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Value of Platelet to Lymphocytes Ratio in Predicting Angiographic Reflow after Primary Percutaneous Coronary Intervention in STEMI Patient

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Abstract

Background: Acute myocardial infarction is a leading cause of death worldwide nowadays and treatment of choice is primary percutaneous coronary intervention (PCI). No reflow is a complication that increases mortality and morbidity post intervention and one of its predictors is platelet lymphocyte ratio. **Aim of Study:** To assess relation between admission platelet to lymphocyte ratio (PLR) and angiographic reflow after primary PCI in acute ST elevation myocardial infarction (STEMI). **Patients and Methods:** This is a prospective study that was conducted from May 2017 to May 2018 at Cardiology Department, Menoufia University Hospital. Sixty patients presented with ST-elevation myocardial infarction who were eligible for primary PCI were enrolled in the study. According to TIMI flow post intervention, patients were arranged into 2 groups: Group 1 (Normal Reflow) included thirty patients with post intervention TIMI flow III and Group 2 (NO Reflow) included thirty patients with post intervention TIMI flow (0, I, II). Comparison between both groups was done regarding platelet lymphocyte ratio (PLR). **Result:** PLR was significantly higher in patients with coronary no reflow than in patients with normal reflow with a P-value of <0.001. Also, timing interval between onset of chest pain to time of intervention and thrombus grading was significantly higher in patients with no reflow than in patients with normal reflow. **Conclusion:** Pre-intervention PLR is an independent predictor of slow flow/no reflow following PPCI in patient with acute STEMI.

Keywords

Acute Myocardial Infarction, Primary Percutaneous Coronary Intervention, No Reflow, Platelet Lymphocyte Ratio

1. Introduction

One of the major causes of mortality and morbidity is acute myocardial infarction [1]. Those patients are liable to develop many complications as heart failure, arrhythmias and cardiogenic shock [2]. Early reperfusion after coronary occlusion in patients with ST-segment myocardial infarction (STEMI) is associated with an improved prognosis [3]. Nowadays primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy in patients with STEMI within 12 h of symptom onset. Impaired angiographic reflow is still a challenging major issue in the management of patients with STEMI undergoing primary PCI. Reduced coronary flow after primary angioplasty (TIMI flow 0 to II) is associated with worse outcome than normal (TIMI III) flow, even when no significant epicardial obstruction remains [4]. Impaired coronary reflow is associated with large infarct size, worse functional recovery, higher incidence of complications, short and long term mortality in acute myocardial infarction [5]. According to many studies, the predictors of No Reflow phenomenon were (age, smoking, previous myocardial infarction (MI), Killip class, serum creatinine, C-reactive protein, time-to-treatment interval, left ventricular ejection fraction, baseline TIMI flow grade, and initial perfusion defect). Micro-embolization leads to platelet and inflammatory cell activation and also vasospasm, which reduce coronary flow in combination with mechanical plugging of the microcirculation [4]. The platelet-lymphocyte ratio (PLR) has recently been investigated as a new predictor for major adverse cardiovascular outcome. It has also been found that high PLR is associated with poor coronary collateral development in stable coronary artery disease and long term mortality [6]. In our study, we aimed to discuss the relationship between admission platelet to lymphocyte ratio (PLR) and angiographic reflow after primary PCI in acute STEMI.

2. Patients and Methods

Sixty patients presented with ST elevation myocardial infarction diagnosed by Ischemic symptoms as chest pain typical of myocardial ischemia, ECG changes indicative of ischemia: new ST elevation at the J point in two contiguous leads of >0.1 mV in all leads other than leads V2-V3, For leads V2-V3 the following cut points were applied: ≥0.2 mV in men ≥40 years, ≥0.25 mV in men <40 years, or ≥0.15 mV in women [7] who presented at emergency room of Menoufia university hospitals within 12 hours from onset of chest pain and who were eligible for primary PCI were included in the study from the period between May 2017 and May 2018. The sample size was decided according to the facility and supplies in the catheter laboratory. All participants provided informed written consent and the study protocol was accepted by the institutional ethics committee. Patients with NON-ST elevation myocardial infarction, history of old myocardial infarction, history of coronary artery bypass graft, contraindication of primary PCI, thrombophilia and thrombocytopenia, recent infection and active inflammation and patients with known hematological abnormalities were excluded.

