

Varasteh-ravan H. R.,  
Ali-Hassan-Sayegh S.,  
Shohre Shokraneh,  
Mohammad R. Mozayan,  
Ali Akbar  
Karimi-bondarabadi

Department of Cardiovascular Disease,  
Yazd Cardiovascular Researches Center;  
Afshar Hospital, Shahid Sadoughi  
University of Medical Sciences,  
Yazd, Iran

**Address for correspondence:**  
Dr. Sadegh Ali Hassan Sayegh,  
Medical Student and Researcher of  
Cardiac Surgery, Yazd Cardiovascular  
Surgery Center, Afshar Hospital,  
Jomhouri Blvd, Yazd, Iran.  
E-mail: s.alihasan.cardiosurg@  
gmail.com

## Abstract

# Relationship of admission mean platelet volume, platelet distribution width and white blood cells with ST resolution in patients with acute ST segment elevation myocardial infarction treated with streptokinase without history of previous cardiovascular surgery

**Background:** Mean platelet volume (MPV) and platelet distribution width (PDW), markers of platelet reactivity, and white blood cell count (WBC-C), a marker of inflammation, have been shown to be predictive of unfavorable outcomes among survivors of ST elevation myocardial infarction (STEMI). We aimed to evaluate the value of admission of MPV, PDW and WBC-C for the prediction of ST segment resolution, in patient with acute STEMI treated with Streptokinase. **Materials and Methods:** This cross sectional study conducted on 280 patients with STEMI treated with streptokinase, from August 2009 until August 2011, in Afshar cardiovascular center, Yazd, Iran. Blood samples were obtained on admission in 280 patients with STEMI. According to sum of ST segment resolution and Schroder's method, patients divided two groups ((patients with ST resolution  $\geq 70\%$  versus group with ST resolution  $< 70\%$ )). The best cut off value of MPV, PDW and WBC-C for prediction of ST resolution (STR) were identified by using the receiver operating characteristic curve. The optimum cut off level was determined by selecting points of test value that provided the greatest sum of sensitivity and specificity. **Results:** Of 280 patients enrolled this study, 39.3% of the patients with STR  $\geq 70\%$  and in 60.7% with STR  $< 70\%$  were found. Patients in the STR  $< 70\%$  group had higher admission MPV ( $10.6 \pm 0.8$  vs.  $9.5 \pm 0.8$ ,  $P = 0.00$ ) and higher PDW ( $13.8 \pm 1.8$  vs.  $11.8 \pm 1.7$ ,  $P = 0.00$ ) and higher WBC-C ( $12.1 \pm 3.1$  vs.  $10.5 \pm 2.5$ ,  $P = 0.00$ ) compare with patients with ST resolution  $\geq 70\%$ . The best cut off value of MPV for predicting STR  $< 70\%$  was  $10/05$  fl (sensitivity 71.8 and specificity 80.9%) and for PDW was  $12.85$  fl (sensitivity 71.2% and specificity 83.6%) and for WBC-C was  $12.65 \times 1000$  (sensitivity 42.9% and specificity 82.7%). The greatest area under the receiver operating characteristic (ROC) curve and greatest predicting value for ST resolution lower 70% was due to PDW (area = 0.812,  $P = 0/00$ ). **Conclusion:** MPV, PDW and WBC-C at admission might be valuable in the prediction of impaired STR and in planning the need for adjunctive therapy to improve outcomes with STEMI treated with Streptokinase. We can speculate that acute STEMI patients having MPV-PDW and WBC-C values above their's cut off patients should be

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considered for stronger antiplatelet and helps anti inflammation treatment to be able to attain a favorable ST resolution and better clinical outcome.

**Key words:** Mean platelet volume, platelet distribution width, ST segment resolution, white blood cell count

## INTRODUCTION

Ischemic Heart disease (IHD) is the most important factor of morbidity and mortality in developed countries. The patients affected with this disorder are classified into two groups; stable angina patients or cases with acute coronary syndromes such as acute ST segment elevation Myocardial infarction (STEMI), unstable angina and non ST segment elevation Myocardial infarction (NSTEMI). Early morbidity rate (30 days) resulting from MI is 30% and more than half of the mortalities occur before patient's arrival into the hospital<sup>[1]</sup> After bursting atherosclerotic plaque, thrombogenesis increases so that a platelet layer is formed at the burst and with releasing agonists such as collagen, epinephrine and serotonin, platelets become active.<sup>[2]</sup>

