

EVALUATION OF THE RELATION BETWEEN PLATELET COUNT AFTER PRIMARY PCI AND LEFT VENTRICULAR ANEURYSM IN PATIENTS WITH ACUTE ANTERIOR ST ELEVATION MYOCARDIAL INFARCTION

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Contribution

MG conceived the idea and designed the study. Data collection and manuscript writing was done by SFM, NM, SN, AS, MMR, FM, AA, and PP. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To evaluate the relationship between platelet count after primary percutaneous coronary intervention (p-PCI) and left ventricular aneurysm (LVA) in patients with acute anterior ST-elevation myocardial infarction (STEMI).

Methodology: This descriptive study was performed on a population of patients with acute anterior STEMI, who had undergone p-PCI. Sampling was carried out by a consecutive survey of patients, who were admitted to the Medical Center in summer and fall of 2018. Blood samples were collected intravenously from all the patients at admission to the emergency department before and after p-PCI. Echocardiographic examinations were routinely performed by a specialist assistant as the co-author 8 to 12 hours after p-PCI and at follow-up (10 to 14 months after acute MI). The TIMI flow was observed immediately after p-PCI. In all the patients undergoing p-PCI, the location of left anterior descending (LAD) artery involvement during coronary arteries angiography was divided into three sections based on LAD artery length.

Results: The mean WBC and PMN before p-PCI were statistically higher in the group of patients with LVA compared to individuals without LVA ($p < 0.001$). Based on multivariate analysis platelet count (OR=0.999, age (OR=1.07), PMN before P-PCI (OR=1.001) had a significant additive effect on the probability of LVA formation.

Conclusion: Platelet count can be used for prediction of the risk of future LVA formation in acute STEMI patients.

Key words: ST-segment elevation myocardial infarction; platelet count; mortality; percutaneous coronary intervention; left ventricular aneurysm

INTRODUCTION

Left ventricular aneurysm (LVA) is a common complication of acute myocardial infarction (MI) with a prevalence of about 10 to 38%.^{1,2} The mortality rate in LVA patients is six times higher than in patients without aneurysm.³ Clinical risk factors for LVA formation include anterior MI, underdeveloped collaterals, and smoking.⁴ However, no evidence of a reliable biomarker yet exists for predicting the future risk of LVA formation, especially in the early phase of MI onset.

Various hematological parameters can be readily and routinely available prior to primary angioplasty (P-PCI) in ST-elevation myocardial infarction (STEMI) patients. High levels of neutrophils have been shown to be associated with an increased risk of adverse clinical outcomes after acute MI.⁵ Platelets can release inflammatory markers and also directly activate other inflammatory cells, leading to greater release of inflammatory cytokines and enhancement of inflammatory response in the microvascular system.⁶ Early risk prediction is critical for identifying patients with high-risk of LVA formation after primary percutaneous coronary intervention (PCI) in order to prevent or treat the disease.⁷

Despite numerous reports demonstrating the predictive value of hematological parameters for the prognosis of acute MI patients undergoing primary PCI, limited studies have investigated the link between hematological parameters and LVA formation. Accordingly, we conducted a study aimed at examining the relationship between intra-procedure hematological parameters and future LVA formation. Of interest was to evaluate the potential predictive value of intra-procedure hematological parameters for LVA so that the timely diagnosis and treatment of the disease can prevent its potential complications.

METHODOLOGY:

This descriptive study was performed on a population of patients with acute anterior STEMI, admitted to the emergency department at the Heshmat Medical Center, Rasht, Iran, who had undergone primary PCI. Sampling was carried out by a consecutive survey of patients, who were admitted to the Medical Center in summer and fall of 2018 and met the inclusion criteria, and continued until data saturation. The inclusion criteria were diagnosis of acute anterior STEMI by a specialist physician at admission and primary PCI as well as no LVA formation. The exclusion criteria included cardiogenic shock at admission, thrombolytic drug use within the last 24 hours, active infection, history of systemic inflammatory diseases, clinical evidence of autoimmune or proliferative blood diseases, known malignancy, liver and kidney diseases, and LVA defined as outward dyskinetic or akinetic motion of the

ventricular wall during the entire cardiac cycle.

