myocardial infarction flow; Myocardial blush grade; ST-elevation myocardial infarction; Percutaneous coronary intervention.

INTRODUCTION

Atherosclerotic CAD is a leading cause of death worldwide, is on the rise, and has become a true pandemic that respects no borders. Results from recent reports do suggest that mortality and morbidity from CAD are leveling, especially in younger adults. Because it offers prompt and complete recanalization of an occluded infarct-related artery (IRA), primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for STEMI at PCI-capable hospitals. However, in a significant proportion of patients, microvascular and myocardial reperfusion cannot be regained despite successfully restoring TIMI grade 3 epicardial blood flow. This occurrence, better known as the 'no-reflow phenomenon', is associated with progressive left ventricular dysfunction and increased risk of congestive heart failure, myocardial infarction (MI), and mortality[1]. Platelets play a significant role during the occlusion and reperfusion period of myocardial infarction and they also strongly contribute to the microvascular obstruction, tissue level perfusion, and

maintenance of vessel patency. Their reactivity is a key pathophysiological issue and it has been shown that platelet size, simply measured by mean platelet volume (MPV) is correlated with platelet activity. It is known that larger platelets are more reactive due to higher concentration of active substances in micro granules (e.g. thromboxane A2, platelet factor 4, P-selectin, platelet-derived growth factor) and expression of adhesive receptors (glycoprotein IIb/IIIa). Furthermore, increased MPV values are associated with shortened bleeding time.

MPV is considered a useful prognostic marker of cardiovascular risk[2].

In the general population, a higher MPV value is associated with an increased occurrence of MI. MPV was found to be a useful hematological marker allowing the identification of patients with stable CAD who are at higher risk of post-PCI low-reflow[3]. Elevated mean platelet volume (MPV) has been recently discussed as a predictor of death in patients with acute coronary syndrome (ACS), but the cut-off point of MPV in relation to poor prognosis has not been estimated so far[4]. In some studies, conducted in AMI, elevated MPV was associated with a higher risk of death and recurrent infarction not only in the hospital but also during the 2-year observation after ACS. The baseline mean MPV in patients who developed restenosis or stent thrombosis was significantly higher than in those who did not develop such a complication[5].

AIM OF THE WORK

To investigate the association of mean platelet volume with angiographic thrombus burden and its prognostic value in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.

PATIENTS AND METHODS

This study was carried out on 72 patients, presented with acute STEMI to the Cardiology Department of Ain Shams University Hospital, in

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the period between August 2016 and December 2017 with pain to door less than 12 hours and underwent primary percutaneous coronary intervention (PCI). Patients were followed up for 3 to 6 months.

Exclusion criteria

Patients with atrial fibrillation, structural heart diseases like (cardiomyopathy, moderate to severe valvular heart disease, congenital heart diseases), mechanical complications of myocardial infarction like (acute ventricular septal rupture, and acute ischemic mitral regurge), hepatic insufficiency, renal failure, history of CABG, hypovolemic patients, patients with concomitant infectious diseases, neoplastic diseases, inflammatory diseases or hematological disorders, and patients receiving oral anticoagulation medicine were excluded from the study.

Methods:

All patients were subjected to:

1) History taking, with special emphasis on

(A) Cardiovascular risk factors.

(B) Chest Pain: type, onset, pain to balloon time.

(C) History: especially of previous ischemic events.

2) Full physical Examination.

3) 12-lead surface ECG was recorded within the first 10 minutes of presentation and 90 minutes post catheterization, then daily till discharge to check for ST-segment elevation, and resolution and to identify tachyarrhythmia or heart block.

4) Laboratory investigation:

- Routine lab investigations including CBC, kidney function tests, and liver function tests.
- Blood samples for total creatine kinase (CK) and CK-MB (on admission then serially every 8 hours for the first 24 hours then once daily) to detect peak enzymatic elevation and their resolution to normal baseline.
- Blood samples for the assessment of MPV were drawn into standardized test tubes containing dipotassium ethylenediaminetetraacetic acid (EDTA). All measurements were performed within 1 h of blood collection. All samples were analyzed on the Sysmex K-4500 automated cell counter (Sysmex Corporation Japan, Koebe, Japan); with time to result in approximately 1 min. MPV and platelet count were assessed.

5) Primary PCI:

PCI was performed aiming at obtaining TIMI 3 flow in the infarct-related artery (IRA), which was identified based on ECG and coronary angiography (CA) findings. In general, only the IRA was targeted during emergency catheterization.

