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White blood cell count and mortality in acute myocardial infarction

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ABSTRACT

Introduction: Coronary atherosclerosis is increasingly viewed as an inflammatory process. We assessed the relation between WBC count on admission and mortality in STEMI patients treated with primary PCI. Material & Method: Totally 205 patients with STEMI less than 24 hours before admission who admitted for primary angioplasty enrolled in study. Study end points were defined as myocardial adverse cardiac event (MACE) and mortality at one month and one year follow-up. Result: Totally 205 patients (166 men) with mean age 56 ± 11 were enrolled in study. The mean WBC count was 8983 ± 34 and mean follow-up was 12.24 months. WBC count remained a significant predictor of mortality after multivariable adjustment in one month and 12 months follow-up (p = 0.02, p = 0.04). Conclusion: Our results extend previous findings that WBC count is an independent marker of cardiac mortality.

Keywords: Myocardial Infarction; Primary Percutaneous Coronary Intervention; WBC Count; Inflammation

1. INTRODUCTION

Coronary atherosclerosis is increasingly viewed as an inflammatory process [1-3]. Previous studies confirmed an association between inflammatory markers and atherosclerosis plaque formation, progression, and instability of plaque, adverse clinical outcome and development of myocardial infarction [4,5]. Leucocytes are major mediators of inflammation. They have a key role in host defense to injury. Increasing of white blood cell (WBC) count is a risk factor for future cardiovascular events in individuals without cardiovascular disease [6,7]. It is associated with worse outcome in patients with stable angina and acute coronary syndrome [8-15]. The baseline WBC count is an independent predictor of mortality in ST elevation myocardial infarction (STEMI) patients [16, 17]. Moreover, in STEMI patients undergoing primary percutaneous coronary intervention (PCI) WBC count predicts short term mortality [18]. Although in one study this association was not significant. Gurm *et al*. showed that WBC count is an independent predictor for long term mortality in patients undergoing PCI either in the setting of stable angina or primary PCI [19,20]. The aim of our study was to assess the relation between on admission WBC count and clinical data and short term and long term mortality in STEMI patients treated with primary PCI.

2. MATERIAL & METHOD

This prospective study was done from Nov 2008 to Dec 2011. Totally 205 patients with STEMI (ST elevation ≥0.1 mV in more than 2 limb leads or ≥0.2 mV in chest lead or new LBBB at presentation, patients with chest pain during less than 24 hours before presentation who admitted for primary angioplasty in Shahid Rajaie hospital in Tehran, Iran enrolled in study.

In all patients, primary angioplasty was performed

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according standard technique after loading dose of ASA 325 mg and 600 mg of clopidoigrel. Integrilin prescribed based on discretion physician performing procedure. Demographic, clinical and angiographic data including sex, age, coronary risk factor, MI location, blood pressure, heart rate, previous presentation before MI and time from onset to admission was determined and recorded. Exclusion criteria included the following: any form of steroid medication or non steroidal anti-inflammatory drugs or antibiotics use in the preceding month, acute infection in the last 2 weeks, surgery within the last 2 weeks, history of liver or renal failure, history of malignancy or vacuities and admission more than 24 hour from onset of symptoms. Pre- and post-procedural angiograms were analyzed by two operators blinded to the study. Study protocol was approved by the local ethics committee.

Study end point was major adverse cardiac events (MACE) including mortality, MI, target vessel revascularization (TVR) and stent thrombosis. Follow up performed based on records of monthly visits in outpatient clinic and telephone interview to evaluate symptoms and admission note.

Baseline WBC count values were analyzed as continuous variable. To assess the relation between WBC count and baseline clinical data multivariable linear regression was applied.

Study end points were defined as MACE and mortality at one month and one year follow-up (minimum 1moth to 33 months for all subjects). Continuous data are presented as mean values with standard deviation and compared by use of Student's t-test. Categorical data are presented as frequencies and analyzed with χ^2 tests. The relation between one-year mortality and clinical factors' including WBC count is examined with stepwise, multivariable logistic regression. Risk ratios are reported with regression model that adjust for factors that are independently associated with the outcome variable. Data analysis is performed using SPSS 16.0.