Venous blood sample were withdrawn in the emergency room on admission and stored in citrate based anti-coagulated tubes and common blood counting CBC were measured by Sysmex K-1000 auto analyzer within 5 minutes of sampling. PLR was calculated as a ratio of platelet count to lymphocyte count.

All patients were orally pretreated with 300 mg aspirin and 600 mg clopidogrel or 180 mg ticagrelor. 10,000 units heparin was given intravenous before PPCI. By using standard technique using Siemens Axioum Artis Zee 2011 machine, coronary angiography through femoral artery approach and by using seldinger technique was performed. Each coronary artery was evaluated using at least 2 views aiming to identify the culprit artery and grading of culprit vessel thrombus using Thrombolysis in myocardial infarction (TIMI) thrombus burden classification into grades from grade 0 with no angiographic evidence of thrombus to grade 5 with definite complete thrombotic occlusion of a vessel was done [8]. After assessment other coronaries the culprit vessel was treated by primary PCI and stenting with DES with absence of signs of dissection or perforation Then TIMI flow after the procedure was estimated as follows [9]:

I. Grade 0 (no perfusion): There is no antegrade flow beyond the point of occlusion.

II. Grade 1 (penetration without perfusion): The contrast material passes beyond the area of obstruction but "hangs up" and fails to opacify the entire coronary bed distal to the obstruction for the duration of the cineangiographic filming sequence.

III. Grade 2 (partial perfusion): The contrast material passes across the obstruction and opacifies the coronary bed distal to the obstruction. However, the rate of entry of contrast material into the vessel distal to the obstruction or its rate of clearance from the distal bed (or both) is perceptibly slower than its entry into or clearance from comparable areas not perfused by the previously occluded vessel (e.g. the opposite coronary artery or the coronary bed proximal to the obstruction).

Grade 3 (complete perfusion): Antegrade flow into the bed distal to the obstruction occurs as promptly as antegrade flow into the bed from the involved bed and is as rapid as clearance from an uninvolved bed in the same vessel or the opposite artery.

The patients were then divided into 2 groups based on the post intervention TIMI flow grades: Group 1 normal-reflow group with post intervention TIMI flow III and Group 2 non-reflow group with post intervention TIMI flow (0, I, II).

Use of tirofiban and thrombus aspiration device was left to operator's discretion.

3. Statistical Analysis

The data collected were tabulated and analyzed by SPSS (statistical package for social science) version 22.0. Two types of statistics were done:

Descriptive statistic: e.g. percentage (%), mean and standard deviation (SD).

Analytic statististics:

*Chi-square test (X^2): was used to study association between two qualitative variables.

*Student t-test: is a test of significance used for comparison between two groups having quantitative variables.

*P-value of <0.05 was considered statistically significant.

*The receiver operating characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of PLR, optimal cut-off value for predicting post-intervention angiographic none-reflow [10].

4. Results

In our study population we had 48 males (80%) and 12 females (20%), 18 diabetic patients (30%), 34 patients had hypertension (56.7%) and 48 patients were current cigarette smokers (80.0%). The mean serum creatinine was 1.01 ± 0.25 mg/dl. By using complete blood picture. The means hemoglobin level was 12.7 ± 1.28 gm/dl, The mean platelet count was 147.76 ± 630.70 ($\times 10^9$/L), The mean lymphocytic count was 2.05 ± 0. 4 ($\times 10^9$/L).

The demographic data and risk factors were comparable between both groups as shown in Table 1.

On studying the CBC parameters it was found that platelets count was significantly higher in the no reflow group while the lymphocytic count was significantly higher in the normal reflow group with PLR value significantly higher in no reflow group than normal flow group (139.65 ± 29.05 vs 85.5 ± 20.68 respectively with P value < 0.001) as shown in Table 2.