All patients received 300 mg aspirin and 600 mg clopidogrel before primary PCI. All patients received heparin according to their body weight (100 IU/kg). Glycoprotein IIb/IIIa inhibitors were used as bailout. The angiographic severity of coronary artery disease (CAD) was assessed visually using 2 orthogonal views. Single-vessel CAD was defined as at least 70% stenosis of only one major epicardial artery and multi-vessel disease was defined as the occurrence of significant stenosis of at least 70% in more than one major coronary artery and/or of at least 50% in the left main coronary artery. Thrombus grading was assessed after the passage of an angioplasty guide wire or a deflated 1.5 mm balloon into the IRA) and it was angiographically scored into five grades: G0 (no thrombus), G1 (possible thrombus), G2 (definite thrombus <0.5 reference vessel diameter), G3 (definite thrombus 0.5–2 reference vessel diameters), G4 (definite thrombus >2 reference vessel diameters) and G5 (complete vessel occlusion). Patients with thrombus G0 to G3 were stratified into a single category defined as low thrombus burden (LTB) [(5)].

The angiographic outcome of PPCI was assessed by the final TIMI flow grade and MBG.

i. TIMI flow that is defined as TIMI O (no perfusion); TIMI I (faint antegrade flow with incomplete filling of the distal coronary bed); TIMI II (delayed or sluggish flow beyond the occlusion with complete filling of the distal coronary bed); TIMI III (normal flow, which fills the distal coronary bed) [(6)].
ii. Myocardial blush grade (MBG) is defined as a visual assessment of relative contrast opacification of the myocardial territory subtended by the IRA in relation to epicardial density. MBG 0: Absence of contrast opacification in the myocardial zone; MBG 1: Minimal contrast opacification or persistent stain without washout; MBG 2: Reduced but clearly evident blush in the infarct zone compared to the contralateral non-involved territory; MBG 3: opacification of the myocardium cleared normally at the end of the washout phase, similar to that in the non-involved territory [(7)].

6) Echocardiography

Full ECG gated echocardiographic study was done on each patient within the hospital stay following primary PCI. Full 2D, M-mode, and Doppler echocardiographic examination were done for all patients in standard precordial apical (2- and 4-chamber images) and parasternal (long- and short-axis images) views according to the American Society of Echocardiography guidelines, 2015). Modified Simpson's method was used for calculating LV ejection fraction [(8)].

Peak longitudinal strain of the left ventricle was measured using speckle-tracking echocardiography. Data analysis was performed offline using the original raw data sets on an EchoPAC software workstation (version BT11, 4D Auto LVQ; GE Vingmed Ultrasound AS) for semi-automated endocardial surface detection as the endocardial

surface of the myocardial wall was manually traced by a point-to-click approach from which the software generated strain curves for each selected myocardial segment. Color-coded parametric images that provide a quick, visual impression of the timing and the extent of segmental myocardial deformation were also generated. The strain values for all the segments were recorded and averaged to obtain the global longitudinal strain (GLS). A topographic representation of the regional and global longitudinal strain of all 17 analyzed segments (Bull's eye configuration) was then automatically generated. The normal value of Global Longitudinal strain is -19.7 ± 3% [(9)].

Follow up

The patients were followed up clinically and by echocardiography for a mean time of three to six months. Follow-up echocardiography was done within 3-6 months from hospital discharge. Clinical follow-up data were obtained from all patients using available medical records, telephone, or personal contact. The following clinical events were defined as secondary endpoints: cardiovascular death, non-fatal re-infarction, repeat revascularization either percutaneous or surgical (CABG), stroke and heart failure (HF) requiring hospitalizations.

Cardiovascular death included death resulting from an acute myocardial infarction, sudden cardiac death, or death due to heart failure. The diagnosis of MI required the combination of: Evidence of myocardial necrosis (changes in cardiac biomarkers) and supporting information derived from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging. Stroke was defined as an acute episode of neurological dysfunction caused by focal or global brain, spinal cord, or retinal vascular injury. Heart failure (HF) requiring hospitalization was defined as symptoms or signs of HF that need an admission to an inpatient unit or a visit to an emergency department that results in at least a 24-hour stay in the absence of other non-cardiac etiology (liver cirrhosis, COPD, renal failure) [(10)]. A composite primary endpoint was defined as a composite of the secondary endpoints.

Ethical Considerations

The research protocol and its procedures followed the declaration of Helsinki. Approval was obtained from The Ethical Committee at Ain Shams University. All participants signed informed written consent with consideration of adequate privacy and confidentiality.

Statistical analysis

Analysis of data was done using the Statistical Package for the Social Sciences (SPSS) version 16 as follows: Quantitative variables were described as mean, standard deviation (SD), and range. Qualitative variables were described as numbers and percentages. Unpaired t-test was used to compare quantitative variables between 2 groups and paired t-test was used to compare pre- and post-interventional quantitative variables in the same group.

Spearman correlation coefficient test was used to rank variables versus each other positively or inversely. The receiver operator characteristic (ROC) curve was used to find out the best cut-off value, and validity of certain variables. Univariate and multivariate regression analysis were done to identify the independent predictors of the primary composite end point of the study. P value > 0.05 was non-significant (NS), P < 0.05 was significant (S), and P < 0.001 was highly significant (HS).