The reduction of infarct area in STEMI is an accomplished through reperfusion by mechanical equipments such as angioplasty.<sup>[3]</sup> ST segment resolution in the ECG of STEMI patients after successful or unsuccessful perfusion to myocardium through fibrinolysis is divided into three groups: Complete resolution of ST segment (fall > 70% of ST primary elevation rate), Partial resolution ST segment (70% > fall > 70% of ST primary elevation) and non-resolution (resolution <30%).<sup>[4]</sup>

Platelets play a vital role in pathogenesis atherosclerosis as well as producing and developing acute thrombotic coronary events. Platelets produced in stressful situation such as acute coronary syndromes are bigger and these bigger platelets have a higher potential for thrombosis, are more compact and have a higher capacity for producing thromboxan B2.<sup>[5]</sup> Mean platelets volume (MPV) and platelet distribution width (PDW) with the aforementioned rates are considered as independent risk factors in MI and stroke and compared with the lower rates; represent aggravated clinical outcomes and higher mortality.<sup>[6-9]</sup> Also, leukocytosis plays a central role in atherosclerosis and acute coronary syndromes (ACS).<sup>[8]</sup> The aim of this study is to evaluate the relationships between hematologic (MPV, PDW, WBC) and clinical indexes at the hospitalization course with ST segment resolution in STEMI patients treated with streptokinase and determining a best cut off point for them in anticipation of ST segment resolution.

## MATERIALS AND METHODS

Our cross sectional study was performed from August 2009 until August 2011 in 280 patients with ST segment elevation MI treated with streptokinase in Afshar heart hospital, Yazd, Iran. Ethical approval for the study was from the human subjects committee of Shahid Sadoughi University of medical sciences. Written informed consent was obtained from all participants. 280 STEMI patients (confidence rate~95% and test potency~80% and standard deviation~1.5) within 12 hours of chest pain onset who had offered to the Yazd Cardiovascular Center were hospitalized and studied. STEMI was defined as typical chest pain lasting longer than 30 min accompanied by ST segment elevation of 1 mm or more in at least two pericardial leads or contiguous inferior leads. All the patients received 160-325 mg aspirin on presentation and 1500000 U streptokinase through infusion in 45-60 min and clopidogrel 300mg. The patients who had referred 12h after chest pain and those who had active infection and those undergoing percutaneous coronary intervention (PCI) excluded from the study. Twelve leads ECG were performed on presentation to ICU and 60 min after beginning treatment with streptokinase. ST segment elevation was measured from the point of 0.06-0.08; from J point on ST segment in (aVL,1), (V1-V6) leads and for anterior MI; In (II-III-aVF), (V3R-V4R), (V1-V9) leads, for inferior leads on presentation to ICU, and for all leads having elevation, 60 min after beginning streptokinase. Intravenous peripheral blood samples was taken from all patients at the time of hospitalization and prior to any treatment to measure MPV, PDW and WBC were put into standard test tubes containing EDTA and then were sent to the laboratory. Data were analyzed using SPSS software version 15. T-test, Chi-square and Mann-Whitney test were used for qualitative and quantitative variables, ROC curve was utilized to determine various cut-off points of WBC, MPV and PDW to predict non-resolution of ST segment and appropriate cut-off point was determine where the sum of sensitivity and characteristics lied at highest level.

## RESULTS

All 280 patients with ST segment elevation myocardial infarction treated with streptokinase enrolled this study. Of

**Table 1: Demographic characteristics of both groups**

Variables	Complete resolution (n = 110)	Non-complete resolution (n = 170)	P value
Age (year)	59.23 ± 9.28	64.34 ± 10.2	0.0001
Sex (M/F)(n)	79/31	122/48	0.99
HTN [n (%)]	42 (38.1)	79 (46.4)	0.17
Diabetic mellitus [n (%)]	36 (32)	70 (41.1)	0.15
Cigarette smoking [n (%)]	36 (32)	51 (30)	0.63
History of CAD [n (%)]	29 (26.3)	39 (22.9)	0.51
Dislipidemia [n (%)]	60 (54.5)	90 (52.9)	0.79
History of used Statin [n (%)]	24 (21.8)	20 (11.7)	0.02
History of used Aspirin [n (%)]	38 (34.5)	43 (25.2)	0.09
Pain to needle time [(time > 3h / time < 3h)]	50/60	99/71	0.03
Subgroup MI [n (anterior wall / inferior wall)]	47/63	115/55	0.0001

