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The relationship between neutrophil/lymphocyte ratio and the TIMI flow grade in patients with STEMI undergoing primary PCI

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Abstract. – OBJECTIVES: ST segment elevation myocardial infarction (STEMI) is an important cause of the morbidity and mortality in coronary artery disease. The aim of this study is to investigate the relationship between hematologic parameters and post primary PCI coronary no-reflow.

PATIENTS AND METHODS: A total of 145 consecutive STEMI patients (mean age=58.2±12.3 years) and healthy volunteer admitted within 6 hours from symptom onset were enrolled to the study in the cardiology clinics. The STEMI patients were divided into 2 groups based on the Thrombolysis In Myocardial Infarction (TIMI) flow grade. No-reflow was defined as post-PCI TIMI Flow Grade 0, 1 or 2 and angiographic success was defined as TIMI Grade 3 Flow.

RESULTS: Diabetes mellitus hypertension and smoking status were similar between groups. With respect to baseline laboratory status, fasting glucose, blood urea nitrogen, creatinine levels were not significantly different between groups. The neutrophil/lymphocyte (N/L) ratio was also significantly higher in STEMI group (7.1±4.6 vs. 2.3±1.7, $p < 0.001$). Additionally, N/L ratio was also significantly higher in No-reflow group (TIMI Flow Grade 0, 1 or 2) group (13.1±4.5 vs. 5.3±2.7, $p < 0.001$).

CONCLUSIONS: The N/L ratio, which is cheaply and easily measurable laboratory data is independently associated with post primary PCI coronary no-reflow.

Key Words:
N/L ratio, ST-segment elevation myocardial infarction, Primary percutaneous coronary intervention, No-reflow.

Introduction

Primary percutaneous coronary intervention (PCI) is a extensively received treatment modality for patients with ST segment elevation myocardial infarction (STEMI)[1]. Nevertheless, no-reflow is still a challenging major issue in the management of the patients wit STEMI undergoing primary PCI. It is well known that angiographic no-reflow is strongly relation with short and long-term morbidity and mortality in acute STEMI. The pathophysiology of no-reflow has not been fully explained and its etiology appears to be multi-factorial and very complex[2,3].

N/L ratio is the sign of balance between neutrophil and lymphocyte levels in the body and an indicator of systemic inflammation[4]. High N/L ratio have been known to be independent prognostic predictors of mortality in patients with coronary artery disease and long term mortality in patients with STEMI[5]. In the present study, we aimed to investigate the relationship between N/L ratio and the Thrombolysis In Myocardial Infarction (TIMI) flow grade in patients with STEMI undergoing primary PCI.

Patients and Methods

Study Population

A total of 145 consecutive STEMI patients (mean age = 58.2±12.3 years) and healthy volunteer admitted within 6 hours from symptom onset were enrolled to the study in the cardiology clinics. All participants were treated with primary PCI. STEMI was defined as: typical chest pain > 30 minutes with ST elevation of > 1 mm in at least two consecutive leads on the electrocardiogram or new onset left bundle branch block. The STEMI

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Table I. Baseline characteristics of patients in groups.

Variable	STEMI group (n: 145)	Normal group (n: 101)	*p* value
Age, years	58.2 ± 12.3	56 ± 7.8	0.08
Gender, Female/Male	41/104	58/43	< 0.001
Smoking, n (%)	27 (18.6)	23 (22.8)	0.42
Hypertension, n (%)	50 (34.5)	31 (30.7)	0.53
Hypercholesterolemia, n (%)	22 (15.2)	5 (4.8)	0.06
Diabetes mellitus, n (%)	28 (19.3)	23 (22.8)	0.51
Biochemical parameters			
Total cholesterol, mg/dl	192.1 ± 41.5	194.1 ± 41.3	0.71
HDL-cholesterol, mg/dl	40.5 ± 9.9	45.5 ± 13.7	0.001
LDL-cholesterol, mg/dl	130.3 ± 38.1	125.5 ± 40.7	0.34
Plasma triglycerides, mg/dl	122.7 ± 115.8	153.3 ± 69.1	0.01
Fasting glucose, mg/dL	127 ± 42.2	123.5 ± 62	0.61
Urea nitrogen, mg/dL	29.5 ± 15.1	27.6 ± 8	0.23
Creatinine, mg/dL	0.91 ± 0.51	0.86 ± 0.36	0.12