RESULTS

This study included 72 patients with acute STEMI who underwent primary PCI. Only 60 patients completed the follow-up process.

1. Demographic data and risk factors

The mean age of the studied cases was 53.22 ± 9.96 years including 62 males (86.1%) and 10 females (13.9%). The most common risk factor for IHD was smoking (Table 1).

Table 1: Demographic data and risk factors

Variables		Total no. = 72
Age (Years)	Mean ± SD	53.22 ± 9.96
	Range	33 – 73
Gender	Female	10 (13.9%)
	Male	62 (86.1%)
Smoking	Negative	15 (20.8%)
	Positive	57 (79.2%)
DM	Negative	33 (45.8%)
	Positive	39 (54.2%)
HTN	Negative	36 (50.0%)
	Positive	36 (50.0%)
Dyslipidemia	Negative	29 (40.3%)
	Positive	43 (59.7%)
Family history	Negative	61 (84.7%)
	Positive	11 (15.3%)

DM: Diabetes Mellitus, HTN: Hypertension.

2. Laboratory findings

The laboratory findings of the studied cases are shown in table 2.

Table 2: Laboratory findings.

Total no. = 72	Mean ± SD
MPV (fl.)	9.97 ± 1.31
Platelet count ($\times 10^3$/ul)	284.83 ± 65.66
Creatinine (mg/dl)	1.02 ± 0.17
Peak CK_{total} (u/l)	3177.38 ± 1454.63
Peak CK_{MB} (u/l)	349.03 ± 186.88

MPV: Mean Platelet Volume, CK: Creatine Kinase.

Site of myocardial infarction: The study included 43 patients with anterior STEMI (Table 3).

Table 3: Site of myocardial infarction

		Total no. = 72
ECG	**Anterior**	**43 (59.7%)**
	Inferior+/- posterior or later	**29 (40.3%)**

3. Pain to balloon time.

The mean pain to balloon time was 6.13 hrs. (Table 4).

Table 4*:* Pain to balloon time.

Pain to balloon (hrs.)	**No.**	**Mean ± SD**	**6.13± 3.02**
	72	**Range**	**1– 11**

4. Angiographic data and PCI

The culprit vessel was LAD in 43 patients. 58 patients had a single vessel disease. Only 33 patients underwent balloon predilatation, 68 patients had PCI by BMS while one patient had PCI by one BMS. Stenting wasn't done during primary PCI in 2 patients due to no-reflow and high thrombus burden (Table 5).

Table 5*:* **Angiographic data and PCI**

		No. (%)
Single vessel disease		**58 (80.6%)**
Multivessel disease		**14 (19.4%)**
Culprit vessel	LAD	43 (59.7%)
	LCX	10 (13.9%)
	RCA	18 (25.0%)
	Ramus	1 (1.4%)
balloon predilatation	**Negative**	**39 (54.2%)**
	Positive	**33 (45.8%)**
Stenting	None	2 (2.8%)
	BMS	68 (94.4%)
	DES	1 (1.4%)
	Both	1 (1.4%)

BMS: Bare Metal Stent, DES: Drug Eluting Stents. LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery.

As regards the angiographic thrombus burden and indicators of reperfusion, 17 cases had a high thrombus burden HTB (i.e. thrombus grade ≥4). 57 cases had a final TIMI III flow. 55 cases had a final MBG (2-3). GP II_b/III_a was used in 18 cases as a bailout (Table 6).

Table 6: **Thrombus burden and angiographic outcome**

		No. (%)
Thrombus grade	< 4	55 (76.4%)
	≥ 4	17 (23.6%)
TIMI	< 3	15 (20.8%)
	3	57 (79.2%)
MBG	(0-1)	17 (23.6 %)
	(2-3)	55 (76.4%)
Use of GP IIb/IIIa	Negative	54 (75.0%)
	Positive	18(25.0%)

TIMI: Thrombus in Myocardial Infarction,
MBG: Myocardial Blush Grade, GP: Glycoprotein.

5. Echocardiographic data

There was a statistically significant change in all the measured echocardiographic after short-term follow-up compared to the initial findings (Table 7).

Table 7*:* Echo parameters

		Baseline	**Follow up**	**Test value ••**	**P-value**	**Sig.**
LVEDD (mm)	**Mean± SD**	52.5± 4.14	53.33± 4.78	2.696 **	<0.001	**HS**
	Range	44 – 59	41 – 70			
LVESD (mm)	**Mean± SD**	38.59± 4.22	38.57± 4.67	2.908 **	<0.001	**HS**
	Range	26 – 43	25 – 43			
EF%	**Mean ± SD**	47.33± 5.54	47.40± 5.94	2.977 **	<0.001	**HS**
	Range	38 – 60	38 – 60			
GLS	**Mean ± SD**	11.1± 2.2	11.3± 2.5	2.515 **	<0.001	**HS**
	Range	7.8 – 16.8	8 – 17.2			

HS: Highly significant. (LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, EF: Ejection Fraction, GLS: global longitudinal strain); ••: Paired t-test.