these, 201 cases (71.78%) were male and 79 cases (28.21%) female. The demographic characteristics of our patients have been presented in Table 1. Of all the patients, 170 (60.7%) had ST segment resolution of lower than 70% and 110 (39.3%) had ST segment resolution higher than 70% in response to streptokinase therapy. Patients with ST segment resolution of lower than 70% had a higher WBC value ( $12.1 \pm 3.1$  versus  $10.5 \pm 2.5$ ), MPV ( $10.6 \pm 0.8$  versus  $9.5 \pm 0.8$ ) and PDW ( $13.8 \pm 1.8$  versus  $11.8 \pm 1.7$ ) compared with the group with a greater resolution of ST segment. The difference was statistically significant. ( $P = 0.0001$ ) [Table 2]. Mean age of the patients with ST segment resolution of lower than 70% was also higher than that of greater than 70% ( $64 \pm 10$  versus  $59 \pm 9$ ) which was statistically significant. ( $P = 0.0001$ ) Out of all patients, previous aspirin consumption were statistically similar between two groups except previous statin consumption was significantly different between both groups ( $P = 0.02$ ).

Out of 280 patients with STEMI, in 149 patients, the time interval between the onset of chest pain till therapy with streptokinase was more than 3h (50 patients (33.6%) of the resolution group more than 70% versus 99 cases (66.4%) in resolution group lower than 70%) and in 131 patients the time interval was less than 3h (60 patients (45.8%) in the resolution group higher than 70% versus 71 patients (54.2%) lower than 70%). Of all the patients, 162 (57.8%) patients were suffering from STEMI at the anterior part of the heart (29% with greater resolution versus 71% with resolution <70%) and 118 patients (42.1%) at the inferior part of the heart (55.4% resolution higher than 70% versus 46.6% resolution lower than 70%). Therefore the patients with MI at the anterior part of the heart had a higher disorder in ST segment resolution which was also statistically significant ( $P = 0.0001$ ).

ROC curve was utilized to determine various cut-off points of WBC, MPV and PDW to predict non-resolution of ST segment and appropriate cut-off point was determined where the sum of sensitivity and characteristics lied at highest level. To predict impaired

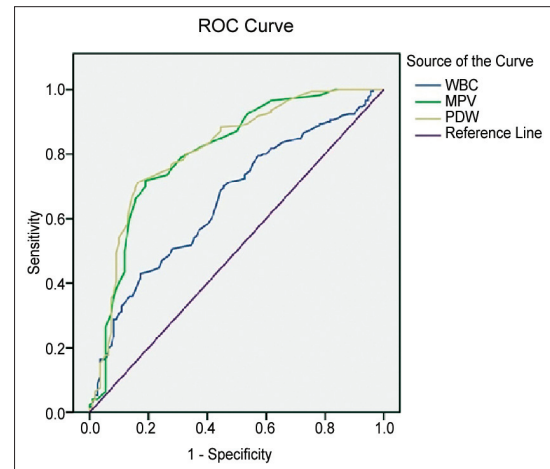
**Table 2: Under area of ROC curve in predicting no-resolution of ST segment**

Groups	PDW	MPV	WBC
ST resolution < 70%	13.84 ± 1.87	10.6 ± 0.85	12.18 ± 3.16
ST resolution > 70%	11.84 ± 1.75	9.59 ± 0.89	10.55 ± 2.54
Total	13.06 ± 2.07	10.2 ± 0.99	11.54 ± 3.04

$P = 0.0001$ , Mann-Whitney test.

**Table 3: Under area of ROC curve in predicting no-resolution of ST segment**

Variables	Area	95% confidence interval	P. value
WBC	0.656	0.592 to 0.721	0.0001
MPV	0.804	0.749 to 0.859	0.0001
PDW	0.812	0.758 to 0.865	0.0001

**Figure 1:** The receiver operating characteristic (ROC) curve for white blood cell, platelet distribution width and mean platelet volume to predict impaired reperfusion in patients treated with streptokinase.

reperfusion, ROC analysis was performed at the cut off points of  $12.65 \times 10^3/\mu\text{L}$ , 10.05 FL, 12.58 FL so we could find the highest sensitivity and specificity for WBC, MPV and PDW respectively with the following values: 0.65, 0.80 and 0.81. As it is shown compared with MPV and WBC, PDW values of 0.81 is the best discriminating value in predicting non-resolution of ST segment ( $P = 0.0001$ ) [Table 3] [Figure 1].