3. RESULT

Total of 205 patients (166 men and 39 women) with AMI with mean age 56.9 ± 11.154 (range 28 - 86 years) were enrolled in study. The mean WBC count was 8983 ± 34 and mean follow up was 12.24 month (range 1 to 33). In patient with current smoking, mean WBC was significantly higher than non smoker patients [10,021 ± 53 versus 8319 ± 55 (p = 0.002)]. Others risk factors such as diabetes mellitus, hypertension, family history of coronary disease, hypercholesterolemia, age and sex had no significant relation with WBC (**Table 1**). **Table 1** Describes baseline characteristics of patients including coronary risk factors and association with mean WBC.

We assessed the relation of MI location, history of previous PCI or CABG, MI history and symptoms before the presentation and presence or absence of shock and their relationship with WBC count. There was a significant statistical relation with history of PCI (**Table 2**).

WBC count in patients with single vessel and multi vessel involvement had no significant difference in our data. LAD lesion diagnosed in 53.7%, LCX lesion in 12.2%, and RCA lesion in 32.7% of patients (p = 0.028). Moreover, 80.5% of patient had thrombotic lesion. Data

Table 1. Baseline characteristics of patients.

Variables		Number	Percent	WBC count mean ± SD	p value
Sex	Male	166	81	9091 ± 65	0.739
	Female	39	19	8535 ± 48	
Smoking	Current	87	42.4	10,021 ± 53	0.002
	Non	118	57.6	8319 ± 55	
Diabetes	Yes	43	21	8323 ± 71	0.179
	No	162	79	9169 ± 36	
Hypertension	Yes	72	35.1	8360 ± 78	0.077
	No	133	64.9	9350 ± 45	
Family history of coronary disease	Yes	24	11.7	8962 ± 38	0.976
	No	181	88.3	8986 ± 38	
Hypercholesterolemia	Yes	82	40	8713 ± 33	0.384
	No	123	60	9190 ± 12	
Age	>70	25	13.2	9204 ± 32	0.765
	Up to 70	178	88.8	8953 ± 25	

Table 2. Clinical and para clinic finding and association with mean WBC count in PPCI.

Variable	Number	Mean ± SD WBC count	*p* value
Anterior MI or new LBBB	111	8882 ± 15	0.694
No anterior MI	94	9096 ± 40	
History of myocardial infarction	41	8058 ± 87	0.100
No history of myocardial infarction	164	9198 ± 18	
History of PCI	22	7320 ± 00	0.047
No history of PCI	183	9156 ± 47	
History of CABG	4	9250 ± 28	0.875
No history of CABG	164	8976 ± 33	
Pre presentation unstable angina	67	8990 ± 76	
Asymptomatic	71	9092 ± 11	0.987
Chronic stable angina	21	8590 ± 95	
Shock in presentation	13	9170 ± 45	0.837
No shock	146	8966 ± 58	
IABP, impella	9.9	9912 ± 22	0.402

Abbreviations: MI = myocardial infarction, LBBB = left bundle branch block.

are summarized in **Table 3**. Moreover, WBC counts were not significantly different between patients with different TIMI frame count (**Table 4**).

In one month follow up mean WBC counts were 8970 ± 13, 9330 ± 97 and 8250 ± 58 in no death (n = 200), cardiac death (n = 4) and non cardiac death (n = 1) groups respectively (p = 0.02). In 12 month follow up, mean WBC count were 8983 ± 14, 11,002 ± 70 and 8992 ± 30 in no death (n = 190), cardiac death (n = 8) and non cardiac death (n = 2) groups respectively (p = 0.04).

The overall rate of MACE (death, MI, re-stenosis, stent thrombosis) was 10.2% in one year follow up. Mean WBC count was 9330 in this group compared to 8970 in patients without MACE which was not significant (p = 0.859) (**Table 5**).

4. DISCUSSION

Based on our study results, a significant relationship observed between baseline WBC count and cardiac mortality in patient with STEMI and primary PCI during one and 12 months follow up. Previous studies investigated the association between increased inflammatory markers and outcome in coronary artery disease [21-25].

