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Original article

The Relationship Between Some Complete Blood Count Parameters and Myocardial Perfusion: *A Scintigraphic Approach*

Semra Ozdemir, Ahmet Barutcu[1], Emine Gazi[1], Yusuf Ziya Tan, Hakan Turkon[2]

Departments of Nuclear Medicine, [1]Cardiology and [2]Biochemistry, Canakkale Onsekiz Mart University, Çanakkale, Turkey

Abstract

Recent studies have shown that there is a relationship between some inflammatory and biochemical markers derived from complete blood count (CBC) such as neutrophil/lymphocyte (N/L) ratio, platelet/lymphocyte (P/L) ratio, platelet distribution width (PDW), red blood cell distribution width (RDW), and coronary artery disease (CAD). The aim of this study was to determine N/L ratio, P/L ratio, PDW values, and RDW values, which are associated with myocardial perfusion in patients diagnosed with CAD. This study included 262 patients (149 with myocardial ischemia/infarction and 113 with normal myocardial perfusion) undergoing myocardial perfusion scintigraphy (MPS) with CBC within 90 days of MPS. Myocardial perfusion parameters such as summed stress score and summed difference score (SDS) were compared with N/L ratio, P/L ratio, PDW values, and RDW values. Neutrophil counts and N/L ratios were significantly higher in patients diagnosed with myocardial ischemia and/or infarct. However, there was no statistically significant relationship between myocardial perfusion abnormalities and P/L ratio, PDW values, and RDW values. This study showed that N/L ratio is related to myocardial ischemia/infarction and correlated to left ventricular ejection fraction (LVEF).

Keywords: Ejection fraction, myocardial perfusion scintigraphy, nutrophil/lymphocyte ratio

Introduction

Coronary artery disease (CAD) is still the most common cause of deaths in the world, which is characterized by atherosclerosis in the epicardial coronary arteries. The atherosclerotic plaque progressively narrows the coronary artery lumen and impairs antegrade myocardial blood flow. Although atherosclerosis is a multifactorial process, inflammatory and immunological factors are considered to play critical roles.[1-3] Recently, there have been many studies investigating the role of inflammatory and biochemical markers derived from complete blood count (CBC) in CAD.[4-7] Although an abundance of studies report strong relationships between neutrophil/lymphocyte (N/L) ratio, platelet/lymphocyte (P/L) ratio, platelet distribution width (PDW) values, red blood cell distribution width (RDW) values, and anatomical CAD, there are few studies evaluating the relationship between N/L ratio, P/L ratio, PDW values, RDW values, and myocardial perfusion. Therefore, this study aimed to investigate the relationship between some inflammatory markers derived from CBC such as N/L ratio, P/L ratio, PDW, RDW, and myocardial perfusion in patients diagnosed with CAD.

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Patients and Methods

Patient population and study protocol

Two hundred and sixty two patients undergoing myocardial perfusion gated single-photon emission computerized tomography (SPECT) scintigraphy were selected among patients who had CBC within 90 days of MPS. There were 145 males and 117 females, ranging from 23 years to 86 years of age (60.3 ± 12.5). The patients were divided into two groups in accordance with MPS results: Group 1: Comprised those who had ischemia and/or infarction positive MPS results (n = 149, 101 males, and 48 females); Group 2 comprised those

Address for correspondence:
Dr. Semra Ozdemir, Department of Nuclear Medicine, Faculty of Medicine, Canakkale Onsekiz Mart University, Çanakkale - 17100, Turkey.
E-mail: semozdemir@yahoo.com

who had normal MPS results (n = 113, 44 males, and 69 females).

All scintigraphic studies were reprocessed. We reviewed the records of the patients' histories, standard 12 lead electrocardiography (ECG) data, and gated myocardial perfusion SPECT image findings. The biochemical values, demographics of all patients, and risk factors for CAD were noted. Written informed consent was obtained from all patients for the scintigraphic study.

