

Value of the Mean Platelet Volume in Evaluation of Patients with Acute Coronary Syndrome

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Abstract

Background: Increased mean platelet volume (MPV) is a central process in the pathophysiology of coronary artery disease (CAD).

Objectives: To investigate whether assessment of MPV, besides the traditional risk factors, enhances the assessment process for the risk of acute coronary syndrome (ACS).

Materials and Methods: This study included 81 patients, divided into 2 groups; group I included 61 patients with acute coronary syndrome (ACS); further subdivided into group I a (37 Tn +ve patients) and group I b (24 Tn -ve patients) and group II included 20 completely healthy age matched as a control group; all patients were subjected to; history taking, clinical examination, ECG, assessment of MPV and lipid profile.

Results: Tn +ve ACS patients had the highest MPV (13.3 ± 2.4 fL), MPV correlated significantly with total cholesterol level, LDL level, and Tn level, $P < 0.001$. By multivariate analysis, only MPV significantly increased the probability of Tn +ve ACS development ($B \pm SE = 0.078 \pm 0.028$, $t = 2.8$, 95% CI 0.022-0.133 with an odds ratio = 0.358, $P = 0.007$). MPV of ≥ 11.1 fL was the best cut-off value in predicting Tn +ve ACS with a sensitivity of 84% and a specificity of 65% ($P = 0.000$).

Conclusion: Our study determined that the MPV can facilitate the risk stratification for ACS occurrence. Which could be used as an alarming sign in follow up of patients with CAD to predict those at risk of Tn +ve ACS.

Keywords: Acute coronary syndrome; Mean platelet volume; Myocardial infarction.

Abbreviations:

ACS; Acute Coronary Syndrome, AMI; Acute Myocardial Infarction, ASA; Acetyl Salicylic Acid, CAD; Coronary Artery Disease, ECG; Electrocardiography, LDL: Low Density Lipoprotein Cholesterol, MPV; Mean Platelet Volume, STEMI; ST-Elevation MI, Tn; Troponin.

Introduction

Increased mean platelet volume (MPV) is a main step in the pathophysiology of coronary artery disease [1-3]. MPV, is a potentially useful biomarker of platelet activity in the setting of cardiovascular disease, as it is a major culprit in atherothrombotic events [4,5]. Platelet volume and its activity had a major role in the atherothrombotic process that was reinforced by the fact that antiplatelet drugs can reduce cardiovascular events [6].

Measuring platelet activity by any of a wide variety of methods has been reported to identify individuals at increased risk for cardiovascular events, but it remains a research tool that is yet to be included in routine clinical decision-making. MPV is the most

commonly used measure of platelet size, so it could be used as a potential marker of platelet reactivity [7].

A lack of enough data about the optimal MPV cut off value for distinguishing increased risk, and the uncertainty about the interpretation and clinical utility of results is a good area for research work.

The study hypothesis

We tried to report the relation between MPV and acute coronary events and so clarify its importance in follow up of patients with CAD.

Aim of the work

To investigate whether assessment of MPV, besides the traditional risk factors, enhances the assessment process for the risk of acute coronary syndrome (ACS).

Materials and Methods

This is a case control study. It included 81 patients, divided into 2 groups; group I included 61 consecutive patients with acute coronary syndrome (ACS) from the emergency room (ER) and group II included 20 completely healthy age matched as a control group. Patients on oral anticoagulant, malignancy, hyperthyroidism, severe renal or liver impairment, were excluded from the study. Approval was

obtained for performing the study from the Ethical Committee of the Zagazig University Cardiology Department after approval of the Institutional Review Board - Zagazig University (IRB-ZU), Egypt.

After giving a written informed consent, all participants were subjected to the following:

1) Full history taking with stress on risk factors of CHD and thorough clinical examination with estimation of the body mass index (BMI in kg/m²).

2) Complete 12-leads electrocardiography (ECG).

Anderson et al. [8] and Thygesen et al. [9] defined ACS on the bases of history and ECG as; new-onset or worsening chest pain occurring at rest or with minimal exertion and not improved by nitroglycerin and or rest. Typical chest pain lasting >20 minute, or atypical chest pain with suggestion of ACS, lasting at least 5 min and occurring within 24 hours before admission and involving an unstable pattern of pain including rest pain, new onset severe or frequent angina or accelerating anginal pain. Evidenced past history of coronary artery disease (CAD) or +ve stress test.