6. Short-term clinical outcomes.

The composite primary endpoint occurred in 12 patients (20%). Those patients developed heart failure requiring hospitalization during the short-term follow-up (Table 8).

Table 8*: short term clinical outcomes*

		No. (%)
Primary Composite Endpoint	Positive	12 (20%)
	Negative	48 (80%)
Cardiovascular death	No	60 (100.0%)
	Yes	0 (0.0%)
Heart failure requiring hospitalization	No	48 (80.0%)
	Yes	12(20.0%)
Non-fatal reinfarction	No	60 (100.0%)
	Yes	0 (0.0%)
Repeat revascularization	No	60 (100.0%)
	Yes	0 (0.0%)
Stroke	No	60 (100.0%)
	Yes	0 (0.0%)

7. Comparative (correlation) analysis between MPV and the other parameters

There was a statistically significant correlation between MPV and smoking and there was a statistically non-significant correlation with Gender, DM, HTN, Dyslipidemia, and family history of CAD (Table 9).

Table 9: Correlation between MPV and different parameters

		MPV		Test value•	P-value	Sig.
		Mean ± SD	Range			
Gender	Female	9.32 ± 1.03	7.6 – 10.8	-1.736	0.087	NS
	Male	10.08 ± 1.32	5.95 – 13.8			
Smoking	Negative	9.27 ± 0.84	7.6 – 10.8	-2.418	0.018	S
	Positive	10.16 ± 1.35	5.95 – 13.8			
Diabetes mellitus	Positive	10.17 ± 1.38	5.95 – 13.8	1.364	0.177	NS
	Negative	9.75 ± 1.2	7.6 – 12.4			
Hypertension	Positive	10.18 ± 1.4	5.95 – 13.8	1.324	0.190	NS
	Negative	9.77 ± 1.19	7.6 – 12.4			
Dyslipidemia	Negative	9.93 ± 1.21	5.95 – 11.9	-0.251	0.802	NS
	Positive	10.01 ± 1.38	7.6 – 13.8			
FH OF CAD	Negative	9.9 ± 1.11	7.6 – 12.4	-1.089	0.280	NS
	Positive	10.37 ± 2.13	5.95 – 13.8			

P-value > 0.05: Non-significant (NS); P-value < 0.05: Significant(S); P-value < 0.01: Highly significant (HS).

There was a statistically significant correlation between MPV and Peak CK_{total}, Peak CK_{mb} (Table 10).

Table 10: Correlation between MPV and platelet count, serum creatinine, and cardiac enzymes

	MPV	
	R	P-value
Platelet count ($\times 10^3$/ul)	-0.010	0.933
Creatinine (mg/dl)	-0.065	0.587
Peak CK_{total} (U/L)	0.324*	0.006
Peak CK_{MB} (U/L)	0.247*	0.036

*: Significant, CK: Creatine Kinase

There was a significantly higher MPV among patients with HTB and patients with impaired reperfusion (MBG (0-1) and TIMI flow<3 (Table 11).

Table 11: Correlation between MPV and angiographic data

		Number	MPV	Test value	P-value	Sig.
			Mean ± SD			
Extent of CAD	Single	58 (80.6%)	9.86 ± 1.25	1.582	0.118	NS
	Multi	14 (19.4%)	10.46 ± 1.48			
THROMBUS GRADE	HTB (≥4)	17	11.42±1.007	6.631	0.00	HS
	LTB (< 4)	55	9.53±1.039			
Need for GP IIb/IIIa	Negative	54 (75.0%)	9.72 ± 1.09	-2.968	0.004	HS
	Positive	18 (25.0%)	10.73 ± 1.63			
MBG	MBG (0/1)	17	11.77±.74	4.761	0.004	HS
	MBG (2/3)	55	9.87±1.26			
TIMI flow	<3	15	10.59±1.839	2.095	0.04	S
	3	57	9.81±1.092			

P-value > 0.05: Non-significant (NS); P-value < 0.05: Significant(S); P-value < 0.01: Highly significant (HS). HTB: high thrombus burden. LTB: low thrombus burden

MPV and the composite primary end point:

MPV was significantly higher among patients of the composite primary endpoint. The primary composite endpoint occurred in 12 patients with a higher MPV (10.95 ± 1.14 vs. 9.73 ± 1.29, p 0.01).