Echocardiography was used to diagnose LVA between 10 to 14 months after acute MI. The patients underwent common medical treatment with aspirin, clopidogrel, and heparin prior to primary PCI, which was performed through the standard femoral route. The TIMI flow was observed immediately after P-PCI and divided into four grades based on coronary perfusion:

- Grade 0 (no perfusion): There exists no antegrade blood flow beyond the point of occlusion.
- 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.
- Grade 2 (partial perfusion): The contrast material passes beyond the area of obstruction and opacifies the coronary bed distal to the obstruction. However, the rate of entry of contrast into the vessel distal to the obstruction and/or its rate of clearance from the distal bed are perceptibly slower than the arterial bed proximal to the obstruction.
- Grade 3 (complete perfusion): Antegrade flow into the bed distal beyond the area of obstruction and its rate of clearance from the distal bed are similar to the bed proximal to the obstruction.

In all the patients undergoing P-PCI, the location of left anterior descending (LAD) artery involvement during coronary arteries angiography was divided into three sections based on LAD artery length: 1) Ostioproximal, 2) midportion, and 3) distal.

Blood samples were collected intravenously from all the patients at admission to the emergency department and 8 to 12 hours after primary PCI. Hematological parameters including neutrophils and platelets were measured. Moreover, creatinine was measured in all the patients. It is noteworthy that blood parameters were routinely measured at the Heshmat Medical Center Laboratory. Echocardiographic examinations were routinely performed by a specialist assistant as the co-author 8 to 12 hours after primary PCI and at followed-up 10 to 14 months after acute MI to measure ejection fraction (EF) using the Simpson's method. This study was approved by the Ethics Committee of Guilan University of Medical Science (Approval No. IR.GUMS.REC.1397.370).

Data analysis

Data analysis was performed in SPSS version 21. Frequency (percent), mean (standard deviation) and median

(range of variation) were used as needed to describe the data. Moreover, logistic regression analysis was used to investigate the relationship between the quantitative and qualitative variables with aneurysm formation. If necessary, t-test or Mann-Whitney test would be used to compare the mean of the quantitative variables between the two groups whereas chi-square test would be used to compare proportions between the two groups. The significance level was considered as $P \leq 0.05$.

RESULTS:

In this study, 255 patients undergoing P-PCI were evaluated in terms of platelet count and LVA formation. The demographic information of the patients along with their history of previous diseases are summarized in Table 1. Moreover, data on LVA formation 10 months after P-PCI are reported in Table 2.

Table 1- The demographic information and underlying diseases of the subjects under study

| | Number | Percentage |
|------------------------------|-------------------------------|------------|
| Age Ranges | | |
| <50 | 37 | 14.5% |
| 51-60 | 80 | 31.4% |
| 61-70 | 84 | 32.9% |
| >70 | 54 | 21.2% |
| Age: Mean \pm SD (max-min) | 61.71 \pm 10.32 (36.0-86.0) | |
| Sex | | |
| Male | 179 | 70.2% |
| Female | 76 | 29.8% |
| Hypertension | | |
| Yes | 167 | 65.5% |
| No | 88 | 34.5% |
| Diabetes mellitus | | |
| Yes | 114 | 44.7% |
| No | 141 | 55.3% |

Table 2- The percentage of LVA in the patients after P-PCI

| Left Ventricular Aneurysm | Number | Percentage | 95% confidence interval | |
|---------------------------|--------|------------|-------------------------|-------------|
| | | | Lower Limit | Upper Limit |
| No | 210 | 82.4% | 77.3% | 86.7% |
| Yes | 45 | 17.6% | 13.3% | 22.7% |

