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Mean Platelet Volume and von Willebrand Factor as Biomarkers for Short-Term Outcomes after Percutaneous Coronary Intervention

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ABSTRACT

Baseline platelet size correlates with future residual platelet reactivity. Mean platelet volume(MPV) is a rapid and simple measure in hospital and outpatient settings. An elevated MPV is a strong independent predictor of myocardial infarction(MI)after percutaneous coronary intervention(PCI) . von Willebrand factor(vWF) is a useful clinical marker strongly correlating with the incidence of MI and prognosis after PCI. There is increased vWF release after PCI contributing to endothelial dysfunction and increased incidence of thrombosis and no reflow. To investigate the association between MPV and vWF and incidence of post-PCI MI, we assessed baseline MPV and pre and post PCI vWF antigen activity in 80 patients presented to our hospital(Mansoura specialized medical hospital) for elective PCI and then follow up of the patients was conducted for 6- months period. Statistical analysis was performed using SPSS, version 21.When the 6-months incidence of MI was stratified by baseline MPV, the incidence of myocardial infarction was significantly more frequent with increasing MPV (21 patients (72.4%) with high MPV had MI at 6 months follow up(p=.002) with mean ± SD of baseline MPV 14.97±3.76 (p=≤.001).When the 6-months incidence of MI was stratified by vWF antigen activity (pre and post PCI), the incidence of MI was significantly more frequent with increasing vWF antigen activity (20 patients (69%) out of 29 patients (100%) with normal pre PCI vWF antigen activity that demonstrated high post PCI vWF activity had MI at 6 months follow up(p=.011) with mean ± SD of vWF antigen activity 190.45±38.62 (p=≤.004).

Keywords: Mean platelet volume, vWF antigen activity

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INTRODUCTION

Platelets play a pivotal role in both normal hemostasis and pathological bleeding and thrombosis [1].Angiographic and pathological studies have demonstrated the critical role of thrombus formation and platelet aggregation in acute coronary syndromes [2]. Occlusive thrombus in coronary arteries begins with deposition of platelets on a ruptured or eroded atherosclerotic plaque [3].

Large platelets have enhanced reactivity compared with normal-size platelets [4]. Platelet size and activity are correlated, and mean platelet volume (MPV) was found to be increased before acute myocardial infarction [5]. MPV has been associated with clinical and angiographic outcomes. Patients with a high MPV before balloon angioplasty have been more likely to develop restenosis [6]. In patients undergoing primary percutaneous coronary intervention (PCI), a high MPV has been associated with impaired angiographic reperfusion and increased 6-month mortality [7].

vWF mediates platelet adhesion to the vascular wall, platelet aggregation and serves as a plasma carrier for factor VIII, stabilizing it in the circulation [8]. Since almost all acute coronary syndromes (ACSs) result from thrombus formation in pre-existing atherosclerosis [9], and given the key role of vWF in arterial thrombus formation, this biomarker attracted considerable interest as a predictor of cardiovascular disease (CVD) [8].In the context of the problem of impaired microvascular circulation and myocardial perfusion after otherwise successful PCI, it may be relevant that PCI and stent implantation are themselves associated with endothelial damage and concurrent vWF release [10], especially in the case of multiple coronary stenting, which induces a rapid increase in vWF expression in the coronary circulation [11].

MATERIALS AND METHOD

The present analysis was a prospective observational study within the University of Mansoura, Specialized Medical Hospital, Cardiovascular Medicine Department. The study group included 80 patients who had undergone elective PCI. The patients were identified at hospital admission and then followed prospectively for a 6-months period. The patients were excluded from the study if PCI had failed and they had undergone emergent coronary bypass surgery or if death had occurred during the index hospital admission. In the event that patients required more than one PCI during the study period, the entry date was recorded as the date of the index procedure. The Human Research Ethic Review Board of the Mansoura faculty of medicine approved the study. All demographic data, coronary risk profile (hypertension, diabetes mellitus, dyslipidaemia and smoking) and previous antiplatelet use (aspirin and clopidogrel) were documented before PCI. A telephone interview was conducted

6-months after the index PCI. If a patient had been rehospitalized for possible cardiac symptoms, the records from the admitting hospital were obtained.