Receiver operating characteristics (ROC) showed that the best cut-off value of MPV for prediction of the occurrence of the primary composite endpoint was 10.5 fl. The area under the ROC curve for MPV was 0.718 (95% CI 0.57–0.65). The value of 10.5 had a positive predictive value (PPV) of 42.9% and a negative predictive value (NPV) of 89.7% (Figure 1).

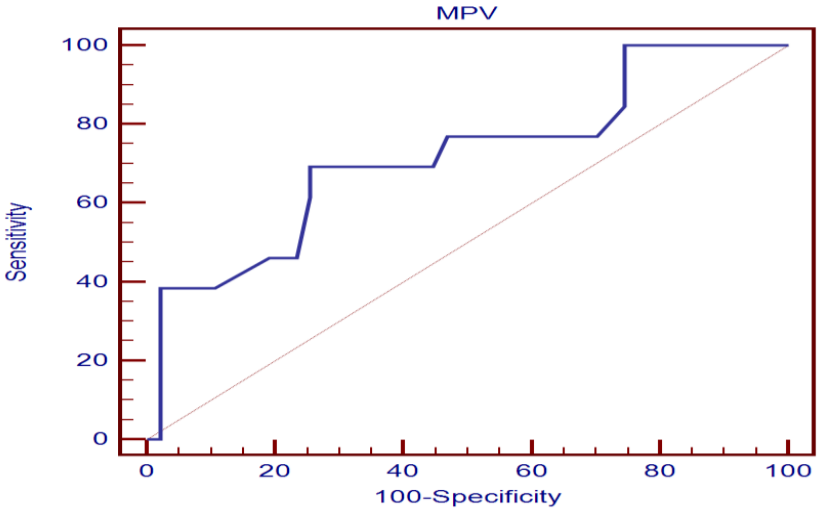

Figure 1: ROC curve analysis of admission MPV for the composite primary endpoint

Univariate regression analysis showed the **MPV, peak CK_{mb}, thrombus grade, TIMI flow, and MBG** are predictors of the primary composite endpoint after AMI in the study (Table 12**).**

Table 12: **Univariate regression analysis for laboratory and angiographic predictors of the primary composite endpoint**

	B	S.E.	Wald	OR	P-value	95.0% C.I. for OR	
						Lower	Upper
TIMI GROUPS	0.563	0.113	0.546	4.965	<0.001	0.336	0.789
TG GROUPS	-0.556	0.105	-0.571	-5.293	<0.001	-0.766	-0.346
PTCA	-0.364	0.098	-0.438	-3.712	<0.001	-0.561	-0.168
MBG GROUPS	0.600	0.097	0.631	6.189	<0.001	0.406	0.794
MPV	-0.101	0.038	-0.328	-2.648	0.010	-0.178	-0.025
PEAK MB	0.000	0.000	-0.299	-2.383	0.020	-0.001	0.000

Multivariate logistic regression analysis showed that **MBG** was the most powerful independent predictor for the composite endpoint after AMI among all statistically significant laboratory and angiographic parameters in the study (Table 13).

Table 13: Multivariate regression analysis for the independent predictors of the primary composite endpoint

	B	S.E.	Wald	P-value	OR	95.0% C.I. for OR	
						Lower	Upper
TIMI GROUPS	2.384	1.389	2.947	0.086	10.846	0.713	164.911
TG GROUPS	-1.210-	1.638	0.546	0.460	0.298	0.012	7.391
MBG GROUPS	**3.147**	**1.114**	**7.973**	**0.005**	**23.258**	**2.618**	**206.604**
MPV	0.311	0.502	0.383	0.536	1.364	0.510	3.649
PEAK MB	-0.005	0.003	2.728	0.099	0.995	0.989	1.001

Univariate regression analysis showed that the MPV, balloon predilatation, pain to balloon time in hours, thrombus grade, and TIMI flow grade were predictors of MBG (0/1) after AMI in the study (Table 14).

Table 14: Univariate regression analysis for predictors of MBG (0/1)

	B	S.E.	Wald	p-value	OR	95.0% C. I. for OR	
						Lower	Upper
MPV	-0.721	0.261	7.626	**0.006**	0.487	0.292	0.811
Balloon predilatation	-1.738	0.637	7.452	**0.006**	0.176	0.050	0.613
Pain to balloon (hrs.)	-0.207	0.106	4.824	**0.041**	0.813	0.661	0.983
Thrombus grade	-1.888	0.618	9.327	**0.002**	0.151	0.045	0.508
TIMI flow	1.414	0.624	5.138	**0.023**	4.112	1.211	13.967

Multivariate logistic regression analysis showed that the balloon pre dilatation is an independent predictor of MBG (0/1) after AMI among all the statistically significant parameters in the study (Table 15).

