The Aging Male

ISSN: 1368-5538 (Print) 1473-0790 (Online) Journal homepage: https://www.tandfonline.com/loi/itam20

Complete blood count parameters in peripheral arterial disease

Yusuf Velioglu & Ahmet Yuksel

To cite this article: Yusuf Velioglu & Ahmet Yuksel (2019) Complete blood count parameters in peripheral arterial disease, The Aging Male, 22:3, 187-191, DOI: 10.1080/13685538.2019.1588873

To link to this article: https://doi.org/10.1080/13685538.2019.1588873

Published online: 29 Mar 2019.

THE AGING MALE
2019, VOL. 22, NO. 3, 187–191
https://doi.org/10.1080/13685538.2019.1588873

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Complete blood count parameters in peripheral arterial disease

Yusuf Velioglu and Ahmet Yuksel

Faculty of Medicine, Department of Cardiovascular Surgery, Abant Izzet Baysal University, Bolu, Turkey

ABSTRACT

Objective: To determine whether complete blood count parameters could be used as the biomarkers of inflammation in patients with in peripheral arterial disease.

Methods: Seventy-five patients with peripheral arterial disease (study group) and 75 healthy subjects (control group) were included in this retrospective study. Their baseline clinical characteristics and laboratory data were recorded and compared. Data were compared using univariate tests including independent samples *t*-test, Mann–Whitney U-test and chi-square test. Moreover, multivariate logistic regression analysis was also conducted to determine independent predictors of peripheral arterial disease.

Results: The groups were statistically similar with regards to baseline clinical and demographic features. The values of C-reactive protein, white blood cell and neutrophil-to-lymphocyte ratio values were found to be statistically significantly higher in study group versus control group, but none of them were considered as an independent predictor of peripheral arterial disease according to multivariate logistic regression analysis. Only mean platelet volume was demonstrated to be a statistically significant predictor of peripheral arterial disease.

Conclusion: Our study deduced that mean platelet volume was an independent predictor of peripheral arterial disease, and could be used as a marker of inflammation in patients with peripheral arterial disease.

ARTICLE HISTORY
Received 10 January 2019
Revised 22 February 2019
Accepted 25 February 2019
Published online 15 March 2019

KEYWORDS
Mean platelet volume; complete blood count; hemogram; peripheral arterial disease

Introduction

Peripheral arterial disease (PAD) is an atherosclerotic disease that causes significant cardiovascular morbidity and mortality, especially observed more frequent in advanced ages. Patients with PAD may be presented as asymptomatic, or symptomatic with intermittent claudication or critical limb ischemia in the course of the disease [1]. Atherosclerotic risk factors play an important role in the development and progression of PAD. Atherosclerosis is a progressive clinical entity that begins in childhood, progresses asymptomatically during adulthood and is ultimately manifested itself by some clinical conditions. In this process, inflammation is the most important pathophysiological factor in the occurrence and development of atherosclerosis. Various growth factors, cytokines and adhesion molecules are responsible for the inflammation [2].

Low-grade inflammation or subclinical inflammation is identified as the clinical conditions characterized by slightly elevated levels of acute phase reactants and proinflammatory proteins and increased immune cell count in the blood of healthy individuals without any sign or symptom of disease [3,4]. Systemic inflammation may be detected using various biochemical and hematological assays. Recent studies have been focused on simple, inexpensive and promising parameters of complete blood count (CBC), which may provide important prognostic and diagnostic information about the diseases associated with chronic low-grade inflammation. Hereby, nowadays CBC parameters are generally used as inflammatory markers and prognostic predictors in a broad spectrum of disease. Among these parameters, red cell distribution width (RDW), mean platelet volume (MPV), white blood cell (WBC) and neutrophil-to-lymphocyte ratio (NLR) are the most common examined examples of noninvasive biomarkers in order to evaluate the status of disease in many different cardiovascular diseases. Although these CBC parameters were frequently studied in various cardiovascular diseases, their role in PAD could not well described due to the fact that the studies investigating CBC parameters in patients with PAD are sparse in the existing literature. We therefore designed this study to investigate whether RDW, WBC, MPV, NLR

CONTACT Yusuf Velioglu yusufvelioglu@gmail.com Faculty of Medicine, Department of Cardiovascular Surgery, Abant Izzet Baysal University, Bolu, Turkey

and other CBC parameters could be used as the biomarkers of inflammation in patients with PAD.

