ORIGINAL ARTICLE

Evaluation of Subclinical Atherosclerosis in Patients with Psoriatic Arthritis

Psöriatik Artrit Tanılı Hastalarda Subklinik Aterosklerozun Değerlendirilmesi

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ABSTRACT

Background/Aims: Psoriatic arthritis (PsA) with peripheral and axial involvement; It is a heterogeneous disease that can cause enthesitis, dactylitis, and nail and skin involvement. The persistence of inflammation in psoriasis may lead to comorbidities such as PsA, cardiovascular disease and metabolic syndrome. Our study aimed to detect subclinical atherosclerosis and prevent possible morbidity and mortality in PsA patients with no known risk factors.
Methods: Fifty-eight patients were evaluated in our study, and 33 patients diagnosed with PsA who met the diagnostic and inclusion criteria constituted the study group. There are 25 healthy individuals of similar age in the control group. Age, gender, disease duration, medical treatment used for the disease, low-density lipoprotein, triglyceride, and total cholesterol levels monocyte-lymphocyte ratio and carotid intima-media thickness (CIMT) obtained from carotid ultrasonography were recorded. Hematological parameters and CIMT were statistically evaluated in the patient and control groups. In addition, correlation analysis was performed to evaluate CIMT, hematological parameters and disease duration. The relationship between PsA and atherosclerosis was evaluated.
Results: A comparison was made between the study and control groups regarding age, triglyceride, low-density lipoprotein, and monocyte-lymphocyte ratio, and no statistically significant difference was observed (p>0.05). Monocyte-lymphocyte ratio, monocyte and lymphocyte count were found to be high in the study group and there was a statistically significant difference (p<0.05). CIMT was higher in the study group and this difference was statistically significant (p<0.05).
Conclusion: Patients with PsA have an increased risk of atherosclerosis compared to the healthy population without any risk factors. CIMT measurements and serum hematological markers have been found useful in predicting this risk. This awareness will be useful in the follow-up of patients and in taking precautions against morbidities that may develop.

Keywords: Psoriatic arthritis, carotid intima-media thickness, subclinical atherosclerosis, ultrasonography

ÖZ

Amaç: Periferik ve aksiyel tutulumlu psöriatik artrit (PsA); entezit, daktilit, tırnak ve deri tutulumuna neden olabilen heterojen bir hastalıktır. Psöriazis de inflamasyonun devam etmesi, PsA, kardiyovasküler hastalık ve metabolik sendrom gibi komorbiditelere yol açabilir. Çalışmamızda bilinen bir risk faktörü olmayan PsA hastalarında subklinik aterosklerozu saptamak, olası morbidite ve mortaliteyi önlemek amaçlandı.
Gereç-Yöntem: Çalışmamızda elli sekiz hasta değerlendirilmiş olup tanı ve katılma kriterlerine uygun 33 PsA tanılı hasta çalışma grubunu oluşturmaktadır. Kontrol grubunda benzer yaşta 25 sağlıklı birey bulunmaktadır. Yaş, cinsiyet, hastalık süresi, hastalık için kullanılan medikal tedavi, düşük dansiteli lipoprotein, trigliserid ve total kolesterol değerleri, monosit-lenfosit oranı, karotis doppler ultrasonografi ile elde edilen karotis intima-media kalınlık (KIMK) ölçüm sonuçları kaydedildi. Hasta ve kontrol grubunda hematolojik parametreler ve KIMK istatistiksel olarak incelendi. Ayrıca KIMK ile hematolojik parametreler ve hastalık süresini değerlendirmede korelasyon analizi yapıldı. PsA ile ateroskleroz arasındaki ilişki istatistiksel olarak incelendi.
Bulgular: Çalışma ve kontrol grupları arasında yaş, trigliserit, düşük dansiteli lipoprotein ve monosit-lenfosit oranı açısından karşılaştırma yapıldı ve istatistiksel olarak anlamlı bir fark gözlenmedi (p>0,05). Monosit/lenfosit oranı, monosit ve lenfosit sayısı çalışma grubun da yüksek bulunmuş olup istatistiksel olarak anlamlı fark saptanmıştır (p<0,05). KIMK çalışma grubunda daha yüksekti ve bu fark istatistiksel olarak anlamlıydı (p<0,05).
Sonuç: PsA'li hastalar, herhangi bir risk faktörü olmayan sağlıklı popülasyona kıyasla artmış ateroskleroz riskine sahiptir. KIMK ölçümleri ve serum hematolojik belirteçleri bu riski ön görmede faydalı bulunmuştur. Bu farkındalık hastaların takibinde ve gelişebilecek morbiditelere karşı önlem alınmasında faydalı olacaktır.