ECG finding as (ST segment deviation >1 mm, inverted T wave, hyper acute T wave in two or more contiguous leads, and new onset Left Bundle Branch Block)

3) Peripheral blood samples were collected for detection of cardiac troponin T and troponin I which are highly specific for myocardial damage to complete diagnosis of ACS [8,9]. Troponin T measurement (Roche diagnostics, detection limit 0.1ng/ml) was done on admission and 6-8 hours later if the first set was negative, values >0.1ng/ml was considered positive. According to the results; group I was farther subdivided into group I a (includes 37 Tn-positive patients) and group I b (includes 24 Tn -ve patients) we selected this classification as Tn +ve carry bad prognosis (means myocyte death).

4) Transthoracic Echocardiography (TTE), by a Vivid 9 system (GE Vingmed Ultrasound AS, Horten, Norway) echo-set and 2.5-MHz transducers were used to calculate the left ventricular ejection fraction (EF %).

5) Lipid profile (total cholesterol, LDL, VLDL and triglyceride levels, expressed as mg/dl) within 24 hours from admission, to assess patients' risk factors of ischemic heart disease.

6) MPV (fL) within 24 hours from admission and analyzed using blood samples with K3 EDTA that were analyzed after 1 hr of venipuncture to allow stabilization of platelet shape and to prevent EDTA-induced swelling, as it is time-dependent [10].

Statistical analysis: All data were analyzed using SPSS version 16 software (SPSS, Inc. Chicago, IL, USA). Results were presented as mean value ± SD for continuous variables and as frequency (%) for categorical variables. Means were compared within groups for significant difference using One Way ANOVA test, Categorical data were compared using chi-squared test. The correlation between MPV and other parameters was done by the Pearson correlation analysis. Regression analysis was done to find the significant independent risk factors of Tn +ve ACS. Determination of cut-off values with associated sensitivity and specificity was performed using Receiver Operating Characteristics (ROC) analysis.

Results

A total of 81 patients were enrolled in the study; group I (n=61 ACS patients) which subdivided into subgroup Ia (n=37 Tn +ve patients) and subgroup Ib (n=24 Tn -ve patients) and group II (n=20 control patients). Table 1 shows baseline clinical and laboratory measures of both groups. There was no gender, age-based or clinical characteristics differences between groups. Tn +ve patients (group Ia) when compared to group Ib & group II; had higher BMI (33.05 ± 4.85 vs. 29.08 ± 3.81 & 21.6 ± 1.65 kg/m² respectively, P=0.000), higher total cholesterol (221 ± 55 vs. 189.8 ± 52.9 & 176.6 ± 27.2 mg/dl respectively, P=0.016), higher LDL cholesterol (132.1 ± 40.4 in Tn +ve vs. 99.3 ± 23.2 mg/dl, in control group P=0.07), and higher mean platelet volume (13.3 ± 2.4 vs. 11.2 ± 1.7 & 10.6 ± 0.8fL respectively, P=0.001). Patients with Tn +ve ACS followed acetyl salicylic acid (ASA) lesser than those with Tn -ve ACS [5 (13.5%) vs. 10 (41.7%), P=0.007]. Table 2 showed highly significant positive correlations between MPV and {BMI (r=0.474, P=0.000), serum total cholesterol level (r=0.481, P=0.000), serum LDL level (r=0.409, P=0.000), and serum Troponin level (r=0.499, P=0.000)}. MPV presented a highly significant -ve correlation with the EF (r=- 0.394, P=0.001). The probability of Tn +ve ACS occurrence, depending on the measured laboratory parameters and calculated ratios, was presented using logistic regression after adjustment for age, gender, diabetes mellitus, hypertension, smoking status, total cholesterol, TG, LDL, VLDL successively. MPV was an independent risk factor for Tn +ve ACS (B ± SE=0.078 ± 0.028, t=2.8, 95% CI 0.022-0.133 with an odds ratio=0.358, P=0.007). MPV of ≥11.1 fL was the best cut-off value considered to predict Tn +ve ACS with a sensitivity of 84% and a specificity of 65 % (P=0.000, 95% CI 0.699-0.906) done by ROC analysis; Figure 1.

