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Blood mean platelet volume and platelet lymphocyte ratio as new predictors of hip osteoarthritis severity

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Abstract

Osteoarthritis (OA) is a low grade systemic inflammatory disease in which many inflammatory mediators are known to be elevated in the peripheric blood. Blood platelet lymphocyte ratio (PLR) and mean platelet volume (MPV) are accepted as novel markers in many of the systemic inflammatory disorders, but have not been investigated in synovitis-free radiographic OA yet.

The aim of this study was to evaluate the levels of blood PLR and MPV in radiographic hip OA. A total of 880 patients were evaluated retrospectively and after certain exclusion criteria, 237 of them who have primary hip OA were included. Age, sex, height, weight, body mass index, neutrophil, lymphocyte and platelet counts, erythrocyte sedimentation rate (ESR), PLR, and MPV levels were recorded, Kellgren–Lawrence (KL) grading of the hip joints were performed. Patients were then divided into 2 groups as KL grades 1 to 2 (mild–moderate) and KL grades 3 to 4 (severe) hip OA.

Mean age, mean neutrophil, lymphocyte and platelet counts, mean MPV, mean PLR, and mean ESR were statistically significantly different between mild/moderate hip OA group and severe hip OA group. In univariate analysis, older age and higher MPV, PLR, and ESR were severely associated with severe hip OA. In multiple logistic regression analysis, MPV, PLR, and ESR emerged as independent predictors of severe hip OA.

The results of the present study, for the first time in the literature, suggest blood PLR and MPV as novel inflammatory markers predicting the radiographic severity of hip OA in the daily practice.

Abbreviations: AS = ankylosing spondylitis, BMI = body mass indexes, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, KL = Kellgren–Lawrence, MPV = mean platelet volume, OA = osteoarthritis, PLR = platelet–lymphocyte ratio, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus.

Keywords: coxarthrosis, inflammation, mean platelet volume, platelet lymphocyte ratio, risk factors

1. Introduction

Osteoarthritis (OA) is one of the most common joint diseases and cause of disability especially in the elderly. Although formerly known as a mechanically activated wear of the cartilage tissue, OA is now known as a low grade inflammatory disease of the entire joint affecting not only the cartilage but also the synovium, synovial fluid, subchondral bone, and adjacent muscles.[1,2] Hip OA is one of the most common forms of OA. Unlike knee OA, mechanical overload is not at the forefront in the pathogenesis. High body mass index or occupations involving regular heavy lifting have a lower level of evidence in the pathogenesis of hip OA compared to knee OA.[3] As mechanical stress and inflammatory response acts simultaneously in OA progression; lower level of evidence about mechanical stress seems to underscore inflammatory mechanisms.

The inflammatory and anti-inflammatory mediators that are known to play a role in OA pathogenesis are, IL-1α, IL-1β, IL-4, IL-6, IL-8, IL-10, IL-11, IL-13, IL-15, IL-17, TNF-α, leukocyte inhibitory factor, IL-1 receptor antagonist, matrix metalloproteinases, proteases, chemokines, nitric oxide, and prostoglandins and leukotriens. These mediators are mainly synthesized by synoviocytes and chondrocytes of the affected joints and disperse into the synovial fluid.[4–7] It is also known that IL-1, IL-6, IL-15, and TNF-α can also be found in the serum of patients with OA.[8,9] Several inflammatory mediators, especially IL-6 is known to stimulate platelet production from megakaryocytes.[10] Moreover, platelet activation and longer platelet survival also takes place giving way to leukocyte activation and vice versa. On the basis of the above mentioned inflammatory state, platelet count in peripheral blood increases.[11–14]

It is known that increased platelet–lymphocyte ratio (PLR) is related to disease activity and severity in rheumatoid arthritis (RA),[15,16] psoriasis, psoriatic arthritis.[17] Moreover, it is also known that alterations of mean platelet volume (MPV) can also be used as an indicator of disease severity in many of the systemic

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inflammatory diseases like RA, ankylosing spondylitis (AS), psoriatic arthritis, . . . etc.[18–29] Nevertheless, MPV and PLR as a marker of OA severity has not been studied in the literature before. So the aim of the present study is to investigate serum MPV and PLR as useful markers demonstrating the severity of hip OA.

2. Patients and methods

Eight hundred eighty consecutive outpatients who were admitted to physical medicine and rehabilitation department of Ankara Physical Medicine and Rehabilitation Education and Research Hospital and orthopedy department of Ankara Atatürk Education and Research Hospital with a preliminary diagnosis of hip OA between January 2014 and January 2016 were evaluated retrospectively. Hospital ethics committee approval was obtained from Atatürk Education and Research Hospital Ethical Committee.