Anahtar Kelimeler: Psöriatik artrit, karotis intima media kalınlığı, subklinik ateroskleroz, ultrasonografi

Introduction

Psoriatic arthritis (PsA) is a chronic autoinflammatory disease that can occur with various clinical phenotypes. It is most commonly seen in people with psoriasis disease. Among the spondyloarthropathies, it is the group that significantly affects the life of the patients and is significantly associated with cardiovascular mortality (1). As a result of increasing awareness and knowledge about the immunological mechanism, psoriasis is increasingly accepted as a disease with systemic effects, different from skin and joint involvement (2). It has been suggested that proinflammatory cytokines are effective in atherogenesis and peripheral insulin resistance. Results compiled from various retrospective and prospective cohort studies and imaging methods show that psoriasis and PsA are associated with increased cardiovascular risk (3,4). Coronary artery disease and ischemic cerebrovascular diseases remain the leading causes of death worldwide (5). It is important to detect subclinical atherosclerosis, which is involved in the common etiopathogenesis of

these two diseases. Atherosclerosis is a multifactorial, chronic inflammatory disease that can affect all parts of the arterial system, characterized by the deterioration of blood supply to organs and limbs such as the heart, brain, and extremities as a result of the narrowing of the lumen of the progressive lesion involving the intima and media layers of the vascular wall (6).

Carotid intima-media thickness (CIMT) is used to detect early atherosclerosis in the demonstration of vascular pathologies that may occur in the future(7,8). Ultrasonographic findings of CIMT correlate with histological findings (9). Studies have also shown that increased CIMT is associated with pathologies such as myocardial infarction and ischemic stroke (10).

Hypercholesterolemia plays a significant role in the development of atherosclerosis. The impact of lipoproteins such as low-density lipoprotein (LDL) and VLDL in the formation of atherosclerosis has been demonstrated in numerous studies (11). It is indisputable that dyslipidemia is a significant risk factor for atherosclerosis. Additionally, in recent years, several studies have shown that inflammation, alongside dyslipidemia, also constitutes an important risk factor (12). There are many markers indicating inflammation. The proportional results of data obtained after blood cell counts provide us with information about inflammation. The effectiveness of the monocyte-to-lymphocyte ratio (MLR), previously obtained by the ratio of monocyte count to lymphocyte count, has been demonstrated in studies concerning the progression and severity of PsA in patients with psoriasis (13). Furthermore, the relationship between MLR and subclinical atherosclerosis has been highlighted in numerous studies (14,15).

This study aims to evaluate subclinical atherosclerosis in patients with psoriatic arthritis using ultrasonography and hematological parameters.