Myocardial perfusion gated SPECT imaging

A same-day rest-stress Tc-99m sestamibi gated SPECT myocardial perfusion imaging protocol was performed. Gated SPECT imaging was acquired in the supine position using the double-head gamma camera equipped with a high-resolution low-energy collimator (Infinia, General Electric Medical Systems, Minnesota, USA), which uses 64 × 64 matrix and 30 projections (rest: 25 s, stress: 20 s). For ECG-gated study, camera acquisition was triggered to R-wave (8 frames collected per R-R interval). The acceptance window for the R-R interval was set to 20%. The SPECT images were analyzed visually and quantitatively by two nuclear medicine specialists. The quality controls of acquisition were performed via sinograms and gating count curves. The images with motion artifacts and low image quality were excluded from the study.

Summed stress score (SSS) and summed rest score (SRS) were calculated automatically in accordance with the conventional 17-segment model of Quantitative Perfusion SPECT (QPS) software (Los Angeles, California, the United States). The SDS, indicating the extent of reversible perfusion defects, was obtained by calculating the difference between SSS and SRS. A normal sestamibi database (Cedars-Sinai Medical Center of normal limits, Los Angeles, California, the United States) was used by the QPS software for perfusion score analysis. The SSS is classified as follows: <4 = normal; 4-8 = mildly abnormal; 9-13 = moderately abnormal; and >13 = severely abnormal. SDS smaller than 2 (<2) was considered as no ischemia; SDS of 2-4 as mild ischemia; SDS of 5-8 as moderate ischemia; and SDS of > 8 as severe ischemia.

The global summed motion score (SMS), global summed thickening score (STS), and left ventricular ejection fractions (LVEF) were obtained from stress studies by using the automated Quantitative Gated SPECT (QGS) program (Los Angeles, California, the United States). For the quantitative scoring of myocardial function, the 17-segment model of the left ventricle was used for SMS (0: normal, 1: mild hypokinesis, 2: moderate hypokinesis, 3: severe hypokinesis, 4: akinesis, and 5: dyskinesis) and STS (0: normal, 1: mildly impaired, 2: moderately to severely impaired, and 3: no thickening).

Biochemical measurements

CBC values were analyzed retrospectively on blood samples taken from vein puncture during admission to the cardiology department. The hemogram parameters were determined with the Beckman Coulter LH 780 (Beckman Coulter Ireland Inc. Mervue, Galway, Ireland). The white blood cell (WBC), hemoglobin, hematocrit, platelet, neutrophil, lymphocyte, RDW, and PDW count were recorded and the N/L and P/L ratios were calculated from these parameters. Patients with elevated WBC count (>11,000/mL), neutrophilia (>70%), and any inflammatory, infective, or malignant diseases were excluded from the study.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences version 19.0 computer program (USA). Continuous data were expressed as mean ± SD and categorical data were expressed as percentage. Mean values were tested for significance using test for paired samples. After analyzing the normality, Student's t-test and Mann-Whitney U test were used to test the differences in continuous variables between groups. Pearson's Chi-square tests were also used to compare the categorical variables between these two groups. Spearman correlation analysis was used to determine the relationship between N/L ratio with stress and motion parameters. Except for multiple comparisons, $P < 0.05$ was regarded as statistically significant in all of the analyses.

Results

There were 149 patients with abnormal MPS results (Group 1) and 113 patients with normal MPS results (Group 2) in the current study. The clinical characteristics of patients are summarized in Table 1. There were no differences between these two groups in terms of clinical characteristics such as age, body mass index (BMI), hypertension, diabetes mellitus, and family history of CAD. The (percentage of male patients) rate of male/female was higher in Group 1 compared to Group 2 ($P < 0.001$), [Table 1]. Smoking was more prevalent among Group 1 compared to Group 2 ($P = 0.01$). In addition, there was significantly higher hyperlipidemia in Group 1 ($P < 0.001$).

When the electrocardiographic parameters were compared, a statistically significant difference was found only in the QRS parameters ($P < 0.001$). The differences between these two groups in terms of heart rate, QT, and PR interval parameters were not statistically significant [Table 1].