Table 3-Comparison of the percentage of LVA formation according to individual variables, underlying diseases and blood factors

| Characteristics | Total | Left Ventricular Aneurysm | | p-value |
|--------------------------------------|----------------------|---------------------------|----------------------|---------|
| | | Yes (n=45) | No (n=210) | |
| Sex | | | | |
| Male | 100% (179) | 17.9% (32) | 82.1% (147) | 0.882 |
| Female | 100% (76) | 17.1% (13) | 82.9% (63) | |
| Age (years) | 61.71 ± 10.32 | 66.6 ± 10.19 | 60.67 ± 10.07 | <0.001 |
| Hypertension | | | | |
| Yes | 100% (167) | 22.2% (37) | 77.8% (130) | 0.009 |
| No | 100% (88) | 9.1% (8) | 90.9% (80) | |
| Diabetes mellitus | | | | |
| Yes | 100% (114) | 32.5% (37) | 67.5% (77) | <0.001 |
| No | 100% (141) | 5.7% (8) | 94.3% (133) | |
| LAD | | | | |
| Proximal | 100% (90) | 30% (27) | 70% (63) | 0.009 |
| Mid | 100% (110) | 10.9% (12) | 89.1% (98) | |
| Distal | 100% (55) | 10.9% (6) | 89.1% (49) | |
| Baseline laboratory parameter | | | | |
| White blood cells (WBC) | 11175.69 ± 11364.81 | 12375.33 ± 15290.99 | 10918.63 ± 10361.85 | <0.001 |
| polymorphonuclear neutrophil (PMN) | 8128.78 ± 5040.14 | 9996.44 ± 11811.16 | 7728.57 ± 769.05 | <0.001 |
| Platelet | 235207.84 ± 65607.22 | 248644.44 ± 63017.01 | 232328.57 ± 65938.14 | 0.074 |

In Table 3, univariate analysis compared LVA formation based on individual variables, underlying diseases and blood factors. According to the data shown in the table, the mean age of patients with LVA was significantly higher ($P < 0.001$) than those without LVA. Similarly, the percentage of LVA formation was significantly higher ($P = 0.009$) in patients with HTN (22.2%) compared to those without HTN (9.1%). Moreover, LVA formation was observed to have significantly higher ($P < 0.001$) percentage in patients with DM (32.5%) as compared to those without DM (5.7%). In a similar vein, the percentage of LVA formation was meaningfully ($P = 0.009$) more in LAD with proximal occlusion (30%) than in those with midpart (10.9%) and distal (10.9%) occlusion. In addition, the mean white blood cell (WBC) and

polymorphonuclear neutrophil (PMN) before PCI-P were statistically significant in the two groups of patients with and without LVA ($P < 0.001$), with WBC and PMN being higher in the group of patients with LVA compared to the other group. Furthermore, Cr levels prior to P-PCI were higher in patients with LVA than in those without LVA ($P < 0.001$). According to the data of this study, the final TIMI was statistically significant in patients with LVA with the median equal to 2 compared to patients without LVA ($P = 0.001$). In multivariate analysis, a logistic regression model was used to correlate platelet count after P-PCI with LVA formation. The main research variable (platelet count) along with individual and contextual variables as well as significant blood factors in univariate analysis were included in the initial model.

