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ARAŞTIRMA/RESEARCH

Diagnostic value of hematological parameters in patients with osteoarthritis

Osteoartrit hastalarında hematolojik parametrelerin tanısal değeri

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Abstract

Purpose: The aim of the present study was to investigate the diagnostic value of routine hematological parameters on osteoarthritis and to explore their clinical significance.

Material and Methods: The study included 118 patients with osteoarthritis and 145 healthy individuals. Medical records, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell count (WBC), neutrophil-lymphocyte ratio (NLR), platelet count (PLT), platelet distribution width (PDW), platecrit (PCT), red cell distribution width (RDW), RDW-platelet ratio (RPR), platelet-lymphocyte ratio (PLR) and mean platelet volume (MPV) levels were retrospectively recorded from patient files.

Results: There were no significant differences in WBC, RDW, PLT, RPR levels between two groups. NLR and PLR values were significantly higher in the OA group than in the control group. RBC, MPV, PCT and PDW values were significantly lower in the osteoarthritis group than in the control group. MPV and RBC were negatively correlated with ESR and CRP in osteoarthritis patients.

Conclusions: Hematological inflammatory markers might be useful parameters that could be used in patients with osteoarthritis.

Key words: Osteoarthritis, inflammation, MPV, hematological indices

Öz

Amaç: Bu çalışmanın amacı, osteoartrit hastalığında hematolojik parametrelerin tanısal değerini araştırmak ve klinik önemlerini ortaya koymaktır.

Gereç ve Yöntemler: Çalışmaya 118 osteoartrit hastası ile yaş ve cinsiyeti benzer 145 sağlıklı birey dahil edildi. Tıbbi geçmişi, eritrosit sedimentasyon hızı (ESR), C-reaktif protein (CRP), beyaz küre sayısı (WBC), nötrofil-lenfosit oranı (NLR), platelet sayısı (PLT), platelet dağılım genişliği (PDW), platecrit (PCT), kırmızı küre dağılım genişliği (RDW), RDW-platelet oranı (RPR), platelet-lenfosit oranı (PLR) ve ortalama platelet hacmi (MPV) değerleri retrospektif olarak hasta dosyalarından elde edildi.

Bulgular: İki grup arasında WBC, RDW, PLT, RPR değerleri arasında fark bulunamamıştır. NLR ve PLR değerleri osteoartrit hastalarında istatistiksel olarak kontrol grubuna göre anlamlı şekilde daha yüksek bulundu. RBC, MPV ve PDW değerleri, osteoartrit hastalarında istatistiksel olarak anlamlı şekilde daha düşük bulundu. Hasta grubunda ESR ve CRP değerleri, MPV ve RBC ile negatif şekilde korelasyon gösterdi.

Sonuçlar: Bu çalışma, hematolojik inflamatuar parametrelerin osteoartrit hastalığında tanısal belirteçler olarak kullanılabileceğini göstermiştir.

Anahtar kelimeler: Osteoartrit, inflamasyon, MPV, hematolojik parametreler.

INTRODUCTION:

Ostearthritis (OA) is most common form of joint disease and one of the leading causes of disability and pain in elderly people worldwide. In the near future it is estimated that increasing age, obesity and extended life expectancy will result in a greater occurrence of the disease. OA is a dynamic disease process developing as a result of a disorder in the normal balance between the breakdown and repair of joint cartilage and subchondral bone.

The disease is characterized by progressive cartilage degradation, joint space narrowing, remodeling of adjacent bone. It is regarded as a complex disease whose pathogenesis is not completely understood. Historically, OA has been considered a non-

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inflammatory disease, but more recently studies revealed that inflammation is a risk factor associated with both progression of cartilage destruction and signs and symptoms of disease, including joint pain, palpable joint swelling, synovial fluid effusion, indicators of synovitis[1, 2]. Inflammation in synovium involved infiltration of mononuclear cells (including monocytes, macrophages, activated B and T cells) and production of proinflammatory mediators, including interleukin-1β and tumor necrosis factor-α[3, 4]. These cytokines are secreted from cartilage, bone and synovium, and stimulate the production of other proinflammatory mediators such as matrix metalloproteinases, Prostaglandin E2, nitric oxide and cytokines (IL-6, IL-8, IL-15, IL-17 and IL-21 etc.), resulting in degenerative changes in cartilage and contributing to the development of symptoms[1,3-6].