Methods

Ethical declaration

The current study was approved by the institutional review board (approval date: December 13, 2018 and decision number 2018/254). The study was conducted in accordance with the principles of Declaration of Helsinki. All relevant guidelines and regulations were completely complied.

Study population and design

This was a retrospective cohort study and conducted in the cardiovascular surgery department of our hospital. Seventy-five patients with PAD and 75 healthy subjects who admitted to the outpatients clinics of our hospital for a routine checkup were enrolled to this study and divided into two groups as PAD and control groups. The clinical and demographic features and laboratory data of the participants were obtained from the computerized medical database of our hospital, and all recorded for analysis. The recorded data were compared statistically between study and control groups. The recorded and compared clinical and demographic data were age, gender, body mass index, systolic and diastolic blood pressures, smoking habit, and comorbid diseases including obesity, diabetes mellitus and hyperlipidemia, whereas the laboratory data included CBC parameters such as RDW, WBC, MPV, NLR, hemoglobin (HGB), hematocrit (HCT), platelet count (PLT), mean corpuscular volume (MCV), neutrophil (NEU), lymphocyte (LYM), platelet distribution width (PDW), plateletcrit (PCT) and platelet-to-lymphocyte ratio (PLR) as well as C-reactive protein (CRP).

Patients with lower extremity PAD were admitted to our outpatient clinic with the symptoms of intermittent claudication or critical limb ischemia between May 2018 and August 2018. These patients with PAD were initially diagnosed with resting ankle brachial index (ABI) measurement. After a 5–10 min rest, in supine position ABI was measured with a blood pressure cuff placed just above the ankle. Systolic blood pressure (SBP) was measured by a Doppler probe on the posterior tibial or dorsal pedis artery of each foot and on the brachial artery of each arm. ABI of each leg was calculated by dividing the highest ankle SBP by the highest arm SBP. A measured resting ABI value <0.9 was abnormal and accepted as the initial diagnostic criterion of PAD, then all patients with ABI value <0.9 were confirmed with radiological imaging methods such as duplex ultrasound, computed tomography angiography, magnetic resonance angiography or invasive angiography.

Participants under 18 and over 80 years, participants with an ABI greater than 1.4, patients with chronic heart, lung, liver or kidney failure, chronic inflammatory disease, hematological disease, active infection, and primary immunodeficiency were excluded from this study.

Blood sample analyses

Peripheral venous blood samples were taken from all participants and placed into sterile standard tubes containing a constant amount of anticoagulant. In order to obtain the values of hemogram parameters, all samples were analyzed in an automatic analyzer of LH 780 model of Beckman Coulter device (Beckman Coulter In.; Bre CA) within one hour after the blood samples were taken. Original kits of the manufacturer were utilized in laboratory tests.

Statistical analyses

All statistical analyses were performed using the Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, Illinois, USA). For the analyses of normally distributed continuous variables, independent samples *t*-test was used. Nonparametric Mann–Whitney U-test was used for non-normal data. Categorical variables were analyzed using chi-square tests. In addition to univariate tests, logistic regression analysis was conducted to determine independent predictors of PAD after adjusting for other variables. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. A p values of less than .05 was accepted as statistically significant.

Results

Both groups were similar with regards to age and gender. Also in terms of the other analyzed clinical and demographic features, both groups were similar and there were no statistically significant differences between the study and control groups (All p values $>.05$).

When laboratory data were considered, it was observed that mean CRP value was statistically higher in PAD group than control group (15.77 ± 25.40 in PAD group and 5.84 ± 4.81 in control group, $p = .008$).

Table 1. Clinical and demographic features, and laboratory data of the groups.