Materıal and Methods

Our study was approved by the relevant unit of our institution (decision no: 2023-05/03). After ethics committee approval, medical records were analyzed retrospectively between January 2020 and March 2023. Patients who applied to the rheumatology clinic of the university hospital between January 2022 and March 2023 and had a confirmed diagnosis of PsA according to the internationally accepted were included in the study. The data of 58 patients were examined retrospectively. Exclusion criteria were Diabetes Mellitus, Hypertension, Presence of Coronary Artery Disease, Hyperlipidemia diagnosis, body mass index above 30, and smoking. 33 patients diagnosed with PSA and meeting the criteria formed the study group. The control group comprised 25 healthy individuals of similar age and without any disease. An automatic blood counter (Beckman Coulter LH 780, USA) was used for the analysis of hematological parameters. The enzymatic colorimetric method (Roche Diagnostics, Mannheim, Germany) was used to measure LDL and triglyceride concentrations. In routine carotid ultrasonography (US) in our institution,

CIMT is found by taking the average of 3 different measurements from the posterior wall, 1 cm distal to the common carotid artery bulb level (Figure 1).
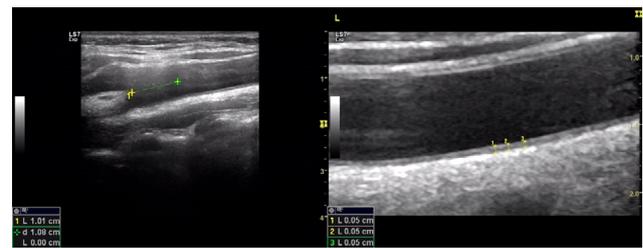
Figure 1. Measurement of common CIMT in carotid artery Doppler ultrasonography

The Laboratory and ultrasonographic findings of individuals in the patient and control groups were evaluated. Patients' age, gender, disease duration, medical treatment used for the disease, LDL, triglyceride levels, lymphocyte and monocyte count, MLR, and CIMT measurements were recorded.

Statistical analysis:

SPSS 22.0 was used for data analysis. Visual and analytical methods analyzed the normality of the variables. For quantitative data suitable for normal distribution, a t-test was performed on independent groups according to the number of groups. For quantitative data unsuitable for normal distribution, analyses were made using the Mann-Whitney U test according to the number of groups. The Spearman Correlation test was used to correlate the data in the patient group. The error level was taken as 0.05.

Results

Fifty-eight patients were evaluated in our study, and 33 patients diagnosed with psoriatic arthritis who met the diagnostic and inclusion criteria constitute the study group. There are 25 healthy individuals of similar age in the control group. Of the 33 patients in the study group, 15 were female, and 18 were male. Of those in the control group, 12 were female and 13 were male. The median age was 45 (32-55) in the study group and 40 (33-51 years) in the control group. There was no significant difference between the groups in terms of age (p:0.47) and gender (p:0.84) (p>0.05).

In the patient group, 14 people were using biologic agents (9 secukinumab, 1 ixekizumab, 1 tofacitinib, 1 adalimumab), 11 patients were using conventional synthetic DMARDs (9 methotrexate, 1 leflunomide), and 8 patients were using NSAIDs (Figure 2).
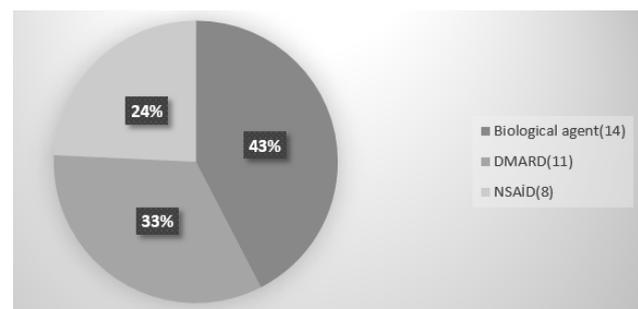
Figure 2. Drug use in the patient group

No significant difference was found when the study and control groups were compared in terms of LDL and triglyceride values (p>0.05). When the study and control groups were compared, CIMT, lymphocyte and monocyte counts were found statistically significant and high in the patient group (Table 1).

