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Original Article

Evaluation of the relation between monocyte count and angiographic thrombosis burden in patients with myocardial infarction with STEMI under primary percutaneous coronary intervention: A cross–sectional study

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Abstract

Introduction: Complete thrombotic blockage of a major epicardial coronary artery is the common pathophysiological mechanism of acute ST-segment elevation myocardial infection (STEMI). Intravascular thrombosis is associated with poor prognosis in STEMI patients. In this study, we assessed the association of monocyte count and angiographic thrombosis burden in STEMI patients.

Methods: In this study, 400 STEMI patients who were undergoing primary percutaneous coronary intervention (PPCI) were enrolled. Based on TIMI ratings of the patients and reviewing their angiographic film, they were divided into two groups with high thrombus burden and low thrombus burden. Then, monocytes were measured in two groups with higher and lower thrombus.

Results: 400 patients with STEMI (mean age of 58.71 ± 12.31, 80.5% male) who underwent PPCI enrolled in this study. There were no considerable differences between the high thrombus and low thrombus groups, regarding diabetes, high blood pressure, previous history of MI and cardiac troponin levels. However, patients with high thrombus burden had lower left ventricular ejection fraction (LVEF) (P value < 0.001). Multivariate analysis showed that higher amount of monocytes was an independent factor in predicting thrombus burden (Odds ratio = 3.099, $P = 0.019$) Receiver-operating characteristic found a cut-off value of 0.60×10^9/L for monocyte count in predicting a high thrombus burden score.

Conclusions: Our study indicated that higher monocytes count is a predictor of high intra-coronary thrombus burden in patients with acute STEMI, and patients can be treated with antithrombotic treatments.

Introduction

In recent years, cardiovascular disease, especially coronary artery disease (CAD) has become the most common cause of mortality worldwide. [1]

Complete obstruction of the thrombus of the major coronary arteries of the epicardium is a common pathophysiological mechanism of myocardial infarction (MI) with an exacerbated ST-segment elevation myocardial infection (STEMI).[2] The main pathophysiology of the STEMI is the formation of intravascular thrombus due to rupture of the atherosclerotic plaque and cessation of coronary blood flow. The amount of intravascular thrombus is associated with poor prognosis in patients with STEMI. [3]

Primary percutaneous coronary intervention (PPCI) for MI in patients with STEMI leads to rapid restoration of normal blood flow and enhanced clinical outcomes. Nevertheless, clinical studies have demonstrated that the amount of intravascular thrombus plays a key role in low thrombolysis in myocardial infarction (TIMI) and impaired myocardial perfusion.[4] Identifying the correlation between blood cell-dependent biomarkers and blood flow status during PPCI is a common focus in research.[5]

Studies have shown that monocytes might be connected with the pathogenesis of CAD, and an increase in their number might be a risk factor for MI.[6] Based on the previous studies, monocytes play an important role in the secretion of coagulation factors, such as tissue factor and in the stimulation of inflammatory processes in

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thrombotic disorders.[6]

During the first and second weeks after MI, the tissues in the infarct area undergo rapid circulation including extracellular matrix digestion and fibrosis. The accumulated monocytes in the infarcted area remove debris and residual tissue and facilitate the process of repair.[7] After MI, the monocytes produced in the bone marrow enter the bloodstream and damage the myocardium in two stages. The first stage is dominated by Ly-6chigh monocytes and the next one is dominated by Ly-6clow monocytes.[6]

Given that MI is the deadliest type of acute coronary heart disease with elevated ST segment, the risk assessment of these patients for short-term and long-term prognosis is increasingly important. Various methods have been used to evaluate these patients, which often have many problems. Therefore, finding a simple way to prognosis the patients who have often undergone mechanical perfusion or primary angioplasty has become increasingly important. According to the mentioned contents and due to the fact that very few studies have been conducted on the relationship between the number of monocyte cells and the amount of thrombus in patients treated with PPCI, we decided to assess the correlation between the number of monocytes and the amount of angiographic thrombus in patients with MI with STEMI treated with PPCI.