Table 1. Comparison between two groups regarding demographic data and risk factors.

	Group 1 (n = 30)		Group 2 (n = 30)		t. test or X^2	P value
	yes	No	Yes	No		
HTN	16(53.3%)	14(46.7%)	18(60%)	12(40%)	**0.494**	**0.625**
DM	9(30%)	21(70%)	9(30%)	21(70%)	**0.00**	**1.00**
Smoker	22(73.3%)	8(26.7%)	26(86.7%)	4(13.3%)	**1.43**	**0.161**
Family History of CAD	**13(43.3%)**	**17(56.7%)**	**12(40%)**	**18(60%)**	**0.273**	**0.787**

N: Number, HTN: Hypertension, DM: Diabetes Mellitus, CAD: Coronary Artery Disease.

Table 2. Comparison between two groups regarding admission platelets count, lymphocytic count and PLR value.

	Group I (n = 30) Mean ± SD	Group II (n = 30) Mean ± SD	t. test or X^2	P value
Platelet count ($\times 10^9$/L)	214.26 ± 49.374	285.70 ± 37.569	5.089	**0.001**
Lymphocytic count ($\times 10^9$/L)	2.5 ± 0.256	2.08 ± 0.260	6.725	**0.001**
PLR	**85.5 ± 20.68**	**139.65 ± 29.05**	**7.97**	**0.001**

The timing interval between onset of symptom of myocardial infarction and starting intervention was significantly higher in non reflow group than normal flow group (7.473 ± 1.75 hrs vs 3.036 ± 1.34 hrs, P < 0.001) (Table 3).

By differentiating pre-intervention thrombus grading into mild degree (contain grade 0, grade 1) and moderate degree (contain grade 2, grade 3) and sever degree (contain grade 4, grade 5), the thrombus grading was significantly higher in non reflow group than in normal flow group (6.03 ± 1.15 Vs 2.66 ± 1.1, P < 0.002) as shown in Table 4.

Using the ROC curve a PLR of value ≥ 167.6 predict no reflow with area under the curve was (0.81) with a sensitivity 75% and specificity 64% as shown in Figure 1.

5. Discussion

ST elevation acute myocardial infarction one of the causes that increase mortality

Table 3. Timing interval between onset of chest pain and PCI (hours).

	Group 1 (n = 30)	Group 2 (n = 30)	t. test or X^2	P value
Timing interval of intervention (hours)	3.036 ± 1.34	7.473 ± 1.75	9.76	0.001

Table 4. Thrombus grading among studied population.

Thrombus grade	Group 1 (n = 30)	Group 2 (n = 30)	t. test or X^2	P value
Mild	8	0		
Moderate	11	13	6.7	0.001
Sever	11	17		