The MPV measurements were determined from the first available venous blood sample within the preceding 2 weeks before PCI. All samples were obtained in standardized dipotassium ethylenedinitrotetraacetic acid (EDTA) tubes. The measurements were performed using automated hemograms (Bayer Advia 2120, Bayer Diagnostics, and Tarrytown, New York) normal value ranging from 7.2 to 11.7 fl.

Qualitative vWF antigen activity assessment was done by REAADS ® vWF antigen test kit (Corgenix ^{TM}, USA); which is ELISA with normal value ranging from 50% to 200%.

The primary outcome was nonfatal MI at 6 months. For patients with > 1 MI, only the first event was counted as an end point.

Data were analyzed with SPSS version 21. The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test while McNemar Test used to compare paired categorical variables. Continuous variables were presented as mean ± SD (standard deviation). The two groups were compared with Student t test. Pearson correlation used for correlation between continuous parametric data. Sensitivity and specificity at different cutoff point tested by Roc Curve. For all statistical tests done, the threshold of significance is fixed at 5% level (p-value).The results was considered Significant when the probability of error is less than 5% ($p \leq 0.05$) Non-significant when the probability of error is more than 5% ($p > 0.05$) Highly significant when the probability of error is less than 0.1% ($p \leq 0.001$). The smaller the p-value obtained, the more significant are the results.

RESULTS AND DISCUSSION

Our study included 80 adult patients (41 men and 39 women) whose age ranging from 35 to 72 years (mean 56.13±8.30 years) that underwent elective PCI procedures. The baseline demographics of the study population stratified according to the risk factors (diabetes mellitus hypertension dyslipidemia and smoking), previous antiplatelet use, baseline MPV, vWF antigen activity (pre & post PCI) and primary outcome (myocardial infarction). There was 42 (52.5%) diabetic, 65 (81.2%) hypertensive, 56 (70.5%) dyslipidaemic and 25 (31.2%) smoker**,** 48 patients (60%) on aspirin and 26 patients (32.5%) on clopidogrel as and 29 patients (36.2%) who developed MI as shown in Figure(1). Subgroups of myocardial infarction group stratified by sex, age, DM, hypertension, dyslipidaemia, smoking status and previous antiplatelet use showed no significant sex difference but there was significant increase of myocardial infarction above the age of 50 yrs (26 patients above 50 years (89.7%) developed MI versus 3 patients below 50 yrs (10.3%) (p=.006) with Mean ± SD 59.93±6.60

(p=.002), DM was significant in the MI group (69 % with p=.026*) while hypertension, dyslipidemia and smoking did not demonstrate significant difference between the MI and non MI groups. There was no significant difference between MI group and non MI group. There were 40 patients (50%) with normal baseline MPV and 40 patients (50%) with high baseline MPV, with MPV level ranging from 7.5 to 19.7 (mean± SD 12.83± 3.76) as shown in Table 1

Table 1: Baseline MPV

Baseline MPV	**Study group (n=80)**	
	No	**%**
Normal (7.2 -11.7)	40	50.0%
High (>11.7)	40	50.0%
Mean ± SD	12.83±3.76	
Min-Max	7.5-19.7	