According to the medical records 643 patients were excluded from the study; 433 patients with referring pain unrelated to hip pathology, 80 patients with developmental dysplasia of the hip, 26 patients with a history of avascular necrosis of the hip, 25 patients with high levels of infection tests (white blood cell, sedimentation, C-reactive protein), 18 patients with accompanying rheumatologic disease, 18 patients with a history of hip/knee prosthesis, 10 patients with accompanying malign disease, 10 patients with trochanteric bursitis, 4 patients with a diagnosis of tumoral lesion of the hip, 3 patients with a history of hip fracture, 2 patients with a history of traumatic dislocation of the hip, 2 patients with inguinal lymphadenopathy, 2 patients with a history of lumbar stabilization operation, 2 patients with a history of hemiplegia, 2 patients with a diagnosis fibromyalgia, 1 patient with scoliosis, 3 patients with a history of cardiac disease, 1 patient with Wilson disease, 1 patient with hyperparathyroidism. Finally a total of 237 patients (167 females, 70 males) with a diagnosis of primary OA of the hip were included into the study. Age, sex, height, and weight of the patients were recorded. Body mass indexes (BMI) were calculated. Kellgren–Lawrence (KL) grading of the mostly affected hip joint was performed for each patient through the evaluation of X-ray images. Neutrophil, lymphocyte and platelet counts, MPV, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) values of each patient obtained at the same time with the X-ray images were recorded. Blood PLR levels were calculated. For missing information, patient interviews were carried out by telephone calls. Patients were then divided into 2 groups as patients with KL grades 1–2 (mild-moderate) hip OA and patients with KL grades 3–4 (severe) hip OA.[30]

The KL grading was used for classifying OA according to radiographic signs. Four different radiographic features: joint space narrowing, osteophytes, subchondral sclerosis, and subchondral cysts are evaluated and X-rays are graded from 1 to 4. Higher grades are associated with more severe OA.[31] Although it was firstly developed for knee joint, KL grading can also be used for most of the joints including hip.[30,32] KL grading of both knees were usually the same but, if obvious difference was present between knees, the most severely affected knee's grading was recorded as a single score.

2.1. Statistical analysis

Analyses were performed using SPSS. Continuous data were presented as mean ± SD. Categorical variables were summarized as percentages. Comparisons between groups were made using Chi-square tests for categorical variables, independent samples Student *t* tests for normally distributed continuous variables and Mann–Whitney *U* tests when the distribution was skewed. A *P*-value < 0.05 was considered statistically significant.

Effects of different variables on severe knee OA were calculated in univariate analysis for each. Variables, for which the unadjusted *P*-value was <0.10 in logistic regression analysis, were identified as potential risk markers and included in the full model. We reduced the model using stepwise multivariate logistic regression analysis and eliminated potential markers using likelihood ratio tests. A *P*-value <0.05 was considered statistically significant, and the confidence interval was 95%.

3. Results

Of the 237 patients, 167 (70.46%) were females and 70 (29.54%) were males. Mean age was 62.09 ± 11.18 years and mean BMI was 28.64 ± 7.1 kg/m^2. Demographic and laboratory parameters of the patients according to hip OA severity (mild/moderate OA, KL grades 1–2 vs severe OA, KL grades 3–4) are presented in Table 1.

Mean age ($P < 0.001$), mean neutrophil ($p = 0.02$), lymphocyte ($P = 0.04$) and platelet ($P = 0.03$) counts, mean MPV ($P < 0.001$), mean PLR ($P < 0.001$), and mean ESR ($p < 0.01$) were statistically significantly different between mild/moderate hip OA group and severe hip OA group (Table 1). Mean BMI and mean CRP were similar in both groups (Table 1).

In univariate analysis; older age ($P < 0.001$), higher MPV ($P < 0.001$), higher PLR ($P < 0.001$), and higher ESR ($P < 0.001$) were severely associated with severe hip OA. In multiple logistic regression analysis, MPV ($P < 0.001$), PLR ($P < 0.001$), and ESR

Table 1

Demographic and clinical characteristics and laboratory findings of hip osteoarthritis patients according to hip osteoarthritis severity.

