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Retrospective evaluation of hematological parameters for the differentiation between non-st elevation myocardial infarction and unstable angina

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Abstract

Aim: In this study, we aimed to investigate the utility of hematological parameters associated with acute coronary syndrome (ACS) in the differentiation of non-ST elevation myocardial infarction (NSTEMI) from unstable angina (UA).

Material and Methods: The retrospective study included patients aged over 18 years who presented to the emergency department with a prediagnosis of ACS and were diagnosed with NSTEMI and UA between January 1, 2014 and February 28, 2018. Sociodemographic and clinical characteristics, including age, gender, and white blood cell count (WBC), platelet count (PLT), mean platelet volume (MPV), red cell distribution width (RDW), and neutrophil-to-lymphocyte ratio (NLR) were recorded for each patient.

Results: The study included a total of 1005 patients (749 NSTEMI and 256 UA). In multivariate logistic regression analysis, the mean WBC level was 1.375(1.258-1.503) times and the mean NLR was 3.631(range, 2.864-4.602) times higher in the NSTEMI group compared to the UA group($p<0.001$). In the ROC analysis, the cutoff value of NLR for the differentiationof NSTEMI from UA was 2.237, with a sensitivity of 84.1% and a specificity of 81.6%.

Discussion: WBC and NLR values can be used as inflammatory markers in the differentiation of NSTEMI from UA.

Keywords

Hematological parameters; Unstable angina; NSTEMI; Neutrophil-to-lymphocyte ratio

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Introduction

The clinical spectrum ofacute coronary syndrome (ACS) is classified into ST-elevation myocardial infarction (STEMI) and non-ST elevation ACS (NSTE-ACS) based on electrocardiography (ECG) findings. The NSTE-ACS group is further divided into non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA)[1]. A pathological correlate for ACS at the myocardial level is cardiomyocyte necrosis in patients with NSTEMI and myocardial ischemia without cell damage in patients with UA [2]. Due to the differences in their pathophysiological processes and treatment strategies, the differentiationof these two clinical conditions in the early period in the emergency department is of paramount importance.

Diagnosis, treatment, and risk management ofpatients with suspected NSTE-ACS often includes clinical evaluation, 12-lead ECG, and biomarkers. Moreover, measurement of cardiac troponin, the most important biomarker of cardiomyocyte damage, is mandatory, sincetroponin levels are often positive in NSTEMI and are often negative in UA [3-5]. Additionally, troponin is the most sensitive and tissue-specific cardiac markerand is also considered the golden-standard biochemical tool for ACS risk stratification. Nonetheless, troponin positivitymay not be detected in approximately 40-60% of patients with ACS [6].

There have been recent studies investigating the inflammatory mechanism in the ACS processand these studies have shown the efficacy of numerous hematological parameters in the diagnosis of ACS, including white blood cell count (WBC), platelet count (PLT), mean platelet volume (MPV), red cell distribution width (RDW), and neutrophil-to-lymphocyte ratio (NLR) [7-9]. However, to our knowledge, there have been no large-scale studies investigating the utility of hematological parameters in the differential diagnosis of NSTEMI and UA.

The aimedthis studywas to investigate the utility of hematological parameters, along with cardiac troponin measured at the time of admission to the emergency department in the differential diagnosis of NSTEMI and UA.

Material and Methods

Study design and setting

Ethics committee approval was obtained before starting the study (Erciyes University Ethics Committee approval date: 20.06.2018 and the Decision Number: 2018/325). The study was conducted in an emergency department, which is visited by approximately 300.000 patients a year. The retrospective study included patients aged over 18 years who presented to the emergency departmentwith a prediagnosis of ACS and were diagnosed with NSTEMI and UA between January 1, 2014, and February 28, 2018.The patients included in the study were selected from the hospital data registry system, taking into account the relevant ICD codes (chest pain R07.4, unstable angina pectoris I20.1, acute subendocardial myocardial infarction I21.4).The NSTEMI group was determined as the patients with non-ST elevation, with troponin positivity and having lesion, detected in coronary angiography. The unstable angina group, on the other hand, was composed of patients with clinical symptoms of unstable angina, with the negativity of troponin, and lesions detected in coronary angiography. Sociodemographic and clinical characteristics including age, gender, and WBC, NLR, RDW, MPV, and PLT levels were recorded for each patient.

Inclusion and exclusion criteria

All male and female patients over the age of 18 who met the diagnostic criteria for UA and NSTEMI were included in the study. Patients agedunder the age of 18 and those with a diagnosis of STEMI, patients with missing data, patients with a normal coronary artery in coronary angiography, patients with a history of hematological disease (anemia, thrombocytopenia, bicytopenia, pancytopenia, immune thrombocytopenic purpura, thrombotic thrombocytopenic purpura, leukemia, lymphoma etc.),and patients with evidence of infection (those who were started antibiotic treatment during hospitalization due to infection, such as pneumonia, urinary tract, etc., or who were asked for an infectious diseases consultation during hospitalization)were excluded from the study (Figure 1).