Table 15: multivariate regression analysis for independent predictors of MBG (0/1)

	B	S.E.	Wald	P-value	OR	95.0% C.I. for OR	
						Lower	Upper
MPV	-0.325	0.326	0.994	0.319	0.723	0.382	1.369
Pain to balloon (hrs.)	-0.200	0.131	2.335	0.127	0.819	0.634	1.058
Balloon predilatation	**-1.735**	**0.801**	**4.689**	**0.030**	**0.176**	**0.037**	**0.848**
Thrombus grade	-1.101	1.162	0.898	0.343	0.332	0.034	3.243
TIMI flow	-0.480	1.108	0.188	0.665	0.619	0.070	5.431

Receiver operating characteristics (ROC) showed that the best MPV cut-off value for prediction of MBG (0, 1) was 11.9 fl. The area under the ROC curve for MPV was 0.906 (95% CI 0.57–0.65). The value of 11.9 had a positive predictive value (PPV) of 98.5% and a negative predictive value (NPV) of 50% (Figure 2).

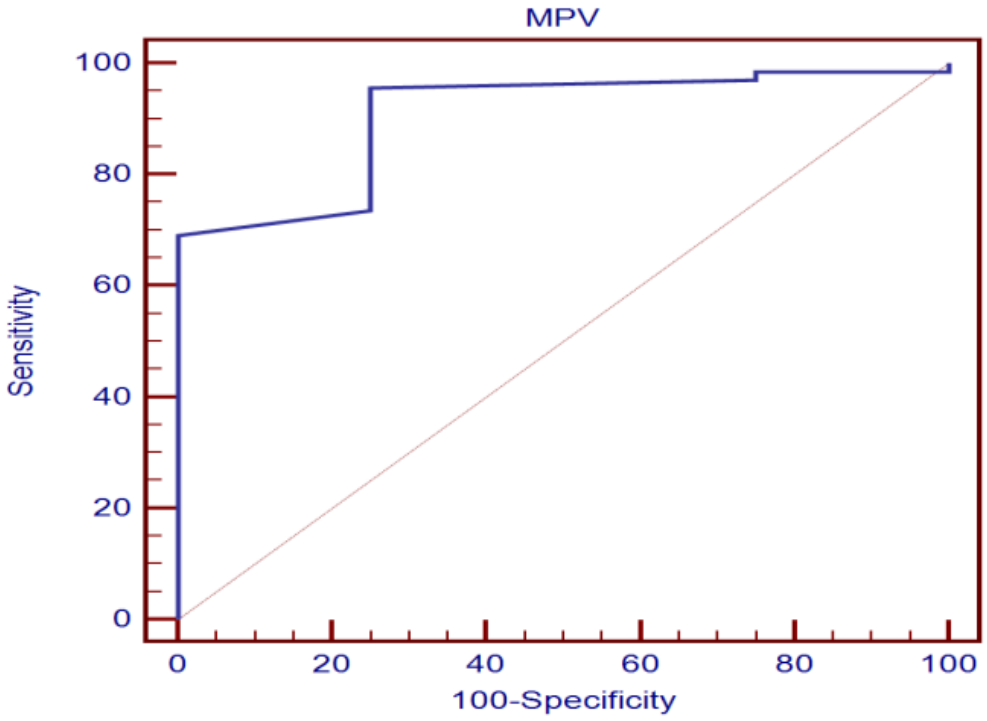

Figure 2: ROC curve analysis of admission MPV for MBG (0, 1).

Univariate regression analysis showed that the MPV, pain to balloon time in hours, thrombus grade, and Balloon pre-dilatation were predictors of TIMI flow after AMI in the study (Table 16).

Table 16: Univariate regression analysis for predictors of TIMI flow.

	B	S.E.	Wald	p-value	OR	95.0% C. I. for OR	
						Lower	Upper
MPV	**-0.076**	**0.036**	**-0.243**	**0.040**	**-2.095**	**-0.148**	**-0.004**
Pain to balloon time in hours	**-0.031**	**0.017**	**-0.212**	**0.074**	**-1.812**	**-0.064**	**0.003**
Thrombus grade	**-0.574**	**0.091**	**-0.601**	**0.000**	**-6.285**	**-0.757**	**-0.392**
Balloon predilatation	**-0.287**	**0.091**	**-0.352**	**0.002**	**-3.144**	**-0.469**	**-0.105**

Multivariate logistic regression analysis showed that the most powerful independent predictor for TIMI flow after AMI for all statistically significant parameters in the study is the TG followed by PTCA (Table 17).

Table 17. multivariate regression analysis for the independent predictors of TIMI flow

	B	S.E.	Wald	P-value	OR	95.0% C.I. for OR	
						Lower	Upper
MPV	0.764	0.418	3.335	0.068	2.146	0.946	4.870
Pain to balloon in hours	-0.050-	0.168	0.087	0.768	0.951	0.684	1.324
Thrombus grade	**-4.765-**	**1.378**	**11.965**	**0.001**	**0.009**	**0.001**	**0.127**
Balloon predilatation	**-2.291-**	**0.945**	**5.877**	**0.015**	**0.101**	**0.016**	**0.645**

DISCUSSION

MPV was proved to be higher in patients with ACS, with an apparent stepwise decrease from AMI to unstable angina to stable chronic coronary disease or non-ACS patients **(11)**. This finding can be explained as an expression of enhanced platelet reactivity in the acute setting of IHD and suggests that MPV could be useful in the evaluation of patients with chest pain **(12)**.