Methods

This cross-sectional study assessed 400 patients with STEMI undergoing PPCI at Shahid Madani hospital, the main tertiary hear center of the north-west of Iran, during 2016-2018. Demographic information (age, sex, blood pressure, diabetes, blood lipids, smoking, history of smoking) and information from echocardiography and medications during treatment and laboratory information including counting monocytes and other components of white blood cells were included in the checklist. By reviewing patients' angiographic film according to the TIMI rating, the individuals were divided into two groups of high thrombus and low thrombus. TIMI thrombus burden grading divides patients into 5 groups; grade 0 patients have no evidence of thrombus in their angiography, and grade 5 shows complete vessel obstruction by thrombus. [8] Then, complete blood count test and monocyte count was done in two groups of high and low thrombus burden. Before prescribing aspirin and clopidogrel, the number of white blood cell counts, the number of monocytes, and other biochemical related parameters were calculated by EDTA tubes in the inpatient ward. complete blood count analysis was performed by an auto-analyzer. For all patients, Creatinine and heart enzymes were measured by standard methods. Based on the previous studies, our sample size should be more than 100 patients, but we reached 400 patients to get a more accurate result.

Statistical analysis

In this study, we used descriptive statistics methods (mean ± standard deviation and frequency (percentage)). To evaluate the average number of monocytes in two groups with high and low thrombus burden, if the values were normal, *t* test was performed. Otherwise, the nonparametric equivalent of the Mann–Whitney U test was used. Chi-square tests, single-variable, and multivariate logistic regression tests were also used to investigate the prediction of a dependent variable based on independent variables. SPSS 19 used for data analysis.

Results

In this study, we enrolled 400 STEMI patients who underwent PPCI (mean age of 58.71 ± 12.31 years; 80.5% male). Demographic and laboratory data were shown in two groups according to high thrombosis and low thrombosis burden (Table 1). There was no statistically significant difference between the two groups regarding diabetes, hypertension, hyperlipidemia, smoking, previous history of MI and cardiac troponin levels. However, the left ventricular ejection fraction (LVEF) of patients was notably lower in high thrombus burden group (P value < 0.001)

Patient angiographic specifications are summarized in Table 2. Blood test parameters is summarized in Table 3. Our study showed no special difference between two groups regarding white blood cell count, neutrophil count, mean

Table 1. Baseline clinical and laboratory elements of the study population divided based on thrombus burden

	Low thrombus burden (n = 144)	High thrombus burden (n = 256)	*P* value
Age	59.85±11.68	58.71±12.31	0.366[a]
Male sex, n(%)	112 (77.8)	213 (83.2)	0.182[b]
Diabetes mellitus, n (%)	48 (33.3)	65 (25.4)	0.090[b]
Hypertension, n (%)	86 (59.7)	159 (62.1)	0.638[b]
Hyperlipidemia, n (%)	18 (12.5)	46 (18.0)	0.152[b]
Active smokers, n (%)	83 (57.6)	148 (57.8)	0.973[b]
Prior MI, n (%)	5 (3.5)	8 (3.1)	0.851[b]
LVEF (%)	41.17±6.82	38.32±8.51	<0.001[a]
Peak cTnI (ng/mL)	30.1(1.4-90.2)	55.9 (14.7-99.9)	0.035[c]

MI: myocardial infarction; LVEF: left ventricular ejection fraction; cTnI: cardiac troponin I.
[a] Independent samples *t* test; [b] Chi-square test; [c] Mann-Whitney U test.

platelet volume hemoglobin, platelet count, lymphocyte count and hematocrit. Nonetheless, the monocyte count was statistically higher in the high thrombosis group in comparison with low thrombosis group (*P* value < 0.001). We entered all parameters with significant correlation with high thrombus burden in univariate analysis to find independent factors. Multivariate analysis showed that monocyte count was independent factor for predicting high thrombus burden in STEMI patients undergoing PPCI. (Table 4) (Odds ratio = 3.099, 95% CI = 1.205–6.988, *P* value = 0.019)

Receiver-operating characteristic curve showed an optimal monocyte count cut-off value of 0.60×10^4 with a sensitivity of 71.13% and specificity of 73.44% (AUC: 0.741; 95% CI: 0.695- 0.783, *P* value < 0.001) in predicting a high thrombus burden score (Figure 1).