Table 1: Comparison of laboratory and imaging results of patient and control groups

	Patient Group	Control Group	P value
LDL count(mg/dl)[a]	119.42±34.84	112.12±22.44	0.36
Triglyceride count (mg/dl)[b]	103(52-178)	97(47-169)	0.41
Monocyte count (10⁹/L)[a]	0.6±0.17	0.5±0.14	0.016*
Lymphocyte count (10⁹/L)[b]	2.36(1.27-4.19)	1.77(1.48-2.86)	0.018*
MLR[a]	0.26±0.08	0.24±0.06	0.2
Right CIMT (mm)[b]	0.70(0.40-1)	0.43(0.30-0.53)	0.0001*
Left CIMT (mm)[b]	0.70(0.50-1)	0.43(0.27-0.53)	0.0001*

LDL: Low-density lipoprotein, MLR: Monocyte/lymphocyte ratio, CIMT: Carotid intima-media thickness

*p<0.05: Statistically significant

[a]: Values are given as mean±standard deviation.

[b]: Values are given as median (min-max).

Spearmen correlation analysis was performed to evaluate the relationship between CIMT and disease duration. A positive correlation was found between right and left CIMT and disease duration, and the results were statistically significant (p<0.05)(Table 2).

Table 2: The relationship between CIMT and disease duration, lymphocyte, monocytes, and MLR

	MLR	Lymphocyte	Monocyte	Disease Duration
Right CIMT (mm)	r:0.08 p:0.53	r:0.11 p:0.39	r:0.12 p:0.35	r:0.454** p: 0.008*
Left CIMT (mm)	r:0.079 p:0.55	r:0.20 p:0.13	r:0.21 p:0.11	r:0.472** p:0.006*

CIMT: Carotid intima-media thickness, MLR: Monocyte/lymphocyte ratio

*p<0.05: Statistically significant

**r: Correlation coefficient

Discussion

In this study, subclinical atherosclerosis was investigated in patients diagnosed with PsA. CIMT was found to have increased in patients diagnosed with PsA. A positive correlation was found between CIMT and disease duration.

Psoriatic arthritis belongs to the spondyloarthritis group and exhibits a heterogeneous clinical presentation often associated with psoriasis. Patients with PsA may experience various comorbidities alongside skin and joint involvement. Particularly notable is the heightened risk of cardiovascular disease within this patient population (4).

Ultrasonographic measurement of CIMT is a non-invasive, reproducible, and sensitive test for detecting subclinical vascular disease and assessing cardiovascular risk factors (16). CIMT has been widely utilized in numerous studies to identify atherosclerosis

presence in rheumatological diseases (17,18).

In a meta-analysis conducted by Bai et al., the presence of subclinical atherosclerosis in patients diagnosed with ankylosing spondylitis (AS) was investigated, and it was concluded that AS patients were at high risk. It was emphasized that these patients might require early evaluation and intervention (18). In a systematic review investigating the presence and prevalence of subclinical atherosclerosis in patients with PsA, it was concluded that CIMT was higher in patients with PsA compared to healthy controls. It was found that increased CIMT was correlated with disease activity parameters (19). In Eder et al.'s study, a positive correlation was found between inflammation intensity and disease duration. Compatible with this, our study found a positive significant correlation between CIMT and disease duration. These results also show the relationship between PsA and atherosclerosis (20).

Monocyte-to-lymphocyte ratio has been used in many studies and has been associated with many diseases (21-24). MLR is a marker that has been studied and shown to be important in malignancies (22), rheumatological (24), cardiovascular (21) and psychiatric (23) diseases. Dincer et al. found in their study in patients with PsA that MLR was high and it was associated with disease activity (24). In the study conducted by Si et al., MLR was stated as an independent risk factor for subclinical atherosclerosis and it was stated that it might be useful in the diagnosis of coronary artery disease (21). In our study, we investigated the effect of monocyte-to-lymphocyte ratio on the development of subclinical atherosclerosis in patients with PsA. When we compared the monocyte-to-lymphocyte ratio between the control group and the patient group, no significant difference was found. In addition, there was a low positive correlation with CIMT, but this correlation was not statistically significant. We think that this result is due to the relatively low clinical disease activity of the patients included in the study. We believe that there is a need for studies in which more patients are included, patients are classified according to disease activity, and additionally, different serum inflammation markers are used.

