




Correlation of Platelet Indices with Thrombolysis in Myocardial Infarction Frame Count in Patients Undergoing Primary Percutaneous Coronary Intervention

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Abstract

Introduction: Given the fundamental role of platelet indices in the development of atherosclerotic plaque, these indices may play a predictive role for the occurrence of disturbed coronary reperfusion. The present study evaluated the association between platelet indices and coronary reperfusion status based on the Thrombolysis in Myocardial Infarction (TIMI) frame count.

Methods: This cross-sectional study was conducted on 98 consecutive patients with ST elevation myocardial infarction who were candidate for primary Percutaneous Coronary Intervention (PCI) at Modarres Hospital in Tehran between January 2016 and January 2018. Venous samples were extracted from all patients before primary PCI. To assess the condition of coronary reperfusion after primary PCI, the TIMI frame count related to culprit artery in acute myocardial infarction was determined.

Results: The TIMI frame count was positively associated with platelet count ($r = 0.320$, $P = 0.001$) and more strongly with platelet to lymphocyte ratio ($r = 0.375$, $P < 0.001$), but not with other platelet indices such as platelet distribution width (PDW), mean platelet volume (MPV) or Platelet large cell ratio (PLCR). According to the ROC curve analysis, platelet to lymphocyte ratio was introduced as a valuable parameter for differentiating complete from disturbed reperfusion (AUC = 0.735, 95%CI: 0.613 – 0.858, $P = 0.001$). The best cutoff value for platelet to lymphocyte ratio in predicting disturbed reperfusion was 146.5 with a sensitivity of 81.8% and a specificity of 60.5%. However, other platelet indices could not present this predictive role.

Conclusion: The platelet to lymphocyte ratio with predictive accuracy and sensitivity predicts coronary perfusion impairment based on the increase in TIMI frame count.

INTRODUCTION

Myocardial infarction is one of the most common cardiac diseases, often due to a sudden decrease in coronary flow, following a thrombotic occlusion in at least one of the coronary arteries previously having atherosclerosis. In the United States, one person is affected by myocardial infarction every 20 seconds and still accounts for one third of deaths [1]. Platelets play a major role in vascular responses to injuries. Platelets

have a high tendency to adhere to the wall of damaged vessels, where platelet granules are released, resulting in platelet adhesion to the wall and formation of platelet aggregation [2]. This process begins atherosclerosis leading to acute coronary syndrome [3]. Increasing the use of platelets at the site of coronary atherosclerotic plaque allows releasing larger platelets of bone marrow. Based on the recent studies, platelet indices such as

platelet distribution width (PDW) and mean platelet volume (MPV) may be the potential predictors of cardiac death [4-6]. Regarding the ease of measurement and availability of the tests measuring platelet indices, proving the association between platelet indices and the extent of coronary artery disease can be an important step in risk assessment and identifying risky patients.

Measurement of Thrombolysis in Myocardial Infarction (TIMI) flow grade or TIMI frame count in myocardial infarction is one of the common methods for assessing coronary artery blood flow in acute coronary syndrome [7]. TIMI frame count is defined as the number of cine frames from initial contrast opacification of the proximal coronary artery to opacification of distal arterial landmarks in the culprit vessel [8]. Over the past 15 years, the TIMI flow indicator has been used to evaluate the success of revascularization procedures [9]. In the present study, the association between platelet indices and coronary reperfusion condition was studied based on TIMI frame count in patients with ST elevation myocardial infarction (STEMI) who underwent primary Percutaneous Coronary Intervention (PCI).

METHODS

This cross-sectional study was conducted on 98 consecutive patients with STEMI who were candidate for primary PCI at Modarres Hospital in Tehran between January 2016 and January 2018. In this study, patients with typical chest pain and ST elevation equal to or greater than one millimeter in two contiguous leads were candidate for primary PCI. Sampling was performed with the same syringes from the antecubital region to assess the platelet indices including platelet count, platelet to lymphocyte ratio, PDW, MPV and Platelet large cell ratio (PLCR) before coronary angiography. If STEMI was approved in angiography the patient was enrolled into the study. Standard therapy was performed for all the patients according to the last American heart association guidelines. Eligible patients were evaluated after primary PCI during the hospitalization period and the information of each patient was recorded in specific checklist.

To assess the condition of coronary reperfusion, TIMI frame count related to culprit artery in acute myocardial infarction was determined as the number of cine frames from initial contrast opacification of the proximal coronary artery to opacification of distal arterial landmarks in the culprit vessel. For the longer lengths of left anterior descending coronary artery (LAD) compared to the right coronary artery (RCA) or left circumflex coronary artery (LCX), its TIMI frame count was calculated by dividing its value by 1.7. TIMI frame count values categorized as less than 28 (indicating complete reperfusion) and equal or more than 28 (indicating disturbed reperfusion) [10]. The study endpoint was to determine the association between platelet indices and TIMI frame count.