Variables (units)	Control group ($n = 75$)	PAD group ($n = 75$)	p value
Gender (n, %)			
Male	60 (80.0%)	51 (68.0%)	.094
Female	15 (20.0%)	24 (32.0%)	
Age (years)	58.37 ± 9.47	58.48 ± 7.91	.795
BMI (kg/m^2)	27.87 ± 3.93	27.55 ± 3.61	.597
Obesity (n, %)	19 (25.3%)	15 (20.0%)	.435
DM (n, %)	13 (17.3%)	22 (29.3%)	.082
HL (n, %)	17 (22.7%)	21 (28.0%)	.453
Smoking (n, %)	23 (30.7%)	26 (34.7%)	.601
SBP (mmHg)	122.3 ± 17.04	125.91 ± 17.03	.269
DBP (mmHg)	74.08 ± 11.07	74.25 ± 11.79	.941
CRP (mg/dL)	5.84 ± 4.81	15.77 ± 25.40	**.008**
HGB (g/dL)	13.49 ± 1.98	13.48 ± 2.00	.967
HCT (%)	40.81 ± 5.88	40.45 ± 5.89	.709
WBC ($\times$ 10^9/L)	9.56 ± 3.81	10.89 ± 4.32	**.042**
RDW (%)	15.88 ± 1.65	16.39 ± 2.63	.254
MCV (fL)	89.40 ± 5.30	89.13 ± 5.63	.709
MPV (fL)	15.88 ± 1.65	16.39 ± 2.63	.177
NEU ($\times$ 10^9/L)	7.56 ± 4.73	8.61 ± 4.56	.091
LYM ($\times$ 10^9/L)	1.29 ± 0.60	1.24 ± 0.76	.225
PLT ($\times$ 10^9/L)	15.88 ± 1.65	16.39 ± 2.63	.927
PCT (%)	232.84 ± 83.32	226.95 ± 66.00	.943
PDW (%)	17.97 ± 1.32	18.06 ± 1.34	.703
NLR	6.81 ± 6.17	9.80 ± 9.87	**.034**
PLR	226.13 ± 158.92	270.62 ± 212.31	.263

BMI: body mass index; CRP: C-reactive protein; DBP: diastolic blood pressure; DM: diabetes mellitus; HCT: hematocrit; HGB: hemoglobin; HL: hyperlipidemia; LYM: lymphocyte; MCV: mean corpuscular volume; MPV: mean platelet volume; NEU: neutrophil; NLR: neutrophil-to-lymphocyte ratio; PAD; peripheral arterial disease; PCT: plateletcrit; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; PLT: platelet; RDW: red cell distribution width; SBP: systolic blood pressure; WBC: white blood cell.
Data were expressed as mean ± standard deviation for continuous variables or n (%) for categorical variables.
BMI, HGB, HCT, MCV variables were compared using independent samples t-test.
Mann Whitney U test was used for the other variables.
Categorical variables were reported as frequency (percent) and compared using chi square tests.
Bold values indicate $p < 0.05$.

Among CBC parameters, mean WBC and NLR values were found to be statistically significantly higher in PAD group versus control group (10.89 ± 4.32 vs. 9.56 ± 3.81, $p = .042$ for WBC, and 9.80 ± 9.87 vs 6.81 ± 6.17, $p = .034$ for NLR). The other studied CBC parameters were found to be statistically similar between the groups (All p values>.05). General clinical characteristics and laboratory data of the study and control groups were presented in Table 1.

In order to assess the independent predictors of PAD after adjusting for other variables logistic regression analysis was used (Table 2). According to the multivariate logistic regression analysis; elevated MPV was a statistically significant predictor of PAD, that was the risk of PAD increased by %24 with one unit increase in the patients' MPV (OR = 1.240; 95% CI: 1.001–1.538; $p = .049$) when other variables were controlled. However, the univariate analysis did not relieve any significant differences between the cases and controls for MPV.

Table 2. Independent predictors of peripheral arterial disease by logistic regression analysis.

Variables	p value*	Odds ratio (95% CI)
Gender (Male)	.139	0.544 (0.243, 1.219)
Age	.965	1.001 (0.959, 1.045)
DM	.086	2.077 (0.901, 4.792)
HL	.847	1.085 (0.474, 2.481)
Smoking	.655	0.838 (0.386, 1.82)
SBP	.076	1.019 (0.998, 1.041)
WBC	.302	1.072 (0.939, 1.224)
RDW	.114	1.155 (0.966, 1.381)
MPV	**.049**	1.240 (1.001, 1.538)
NEU	.648	0.963 (0.819, 1.132)
LYM	.456	1.362 (0.605, 3.069)
NLR	.289	1.060 (0.952, 1.181)
PLR	.557	1.001 (0.998, 1.004)

CI: confidence interval; DM: diabetes mellitus; HL: hyperlipidemia; LYM: lymphocyte; MPV: mean platelet volume; NEU: neutrophil; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; SBP: systolic blood pressure; WBC: white blood cell.
*Results of multivariate logistic regression analysis of peripheral arterial disease as the dependent variable.
The goodness of fit of the model was confirmed by a p values of .721 in the Hosmer–Lemeshow test.
Bold values indicate $p < 0.05$.