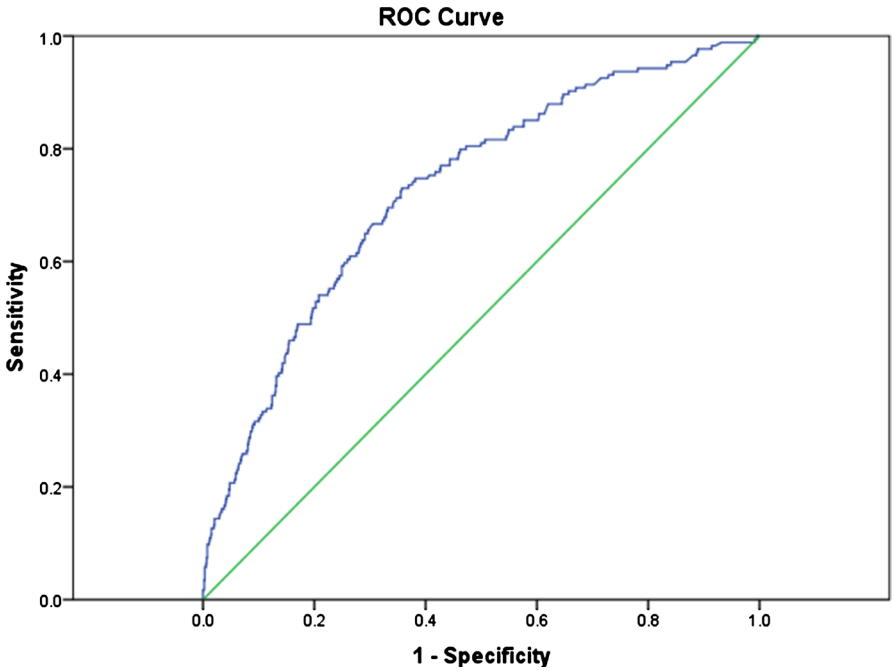

Figure 1. ROC curve to assess cut off value of PLR to predict no reflow.

and morbidity worldwide [11], Rapid restoration of infarct-related arterial flow is associated with improved ventricular performance and lower mortality in patients with STEMI [4]. However, poor post-interventional reflow may limit the benefits of re-canalization of the culprit vessel [11]. Impaired angiographic reflow is strongly correlated with morbidity and mortality in acute STEMI. It is also associated with larger infarct size, worse functional recovery, and higher incidence of complications [11].

The pathophysiology of none-reflow has not been fully explained and its etiology appears to be multifactorial. These factors include ischemic endothelial damage, micro-vascular leukocytes and platelet plugging and complex interactions between leukocytes and platelets induced by the inflammatory process [12].

Endothelial injury is induced by an acute inflammatory response, generation of reactive oxygen species. Ultra structural changes are confined to the necrotic zone, appear first in the sub endocardium, and subsequently progress toward the sub epicardium after longer periods of occlusion. Endothelial cellular swelling and protrusions, as well as myocyte swelling and tissue edema, may occlude the microvasculature and vasospasm and downstream embolization of thrombus compound the microvascular obstruction that increase thrombus burden and increase susceptibility of coronary no reflow [13]. In our study we studied the importance of PLR as a predictor of TIMI flow post primary PCI in acute ST myocardial infarction which was significant higher in no reflow group than in normal flow group with (P value < 0.001) and this may be related to underlying mechanism that increase inflammatory mediators which stimulate megakaryocytic proliferation and produce relative thrombocytosis. On the other side, lymphocyte mediated apoptosis is less destructive to adjacent myocardial cells [14]. Abdulkadir Yildiz *et al.* found that preprocedural PLR value was associated with no reflow by logistic regression analysis [15]. Similarly Turgay Celik *et al.* found that PLR was independent predictor of no reflow in young patients with STEMI after primary PCI [12]. Also Alpraslan Kuturl *et al.* found that pre intervention PLR is a strong and independent predictor of slow flow/no-reflow after PPCI in patients with acute STEMI [16]. In our study we demonstrated that the cut off value of PLR to indicate possibility of no reflow was 167.6 with a sensitivity 75% and specificity 64%. Another important predictor of no reflow the thrombus grading and TIMI flow pre intervention which was higher in no reflow group than in normal flow group with (P value < 0.001). Cervat Karima *et al.* showed that TIMI flow 1 or 0 prior to primary PCI is related to increase incidence of no reflow [17]. Also Hua Zhou found that TIMI flow grade before primary PCI is a predisposing factor of no reflow [11]. Another important predictor of no reflow is the timing interval between onset of chest pain and timing of intervention that was higher in group of no reflow than in group of normal flow (P value < 0.001). Hon Kan Yip *et al.* found that early reperfusion reduces the incidence of no reflow phenomenon in infarct related artery [13]. Also Hua Zhou *et al.* found that time from onset of chest pain to reperfusion is related to no reflow phenomenon

[11]. And Giampaolo Niccoli *et al.* that found a longer time to reperfusion is associated with a higher prevalence of no reflow and with a larger no reflow region [18].

6. Conclusion

Elevated level of platelet lymphocyte ratio in acute ST myocardial infarction patients before primary PCI can predict occurrence of no reflow phenomenon post intervention.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

STEMI	ST-myocardial infarction
PLR	Platelet lymphocyte ratio
TIMI flow	Thrombolysis in myocardial infarction
PPCI	Primary percutaneous coronary intervention