With correlation between baseline MPV, and age, DM, and previous antiplatelet use, there was a trend for patients with high MPV to be Older (P ≤.001), diabetic; 31 patients (73.8%) of the diabetic group had high MPV (p=≤.001) with mean ± SD of MPV (14.64±3.52) (p=≤.001) and On clopidogrel; use of clopidogrel was inversely related to MPV (69.2% of clopidogrel user had normal baseline MPV (p=.017) with mean ± SD 11.52±3.75 (p=.03*). The study group was stratified into 2 subgroups based upon vWF antigen activity; as shown in Figures (2) and (3); Pre PCI vWF antigen activity subgroup (80 patients (100%) with normal value) with level ranging from 90 to 190% (mean ± SD 152.28±29.01). PostPCI vWF antigen activity subgroup (40 patients (50%) with high value and 40 patients (50%) with normal value p=≤.001) with level ranging from 91 to 221% (mean± SD 172.29±43.01) (p=≤.001). When the 6-months incidence of myocardial infarction was stratified by baseline MPV, the incidence of myocardial infarction was significantly more frequent with increasing MPV (21 patients (72.4%) with high MPV had myocardial infarction at 6 months follow up(p=.002) with mean ± SD of baseline MPV 14.97±3.76 (p=≤.001) as shown in Figure (4). When the 6-months incidence of myocardial infarction was stratified by vWF antigen activity (pre and post PCI), the incidence of myocardial infarction was significantly more frequent with increasing vWF antigen activity (20 patients (69%) out of 29 patients (100%) with normal pre PCI vWF antigen activity that demonstrated high post PCI vWF activity had myocardial infarction at 6 months follow up(p=.011) with mean ± SD of vWF antigen activity 190.45±38.62 (p=≤.004) as shown in Figure (5) and Figure(6). By applying ROC curve for detection of myocardial infarction as shown in Figures (7),(8) and(9), the true positive rate (sensitivity) was plotted against false positive rate (1-specificity), with Baseline MPV**;** the predictive value of serum MPV level for detection of myocardial infarction (sensitivity of 82.8 % and specificity of 35.3%, area under the ROC curve = 0.756) was 9.8

fl. Pre PCI vWF antigen activity; the predictive value of pre PCI vWF antigen activity for detection of myocardial infarction (sensitivity of 82.8 % and specificity of 35.3%, area under the ROC curve = 0.648) was 137.5%. Post PCI vWF antigen activity; the predictive value of post PCI vWF antigen activity for detection of myocardial infarction (sensitivity of 82.8 % and specificity of 41.2%, area under the ROC curve = 0.764) was 146 %.

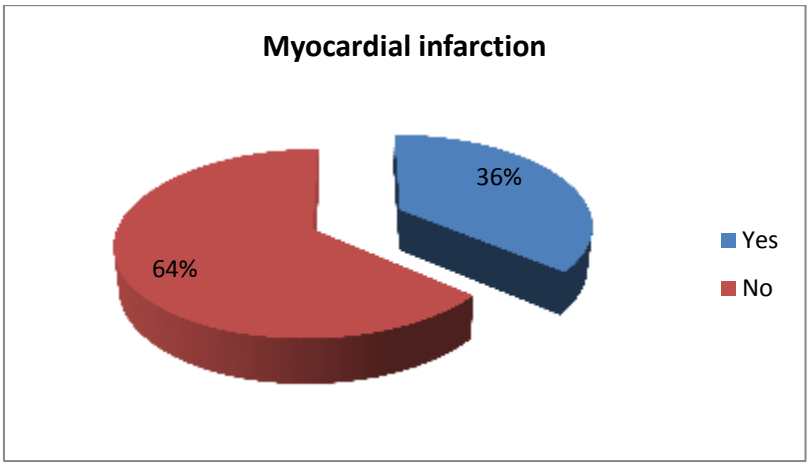

Figure 1: Primary outcome (myocardial infarction)