Our study tested the predictive value of MPV for angiographic thrombus burden and short-term outcomes in patients with ST segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. The main findings were as follows:

- MPV is an independent predictor of the thrombus grade (TG) after STEMI.
- The TG and balloon predilatation are independent predictors of post-interventional TIMI flow in the study.
- Linear regression analysis showed that admission MPV is significantly associated with post-interventional MBG.
- MBG is an independent predictor of the primary composite endpoint in the study.

We studied 72 patients (62 male and 10 female), with a mean age of 53.22 ± 9.96 years. STEMI was more common among males but, our study did not show any significant correlation between MPV and both age and gender similar to observations made by **Ilavarasi *et al.*** **(13)**.

In concordance with **Ilavarasi *et al.*** (13), we found that the MPV was higher in patients with diabetes mellitus, hypertension, and or dyslipidemia but the correlation was not significant. Among the study group, 57 patients were smokers (79.2%) and the mean MPV was significantly higher among smokers. Similar results were observed by **Varol *et al.*** (14) who found also, a decrease in the MPV after cessation of smoking. These results may indicate that there is a common mechanism by which these risk factors increase the risk of cardiovascular disease.

The mean platelet count of the study population was 284.8 ± 65.6 /mm^3. There was no significant relationship between platelet count and MPV similar to observations made by **Ilavarasi *et al.*** (13). On the contrary to MPV, the platelet count itself did not show any diagnostic nor prognostic value in patients with ACS (15).

In the present study, there was a significant correlation between MPV and LVESD, LVEDD ejection fraction, and global longitudinal strain in both baseline and follow-up echocardiography. **Ilavarasi *et al.*** (13) observed that increased MPV on admission is associated with impairment in left ventricular systolic function. We assume that fractions of larger platelets wielding greater thrombotic potential may cause recurrent thrombosis in an environment of microcirculation injured due to ischemic-reperfusion.

In concordance with the present study, several studies have reported that there is no relationship between MPV and the extent of CAD (16-18).

Preprocedural high-thrombus burden (HTB i.e. thrombus grade ≥4) of infarct-related artery (IRA) is a harbinger of procedural complications following primary PCI in patients with STEMI. It can lead to poor outcomes by various mechanisms, including the no-reflow phenomenon, and increased myocardial necrosis with subsequent reduced survival benefit at follow-up **(16).** In concordance with **Lai and his colleagues (17)**, (23.6%) of patients with HTB in our study had a significantly higher admission MPV than the patients with LTB. We found in a receiver operating characteristics analysis that an MPV cut-off value of ≥ 11.3 fl predicted HTB with 98% sensitivity and 47% specificity. At the same time, **Lai *et al.*** (17) found that a cut-off value of ≥ 10.2 fl predicted HTB with 73.5% sensitivity and 68.9% specificity. Increased MPV has been shown to be an indicator of larger and more reactive platelets (16). Larger platelets aggregate more rapidly upon collagen challenge and have a greater prothrombotic potential, with higher levels of intracellular thromboxane A2 as well as increased levels of procoagulant surface proteins, thereby contributing to thrombus formation (17).

Angiographic successful reperfusion in acute myocardial infarction has been defined as TIMI 3 flow. Failure to achieve TIMI flow grade 3 after the successful opening of the artery without angiographic evidence of mechanical obstruction, observed in 5% to 20% of patients treated with primary PCI and defined as a no-reflow phenomenon, is associated with more extensive myocardial necrosis, worse segmental and global contractility of the left ventricle, malignant arrhythmias, and increased mortality(6). In our study, admission MPV was significantly higher in patients with TIMI flow ≤ II (20.8% of cases) than the patients with TIMI III flow. Univariate regression analysis showed that MPV, pain to balloon time in hours, thrombus grade, and balloon predilatation are predictors of post-interventional TIMI flow after acute myocardial infarction in the study. Similar results were observed by **Elbasan *et al*.** (18), who found that the incidence of post-PCI normal TIMI flow was significantly decreased with increased MPV. Furthermore, they showed that MPV was independently associated with post-PCI TIMI flow.

Also, **Lai *et al.*** (17) found that post-interventional TIMI 3 flow was less achieved in patients with MPV>10.2 fl (87.8% vs. 93.3%)**.** Furthermore, **Estévez and his co-workers** (19) published that increased MPV was an independent predictor of IRA patency in patients with STEMI treated with primary PCI.