Statistical analysis

Data were analyzed using SPSS for Windows version 25.0 (Armonk, NY: IBM Corp.). Normal distribution of continuous variables was assessed using the Lilliefors-corrected Kolmogorov-Smirnov test. Continuous variables (age, WBC, NLR, RDW, MPV,and PLT) were compared between the two groups (NSTEMI and UA) using the Mann-Whitney U Test with Monte Carlo Simulation. Categorical variables (treatment method and gender) were compared between the two groups usingPearson's Chi-Squared test, followed byFisher's exact test for gender and Monte Carlosimulation for treatment method.Subsequently,column proportions were compared and expressed according to the Benjamini-Hochberg adjustedp-value.Multivariate Logistic Regression (method=enter)was used to determine the cause-effect relationship between the diagnosis (NSTEMI and UA) and continuousvariables (age, WBC, NLR, RDW, MPV,and PLT)and categorical variables (treatment method). Continuous variables were expressed as medians (minimum/maximum), and categorical variables were expressed as frequencies (n). A p-value <0.05 was considered significant.

Results

The study included 1005 patients (749 NSTEMI and 256 UA). Table 1 presents the demographic data of the patients. The mean WBC level in all patients was 9.5 (range, 4.0-27.6) x103/uL, mean NLR was 2.9 (range, 0.5-42.4), mean RDW was 42.1 (range, 31.8-69.2) fL, mean MPV was 10.2 (range, 7.7-14.0) fL, and mean PLT was 240 (range, 54-736) x 103/uL.

A significant difference was found between the two groups with regard to WBC, PLT, RDW, and NLR values ($p<0.05$), whereas no significant difference was found with regard to MPV values ($p= 0.123$) (Table 1).

The mean WBC level was 1.375(1.258-1.503) times and the mean NLR was 3.631(range, 2.864-4.602) times higher in the NSTEMI group compared to the UA group (Figure 2).

The multivariate logistic regression model indicated that both NLR and WBC predicted NSTEMI and UA with a sensitivity of 92.8% and 66.8%, respectively, and also had an overall sensitivity of 86.2% (model, $p=0.001$), which suggests that both NLR and WBC were significant independent predictors of NSTEMI (Table 2).

Table 1. Numerical data of patients and analysis of quantitative and categorical variables with respect to NSTEMI and UA diagnosis

	NSTEMI (n=749)	UA (n=256)	Total (N=1005)	P
	Median (IQR)	Median (IQR)	Median (IQR)	
Age	66 (18)	62 (15)	64 (18)	<0.001 [1]
	n (%)	n (%)	n (%)	
Gender (Female)	244 (32.6)	75 (29.3)	319 (31.7)	0.351 [2]
	Median (IQR)	Median (IQR)	Median (IQR)	
WBC (10^3/uL)	10.435 (3.98)	7.86 (2.63)	9.545 (4.17)	<0.001 [1]
RDW (fL)	42.4 (5.2)	41.35 (4.66)	42.1 (5.2)	0.001 [1]
MPV (fL)	10.2 (1.3)	10.15 (1.3)	10.2 (1.2)	0.123 [1]
PLT (10^3/uL)	242 (92)	234 (70)	240 (87)	0.029 [1]
NLR	3.61 (3.27)	1.7 (0.75)	2.91 (2.75)	<0.001 [1]
	n (%)	n (%)	n (%)	
NLR				
<2.237	119 (36.3) (15.9)	209 (63.7) [npv] (81.6) [sp]	328 (32.6)	<0.001 [3]
>2.237	630 (93.1) [ppv] (84.1) [ss]	47 (6.9) (18.4)	677 (67.4)	AUC (SE): 0.894 (0.011)

[1] Mann-Whitney U Test (Monte Carlo), [2] Pearson Chi-Square Test (Exact), [3] Roc Curve Analysis (Youden index J - Honley&Mc Nell), AUC: Area under the ROC curve,ss Sensitivity, sp Specificity, ppvPositive predictive value, npv negative predictive value, IQR: Interquartile Range

Table 2. Multiple Logistic Regression Analysis Findings for Age, Treatment Type, WBC, NLR, RDW, PLT Variables with NSTEMI and UA Dependent Variables

	B	S.E.	P	Odss Ratio	95% C.I.forOdss Ratio	
					Lower	Upper
Age	-0,0005	0,0085	0,954	1,000	0,983	1,016
WBC	-0,3174	0,0454	<0.001	1,375	1,258	1,503
NLR	-1,2854	0,1210	<0.001	3,631	2,864	4,602
RDW	-0,0439	0,0243	0,089	0,959	0,915	1,006
PLT	0,0003	0,0015	0,859	1,000	0,997	1,003
Constant	7,4518	1,1893	<0.001			

Dependent Variable: Diagnosis Predicted; NSTEMI = 92.8, UA=66.8 Overall: 86.2
P Model<0,001

Multiple Logistic Regression (Method = Enter), C.I.:Confidence interval B: regression coefficients SE: Standard error