The quantitative myocardial perfusion gated SPECT parameters are presented in Table 1. When the

quantitative stress summed score (SSS), summed difference score (SDS), stress motion score (SMS), and stress thickening score (STS) values are compared with each other, higher values that are statically significant stand out in Group 1. Furthermore, it was noted that the ejection fraction (EF) values in Group 1 were statistically lower ($P < 0.001$). While the mean values of EF were 68.04% in Group 2, they were 52.02% in Group 1 [Table 1].

The results of statistical analysis of inflammatory markers derived from CBC between the two groups are given in Table 2. There were no significant differences between the two groups regarding WBC, hemoglobin, hematocrit, platelet, lymphocyte, RDW values, PDW values, and P/L ratios. However, as shown in Table 2, neutrophil counts and N/L ratios were significantly higher in Group 1. Moreover, a significant correlation was found between N/L ratio and SMS, STS, and EF (which were *r*: 0.147, *P*: 0.018: *r*: 0.157, *P*: 0.011: and *r*:-0.208, *P*: 0.001, respectively) [Table 3].

Discussion

Atherosclerosis is a widespread health problem that can cause serious clinical consequences such as CAD. Recent studies have focused on inflammation, which has an important role in the pathogenesis of atherosclerosis.[8-10] Hence, we evaluated the relationship between N/L ratio, P/L ratio, PDW values, and RDW values, and myocardial perfusion parameters in patients diagnosed with CAD using myocardial perfusion scintigraphy (MPS). Our study results demonstrated that only the N/L ratio significantly increased in patients with myocardial ischemia and/or infarct and positively correlated with SMS and STS scores.

Previous studies have also reported that the ratio of P/L, PDW values, and RDW values are related to the severity of acute CAD. Temiz *et al*. showed that P/L ratio is an independent predictor factor of cardiovascular mortality.[11] Also, Kurtul *et al*. noticed similar results in patients with acute coronary syndrome.[12] Although platelets play an important role in pathogenesis of acute coronary events, our results showed that P/L ratio was not correlated to chronic coronary events. Although the underlying pathophysiology is unknown, a relationship between RDW and CAD has been reported in the literature.[13,14] Osadnik *et al*. claimed that higher RDW is an independent predictor of mortality in patients with stable CAD. It has been reported that higher values of RDW may be associated with adverse outcomes in patients with both acute and chronic CAD.[15] Wang *et al*. reported that a high RDW may be associated with the severity and instability of acute myocardial infarction.[16] Additionally, in our study, the RDW values were higher

Table 1: Shows some demographic and clinical parameters such as age, gender, comorbidities, and myocardial perfusion gated imaging findings in the presented patients

Clinical characteristics	Patients cohort (*n*: 262)		
	Group 1 (*n*=149)	Group 2 (*n*=113)	*P*
The mean age (y)	60.84±13.74	56.75±10.89	0.086
Gender (male) (*n*, %)	101 (67.8)	44 (38.9)	<0.001
BMI (kg/m^2)	28.14±4.80	29.16±4.75	0.070
Comorbidities (%)			
Hypertension	65.8	62.8	0.623
Diabetes mellitus	38.9	31	0.184
Hyperlipidemia	51.7	28.3	<0.001
Smoking	36.9	22	0.010
Family history of CAD	45	46	
ECG			
QRS interval (ms±SD)	98.32±14.91	90.63±8.85	<0.001
QTc (corrected) (ms±SD)	418.84±21.51	415.64±20.50	0.253
PR interval (ms±SD)	154.91±42.20	151.02±21.60	0.807
Heart rate (bpm)	79.41±13.29	80.99±14.57	0.437
Myocardial perfusion imaging			
Stress EF (%)	52.02±12.89	68.04±6.71	<0.001
SSS	12.17±6.82	0.81±1.16	<0.001
SDS	5.13±3.27	0.50±0.74	<0.001
SMS	10.11±10.85	0.94±1.57	<0.001
STS	7.28±7.69	0.26±0.83	<0.001