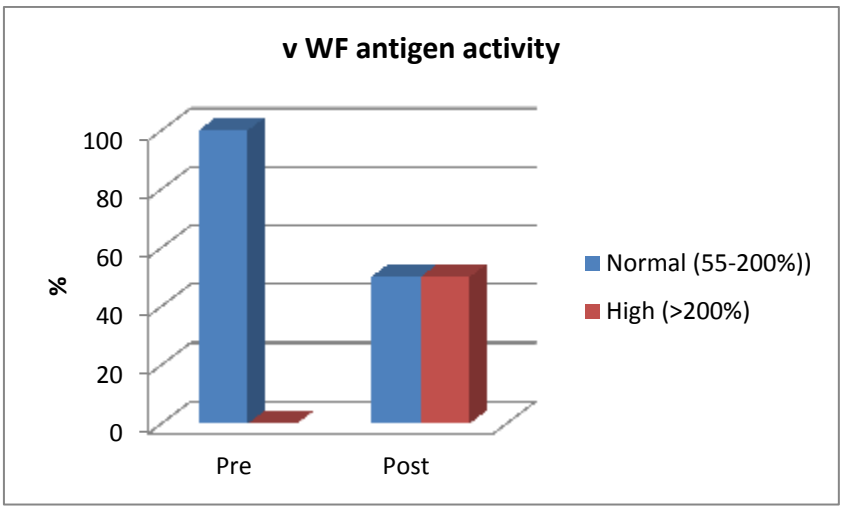

Figure 2

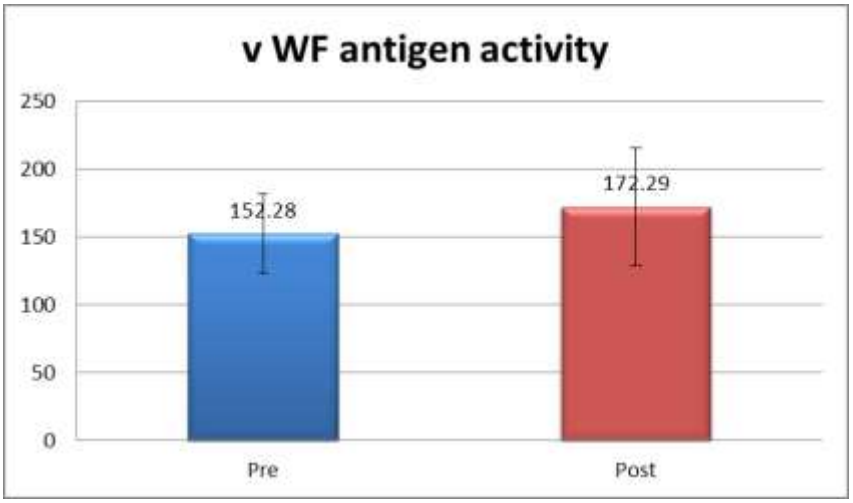

Figure 3

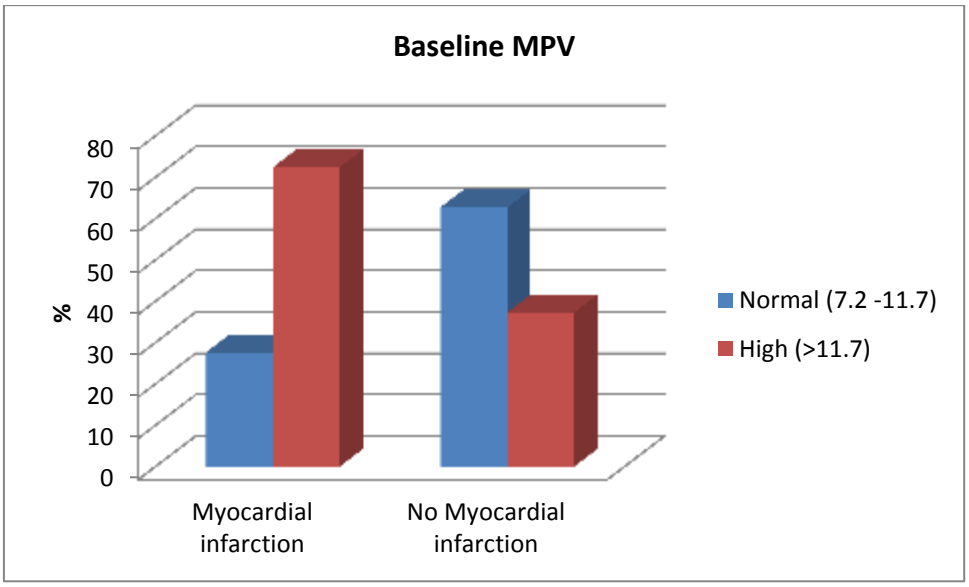

Figure 4: Correlation between baseline MPV and myocardial infarction