Table 4- Regression coefficients and odds ratios of factors associated with LVA

| | | B | S.E. | Sig. | Odds Ratio | 95% C.I. for OR | |
|----------------------|--------------------|----------|---------|--------|------------|-----------------|------------|
| | | | | | | Lower | Upper |
| Primary model | Sex | .36441 | .54547 | .50409 | 1.440 | .494 | 4.193 |
| | Age | .08208 | .02834 | .00377 | 1.086 | 1.027 | 1.148 |
| | Hypertension | -.59320 | .64063 | .35447 | .553 | .157 | 1.939 |
| | Diabetes mellitus | .68589 | .84954 | .41946 | 1.986 | .376 | 10.496 |
| | begining.Cr | -.99267 | 3.51470 | .77761 | .371 | .000 | 363.586 |
| | begining.WBC | -.00001 | .00002 | .74480 | 1.000 | 1.000 | 1.000 |
| | after.WBC | .00001 | .00003 | .78744 | 1.000 | 1.000 | 1.000 |
| | after.Cr | 7.60472 | 2.35663 | .00125 | 2007.646 | 19.802 | 203543.979 |
| | time.8_12.hours.EF | .08772 | .11763 | .45586 | 1.092 | .867 | 1.375 |
| | time.10.months.EF | -.23121 | .12453 | .06336 | .794 | .622 | 1.013 |
| | begining.PMN | .00104 | .00052 | .04804 | 1.001 | 1.000 | 1.002 |
| | Final TIMI | -1.86874 | .54002 | .00054 | .154 | .054 | .445 |
| | after.PLT | -.00001 | .00001 | .03511 | 1.000 | 1.000 | 1.000 |
| Constant | -11.88492 | 7.41977 | .10920 | .000 | | | |
| Final model | Age | .07346 | .02667 | .00588 | 1.076 | 1.021 | 1.134 |
| | after.Cr | 6.08838 | 1.45961 | .00003 | 440.70677 | 25.21884 | 7701.48357 |
| | time.10.months.EF | -.16720 | .09331 | .07314 | .84603 | .70463 | 1.01580 |
| | begining.PMN | .00100 | .00049 | .04140 | 1.00100 | 1.00004 | 1.00197 |
| | Final TIMI | -1.73525 | .49492 | .00045 | .17636 | .06685 | .46523 |
| | after.PLT | -.00001 | .00001 | .04442 | .99999 | .99998 | .999999 |
| | Constant | -9.27619 | 6.45797 | .15089 | .00009 | | |

a. Variable(s) entered on step 1: Sex, Age, Hypertension, Diabetes mellitus, begining.Cr, begining.WBC, after.WBC, after.Cr, time.8_12.hours.EF, time.10.months.EF, begining.PMN, Final TIMI, after.PLT.

Based on the data in Table 4, in multivariate analysis, after adjusting for the effects of individual variables, underlying diseases and LVA-related blood factors, the correlation between platelet count after P-PCI and LVA formation was observed to be statistically significant ($P=0.044$). Accordingly, every one-unit increase in platelet count decreased the risk of LVA formation (OR=0.999) (CI OR=0.0-99998.99999). Based on multivariate analysis, in addition to platelet count, the variables of age (OR=1.07), PMN before P-PCI (OR=1.001), and Cr after P-PCI (OR=440.7) had a significant additive effect on the probability of LVA formation. However, EF (OR=0.846) and final TIMI (OR=0.176), similar to platelet count, had a reducing effect on the risk of LVA formation.

DISCUSSION

Most cases of LVA occur at ventricular apex and only a few

cases occur near the lower part of the posterior wall. LVA formation may spatially damage the ventricle and result in decreased systolic and diastolic ability,⁸ thereby resulting in worse prognosis following MI, including angina pectoris,⁹ malignant arrhythmia,¹⁰ embolism¹¹ and even death.¹² Necrotic myocardium is gradually replaced by fibrous tissue, causing the ventricular wall to become thinner.⁹ LVA progressively destroys the remaining active myocardial function. Therefore, it is necessary to diagnose LVA early and treat it appropriately after MI. Diagnostic methods for LVA are currently expanding rapidly. Electrocardiography, echocardiography, ventricular angiography, MRI, radionuclide ventriculography and myocardial perfusion imaging can be used to diagnose ventricular aneurysms. Clinical risk factors for LVA formation include anterior MI, underdeveloped collaterals, and smoking.⁴ Early risk prediction is essential for recognizing patients highly susceptible to LVA formation after PCI so that the disease