Group 1: Patients with abnormal MPS results; Group 2: Patients with normal MPS results; CAD: Coronary artery disease; EF: Ejection fraction; SSS: Summed stress score; SDS: Summed difference score; SMS: Summed motion score; STS: Summed thickening score

Table 2: Laboratory findings of patients

Variable	Group 1	Group 2	*P**
WBC count (10^3/mm^3)	7.74±1.67	7.46±1.64	0.117
Hemoglobin (g/dL)	13.29±1.65	13.06±1.50	0.066
Hematocrit (%)	40.57±5.04	39.91±4.29	0.068
RDW (%)	14.51±1.52	14.28±1.62	0.076
PDW	16.81±0.60	16.58±0.51	0.120
Platelet count (10^3/mm^3)	239.54±62.40	251.57±67.06	0.168
Neutrophil count (10^3/mm^3)	4.78±1.26	4.33±1.37	0.010
Lymphocyte count (10^3/mm^3)	2.16±0.66	2.21±0.77	0.957
N/L ratio	2.49±1.49	2.16±1.03	0.031
P/L ratio	120.24±51.92	126.03±56.69	0.487

WBC: White blood cell; RDW: RBC distribution width; PDW: Platelet distribution width; N/L: Neutrophil/lymphocyte ratio; P/L: Platelet/lymphocyte ratio. *: Significant Pearson's Chi-square test

Table 3: Spearman's correlation coefficients of N/L ratio and gated myocardial perfusion SPECT parameters

	rho	*P*
SSS	0.115	0.063
SDS	0.108	0.080
SMS	0.147	0.018
STS	0.157	0.011
EF	0.208	0.001

SSS: Summed stress score; SDS: Summed difference score; SMS: Summed motion score; STS: Summed thickening score; EF: Ejection fraction

in patients with myocardial ischemia and/or infarction than in patients with normal myocardial perfusion; however, the difference was not statistically significant. The results of a study conducted by De Luca *et al*. are consistent with the results of our study. De Luca *et al*. have concluded that the combined information on mean platelet volume (MPV) and PDW is not related to the extent of CAD.[17] Thus, both MPV and PDW cannot be considered as risk factors for CAD.

In many studies, there is a correlation between N/L ratio and the progression of atherosclerosis in coronary arteries.[18-20] However, most of the studies designed to evaluate this subject are carried out in acute cardiac events. It is now known that there is a strong neutrophilic response in the acute myocardial ischemia and infarction. Recent studies indicate that high N/L ratio may be associated with poor adaptive mechanisms in myocardial tissue.[21] In addition, both neutrophilia and lymphopenia indicate a high inflammatory process and inflammation is an important factor for myocardial damage.[22] On the other hand, a limited number of studies have presented a relationship between N/L ratio and chronically impaired myocardial perfusion. For example, Brent *et al*. demonstrated a strong relationship between N/L ratio and myocardial perfusion. They showed this relationship in patients with known CAD or suspected of CAD using cardiac positron emission tomography (PET) imaging.[23] Some studies reported that lymphopenia and low CD4 count are related to systolic dysfunction and high myocardial mass destruction because of the lymphocyte apoptosis and proinflammatory cytokines.[24] Additionally, the high N/L ratio negatively correlated with EF and is an independent predictor of left ventricular systolic dysfunction (LVSD) in stable multivessel CADs.[25] Our results also showed that the elevated neutrophil and depressed lymphocytes are related to chronically myocardial ischemia and/or infarction. Furthermore, our results showed that high N/L ratio is related to poor wall motion and thickening scores and low EF. These findings suggest that high inflammatory response may lead to severe tissue damages in patients diagnosed with CAD. On the other hand, although there is no statically significant relationship between SSS and SDS scores and N/L ratio, some values have been obtained that are close to significance levels. We think that these significance levels can be reached in future studies by increasing the number of patients to be included in the study.

Conclusion

In conclusion, we have found that patients diagnosed with ischemia and/or infarct in SPECT analysis have higher N/L ratio, where N/L ratio is correlated to SMS and STS scores and low EF values. Our results are consistent with the opinion suggesting that high N/L ratio may be a predictor of severe CAD and myocardial damage.

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