Complete blood count (CBC) analyses are inexpensive and easy, give quick results and have a significant place in the assessment of various diseases and conditions. Mean platelet volume (MPV) is a measure of platelet size and an indicator of platelet function and activation. MPV levels have been studied in many diseases, and have been found to have diagnostic value in detecting inflammatory disease such as rheumatoid arthritis, ankylosing spondylitis, acute rheumatic fever, familial mediterrean fever, ulcerative colitis and acute pancreatitis[7-11]. Red blood cell distribution width (RDW), the measure of the range of variation of red blood cell (RBC) volume, is used in the diagnosis of many diseases such as anemia. It has been postulated that RDW levels correlate with inflammatory markers and disease activity in several chronic inflammatory diseases[12, 13]. Neutrophil to lymphocyte ratio (NLR), calculated as a simple ratio between neutrophil and lymphocyte counts, was used as a systemic inflammation index, and were assessed in studies of rheumatologic diseases and malignancy[14, 15]. Platelet to lymphocyte ratio (PLR) reflects systemic inflammatory response[15]. The RDW to platelet ratio (RPR) is also used in showing the severity of inflammation[16].

The aim of this retrospective study was to compare the levels of MPV, NLR, RDW, platelet distribution width (PDW), PCT, PLR, RPR and other inflammatory parameters (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)) levels between OA patient group and the control group and to contribute new findings to OA disease pathogenesis.

MATERIAL AND METHODS:

The data used in the present study were obtained retrospectively from patients who had osteoarthritis diagnosis with based on Kellgren-Lawrence grading system and physical examination in January 2014 – November 2015 period in Orthopedic Clinic of the Tatvan Military Hospital (Bitlis, Turkey). Ethical approval for the study was obtained from the local ethics committee and conducted in accordance with the ethical principles described by the Declaration of Helsinki.

The study consisted of 118 grade 2 and grade 3 osteoarthritis patients, and 145 healthy individuals who were established by routine physical examination at the same hospital as a control group. Participants with a history of smoking, acute or chronic infectious diseases, hypertension, coronary heart disease, angina pectoris, myocardial infarction, heart failure, diabetes mellitus, obesity, asthma, chronic obstructive pulmonary disease, peripheral or cerebral vascular disease, hematological disorders (such as hemoglobin >16.5 g/dl, thrombocytopenia, anemia, myeloproliferative disorders etc.), dyslipidemia, musculoskeletal surgery or injury within past 2 months, other musculoskeletal disease (rheumatoid arthritis etc.), autoimmune or metabolic disorders, cancers, pregnancy, abnormal liver or renal function tests, malignancies, thrombosis or chronic renal insufficiency were excluded from the study. None of the patients were taking any medications (such as oral anticoagulants, antiepileptics etc) that might have caused platelet or coagulation abnormalities during the last eight weeks before blood sampling. 48 patients were excluded from the study according to the exclusion criteria.

Medical records, ESR, CRP, white blood cell count (WBC), NLR, platelet count, PDW, RDW, RPR, PLR and MPV levels were retrospectively recorded from patients' files. Standard tubes with constant amount of ethylenediaminetetraacetic acid (EDTA) were used for complete blood count. All blood samples were studied within less than one hour after the sampling. The complete blood count analyses which based on technique of laser flow cytometry scattergrams, were performed in the same analyzer (Medonic CA-620, Sweden) in the central laboratory of our institution which is routinely checked every day. Complete blood count parameters of

participants were recorded from the same computerized database. ESR was determined by the Westergren method. ESR levels were considered to be elevated if they were greater than 20 mm/h. CRP level was determined by the immunoturbidimetric method. CRP levels were considered to be elevated if they were greater than 5 mg/dl.

Statistical analysis

Statistical analysis was performed with the program SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Distributions of variables were evaluated with the Shapiro-Wilk test. Data was expressed as mean±standard deviation. In the comparison of continuous variables, the Student *t*-test and the Mann-Whitney's *U* test were used. The correlations between the variable pairs were analyzed using Spearman's correlation test. A level of $p < 0.05$ was considered significant.