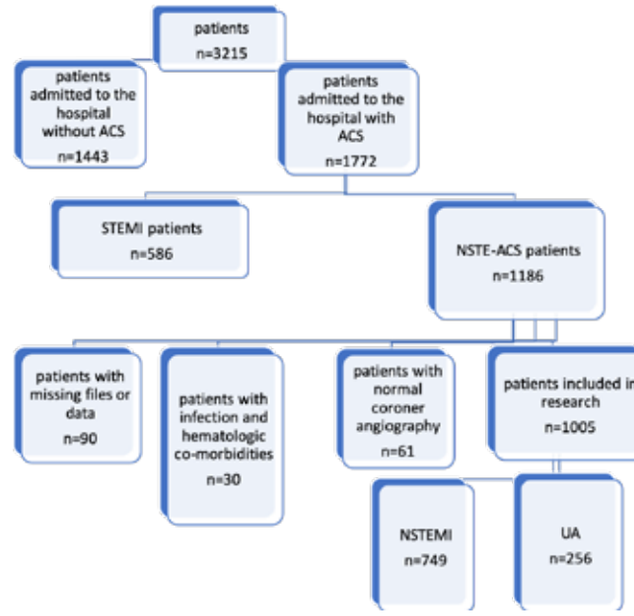

Figure 1. Flowchart of the study

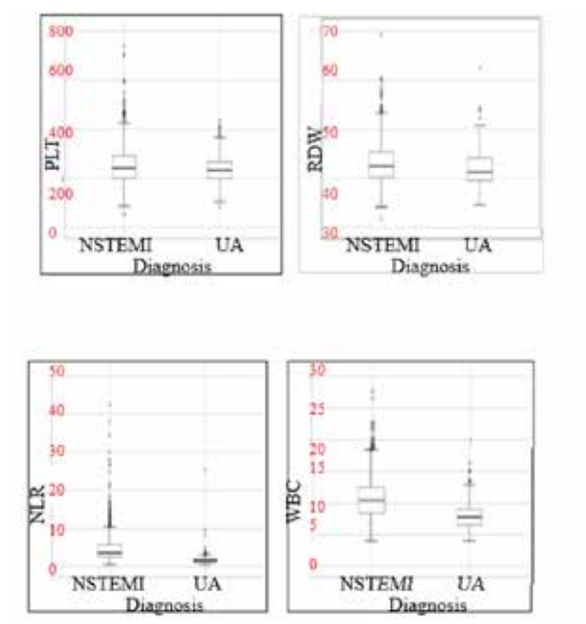

Figure 2. Comparison of PLT, WBC, RDW, NLR between diagnosis NSTEMI and UA

Discussion

Troponin is the most important biomarker in patients admitted tothe emergency department with a prediagnosis of ACS[10]. Our findings indicated that hematological parameters could be beneficial when used togetherwith the troponin value in the differential diagnosis of NSTE-ACS in the emergency department. To our knowledge, there have been no studies evaluating the utility of hematological parameters in the differential diagnosis of NSTE-ACS.

Studies have shown that inflammation plays akey role in the pathogenesis and progression of atherosclerosis by participating in many processes such as endothelial damage and plaque formation[11,12]. In the literature, proinflammatory functional responses of neutrophils have been shown to be associated with cardiovascular risk factors in atherosclerosis, andthe role of neutrophils has been shown in both acute and chronic vascular damage [13,14]. Lymphocytes constitutea heterogeneous subgroup of WBC, along with pro-atherogenic and pro-inflammatory cells, and also may influence immune regulatory pathways [15]. NLR has recently emerged as a novel potential biomarker in the detection of individuals at risk for new cardiovascular events. Aprevious reviewindicated that NLR is the best predictor of death and major adverse cardiovascular events in patients with ACS[16].Another studyreported that the NLR value, assessed on admission, is a strong and independent predictor of cardiovascular mortality in NSTEMI and UA patients [17]. Tahto et al. evaluated the inflammatory parameters of 50 acute myocardial infarction (AMI) and 50 UA patients and reportedthat the mean NLR value was significantlyhigher in the AMI group compared to the UA group (7.22 vs.4.62) [18]. In our study, the mean NLR was 3.6 in the NSTEMI group as opposed to 1.7 in the UA group. Moreover, the mean WBC level was 1.375(1.258-1.503) times and the mean NLR was 3.631(range, 2.864-4.602) times higher in the NSTEMI group compared to the UA group. Accordingly, the higher levels of WBC and NLR

in our NSTEMI group compared to the UA group support the literature findings.In addition to these findings, multivariate logistic regression analysisrevealed that WBC and NLR were strong predictors in the differentiation between NSTEMI and UA.

Limitations

The fact that our study was retrospective and conducted as a review of the data recording system caused difficulties in the classification of patients and in determining the missing parts in the history. Again, it is possible that we have no idea about the way and duration of taking the hemogram panel, determining other factors that will cause variations in the parameters. Another problem is that the approach of the cardiologist in determining the treatment method is uncertain. Another limitation is that we cannot include patients with unstable angina who were discharged despite admitting to the emergency department and could not be detected.

Conclusion

Our study is the first step towards using hematological parameters in the differential diagnosis of NSTE-ACS. WBC and NLR can be safely used as independent markers in the differential diagnosis of NSTEMI and UA. Further multi-center and comprehensive studies are needed to substantiate our findings.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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