Because TIMI 3 flow does not always result in effective myocardial reperfusion we used myocardial blush grade (MBG) as an angiographic measure of myocardial reperfusion, in our study, (76.4%) cases had a final MBG (2-3), while MBG (0-1) occurred in (23.6%) cases. In concordance with **Lai and his colleagues** (17), we found that patients with MBG (0-1) had a significantly higher admission MPV than patients with good MBG. In a receiver operating characteristics analysis, an MPV cut-off value of ≥11.9 fl predicted MBG (0, 1) with a sensitivity of 95.59% and a specificity of 75%. Linear regression analysis showed that admission MPV was significantly associated with post-interventional MBG and this is concordant with **Sarli and his co-workers**(20). **Elsherbiny *et al.***, have shown that the MPV is higher in slow coronary flow (SCF) compared to normal coronary flow (NCF) (21). Furthermore, **Nurkalem *et al.*** have reported that SCF cases with unstable angina have higher MPV compared to SCF ones with stable coronary artery disease and NCF cases (22). Other studies have also confirmed that elevated MPV is associated with the presence of coronary slow flow **(23,24).**

In our study, patients with worse short-term outcomes had a significantly higher MPV than those with better short-term outcomes. In our study, an MPV cut-off value of >10.5 predicted the primary composite endpoint with a sensitivity of 69.23 % and a specificity of 74.47 %. In concordance with different studies where MPV cutoff values for predicting poor clinical outcomes in STEMI patients treated via PCI are 8.9 to 11.7 fl. (18-20). **Choi *et al.*** pooled results from three cohort studies involving patients with AMI and concluded that elevated MPV (two studies used a cut-off MPV of ≥10.3 fL and the other >9 fL) increased the odds of death as compared with a normal MPV and when the two studies that used a cut-off MPV of ≥ 10.3 fL were analyzed separately from the study using a cut-off MPV of 9 fL, the increased risk of mortality with an elevated MPV was two-fold greater (25). Also, **Sun *et al.*** enrolled Chinese patients with STEMI for almost 6 years in this study, the worst outcomes occurred among patients with larger MPV, either above the normal range (>12.5 fL) or in higher values within the normal range (11.1–12.5 fL), although the relationship between MPV and cardiac death was not specifically assessed in this study, most of the documented events (144 out of 197) during follow-up were due to cardiovascular issues (26).

Also, worse short-term outcomes were significantly higher among patients with HTB, TIMI flow < III and MBG (0-I) (64.3% vs. 8.7%, 66.7 % vs. 10.4%, 100.0% vs. 16.1). This is concordant with **Lai and his colleagues (17)** who found that the cumulative 30-day all-cause mortality rate was significantly higher in the groups with high MPV and HTB (9.8% vs. 2.5% and 8.6% vs. 4.1%, P = 0.036, respectively). Also, **Lai and his colleagues**(17) published that the cumulative 30-day all-cause mortality rate was significantly higher in the groups with high MPV and MBG 0/1 (6.8 vs.

1.5%, and 7.6 vs. 1.9%, respectively). **Huczek *et al.*** stated that high MPV was associated with impaired angiographic reperfusion and increased 6-month mortality in patients undergoing primary PCI [(27)]. **Goncalves *et al.*** reported that elevated MPV was a strong independent predictor of long-term outcomes (death and AMI) after percutaneous coronary intervention, with a comparable predictive value to troponin in patients with an ACS [(28)]. There are several mechanisms through which increased MPV may contribute to adverse outcomes. Increased MPV is an indicator of a larger, hyperactive platelet. Hyperactive platelets may exaggerate platelet adhesion and aggregation and contribute to myocardial injury by releasing a variety of mediators of inflammation and thrombosis. Hyperactive platelets are also implicated in the platelet-mediated microvascular dysfunction and inflammatory response on the tissue level, thereby aggravating tissue injury and extending infarct size, which may suggest a possible mechanistic link between higher MPV values and increased short-term mortality in patients with STEMI undergoing primary PCI[(28)].

Results from the present study support the idea that platelets play an important role in the pathophysiology of no-reflow and suggest that MPV may be considered as a useful, independent, hematological marker allowing for early and easy identification of patients who are at a higher risk of impaired reperfusion after primary PCI. Admission of MPV may be additive to conventional risk factors in patients with STEMI undergoing PCI. Research on the no-reflow phenomenon, where intravascular plugging by platelets was identified as one of the responsible factors, supports this hypothesis. In light of these findings, the necessity of further investigation of platelet function is legitimized.

CONCLUSION

MPV may be a useful biomarker that can help identify large intracoronary thrombus burden in patients with STEMI undergoing primary PCI. So, it may become a valuable contribution to the identification of higher-risk patients, who might require more potent antiplatelet therapy.

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