could be prevented or at least cured. With the development of reperfusion strategies such as PCI, the risk of LVA formation has decreased significantly in recent years.⁷ Investigating the rate of LVA formation in this study within one year after P-PCI revealed that LVA was formed in 17.6% of the patients. Wang et al. found that LVA formation had a rate of 12% at one year after P-PCI.¹³ In the study of Galiuto et al., the rate of LVA formation was 27% and 8% in patients with and without ST-segment elevation at discharge, respectively.¹⁴ Mori et al. in their study reported the rate of LV apical aneurysm to be 18% at 6 to 12 months after P-PCI.¹⁵ Yet in another study, Mori et al. found that in patients undergoing PPCI, peak creatine kinase and the TIMI flow grade were significantly associated with LVA formation.¹⁵ In a study by Shen et al., it was revealed that a large MI can cause LVA formation.³ Celik et al. found that intra-stent thrombosis and in-hospital mortality were significantly higher in TIMI grades 0, 1, and 2.¹⁶ In another research, Galiuto et al. reported no significant relationship between TIMI 3 grade flow and increased risk of LVA formation within 6 months after P-PCI.¹⁴ Different demographic characteristics and PCI procedures can explain the discrepancy between their results and ours. While numerous reports have demonstrated the predictive value of hematological parameters for the prognosis of acute MI patients undergoing primary PCI, limited studies have investigated the link between hematological parameters and LVA formation.

Thus, the main purpose of this study was to investigate the relationship between platelet count after P-PCI and LVA formation in STEMI patients. Based on the results of our study the correlation between platelet count after P-PCI and LVA formation was observed to be statistically significant and every one-unit increase in platelet count after P-PCI led to the decreased risk of LVA formation.

In a study by Liu et al., it was concluded that platelets accumulated in MI may play a role in regional inflammation, ventricular remodeling, and ventricular rupture, and that antiplatelet therapy would reduce inflammation severity and the risk of post-MI complications.¹⁷ Results of Nikolsky's clinical study showed that high initial platelet count in patients with acute MI was a powerful independent predictor of death and re-infarction during the first year after P-PCI.¹⁸ According to the previous research works, platelets enhance the formation of thrombus in the MI pathophysiological process. In addition, they can stimulate the insufficient inflammatory response and ventricular re-modelling.¹⁹

In spite of the involvement of activated platelets in the circulatory inflammation response, they connect to the inflamed microvessels wall. It happens via direct attachment to endothelial cells or via attaching to leucocytes, which previously adhered to the wall of the vessel. Platelets are

able to discharge inflammation markers, and they can cause direct activation of other inflammatory cells, resulting in more discharge of inflammatory cytokines and augmenting the inflammatory response in the microvessels.⁶ The cross talk between leucocytes, endothelial cells, and platelets could diminish the microvascular activity in the infarct zone. It can happen also in patients who have had acceptable mechanical reperfusion therapy. As reported by Yamamuro et al.,²⁰ even if reperfusion is successful in epicardial coronary arteries, microvascular dysfunction, which is evaluated by coronary flow velocity, leads to inadequate infarcted myocardium reperfusion. It results in dysfunction of the left ventricular and formation of LVA.

One of the limitations of our study was that we only investigated patients in a single medical center cross-sectionally. Therefore, we recommend to conduct further research with a larger sample size. Moreover, we did not examine drugs that can be used after P-PCI and alter platelet count. Thus, we suggest to make use of such drugs in future studies.

CONCLUSION

In conclusion, the correlation between platelet count after P-PCI and LVA formation was observed to be statistically significant, so platelet count can be used for a more robust prediction of the risk of future LVA formation in acute STEMI patients. Accordingly, the data from this study can contribute to the optimization of preventive treatments in order to improve outcomes in such patients.

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Conflict of Interest Disclosures

None.

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