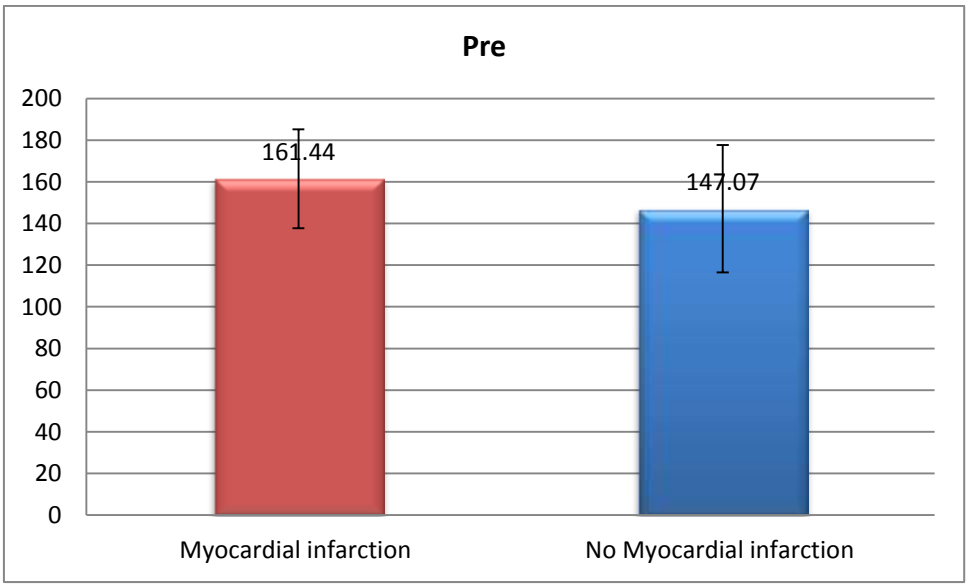

Figure 5: Correlation between pre PCI vWF antigen activity and myocardial infarction

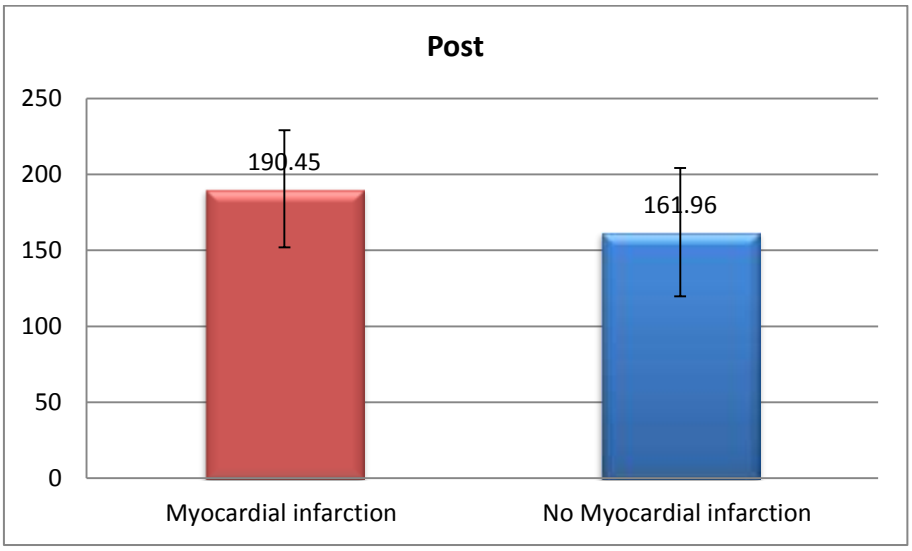

Figure 6: Correlation between post PCI vWF antigen activity and myocardial infarction