RESULTS

Demographic characteristics of the individuals are given in Table I. The mean age of the OA subjects were 50 ± 10 years, while the mean age of controls was 52 ± 7 years. There were 75 (64.1%) females in the patient group and 100 (69%) in the control group. No significant difference was found between the two groups in terms of age and gender distribution (p=0.077, p=0.406, respectively).The comparison between two groups for blood parameters is shown in Table 2. WBC values were found to be 7.51 ± 1.55 x10³/mm³ for the osteoarthritis group and 7.83 ± 1.46 x10³/mm³ for the control group. No difference was found between the two groups in terms of WBC values. NLR levels of patients with OA (2,15 ± 1,12) were significantly higher than control subjects (1,79 ± 0,97) (p=0.006). RBC values of patients with OA (4,68 ± 0,37 x10⁶/mm³) were significantly lower than control group (4,98 ± 0,47 x10⁶/mm³)(p=0,001). No statistically significant difference was found between the PLT, RDW and RPR levels of the two groups (p>0.05) (Table 2).

Mean MPV values were 7,79±0.54 fL in patients with OA, vs. 8,27± 0.4 fL in the control group. MPV values were found to be significantly lower in OA group (p=0.001). PCT and PDW values in the OA group were significantly lower than control group (p=0,028, p=0,001, respectively) (Table 2). Mean PLR values were 139,5 ± 57,7 in patients with OA, vs. 118,9 ± 39,6 in the control group. PLR values were found to be significantly higher in OA group (p=0.009). Patients with OA had significantly higher CRP and ESR values compared to control group (p=0,020, p=0,011, respectively) (Table 2).

Table 1. Characteristics of osteoarthritis patient and control groups

		Osteoarthritis patients (n=118)	Control group (n=145)	p value
Age (years)		50±10	52±7	0.077
Gender	Female	75 (64.1%)	100 (69%)	0.406
	Male	42 (35.9%)	45 (31%)	

Table 2. Relationship of blood parameters between osteoarthritis patients and the control group

	Osteoarthritis (Mean±SD)	Control (Mean±SD)	*p* value
White blood cell count (x10³/mm³)	7.51 ± 1.55	7.83 ± 1.46	0.095
Neutrophil/lymphocyte ratio	2.15 ± 1.12	1.79 ± 0.97	0.006**
Red blood cell count (x10⁶/mm³)	4.68 ± 0.37	4.98 ± 0.47	0.001**
Red blood cell distribution width (fl)	82 ± 6	80 ± 8	0.086
Platelet count (x10³/mm³)	286 ± 70	295 ± 77	0.404
Mean platelet volume (fl)	7.79 ± 0.54	8.27 ± 0.4	0.001**
Platecrit (%)	0.23 ± 0.06	0.26 ± 0.08	0.028**
Platelet distribution width (fl)	10.14 ± 0.78	10.63 ± 1.03	0.001**
Platelet/lymphocyte ratio	139.5 ± 57.7	118.9 ± 39.6	0.009**
Red cell distribution width/platelet ratio	0.30 ± 0.08	0.29 ± 0.08	0.213
C-reactive protein (mg/dl)	4.9 ± 2.9	3.3 ± 1.1	0.020**
Erythrocyte sedimentation rate (mm/h)	16.6 ± 8.7	12.4 ± 3.0	0.011**

Table 3. Analysis of correlation between ESR and blood parameters in the osteoarthritis patient group

		CRP	WBC	NLR	RBC	RDW	PLT	MPV	PCT	PDW	PLR	RPR
ESR	r	0.743	0.031	-0.061	-0.282	-0.152	0.154	-0.198	0.096	-0.223	-0.015	-0.181
	p	0.001	0.739	0.512	0.002	0.101	0.097	0.032	0.304	0.015	0.875	0.051

Abbreviations: ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: White blood cell; NLR: Neutrophil to lymphocyte ratio; RBC: Red blood cell; RDW: Red cell distribution width; PLT: Platelet; MPV: Mean platelet volume; PCT: Platecrit; PDW: Platelet distribution width; PLR: Platelet to lymphocyte ratio; RPR: Red cell distribution width to platelet ratio.