Variables	Tn +ve group (n=37)	Tn -ve group (n=24)	Control group (n=20)	P	Post hoc test
Age (years) X- ± SD	53.4 ± 8.8	52.6 ± 9.5	48.6 ± 11.1	0.36	
Gender (male/female), n (%)	27/10 (73/27%)	16/8 (66.7/33.3%)	14/6 (70/30%)	0.72	
HTN n (%)	16 (43.2%)	16 (66.7%)	10 (50)	0.3	
DMn (%)	15 (40.5%)	13 (54.2%)	6 (30%)	0.37	
Smoker n (%)	15 (40.5%)	5 (20.8%)	6 (30%)	0.72	
BMI(kg/m ²) X- ± SD	33.05 ± 4.85	29.08 ± 3.81	21.6 ± 1.65	0.000	Between the groups 3

Renal impairment	0	0	0	NS	
Duiretics	0	0	0		
ASA n (%)	5(13.5%)	10 (41.7%)	0(0%)	0.007	Tn +ve vs. Tn -ve
ACEI n (%)	10(27%)	10(41.7%)	4(20%)	0.35	
Total Cholesterol (mg/dl) X- ± SD	221.1 ± 55	189.8 ± 52.9	176.6 ± 27.2	0.016	Between the 3 groups
TG (mg/dl) X- ± SD	153.6 ± 100.6	137.7 ± 70	125.1 ± 40.3	0.58	
LDL(mg/dl) X- ± SD	132.1 ± 40.4	117.6 ± 48.5	99.3 ± 23.2	0.07	T+ve vs. control
HDL(mg/dl) X- ± SD	39.9 ± 13.6	44.8 ± 11.7	48.1 ± 9.7	0.12	
VLDL(mg/dl) X- ± SD	30.7 ± 20	27.5 ± 14.0	27.6 ± 11.1	0.74	
MPV(fL) X- ± SD	13.3 ± 2.4	11.2 ± 1.7	10.6 ± 0.8	0.000	Between the 3 groups
EF(%)	62.6 ± 10.5	63.1 ± 5.4	63.9 ± 6.6	0.92	

Table 1: Demographic and clinical characteristics of the study groups: p-value ≤0.05=Significant, p-value <0.01=Highly significant, p-value >0.05=Non-significant; BMI: Body Mass Index; ASA: Acetyl Salicylic Acid; TG: triglycerides; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; VLDL: Very Low Density Lipoprotein; MPV: Mean Platelet Volume; EF: Ejection Fraction; NS: Non Significant.

Variables	r	p-value
HTN	0.241	0.043
Smoking	0.282	0.017
BMI	0.474	0.000
Total cholesterol	0.481	0.000
LDL	0.409	0.000
EF	-0.394	0.001
Tn	0.499	0.000

Table 2: Correlation of MPV (fl) and other parameters. Significant correlation p-value ≤0.05, highly Significant correlation p-value ≤0.01, Tn; troponine.

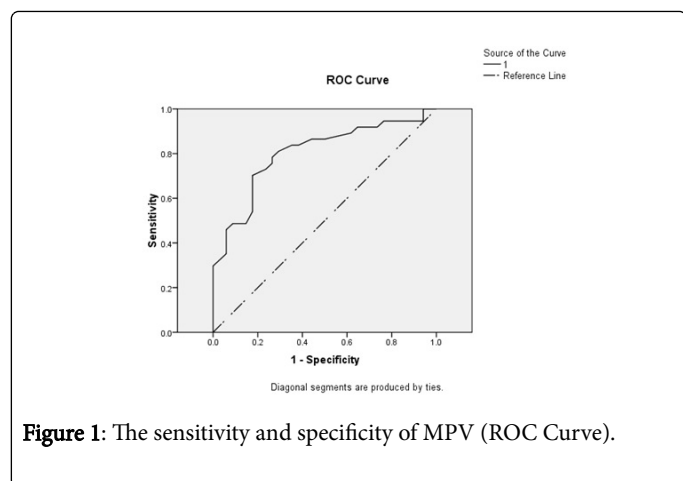


Figure 1: The sensitivity and specificity of MPV (ROC Curve).