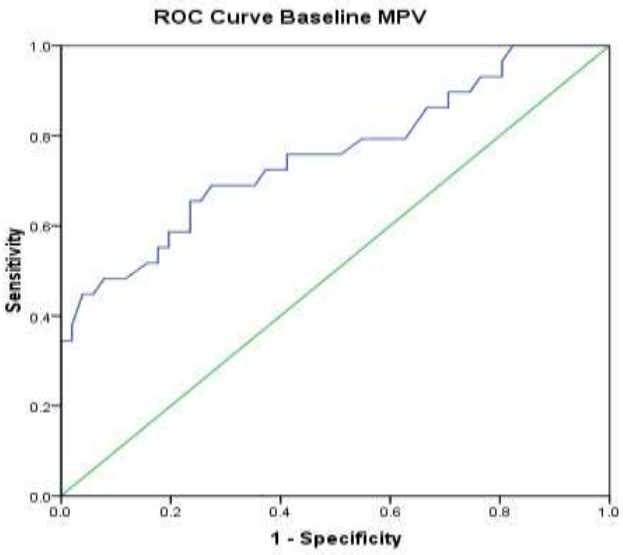

Figure 7:ROC curve for baseline MPV for prediction of MI

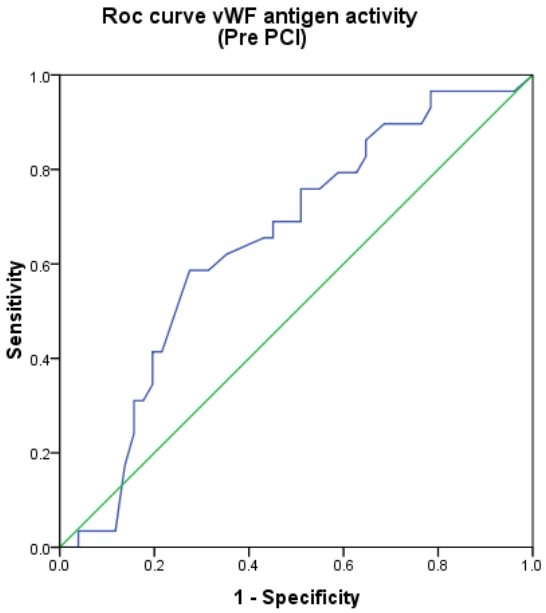

Figure 8: ROC curve for vWF antigen activity (Pre PCI) for prediction of MI.

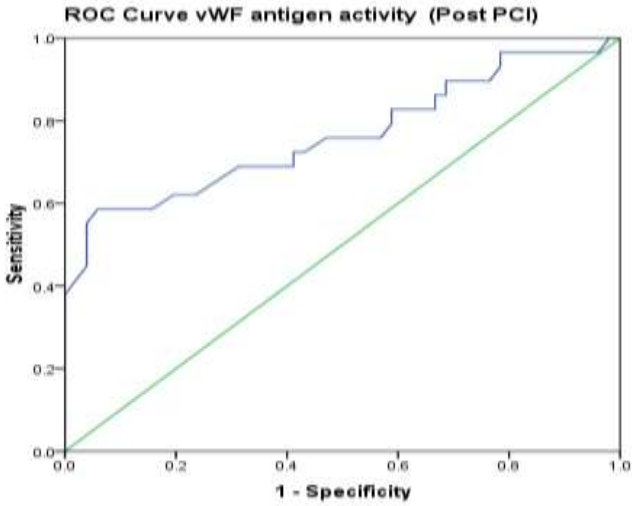

Figure 9:ROC curve for vWF antigen activity (Post PCI) for prediction of MI.

CONCLUSION

An elevated MPV was a strong independent predictor of myocardial infarction after PCI. MPV is increased in diabetic, elderly patients and decreased in patients on clopidogrel therapy. Our study defined cut off point for MPV (9.8 fl) that can help in planning more aggressive antiplatelet treatment to improve the adverse outcomes after PCI. VWF is a useful clinical marker strongly correlating with the incidence of MI and prognosis after PCI. There is increased VWF release after PCI contributing to endothelial dysfunction and increased incidence of thrombosis. Our study defined cut off points for pre & post PCI vWF antigen activity (137.5% and 146 % respectively) that can aid in treatment strategies. Therapies targeting VWF appear to be promising with improvement of periprocedural outcomes by decreasing the endothelial dysfunction and thrombosis.

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