Discussion

The major finding of our research is that the CBC parameters such as WBC, NLR, PLR and RDW are not useful for the prediction of PAD; and although it was not a statistically significant variable in univariate analysis, increased MPV was detected to be an independent predictor of PAD. The situation of that MPV was not a significant variable in univariate analysis, but it was a significant variable in multivariate logistic regression analysis and hereby was considered as an independent predictor, can be explained by that the effect of MPV may be suppressed by other variables which are included in the multivariate analysis.

In addition to the role of platelets in hemostasis and tissue regeneration, platelets also play a role in the pathogenesis of atherosclerotic diseases and thrombus formation. MPV indicates platelet volume and is a potential indicator of platelet activity. Increased MPV is associated with platelet aggregation, thromboxane synthesis and release of adhesion molecules [5,6]. Possible mechanism of that increase in MPV value can be explained as follows: When an inflammatory event occurs, it is clear that the levels of inflammatory cytokines in the systemic circulation increase. These inflammatory cytokines can affect the thrombopoiesis in bone marrow and lead to produce platelets with larger volume from megakaryocytes. Thus, the value of MPV that reflects platelet volume increases.

It has been reported to increase MPV in many cardiovascular diseases such as hypertension [7], coronary artery disease [8], atrial fibrillation [9], and hypertrophic cardiomyopathy [10]. However, the role of

MPV in PAD has not been well described since the investigations examining MPV in patients with PAD are very limited in the literature. Arican Ozluk et al. [11] examined MPV in angiographically documented PAD and did not found any significant changes in the MPV levels. As the result, the authors concluded that the use of MPV as a predictor for PAD was impractical. The evidence from this mentioned study was not in line with the evidence from our study.

Demirtas et al. [12] investigated the relationship between CBC parameters and stages of disease in patients with PAD, and indicated that high MPV level was related to the increased severity of atherosclerotic disease in PAD. In contrast to this study, a recent report interestingly demonstrated a significant relationship of low MPV levels with higher occurrence of critical limb ischemia in a large number of PAD patients [13]. In our study, no analysis was conducted according to the stage or severity of the disease.

NLR has currently become one of the most valuable and popular CBC parameters. It is easily calculated by the proportion of neutrophil and lymphocyte counts in hemogram test, and is nowadays considered as one of the markers of inflammation [14]. There are various reports indicating that it can be used both in the diagnosis and determining the prognosis of many different cardiovascular diseases such as coronary artery diseases [15], hypertension [16], atrial fibrillation [17], and aortic dissection [18], as well as PAD [19].

RDW is an indicator of the size of red blood cells. Increased RDW can be seen in a number of diseases that cause reticulocytes to be released into the circulation without maturation. It has been found that increases in RDW are associated with increases in inflammatory markers [20]. In addition to its use in the differential diagnosis of anemia, there are also studies showing that it can be used as an indicator of the diagnosis and/or prognosis in various cardiovascular diseases such as congestive heart failure [21], acute myocardial infarction [22], and atrial fibrillation [23], as well as PAD [24,25].

As mentioned above, many CBC parameters have been investigated in various cardiovascular diseases, but a relatively small number of data regarding CBC parameters in PAD are available in existing literature. Moreover, those data have been always focused on a specific CBC parameter such as RDW, MPV or NLR instead of all CBC parameters. In our opinion, the most powerful aspect of our study is the examination of almost all CBC parameters in PAD, and to the best of our knowledge, this present study is the first report investigating almost all CBC parameters in PAD. On the other hand, there are also several limitations of our study, and among them retrospective design and relatively small sample size are the major limitations of the study. A prospective design and larger study population could increase the quality and statistical power of our study.

In conclusion, the current study revealed that MPV was an independent predictor of PAD, and could be used as a marker of inflammation in patients with PAD.

Disclosure statement

The authors declare that there is no conflict of interest.