Discussion

In the present study, we investigated the association of monocyte count and angiographic thrombus burden in patients admitted with STEMI underwent PPCI. Our results showed that with a cut-off point of 0.60×10^9/L with a sensitivity of 71.13% and specificity of 73.44% monocyte count could predict high thrombus burden achieved by angiographic findings. There are few studies investigating the relationship between monocyte count and thrombosis burden. According to the results of a study by Wang et al,[5] a group of people with STEMI with high thrombosis burden in coronary arteries had an increased amount of circulating monocytes. In this study monocyte count with a cut-off value of 0.48×10^9/L and a sensitivity of 71.9% and specificity of 46.9% could predict high thrombus burden with is close to our findings.

Monocytosis induced by MI could enhance cardiovascular complications.[6] Similar to our study van der Laan et al by studying 58 patients with STEMI showed that monocyte elevation was associated with severe cardiac damage and poor outcome. They showed that higher monocyte count could induce a pro-inflammatory effect causing more cardiac injury.[9] Furman et al showed that monocyte platelet aggregates were detected in the blood sample of patients with STEMI as early as 4 hours and even before the elevation of cardiac creatine kinase.[10] The pathophysiology ACS is caused by thrombosis and rupture of the atherosclerotic plaque. The rate of residual thrombosis after successful PCI is closely related to the rate of distal coronary perfusion and the LVEF.[11]

Previous studies have suggested that white blood cell

Table 2. Baseline angiographic and procedural characteristics according to thrombus burden

	Low thrombus burden (n = 144)	High thrombus burden (n = 256)	*P* value
Time form symptom onset to PPCI			0.772 [b]
< 3 h (%)	39 (27.8)	70 (27.3)	
3-6 h (%)	53 (28.5)	102 (39.8)	
6-12 h (%)	52 (36.1)	84 (32.8)	
Anterior infarct location, n (%)	77 (53.5)	129 (50.4)	0.714 [b]
Infarct-related coronary artery, n (%)			0.923 [b]
Left main	0 (0.0)	0 (0.0)	
Left anterior descending	77 (53.5)	132 (51.6)	
Left circumflex	18 (12.5)	32 (12.5)	
Right coronary artery	49 (34.0)	92 (36.0)	
Number of used stent, n	1.7±0.6	1.5±0.7	
Total stent length, (mm)	35.9±18.9	36.2±18.6	0.878 [a]
Stent diameter, (mm)	3.28±0.4	3.30±0.4	0.632 [a]
Use of thrombus aspiration, n (%)	14 (9.7)	159 (62.11)	< 0.001 [b]
Tirofiban use, n (%)	75 (52.1)	213 (83.2)	< 0.001 [b]

[a] Independent samples *t* test; [b] Chi-square test.

Table 3. Hematological parameters of the study population

Variable	Low Thrombus burden (n = 144)	High Thrombus burden (n = 256)	*P* value
White blood cell count $\times10^9$/L	10.3 ± 4.0	10.4 ± 4.5	0.879 [a]
Neutrophil count$\times10^9$/L	7.1 ± 1.3	6.8 ± 1.3	0.053 [a]
Hemoglobin g/dL	14.5 ± 1.9	14.6 ± 2.1	0.516
Platelet count$\times10^9$/L	239.5 ± 67.9	234.6 ± 76.3	0.595 [a]
Hematocrit %	42.1 ± 4.5	42.0 ± 4.7	0.836 [a]
Mean platelet volume fl	10.2 ± 0.6	10.1 ± 0.7	0.150 [a]
Lymphocyte count$\times10^9$/L	2.17 ± 1.08	2.23 ± 1.11	0.592 [a]
Monocyte count $\times10^9$/L	0.59 ± 0.28	0.81 ± 0.33	< 0.001 [a]

[a] Independent samples *t* test.