Table 1. Baseline Characteristics of the Study Population

	Values
Male gender	79 (80.6)
Age (year)	58.11 ± 10.79
Hypertension	36 (36.7)
Diabetes Mellitus	27 (27.6)
Smoking	52 (53.1)
Family history of coronary artery disease	20 (20.4)
Previous myocardial infarction	5 (5.1)
Prior cerebrovascular events	2 (2.0)
Drug	
Amiodarone	1 (1.0)
Beta blocker	16 (16.3)
Involved vessels on PCI	
LAD	50 (51.0)
RCA	30 (30.6)
LCX	5 (5.1)
OM	8 (8.2)
Diagonal	5 (5.1)
Number of stent used	
One	90 (91.8)
Two	7 (7.1)
Three	1 (1.0)
Mean TIMI frame count	21.55 ± 8.98
Disturbed reperfusion rate	30 (30.6)
Platelet count (/mm³)	235428.57 ± 75390.25
Platelet to lymphocyte ratio	170.49 ± 95.44
MPV (fL)	9.55 ± 1.62
PDW (fL)	12.45 ± 1.80
PLCR (%)	23.67 ± 6.69

Data in table are presented as Mean ± SD or No. (%)

PCI: Percutaneous Coronary Intervention; MPV: mean platelet volume, PDW: platelet distribution width; PLCR: Platelet large cell ratio; LAD: left anterior descending artery; RCA: right coronary artery; LCX: left circumflex artery; OM: obtuse marginal branch; TIMI: Thrombolysis in Myocardial Infarction

Statistics

Descriptive analysis was used to describe data, including mean ± standard deviation (SD) for quantitative variables and frequency (percentage) for categorical variables. The correlation between quantitative variables was assessed using the Pearson's or Spearman's correlation tests. To determine the main indicators for disturbed reperfusion based on the TIMI frame count, the multivariable logistic regression model was used. The ROC curve analysis was also used to determine the value of each platelet indices to discriminate complete from disturbed reperfusion. For the statistical analysis, the statistical software IBM SPSS Statistics for Windows version 23.0 (IBM Corp. Released 2013, Armonk, New York) was used. P values < 0.05 were considered statistically significant. The institutional review board approved the study protocol and patients provided an informed written consent.

RESULTS

In the present study, 98 patients were studied. The mean age of patients was 58.11 ± 10.79 years ranged from 35 to 85 years and 80.6% were male. Baseline characteristics of patients are summarized in Table 1. The PCI procedure was scheduled commonly on LAD artery (51.0%) followed by RCA (30.6%) and obtuse

marginal branch (8.2%). One, two and three stents were applied in 61.8%, 7.1% and 1.0%, respectively. The mean TIMI frame count was 21.55 ± 8.98 ranged from 8 to 40. Using the cutoff value of 28 for TIMI to determine disturbed reperfusion, 22.0% had incomplete reperfusion due to atherosclerosis.

Table 2. The Association between Platelet Indices and TIMI Frame Count

Parameter	R coefficient	P value
Platelet count	0.320	0.001
platelet to lymphocyte ratio	0.375	< 0.001
MPV	0.060	0.555
PDW	0.156	0.125
PLCR	0.176	0.082

TIMI: Thrombolysis in Myocardial Infarction; MPV: mean platelet volume, PDW: platelet distribution width; PLCR: Platelet large cell ratio

Table 3. Comparing Platelet Indices between the Groups with and Without Successful Reperfusion

Parameter	Group with successful reperfusion	Group without successful reperfusion	P value
Platelet count (/mm ³)	267318 ± 80707	226197 ± 71710	0.02
platelet to lymphocyte ratio	223.60 ± 97.78	155.11 ± 89.65	0.003
MPV (fL)	10.01 ± 0.91	22.51 ± 0.40	0.6
PDW (fL)	13.07 ± 1.94	12.27 ± 1.73	0.06
PLCR (%)	26.15 ± 6.83	22.95 ± 6.51	0.04

Data in table are presented as Mean \pm SD

MPV: mean platelet volume, PDW: platelet distribution width; PLCR: Platelet large cell ratio

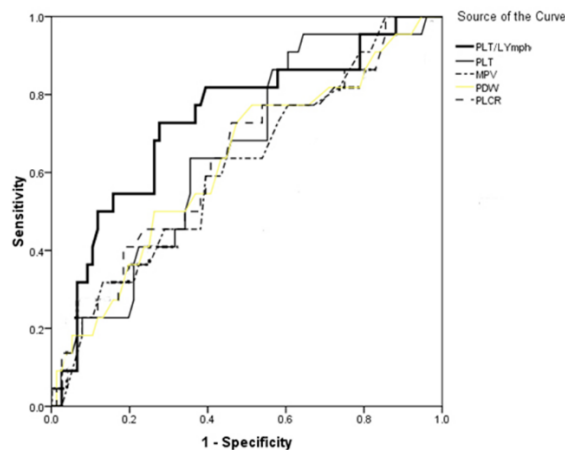


Figure 1. The ROC Curve Analysis to Determine the Value of Platelet Indices in Predicting Incomplete Reperfusion. PLT: Platelet count; PLT/Lymph: Platelet to lymphocyte ratio; MPV: mean platelet volume, PDW: platelet distribution width; PLCR: Platelet large cell ratio