## DISCUSSION

This study attempting to assess the resolution between hematologic (WBC, MPV and PDW) and clinical indexes of STEMI patients with resolution of ST segment treated with streptokinase. Other studies have investigated platelet count index in predicting no-reflow event on the basis of angiography criteria and have considered such high indexes as critical independent predictor in forecasting no-reflow event.<sup>[10,11]</sup> Regarding that recent studies have emphasized the role of ECG in assessing reperfusion and desired resolution of ST segment as successful myocardial reperfusion and have also considered establishment of microvascular circulation, however, patency of epicardium artery as more responsible event for MI<sup>[11-13]</sup> this study investigated the relation between resolution of ST segment and hematological, clinical indexes in patients. Comparing the two groups, our study revealed that the group with lower resolution of ST segment enjoyed higher PDW, MPV and WBC values which are statistically significant. İbrahim SUSAM *et al.* Reported that MPV is not associated with post-intervention reperfusion in patients with STEMI treated with fibrinolysis. They suggested that MPV cannot be a marker of impaired reperfusion.<sup>[14]</sup> In a study conducted by Pereg *et al.* indicated that higher MPV may correlates with thrombolysis failure in patients with STEMI. MPV can be utilized as an available factor for evaluating thrombolysis outcome.<sup>[15]</sup> In a study carried out by Maden *et al.*, the STEMI patients were divided in two groups on the basis of having or not having TIMI flow III and their MPV and WBC were compared. The study demonstrated that occluded infarct-related artery group, compared with patent infarct-related artery group, and had higher MPV and WBC values.<sup>[16]</sup>

In determining the desire cut off point of MPV in predicting non-resolution of ST segment our study revealed 0.05 FL with 71.8% sensitivity and 80.9% specificity on the basis of ROC curve. In Maden's study attempting to detect the desired cut off point for predicting occlusion of coronary artery 8.55 FL had a sensitivity of 74% and specificity of 60%.<sup>[16]</sup> In another study by Huczek, the desired cut off point of MPV in predicting no-reflow after performing PCI, 10.3 FL was found to have sensitivity of 61.9 and specificity of 74.3%.<sup>[6]</sup> This present study found the desired cut off point of PDW in predicting no-resolution of ST segment 12.85 FL with 71.2% sensitivity and 83.6% specificity on the basis of ROC curve. Under area of ROC curve for MPV was 0.76, 0.71, 0.8 for Maden's, Huczek's and our study respectively. This study, like other studies, is indicative of the relation between high values of MPV and WBC with reperfusion disorder in STEMI patients and confirms it. In terms of cut off points, specificity, sensitivity and under area of ROC curve for hematological indexes, the difference

evaluating reperfusion and unequal clinical condition of the patients included in the study.

Also in Maden's research no differences was found between the occluded infarct-related artery group and patent infarct-related artery group in terms of atherogenesis risk factors.<sup>[16]</sup> In terms of pervious consumption of aspirin and statin no difference was detected between the two groups in Maden's *et al.* study while in our research a significant difference was detected between the two group only in pervious consumption of statin with resolution of ST segment (i.e., no difference in consuming aspirin). ( $P = 0.024$ )

This study could find a significant difference between earlier percutaneous coronary intervention and ST segment resolution. ( $P = 0.05$ ) Their study also demonstrated lower prevalence of patent infarct-related artery cases in patients with anterior MI which is in line with that of our study in which those with anterior MI showing poorer response with streptokinase therapy had more disorder resolution of ST segment. We concluded that drawing attention to MPV, WBC and PDW in STEMI patients at the onset of hospitalization, which is routinely controlled in all patients through CBC, in addition to focusing on clinical conditions, can discriminate high risk patients and those who will benefit from pharmacological extra therapy or mechanical strategies. We suggest a prospective study with short-term or long-term follow up of patients with different values of hematologic indexes in terms of reoccurrence of coronary or valvular events demonstrate diagnostic role of these factors related to survival and outcome of the patients. Also a study can be conducted to control the relation between hematologic indexes and no reflow phenomenon following primary PCI in STEMI patients and find a way to stop the probable occurrence of this phenomenon.

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