Table 4. Logistic regression analyses of independent predictors of high-thrombus burden in patients with ST-elevation myocardial infarction

Variable	Univariate		Multivariate	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age	0.985 (0.970–1.009)	0.901		
Sex	0.998 (0.649–1.803)	0.821		
Diabetes mellitus	1.012 (0.597–1.451)	0.802		
Prior MI	2.001 (0.821–8.812)	0.109	1.797 (0.802–9.142)	0.454
LVEF	0.998 (0.998–1.141)	0.811		
Time from symptom onset to PPCI	1.121 (1.098–1.311)	0.102	1.053 (0.998–1.207)	0.575
Creatinine	0.997 (0.982–1.009)	0.209		
Neutrophil count	1.009 (0.942–1.097)	0.786		
Hemoglobin	1.003 (0.981–1.02)	0.776		
Lymphocyte count	1.049 (0.924–1.209)	0.801		
Monocyte count	2.387 (1.014–6.068)	0.046	3.099 (1.205–6.988)	0.019

MI: myocardial infarction; LVEF: left ventricular ejection fraction; PPCI: primary percutaneous coronary intervention.

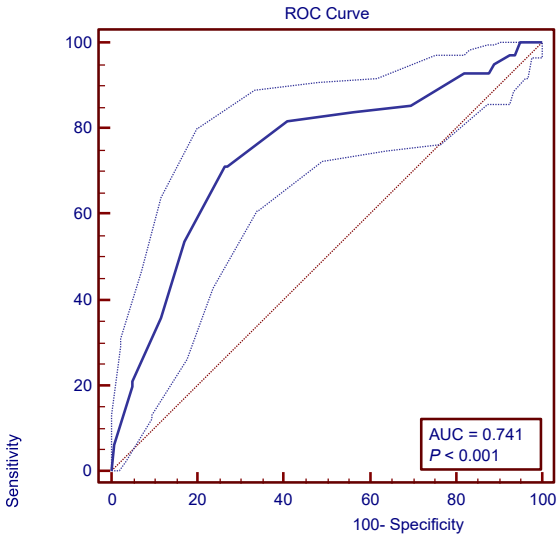

Figure 1. ROC curve of the monocyte in predicting the higher thrombus.

counts and their subtypes play a key role in determining the prognosis of patients with acute STEMI who undergo PPCI. White blood cells and their subtypes in various ways affect thrombotic processes, including hyper coagulopathy and inflammatory conditions.[12]

Activation of monocytes and their conversion to macrophages exacerbates atherosclerotic processes. Blood monocytes enter the intimal and sub-intimal layers of the vessel wall and become LDL foam and other serum lipids. People with hypercholesterolemia have higher rates of monocyte migration.[11]

Inflammation and oxidative stress processes play an essential role in the pathogenesis of plaque rupture and thrombosis. 10% of Blood leukocytes consists of monocytes which are one the most major players in inflammatory processes.[5]

The Palmerini et al study, which examined the histology of asymptomatic thrombosis of coronary arteries in people with STEMI, found that monocytes produced larger amounts of tissue factor, comparing to neutrophils.[13]

Aleman et al found that monocyte microparticles had prothrombinase activity and rapidly produced fibrin.[14]

A study by Mach and colleagues indicated that stimulation of monocytes could cause internal collagenase and platelet destabilization.[15]

Limitations of the study

Our study was a cross-sectional study, and using a cohort study can give more information in this era. We did not have the baseline monocyte count of patients, and the exact decrease or increase of monocyte count regarding base count could be more reliable.

Conclusion

Our study showed that higher monocytes count was a predictor of high intra-coronary thrombus burden in patients with acute STEMI, and patients can be treated with antithrombotic treatments.

Conflict of Interest

The authors expressed no conflict of interest.

Ethical Approval

This study was accepted by the ethical committee of Tabriz University of Medical Sciences (No. IR.TBZMED.REC.1398.1025).

Author's contribution

AS, and AHS, carried out the design of study and manuscript preparation. MA, provided assistance in the design of the study. AHS, AND, HS assisted in statistical analysis and manuscript preparation. HS, and MA participated in data gathering and manuscript editing.

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Study Highlights

What is current knowledge?

- Very few studies have been conducted on
- The relationship between the number of monocyte cells
- The amount of thrombus in patients treated with PPCI.

What is new here?

- Our study showed that higher monocytes count was a predictor of high intra-coronary thrombus burden in patients with acute STEMI, and patients can be treated with antithrombotic treatments

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