	All patients (n = 237)	KL grade 1–2 (n = 136)	KL grade 3–4 (n = 101)	*P*
Gender (%female)	70.46	74.26	65.34	0.13
Age	62.09 ± 11.18	56.22 ± 11.53	65.55 ± 9.45	< 0.001
BMI	28.64 ± 7.1	28.1 ± 4.5	29.23 ± 6.2	0.62
Neutrophil count	4.11 ± 1.28	3.94 ± 1.22	4.33 ± 1.32	0.02
Lymphocyte count	2.29 ± 0.70	2.36 ± 0.70	2.18 ± 0.68	0.04
Platelet count	247.98 ± 67.42	239.66 ± 33.30	259.18 ± 71.39	0.03
MPV	9.88 ± 1.32	9.42 ± 1.31	10.49 ± 1.06	< 0.001
PLR	116.29 ± 41.03	107.42 ± 35.19	128.24 ± 45.25	< 0.001
ESR	17.50 ± 16.40	11.41 ± 10.47	25.54 ± 19.18	< 0.01
CRP	5.16 ± 2.53	4.95 ± 2.14	5.40 ± 2.93	0.19

BMI = body mass indexes, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, KL = Kellgren–Lawrence, MPV = mean platelet volume, PLR = platelet–lymphocyte ratio.

Table 2

Results of univariate and multivariate regression models.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.06 (1.03–1.08)	<0.001	1.02 (0.99–1.06)	0.17
MPV	2.39 (1.80–3.19)	<0.001	2.32 (1.66–3.25)	<0.001
PLR	1.01 (1.01–1.02)	<0.001	1.01 (1.00–1.02)	0.006
ESR	1.08 (1.05–1.1)	<0.001	1.06 (1.03–1.09)	<0.001
CRP	1.07 (0.96–1.1)	0.19		

CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, MPV = mean platelet volume, OR = odds ratio, PLR = platelet–lymphocyte ratio.

($P < 0.001$) emerged as independent predictors of severe OA of the hip (Table 2).

4. Discussion

According to the results of the present study, patients with severe hip OA have elevated blood PLR and MPV levels compared to patients with mild/moderate hip OA and high PLR and MPV are independent predictors of hip OA severity. To our knowledge, this study is the first one demonstrating PLR and MPV, 2 basic, inexpensive and easily available blood tests, can be used as markers to assess the radiographic severity of OA of the hip in the daily practice.

In the literature there is some evidence for elevated ESR in OA patients. Hanada et al[33] found elevated levels of ESR in knee OA patients and moreover ESR levels of patients with KL grade 3 and 4 knee OA were higher than patients with KL grade 1 knee OA. In another study by Sanchez-Ramirez et al, elevated levels of serum ESR have been found to be associated with lower quadriceps and hamstring muscles strength. Their study also demonstrated the association of elevated ESR and OA severity, but in an indirect way, as the muscle weakness and knee OA severity are directly associated.[34] Our results are also in accordance with the literature, with elevated ESR levels in severe hip OA group.

Recently, increased PLR was found to be directly associated with disease activity in RA[15,16] and disease severity in psoriasis,[17] and was also found to be a strong predictor of psoriatic arthritis in psoriasis patients. Apart from rheumatologic diseases, higher levels of PLR, as a marker of systemic inflammation, seems to be associated with reduced survival in gastric, colorectal, and pancreatic cancers[35–37] and poor prognosis in vascular surgery.[38,39] On the contrary, Boyraz et al found lower PLR levels in AS patients compared with controls. But in their study, the patients in the active phase excluded and the study group only consisted of patients who had been under anti-TNF therapy at least for 6 months.[40] There is no study in the literature where PLR levels were investigated in OA before. Nevertheless our results with higher levels of PLR in severe hip OA group are in concordance with the literature owing to the fact that OA is already accepted as a systemic inflammatory disorder.

MPV was also investigated widely in the past decade. It is frequently found to be decreased in the presence of active high grade inflammation; that is, active phase of RA, AS, ulcerative colitis and Chron disease[27,41,42] activation of systemic lupus erythematosus (SLE) arthritis[43] and active SLE.[44] Increased MPV levels were on the other hand mainly found in states of low grade inflammation such as: cellulitis,[45] idiopathic subjective tinnitus,[46] symptom/attack-free periods of familial Mediterranean fever patients[47,48] and irritable bowel syndrome,[49] obstructive sleep apnea syndrome.[50] Being a state of low grade systemic inflammation, OA, is also expected to be associated with higher levels of MPV and this is demonstrated in our study. In our study, higher levels of MPV was found in severe hip OA group and this is in concordance with the present literature as OA (even the severe form) is a low grade inflammatory condition.[1,2]

The most important limitation of the present study is the cross-sectional design giving way to a chicken and egg situation and overshading the pathogenesis of elevated blood PLR and MPV levels in severe hip OA. Moreover, the use of a single blood sample does not allow assessment of the stability of blood levels over the time. So, longitudinal studies should be performed to evaluate the role of blood PLR and MPV in hip OA pathogenesis.

In conclusion, the results of the present study, for the first time, demonstrated that blood PLR and MPV can be used as basic indicators of radiographic severity of hip OA. Our results also support the part of low grade systemic inflammation in OA pathogenesis. According to the data from this study, MPV and PLR are useful in the clinical setting to assess the severity of hip OA.

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