Other studies showed the association between WBC count and short term mortality in AMI. Barron *et al.* demonstrated in patients with AMI that received thrombolytic, higher baseline WBC count was associated with worse short term outcome, reduced myocardial perfusion, thromboresistance and higher incidence of new CHF and death [26-28]. On the other hand in PAMI trial there was no association between WBC count and mortality in AMI and primary PCI [19]. Mehran *et al*. described association between WBC and MACE (MI, death, TVR, stroke) in one month in primary PCI [28]. In another investigation in patients undergoing PCI (other than primary PCI) baseline WBC count in group with history of MI, heart failure, and type C lesion was higher. PCI success rate between groups was equal and three years mortality had linear association with WBC count [29]. In other study, total WBC count could predicted one year's mortality in patients with acute coronary syndrome which treated with percutaneous coronary intervention, leucocytes count had predicted mortality across all of the subgroups [30].

The association between thrombotic and inflammatory pathways in MI has been explored in numerous studies. Leukocytosis is common in acute STEMI. It results from inflammatory response of neurohormonal system. The infiltration of WBCs into necrotic tissue in response to ischemia and reperfusion has major role in secreting mediators which contribute to oxidative and proteolytic injury. Furthermore, the distal embolisation of leukocytes and platelet-leukocyte aggregates may reduce microvascular perfusion and contribute to thrombosis and widespread myocardial inflammation [11]. In addition to inflammatory response in acute MI, post procedural inflammatory response in patients undergoing PCI has a wide range of mechanisms, including mechanical disruption of atherosclerotic plaque, endothelial cell injury

Table 3. Baseline procedural data and association with mean WBC in PPCI.

Variables		Number	Mean ± SD WBC count	*p* value
Multi vessel disease		94	8936 ± 18	0.835
Single vessel disease		65	9051 ± 23	
Culprit vessel	LAD	84	8788 ± 11	0.028
	LCX	17	11,141 ± 18	
	RCA	55	8405 ± 89	
	Ostia	16	9425 ± 39	
Location invessel	Proximal	68	9496 ± 93	0.383
	Mid portion	61	8362 ± 79	
	Distal	8	9088 ± 75	
	Bifurcation	6	8150 ± 44	
Type of Lesion	A	2	9200 ± 55	0.924
	B	29	9202 ± 97	
	C	128	8930 ± 24	
Thrombotic		131	8963 ± 62	0.872
Non thrombotic		28	9077 ± 71	
Stenosis <100		36	9544 ± 61	0.263
Stenosis 100%		123	8818 ± 90	
Glycoprotein IIb/IIIa use		46	9484 ± 59	0.238
No glycoprotein IIb/IIIa use		113	8779 ± 12	

Table 4. TIMI flow before and after PCI.

Variables		Number	Mean ± SD WBC count	*p* value
TIMI flow before PCI	0	123	8818 ± 90	0.765
	1	9	9691 ± 11	
	2	14	10,169 ± 71	
	3	13	8770 ± 58	
TIMI flow after PCI	0	3	7100 ± 81	0.666
	1	3	9966 ± 67	
	2	20	9461 ± 57	
	3	123	8931 ± 66	

Table 5. Clinical outcome and association with mean WBC in PPCI.

Variables	Number	Mean ± SD WBC count	*p* value
Outcome 1 month			
Death	5	8500 ± 40	
Stent thrombosis	3	8066 ± 67	
Restenosis	1	9200 ± 36	0.295
Re-PCI	3	8066 ± 67	
CABG	2	10,800 ± 61	
Outcome 12 month			
Death	10	11002.50	
Stent thrombosis	6	7400 ± 51	
Restenosis	7	8822 ± 35	
Re-PCI	9	8387 ± 41	0.079
CABG	8	8337 ± 50	
Ischemia, MI	10	9567 ± 78	
Total outcome	50	9335 ± 81	

caused by proteolytic and oxidative stress, arterial wall injury, myocardial necrosis due to distal embolisation, vessel plugging effecting the blood flow through the cardiac microvasculature, hyper coagulable state with decrease epicardial patency and increased ischemic burden [31,32]. Moreover, reduced patency of coronary arteries and higher thrombus burden was observed in patients with elevated WBC count [33].

It is possible that endothelial dysfunction and microvascular plugging due to elevated level of WBC play an important role in developing of future heart failure in STEMI patients [34].

5. CONCLUSION

Our results extend previous findings that WBC count can be an independent marker of cardiac mortality, in short term and long-term mortality prediction in STEMI treated with revascularization. Increased WBC count is a simple non-specific marker of inflammation; it may serve as an available and inexpensive tool for risk stratification in acute SEMI.

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