Data expressed mean ± SD

patients were divided into 2 groups based on the TIMI flow grade[6]. No-reflow was defined as post-PCI TIMI Flow Grade 0, 1 or 2 [3], and angiographic success was defined as TIMI Grade 3 Flow. Exclusion criteria included treatment with thrombolytic drugs in the previous 24 hours, cardiogenic shock on admission, active infections, previously proven systemic inflammatory disease history, known malignancy, liver disease and renal failure. Informed consent was obtained from all patients and the local Ethics Committee approved the protocol.

Coronary Angiography and PCI Procedure

All primary PCI procedures were performed using the standard femoral approach with a 6-French guiding catheter. After administration of 5,000 IU of intravenous heparin (70 U/kg) and a 600 mg loading dose of clopidogrel, direct stenting was performed whenever possible, and in the remaining cases, balloon pre-dilatation was performed. The choice of stents was left to the operator's decision. In patients who were treated with tirofiban, the agent was administrated after primary PCI procedure in the Coronary Care Unit. Patients taking fibrinolytic therapy were excluded from our study.

Laboratory Analysis

In all patients, antecubital venous blood samples for the laboratory analysis were drawn on admission in the emergency room. Common blood counting parameters stored in citrate based anticoagulated tubes were measured by *Sysmex* K-1000 auto analyzer within 5 minutes of sampling. Glucose, creatinine, blood urea nitrogen, lipid profile (total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol, triglyceride were determined by standard methods.

Statistical Analysis

Statistical analysis was performed by using the SPSS 15.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA). We used one sample Kolmogorov-Smirnov and Levene tests to determine the distribution characteristics of variables and variance homogeneity. Results are expressed as the mean±SD, median and percentages. The differences between groups were tested by chi-square, independent samples *t*-test and Mann-Whitney *U* tests. A two-sided p value of < 0.05 was considered significant.

Results

The baseline demographic, biochemical characteristics of patients in STEMI and normal groups are shown in Table I. Diabetes mellitus, hypertension and smoking status were similar between groups. With respect to baseline laboratory status, fasting glucose, BUN, creatinine levels were not significantly different between groups.

Table II. Common blood counting parameters of patients.

Variable	STEMI group (n: 145)	Normal group (n: 101)	*p* value
Hemoglobin, g/dL	13.5 ± 1.9	13.7 ± 1.8	0.43
White blood cell count, × 10^9/L	12.4 ± 3.9	8.0 ± 2.0	<0.001
Platelet count, × 10^9/L	250.5 ± 66.8	277.1 ± 61.4	0.001
Hematocrit, %	40 ± 5.6	41.6 ± 4.7	0.02
Red cell distribution width (%)	13.9 ± 1.4	13.8 ± 1.3	0.83
Red blood cell count, × 10^6/mL	4.6 ± 0.6	4.8 ± 0.5	0.03
Mean corpuscular volume, fl	87.0 ± 5.6	86.4 ± 5.9	0.42
Mean platelet volume, fl	10.3 ± 1.2	10.4 ± 0.7	0.60
Platelet distribution width, %	14.5 ± 2.8	12.4 ± 1.3	<0.001
Neutrophil/lymphocyte ratio	7.1 ± 4.6	2.3 ± 1.7	<0.001

Data expressed mean ± SD or percentage

CBC (common blood counting) parameters were showed in Table II. Hemoglobin, platelet count, MPV (mean platelet volume) and RDW (red cell distribution width) were similar between groups. With respect to white blood cell distribution, N/L ratio was also significantly higher in STEMI group (7.1±4.6 vs. 2.3±1.7, $p < 0.001$) (Table II).