As indicated in Table 2, the TIMI frame count was positively associated with platelet count ($r = 0.320$, $P = 0.001$) and more strongly with platelet to lymphocyte ratio ($r = 0.375$, $P < 0.001$), but not with other platelet indices such as PDW, MPV or PLCR. Comparing platelet indices between the groups with and without complete reperfusion (Table 3) showed a significant

difference in platelet count, platelet to lymphocyte ratio and PLCR, but in multivariate logistic regression model with the presence of baseline parameters, only platelet to lymphocyte ratio could predict disturbed coronary reperfusion ($OR = 1.322$, $P = 0.001$). According to the ROC curve analysis (Figure 1), platelet to lymphocyte ratio was introduced as a valuable parameter for differentiating complete from disturbed reperfusion ($AUC = 0.735$, $95\%CI: 0.613 - 0.858$, $P = 0.001$). The best cutoff value for platelet to lymphocyte ratio in predicting disturbed reperfusion was 146.5 yielding a sensitivity of 81.8% and a specificity of 60.5%. However, other platelet indices could not present this predictive role (Fig 1).

DISCUSSION

Evaluation of coronary reperfusion status after revascularization is mainly due to aggressive procedures. In the recent years, the main focus has been on using minimal invasive laboratory indices to evaluate reperfusion defect. In this regard, and given the fundamental role of platelet indices in development of atherosclerotic plaque, it seems that these indices can play a predictive role for the occurrence of disturbed coronary reperfusion. Therefore, the present study evaluated the association between platelet indices and coronary reperfusion status based on the TIMI frame count. Also, the value of these indices in predicting coronary reperfusion defect was investigated. In this study and among different platelet indexes, the only index of platelet to lymphocyte ratio was introduced for predicting reperfusion defect assessed by measuring the TIMI frame count in patients undergoing PCI. This predictive value was confirmed in the presence of all the underlying demographic and clinical factors. Interestingly, the platelet count index alone did not have the predictive power to increase the TIMI frame count and therefore the role of lymphocytic count along with platelet counts should be taken into account. In fact, activation of inflammatory cascade with platelet aggregation would be continuously effective in determining and predicting a reperfusion defect. In this regard, other platelet indications such as PDW or MPV have not been as effective in predicting disturbed reperfusion.

What we found in other studies was to illustrate the role of some platelet indices in predicting the severity of reperfusion defect. In a study by Vakili et al., and quite similar to our study, the platelet-to-lymphocyte ratio had a strong statistical correlation with TIMI frame count and corrected TIMI frame count [11]. In a study by Yaşar et al., there was a weak correlation between the two MPVs and the corrected TIMI frame count. The evaluation by regression model showed that MPV is an undesirable predictive factor for predicting reperfusion status which was not consistent with our findings, because in our study the association between MPV and TIMI was not significant [12]. In a study by Celebi et al.,

patients with complete reperfusion had a much lower MPV content. There was a significant correlation between the MPV and incomplete reperfusion [13], which in our study did not achieve such an effect on the role of MPV. In a study by Shefaee et al. in 2005, 100 patients with chest pain based on diagnosis were classified into three groups, including patients with UA, those with chronic angina and those with non-cardiac chest pain. Patients with UA (unstable angina) had a much higher MPV, as well as higher PDW and PLCR values than other groups [14]. Therefore, the potential role of the platelet to lymphocyte ratio in predicting the severity of coronary reperfusion defect is indicated; hence, it may be valuable for predicting an undesirable clinical outcome associated with coronary involvement. Inflammatory mediators cause proliferation of megakaryocytes and lead to relative thrombocytosis. Therefore, increasing the number of platelets may reflect activation of inflammatory processes. In addition, plaque stability in patients with coronary atherosclerosis is associated with increased platelet aggregation [15, 16]. Conversely, lymphocytes are controller for inflammatory processes [17]. Due to this inflammatory/anti-inflammatory balance, the platelet-to-lymphocyte ratio may reflect the underlying pathology. This index is mainly used to predict the outcome of cardiovascular events [18, 19], with higher rates associated with increased mortality and morbidity in patients with STEMI and Non-STEMI [20]. In addition, an increase in this ratio can predict lack of perfusion following primary PCI. Therefore, the platelet-to-lymphocyte ratio is an important indicator for the diagnosis of perfusion impairment and predicts the likelihood of adverse cardiac events.

CONCLUSION

The platelet to lymphocyte ratio with predictive accuracy and sensitivity predicts coronary perfusion impairment based on an increase in the TIMI frame count. This is probably due to an inflammatory/anti-inflammatory unbalance in the cardiovascular system.

Conflict of Interest

There is no conflict of interests with this article.

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