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WHITE BLOOD CELLS RATIOS IN PATIENTS WITH ACUTE CORONARY SYNDROMES IN ASSOCIATION WITH HYPERTENSION AND DIABETES MELLITUS

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ABSTRACT

Introduction. Evidence now indicates that inflammation contributes considerably to the initiation and progression of atherosclerosis and an active inflammatory processes may trigger plaque rupture and enhance the risk of coronary thrombosis leading to a clinical ischemic event. The purpose of this study was to evaluate of white blood cells ratios in patients with ACS in association with arterial hypertension and 2 type Diabetes Mellitus.

Material and Methods. In this observational cohort trial we observed of 184 patients with ACS. All patients were randomized into four groups: 1st group - 42 patients with ACS without AH or DM; 2nd group – 56 patients with ACS and previous AH; 3rd group – 42 patients with ACS and 2 type DM; and 4th group – 44 patients with ACS and AH and DM. We studied of leukocytes count and their subpopulation ratios: neutrophils to lymphocytes ratio (NLR), neutrophils to monocytes ratio (NMR), neutrophils to lymphocytes+monocytes ratio (N/LMR), lymphocytes to monocytes ratio (NMR).

Results. The mean white blood cells count was significant higher in patients with ASC, compared with control group (p<0.001). In patients with ACS the elevated NMR and NLR were observed: 15.04 ± 1.28 vs 11.09 ± 0.43 in control group (p<0.05), and 3.34 ± 0.20 vs 2.60 ± 0.06 (p<0.05), respectively. No significant differences between WBC ratios were revealed in observed patients with ACS with or without AH and/or DM.

Conclusions. ACS is characterized of raised NLR and NMR which could be indicators of poor prognosis.

Introduction. Each year, about 1.1 million patients are hospitalized with an acute coronary syndromes (ACS) event in the United States [1]. Although the overall incidence of ACS appears to be declining, the direct and indirect costs associated with treating patients with ACS and its downstream sequelae, including congestive heart failure and repeat revascularization, remain a medical and economic burden worldwide.

Evidence now indicates that inflammation contributes considerably to the initiation and progression of atherosclerosis and an active inflammatory processes may trigger plaque rupture and enhance the risk of coronary thrombosis leading to a clinical ischemic event. Due this conception over the past two decades, there has been increasing interest in discovering novel therapeutic agents for reducing residual risk among patients with ACS, including ST-segment elevation myocardial infarction (STEMI), non–ST-segment myocardial infarction (NSTEMI), and unstable angina [2].

Interest in characterizing inflammatory markers that predict clinical events have dominated clinical investigation. White blood cell (WBC) count is considered a marker of inflammation

measured on routine hemograms, and earlier studies demonstrated an association between WBC and MACE in patients with ACS. Thus, in TACTICS-TIMI 18 (Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18) trial in patients with unstable angina or NSTEMI the WBC count was associated with impaired epicardial and myocardial perfusion, more extensive coronary artery disease (CAD), and higher six-month mortality. After adjustment for traditional risk factors and other biomarkers, assessment of WBC count can be used to stratify patients across an eightfold gradation of six-month mortality risk [3]. Similarly, in the Thrombolysis in Myocardial Infarction (TIMI) 10A and 10B trials among patients with acute myocardial infarction (AMI) elevation in WBC count was associated with reduced epicardial blood flow and myocardial perfusion, thromboresistance (arteries open later and have a greater thrombus burden), and a higher incidence of new congestive heart failure and death [4].

There are some controversial data about prognostic role of WBC ratios in patients with ACS.

The purpose of this study is to evaluate of white blood cells ratios in patients with ACS in association with arterial hypertension and 2 type Diabetes Mellitus.

Material and Methods. The study was performed in accordance with the Helsinki Declaration and Good Clinical Practice Guideline. It was approved by the local ethics committee and written informed consent was obtained from all patients. In this observational cohort trial we observed of 184 patients with ACS. The diagnosis was verified by laboratory and instrumental methods according to European Society of Cardiology guidelines (2017, 2020) [5, 6]. All patients were randomized into four groups: 1st group - 42 patients with ACS without AH or DM; 2nd group – 56 patients with ACS and previous AH; 3rd group – 42 patients with ACS and 2 type DM; and 4th group – 44 patients with ACS and AH and DM. 30 apparently healthy persons were included into control group. We studied of leukocytes count and their subpopulation ratios: neutrophils to lymphocytes ratio (NLR), neutrophils to monocytes ratio (NMR), neutrophils to lymphocytes+monocytes ratio (N/LMR), lymphocytes to monocytes ratio (NMR).