Conclusion

This study had some potential limitations. First of all, the study was single-center and conducted with a relatively small study population. The second limitation is that it was designed retrospectively. Finally, numerical differences between the patient and control groups emerged due to the study being conducted within a specific time frame. We believe that studies with long-term follow-up in a larger patient population are required.

As a result, it was found that subclinical atherosclerosis increased in patients with PsA who did not have a known cardiovascular risk factor, compared to the healthy population. Considering the relationship between atherosclerosis and the duration of diagnosis, as emphasized in our study, an awareness of cardiovascular problems is essential in the follow-up

of patients with PsA. To prevent possible morbidity and mortality in this patient group, necessary tests should be performed, prophylactic measures should be taken, diet and lifestyle changes should be explained, and a treatment plan should be made, if necessary, by consulting the relevant departments.

Conflicts of interest: No potential conflict of interest any financial or non-financial interest was reported by the authors.

Author contributions: IA: Conception, Design, Resource, Materials, Analysis, Literature Review, Critical Review, SA: Conception, Supervision, Resource, Data Collection and Processing, Writer, Critical Review, EG: Supervision, Resource, Data Collection and Processing, Analysis, Writer

Ethical approval: The ethics committee approval of the study was obtained from Sivas Cumhuriyet University Medical Faculty Hospital Clinical Research Ethics Committee with the number 2023-05/03.

References

1.Aljohani R. Metabolic Syndrome and Its Components in Psoriatic Arthritis. Open Access Rheumatol. 2022 Feb 17;14:7-16.

2.Menter A, Griffiths CE, Tebbey PW, Horn EJ, Sterry W; International Psoriasis Council. Exploring the association between cardiovascular and other disease-related risk factors in the psoriasis population: the need for increased understanding across the medical community. J Eur Acad Dermatol Venereol. 2010 Dec;24(12):1371-7.

3.Haroon M, Gallagher P, Heffernan E, FitzGerald O. High prevalence of metabolic syndrome and of insulin resistance in psoriatic arthritis is associated with the severity of underlying disease. J Rheumatol. 2014 Jul;41(7):1357-65.

4.Tobin AM, Veale DJ, Fitzgerald O, Rogers S, Collins P, O'Shea D, et al. Cardiovascular disease and risk factors in patients with psoriasis and psoriatic arthritis. J Rheumatol. 2010 Jul;37(7):1386-94.

5.Towfighi A, Saver JL. Stroke declines from third to fourth leading cause of death in the United States: historical perspective and challenges ahead. Stroke. 2011 Aug;42(8):2351-5.

6.Kong P, Cui ZY, Huang XF, Zhang DD, Guo RJ, Han M. Inflammation and atherosclerosis: signaling pathways and therapeutic intervention. Signal Transduct Target Ther. 2022 Apr 22;7(1):131.

7.Karaoğlan B, Öztürk GT, Özdoğan V, Cumaoğlu A, Oktar S, Tas N, et al. Investigation of the correlation between ADMA levels and carotid artery intima-media thickness in rheumatoid arthritis patients. Turk J Phys Med Rehab 2011;57:114-8.

8.Nezu T, Hosomi N. Usefulness of Carotid Ultrasonography for Risk Stratification of Cerebral and Cardiovascular Disease. J Atheroscler Thromb. 2020 Oct 1;27(10):1023-1035.

9.Kiran V R, P M N, Shah MI, Sivaprakasam M, Joseph J. Gaussian-Mixture Modelling of A-Mode Radiofrequency Scans for the Measurement of Arterial Wall Thickness. Annu Int Conf IEEE Eng Med Biol Soc. 2021 Nov;2021:5598-5601.

10.Rosvall M, Janzon L, Berglund G, Engström G, Hedblad B. Incident coronary events and case fatality in relation to common carotid intima-media thickness. J Intern Med 2005;257:430-7.