Table 4. Analysis of correlation between CRP and blood parameters in the osteoarthritis patient group

		ESR	WBC	NLR	RBC	RDW	PLT	MPV	PCT	PDW	PLR	RPR
CRP	r	0.743	0.072	0.013	-0.231	-0.125	0.122	-0.184	0.073	-0.179	0.002	-0.144
	p	0.001	0.441	0.889	0.012	0.180	0.190	0.047	0.436	0.054	0.981	0.121

Abbreviations: ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: White blood cell; NLR: Neutrophil to lymphocyte ratio; RBC: Red blood cell; RDW: Red cell distribution width; PLT: Platelet; MPV: Mean platelet volume; PCT: Platecrit; PDW: Platelet distribution width; PLR: Platelet to lymphocyte ratio; RPR: Red cell distribution width to platelet ratio.

In the correlation analysis, ESR was found to have a positive correlation with CRP and a negative correlation with RBC, MPV and PDW in the patient group (Table 3). Also, CRP was negatively correlated with RBC and MPV (Table 4)

DISCUSSION

Although osteoarthritis is regarded as a non-inflammatory disease, it is thought that low-grade inflammation is part of the pathogenesis of the illness. Low-grade inflammation leads to the production of pro-inflammatory cytokines in the synovial membranes of patients, which contributes to the pathogenesis (17). In this study, it was found that the hematological parameters relating to inflammation showed changes in grade 2 and grade 3 osteoarthritis patients, and the study supports the hypothesis that inflammation plays a part in the pathogenesis of osteoarthritis.

In the literature there is only one study on complete blood count parameters in osteoarthritis patients. In that study, performed in 2013, it was found that MPV values of osteoarthritis patients with synovitis were statistically significantly lower than those of osteoarthritis patients without synovitis and of a control group[18]. No significant difference was found between the MPV values of osteoarthritis patients without synovitis and the control group. Also, a significant negative correlation was found between the MPV values and the CRP values in the osteoarthritis group with synovitis. No correlation was found between MPV and ESR. However, patients' cardiac, hepatic and respiratory system characteristics were also not investigated in the study. Pathologies relating to these systems had the ability to cause changes in MPV values[19-22]. Also in that study, it was not clear how the diagnosis of synovitis was made. There was no information on how the researchers had collected the blood samples in the study or when the study took place. Samples taken in tubes without EDTA and samples not investigated within an hour of collection affect MPV results[23]. In the present study we had wide exclusion criteria and included in these criteria diseases which could affect hematological parameters. In collecting samples, EDTA tubes were used, and the blood samples were examined in the laboratory within one hour. Also, we included in the patient group grade 2 and grade 3 osteoarthritis patients whether or not they had synovitis. This is because a diagnosis of synovitis is given not directly by radiography but by the gold standard of histological examination. Our aim was to perform a retrospective analysis on the usefulness of hematological parameters as an inflammatory determiner.

Our study did not show a difference between the WBC levels of the two groups. This accords with the results of previous studies. Osteoarthritis is a chronic disease. WBC values increase in septic

arthritis but generally do not change in osteoarthritis[24]. We also examined NLR and PLR levels, and found them to be significantly raised in the osteoarthritis patient group. Studies have shown that NLR and PLR levels can be used as indicators of systemic inflammation[14,15]. This supports the inflammatory hypothesis of the pathogenesis of osteoarthritis.

We did not find any difference between the groups' RDW and RPR levels. RDW is an indicator of the distribution of red blood cells, and shows itself when immature erythrocytes appear in peripheral blood with the effect of erythropoiesis of inflammatory mediators in the inflammatory process[25]. In our study, despite expecting an increase in RDW, we did not find a difference between the two groups. This may be because our patient group was a chronic patient group.

In our study, ESR and CRP levels were found to be higher in the osteoarthritis patients than in the control group. This is in accord with previous studies. ESR and CRP levels in osteoarthritis patients are used in studies as inflammation indicators[26-28]. In the present study, we found significant variations in MPV levels in the patient group compared to the control group. Also MPV was seen to correlate negatively with ESR and CRP in the patient group. This suggests that MPV can be used in osteoarthritis patients as an inflammatory indicator like ESR and CRP. This accords with previous studies. In previous studies it was recommended that MPV could be used as an inflammatory indicator in rheumatologic diseases such as rheumatoid arthritis, ankylosing spondylitis, familial Mediterranean fever and acute rheumatic fever[7-9].

In conclusion, we suggest that hematological parameters and especially MPV can be used as diagnostic inflammatory indicators like CRP and ESR. Our findings need to be supported with prospective studies with histological examinations and a larger number of patients.

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