Categorical variables are presented as percentages, whereas continuous variables are presented as mean (M) and standart error of mean (m) if normally distributed, or as median and interquartile range (Me [IQR]), if not. Categorical variables were compared by the χ^2 test and continuous variables by the t test or the Mann–Whitney U test. A p value of <0.05 was considered statistically significant. All tests were 2-sided. Analyses were performed with Statistica system software, version 12.0.

Results. The mean age of all observed patients with ACS was 64.6±11.9 years; 93 (50.5%) were males and 91 (49.5%) females among them (see table 1). ACS without persistent ST segment elevation was diagnosed in 44 (23.9%) cases; instead ACS with persistent ST segment elevation – in 140 (76.1%) cases. 63 (34.2%) patients were identified as current smokers.

ACS with persistent ST segment elevation more often was presented as anterior-lateral myocardial infarction with persistent ST segment elevation (STEMI) – in 70 (50.0%) cases. Other walls of left ventricle were injured in 39 (27.9%) cases – inferior wall, in 21 (15.0%) cases – anterior wall, and in 10 (7.1%) cases necrosis was localized on anterior and lateral parts of left ventricle.

The mean white blood cells count was significant higher in patients with ASC, compared with control group: 8.23 [6.50; 9.40] vs 5.49 [5.20; 5.70] (p<0.001).

In patients with ACS the elevated NMR and NLR were observed: 15.04±1.28 vs 11.09±0.43 in control group (p<0.05), and 3.34±0.20 vs 2.60±0.06 (p<0.05), respectively (table 1).

Table 1: White blood cells ratios in observed persons

Parameter	Observed persons	
	Patients with ACS, n=184	Control group, n=30
NMR	15.04±1.29*	11.09±0.43
LMR	5.76±0.58	4.39±0.12
NLR	3.34±0.20*	2.60±0.07
N/LMR	2.34±0.13	2.14±0.06

Notes: * p<0.05

No significant differences between WBC ratios were revealed in observed patients with ACS with or without AH and/or DM (table 2).

Table 2: White blood cells ratios in patients with ACS

Parameter	Patients with ACS, n=184			
	ACS, n=42	ACS+AH, n=56	ACS+DM, n=42	ACS+AH+DM, n=44
NMR	18.56±4.65	14.63±1.45	14.03±1.67	13.93±1.74
LMR	7.63±2.57	5.25±0.47	6.12±0.67	5.48±0.52
NLR	3.28±0.37	3.46±0.26	2.94±0.39	2.97±0.49
N/LMR	2.41±0.21	2.39±0.18	2.21±0.21	2.12±0.23

Notes: p>0,05

Discussion. WBC ratios is an important predictors of patients with acute or chronic diseases survival [7]. Thus, in medicine NLR is used as a marker of subclinical inflammation. In recent trial with 250 consecutive STEMI patients presenting acutely for revascularization NLR determined as predictors of short- and long-term mortality (OR = 1.05, $p = 0.011$), and both short-term (≤ 30 days) and long-term (≤ 2 years) mortality were predicted with Kaplan-Meier survival curve separation best stratified by a NLR cut off value of 7.4 [8]. In our trial the elevated NLR was observed in patients with ACS.

In last meta-analysis, with enrolment of 5 studies comprising 4343 patients to investigate the prognostic value of the LMR in patients with ACS, lower LMR was associated with higher long-term mortality/MACE in patients with ACS [9]. No difference in LMR parameters between patients with ACS and healthy persons was observed in our trial.

Patients with ACS showed of elevated NMR. Established, that Average values of NLR were significantly higher in patients with AMI in relation to patients with UA, indicating the importance of this inflammatory marker in discrimination of clinical forms of ACS. A positive correlation was established between NLR and markers of myocardial necrosis, and between NLR and CRP, indicating the importance of NLR in the assessment of the extent of the myocardial lesion and in inflammation intensity assessment in ACS [10]. Last meta-analysis of 8 studies with 9406 patients indicated that elevated pretreatment NLR was a poor prognostic marker for patients with recent ACS in predicting medium to long-term mortality/MACEs (OR 1.26, 95%CI 1.13–1.41). This analysis showed that higher pretreatment NLR value was associated with higher in-hospital mortality in ACS patients (OR 6.39, 95%CI 1.49–27.38, $p < 0.001$); and NLR value of 5.0 maybe a cut-off value for ACS risk [11].

Conclusions. ACS is characterized of raised NLR and NMR which could be indicators of poor prognosis.

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