11.Ozkan E, Tuncel P. Erken yaş koroner kalp hastalığı olan erkek hastaların 1. derece erkek akrabalarının da bu riski gösterir ldl oksidasyon duyarlılığının tespiti. International Anatolia Academic Online Journal Health Sciences, 2023, 9(1), 30-42.

12.Libby P. The changing landscape of atherosclerosis. Nature. 2021 Apr;592(7855):524-533.

13.Cosansu NC, Dikicier BS, Yaldiz M, Solak B. Is there any association between the monocyte/lymphocyte ratio and the presence and severity of the disease in patients with psoriasis? A cross-sectional study. Sakarya Tıp Dergisi, 2020, 10(3), 430-436.

14.Urbanowicz T, Michalak M, Olasinska-Wisniewska A, Rodzki M, Krasińska A, Perek B, et al. Monocyte/Lymphocyte Ratio and MCHC as Predictors of Collateral Carotid Artery Disease-Preliminary Report. J Pers Med. 2021 Dec 1;11(12):1266.

15.Zuo B, Zhu S, Meng X, Zhao D, Zhang J. Monocyte/lymphocyte ratio is associated with carotid stenosis in ischemic stroke: A retrospective analysis. Brain Behav. 2019 Oct;9(10):e01429.

16.Urbina EM, Williams RV, Alpert BS, Collins RT, Daniels SR, Hayman L,; American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. Noninvasive assessment of subclinical atherosclerosis in children and adolescents: recommendations for standard assessment for clinical research: a scientific statement from the American Heart Association. Hypertension. 2009 Nov;54(5):919-50.

17.Dimitroulas T, Baniotopoulos P, Pagkopoulou E, Soulaidopoulos S, Nightingale P, Sandoo A, et al. Subclinical atherosclerosis in systemic sclerosis and rheumatoid arthritis: a comparative matched-cohort study. Rheumatol Int. 2020 Dec;40(12):1997-2004.

18.Bai R, Zhang Y, Liu W, Ma C, Chen X, Yang J, et al. The Relationship of Ankylosing Spondylitis and Subclinical Atherosclerosis: A Systemic Review and Meta-Analysis. Angiology. 2019 Jul;70(6):492-500.

19.Jamil M, Aslam R, Patel A, Nadir B, Khan S. Prevalence and Extent of Subclinical Atherosclerosis and Associated Cardiovascular Risk Factors in Adult Patients With Psoriatic Arthritis: A Systematic Review. Cureus. 2021 Aug 3;13(8):e16853.

20.Eder L, Jayakar J, Shanmugarajah S, Thavaneswaran A, Pereira D, Chandran V, et al. The burden of carotid artery plaques is higher in patients with psoriatic arthritis compared with those with psoriasis alone. Ann Rheum Dis. 2013 May;72(5):715-20.

21.Si Y, Fan W, Han C, Liu J, Sun L. Atherogenic Index of Plasma, Triglyceride-Glucose Index and Monocyte-to-Lymphocyte Ratio for Predicting Subclinical Coronary Artery Disease. Am J Med Sci. 2021 Sep;362(3):285-290.

22.Tan D, Fu Y, Tong W, Li F. Prognostic significance of lymphocyte to monocyte ratio in colorectal cancer: A meta-analysis. Int J Surg. 2018 Jul;55:128-138.

23.Zhu X, Li R, Zhu Y, Zhou J, Han X, Tong Y, et al. Neutrophil/lymphocyte, platelet/lymphocyte, monocyte/lymphocyte ratios and systemic immune-inflammation index in patients with depression. Bratisl Lek Listy. 2023;124(6):471-474.

24.Kelesoglu Dincer AB, Sezer S. Systemic Immune Inflammation Index as a Reliable Disease Activity Marker in Psoriatic Arthritis. J Coll Physicians Surg Pak. 2022 Jun;32(6):773-778.