ORCID

Yusuf Velioglu http://orcid.org/0000-0003-4709-4705
Ahmet Yuksel http://orcid.org/0000-0003-0021-6509

References

[1] Yuksel A, Velioglu Y, Cayir MC, et al. Current status of arterial revascularization for the treatment of critical limb ischemia in infrainguinal atherosclerotic disease. Int J Angiol. 2018;27:132–137.
[2] Brevetti G, Giugliano G, Brevetti L, et al. Inflammation in peripheral artery disease. Circulation. 2010;122:1862–1875.
[3] Guthrie GJ, Charles KA, Roxburgh CS, et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. Crit Rev Oncol Hematol. 2013;88:218–230.
[4] Kirbas A, Ersoy AO, Daglar K, et al. Prediction of preeclampsia by first trimester combined test and simple complete blood count parameters. J Clin Diagn Res. 2015;9:20–23.
[5] Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis. 1996;7:157–161.
[6] Karagoz I, Aktas G, Yoldas H, et al. Association between hemogram parameters and survival of critically ill patients. *J Intensive Care Med*. 2017. 885066617703348. doi:10.1177/0885066617703348
[7] Gang L, Yanyan Z, Zhongwei Z, et al. Association between mean platelet volume and hypertension incidence. Hypertens Res. 2017;40:779–784.
[8] Sansanayudh N, Anothaisintawee T, Muntham D, et al. Mean platelet volume and coronary artery disease: a systematic review and meta-analysis. Int J Cardiol. 2014;175:433–440.
[9] Makowski M, Smorag I, Makowska J, et al. Platelet reactivity and mean platelet volume as risk markers of thrombogenesis in atrial fibrillation. Int J Cardiol. 2017;235:1–5.

[10] Icli A, Aksoy F, Dogan A, et al. Increased mean platelet volume in hypertrophic cardiomyopathy. Angiology. 2014;65:420–424.
[11] Arican Ozluk O, Ber I, Peker T, et al. Mean platelet volume levels in the presence of angiographically documented peripheral artery disease. Int J Clin Exp Med. 2015;8:2899–2904.
[12] Demirtas S, Karahan O, Yazici S, et al. The relationship between complete blood count parameters and Fontaine's Stages in patients with peripheral arterial disease. Vascular. 2014;22:427–431.
[13] Rief P, Raggam RB, Avian A, et al. Low mean platelet volume is associated with critical limb ischemia in peripheral arterial occlusive disease. *Sci Rep*. 2018;8:6718.
[14] Yoldas H, Karagoz I, Ogun MN, et al. Novel mortality markers for critically ill patients. *J Intensive Care Med*. 2018;885066617753389. doi:10.1177/0885066617753389
[15] Yilmaz M, Korkmaz H, Bilen MN, et al. Could neutrophil/lymphocyte ratio be an indicator of coronary artery disease, coronary artery ectasia and coronary slow flow? J Int Med Res. 2016;44:1443–1453.
[16] Srinivasagopalane B, Andrew Rajarathinam S, Balasubramaiyan T. Clinical pertinence of neutrophil-to- lymphocyte ratio among hypertensives with different grades and duration of hypertension - an insight. *Clin Exp Hypertens*. 2018;1–6. doi:10.1080/10641963.2018.1510942
[17] Shao Q, Chen K, Rha SW, et al. Usefulness of neutrophil/lymphocyte ratio as a predictor of atrial fibrillation: a meta-analysis. Arch Med Res. 2015;46:199–206.
[18] Kalkan ME, Kalkan AK, Gündeş A, et al. Neutrophil to lymphocyte ratio: a novel marker for predicting hospital mortality of patients with acute type A aortic dissection. Perfusion. 2017;32:321–327.
[19] Paquissi FC. The role of inflammation in cardiovascular diseases: the predictive value of neutrophil-lymphocyte ratio as a marker in peripheral arterial disease. Ther Clin Risk Manag. 2016;12:851–860.
[20] Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med. 2009;133:628–632.
[21] Cauthen CA, Tong W, Jain A, et al. Progressive rise in red cell distribution width is associated with disease progression in ambulatory patients with chronic heart failure. J Card Fail. 2012;18:146–152.
[22] Wang P, Wang Y, Li H, et al. Relationship between the red blood cell distribution width and risk of acute myocardial infarction. J Atheroscler Thromb. 2015;22:21–26.
[23] Adamsson Eryd S, Borné Y, Melander O, et al. Red blood cell distribution width is associated with incidence of atrial fibrillation. J Intern Med. 2014;275:84–92.
[24] Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol. 2011;107:1241–1245.
[25] Zalawadiya SK, Veeranna V, Panaich SS, et al. Red cell distribution width and risk of peripheral artery disease: analysis of National Health and Nutrition Examination Survey 1999-2004. Vasc Med. 2012;17:155–163.