Angiographic characteristics and N/L ratio in respect to TIMI flow grade were shown in Table III. N/L ratio was also significantly higher in No-reflow group (TIMI Flow Grade 0, 1 or 2) group (13.1±4.5vs. 5.3±2.7, $p < 0.001$) when compared to patients with normal TIMI flow.

Discussion

In this study, we demonstrated that preprocedural N/L ratio that measured in the first six hours from symptom onset was different in post primary PCI coronary no-reflow.

ST segment elevation myocardial infarction (STEMI) is an important cause of the morbidity and mortality in coronary artery disease[7]. The management of patients with STEMI in the earliest times after symptom onset are considerably important in both the emergency service and in-hospital period[8]. No-reflow is one of the major problems in patients with STEMI who undergoing primary PCI. Rapid restoration of infarct-related artery (IRA) flow is associated with mortality among patients with STEMI. But, no-reflow phenomena may limit the benefits of recanalization of the IRA[9]. The pathophysiology of no-reflow has not been fully explained and its etiology appears to be multi-factorial. These factors include ischemic endothelial damage, microvascular leukocytes and platelet plugging and complex interactions between leukocytes and platelets induced by the inflammatory process[10]. It is known that angiographic no-reflow is strongly correlated with morbidity and mortality in acute myocardial infarction (AMI).

Table III. Angiographic characteristics of study patients.

Variable	TIMI ≤2 (n = 35)	Flow grade 3 (n = 110)	*p* value
Infarct related artery, n (%)			
Left anterior descending coronary artery	12 (34.2)	39 (35.5)	0.69
Right coronary artery, n (%)	15 (42.9)	43 (39.1)	0.32
Circumflex coronary artery, n (%)	8 (22.9)	28 (25.4)	0.31
Number of coronary arteries narrowed, n (%)			
Single vessel	7 (20)	23 (20.9)	0.78
Multivessel	28 (80)	87 (79.1)	0.89
Neutrophil/lymphocyte ratio	13.1 ± 4.5	5.3 ± 2.7	<0.001

Data expressed mean ± SD or percentage

Thus, there is also a relationship between the recovery of left ventricular function after an AMI and the no-reflow phenomenon[11].

The N/L ratio is the sign of balance between neutrophil and lymphocyte levels in the body and an indicator of systemic inflammation[4]. N/L ratio was evaluated with numerous studies in coronary artery disease[12-14]. In our recently published study[12] we demonstrated that N/L ratio is associated with post primary PCI coronary no-reflow. Papa et al[13] showed in their report that high N/L ratio was associated with increased cardiac mortality in clinically stable patients with coronary artery disease. Duffy et al[14] evaluated the predictive role of N/L ratio in patients who undergoing PCI and they found that elevated preprocedural N/L ratio is associated with an increased risk of long-term mortality.

In the previous work, neutrophil count showed to be significantly associated with cardiovascular death, while an inverse relationship was showed between the lymphocyte count and mortality in patients with ischemic and non-ischemic left ventricular systolic dysfunction[15]. Some authors demonstrated that neutrophils release large amounts of inflammatory mediators and, because of short neutrophil half-life, neutrophilia may be associated with the acute inflammatory response to tissue injury. The neutrophils secrete the chemotactic agent leukotriene B4[16]. The association between neutrophilia and impaired microvascular perfusion may be a manifestation of neutrophil-mediated microvascular plugging[16]. Also, Ommen et al[17] showed a decrease in total and relative number of circulating lymphocytes during AMI and advanced congestive heart failure. Also in the present study, neutrophils and N/L ratio were higher in no-reflow group.

We didn't analyze any parameter of fibrinolysis in this study. This was for avoiding our study to be complicated with extensive data.

Conclusions

CBC is the most widely available laboratory data on admission in hospital. In our study, we suggest that N/L ratio, which is cheaply and easily measurable laboratory data is independently associated with post primary PCI coronary no-reflow. Our results suggest that an preprocedural N/L ratio that an inexpensive and universal available parameter can use for the risk stratification of patients with STEMI.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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