Discussion

This is the first clinical study searching for the best cut-off value of MPV in Tn +ve ACS patients in Egypt and whether it could be used as a risk factor in this group of patients. The main findings of this study were as follows: (1) MPV was higher in ACS patients, with the highest level in Tn +ve ACS than Tn -ve ACS patients, and (2) MPV of ≥11.1 fL was the best cut-off value considered to predict Tn +ve ACS.

Platelets play the main role in atherothrombosis which is the major cause of most ACS events [1]. The main factor in pathogenesis of occlusive arterial disease is activation of platelets at sites of vascular injury via pathologically exaggerated and deregulated protective mechanisms involved in hemostasis [5]. Platelets express and secrete a large number of mediators of coagulation, inflammation, atherosclerosis and thrombosis process [1,3]. Antiplatelet can reduce the cardiovascular events; this fact reinforces the major role of platelets in the atherothrombotic process [4].

The insufficient data about the best MPV cut off value to distinguish increased risk, and the lack of data about the interpretation and clinical utility of results open the research gate.

Previous studies concluded that MPV was higher in patients with acute myocardial infarction (AMI) than in those without [2-13], that with meta-analysis expressed a mean value of (9.24 fL, 95% CI 8.39-10.08 vs. 8.48 fL, 95% CI 7.77-9.19) [4].

In our study, we found that MPV was higher in Tn +ve ACS subgroup than Tn -ve ACS subgroup (P<0.001), consistent with those of above publications.

Increased MPV was noted in patients with risk factors of CAD, such as smoking, diabetes, obesity, hypertension, and hyperlipidemia [14-18], in consistence with our results.

Huczek, et al. [19] suggested that MPV may have a role in guiding therapy in the setting of ST-elevation MI (STEMI); only patients with elevated MPV developed a reduction of mortality from abciximab

administration. So, it would be clinically helpful to study whether the use of glycoprotein IIb/IIIa inhibitors (or other antiplatelet agents) is effective or not. But no study to date has shown that lowering MPV lowers cardiovascular risk [4].

We found that patients with Tn +ve ACS were less adherent to ASA, which may play a major role in modulation of the MPV and so reduction of ACS specially Tn +ve.

The optimal cut-off to sign the increased risk is unknown, the interpretation and clinical utility of results are uncertain [4]. In our study, we revealed by logistic regression analysis that the MPV was an independent risk factor in Tn +ve ACS. We determined the MPV cut-off value that is most useful for predicting Tn +ve ACS in clinical practice was ≥ 11.1 fL.

The relationship between MPV and platelet count is not completely understood [13]. There was significant correlation between MPV and other cardiovascular events, even after adjusting for platelet count [13,19,20]. An increased MPV pre-dates AMI, as the average platelet lifespan in blood is 7-10 days so; the vast majority of platelets sampled on admission, would have been circulating before the event of AMI [21]. Martin et al. showed that elevation in MPV remained elevated for 6 weeks after hospital discharge; this explained that it is a chronic rather than acute process [21]. Our study supported the hypothesis that platelet size may play a role in the development and the consequences of CAD.

Study limitations

The present study was limited by the small sample size. No long follow up strategy as we began from the end point to pick up the target.

Conclusion

We determined that the MPV at a cut-off value of ≥ 11.1 fL was the best predictor for Tn +ve ACS, with a sensitivity of 73% and a specificity of 76.5 % (P=0.000), accordingly this parameter might be considered a simple non invasive parameter for risk stratification during follow up of patients with stable CAD.

Clinical implications and recommendations

MPV is simple to obtain, easy to interpret, and inexpensive routinely measured by automated cell counters, so it could be used in follow up of patients with CAD to predict the future attacks of ACS specially those with Tn +ve.

It is recommended to do a larger study, with long follow up and meticulous medication history to determine the relation between: ACS, MPV and medications. We recommend doing genetic studies to determine the relationship between MPV genetic basis and the cardiovascular phenotype for accurate MPV cut-off values.

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