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Evaluation of subclinical atherosclerosis by ultrasound radiofrequency data technology in patients with psoriatic arthritis

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SUMMARY

OBJECTIVE: This study aimed to assess the presence of subclinical atherosclerosis in patients with psoriatic arthritis using ultrasound radiofrequency data technology.

METHODS: In all, 29 psoriatic arthritis patients and 42 age- and sex-matched healthy controls were included in this cross-sectional study. Arterial stiffness and carotid intima-media thickness measurements were performed in bilateral common carotid arteries using ultrasound radiofrequency data technology in all participants.

RESULTS: In psoriatic arthritis patients, the mean carotid intima-media thickness, α and β stiffness indices, and pulsed wave velocity value were significantly higher than those in the control group (542.3 (81.3) vs. 487.9 (64.1), 9.3 (6.3) vs. 3.9 (0.1), 18.7 (17.7) vs. 8.04 (4.2), and 10.2 (3.8) vs. 6.4 (1.5), p<0.05). The mean distensibility coefficient and compliance coefficient values of the patient group were significantly lower than those of the control group (0.014 (0.01) vs. 0.03 (0.01) and 0.57 (0.33) vs. 1.02 (0.4), p<0.05). No significant correlation was found between carotid artery hemodynamic parameters and symptom duration, duration of diagnosis and treatment, disease activity ındex for psoriatic arthritis scores, erythrocyte sedimentation rate, and C-reactive protein levels (p>0.05).

CONCLUSION: In the results of our study, evidence of subclinical atherosclerosis has been detected in psoriatic arthritis patients without clinically evident cardiovascular disease or traditional cardiovascular risk factors.

KEYWORDS: Arterial stiffness. Carotid intima-media thickness. Psoriatic arthritis. Atherosclerosis. Ultrasonography.

INTRODUCTION

Psoriatic arthritis (PsA) is a heterogeneous and inflammatory joint disease that occurs in patients who have psoriasis, will develop psoriasis, or have a family history of psoriasis. Patients with PsA have heterogeneous clinical manifestations, including synovitis, enthesitis, dactylitis, axial inflammation, and skin and nail involvement[1,2]. Recently published data revealed that the pooled prevalence and incidence rates of PsA are 133 patients per 100,000 subjects and 83 per 100,000 person-years, respectively[3].

Atherosclerosis is a chronic inflammatory vascular disease characterized by the accumulation of lipids, inflammatory cells, and fibrous elements in the walls of arteries, causing progressive luminal narrowing of these vessels[4,5]. Vascular inflammation plays a critical role in pathophysiology of atherosclerosis, but the contribution of inflammation to this pathophysiology is complex and probably not fully understood[5,6]. It is widely accepted that both innate and adaptive immune responses are important for initiation and progression of atherosclerosis[5].

Carotid intima-media thickness (CIMT) is measured between the intima-lumen and the media-adventitia interfaces of the carotid artery[7]. The CIMT measurements are used as a surrogate marker for atherosclerosis and subclinical cardiovascular diseases (CVD), and as a variable predictor of cardiovascular events[7,8].

Arterial stiffness is a term used to qualitatively describe the reduction in the elastic vessel wall properties. It is one of the earliest markers of functional and structural changes in arterial walls[4,9]. Measurement of arterial stiffness is important because it is an independent predictor of the risk of future fatal and nonfatal cardiovascular (CV) events[4,10]. The pulse wave velocity (PWV) is the most widely used measure of arterial stiffness[4].

Ultrasound (US) radiofrequency (RF) data technology is a novel sonographic method for the evaluation of vascular disease. The innovations in the US technology have allowed the automatic and accurate measurement of CIMT and arterial stiffness[11,12]. During examinations with this technology, the pulsation of the arterial wall can be automatically monitored

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using RF energy, and it also gives feedback on the quality of the measurement. Thus, this measurement method is less dependent on the experience of the operator[11,13]. The quality arterial stiffness software provides real-time measurement of the expansion of blood vessel walls caused by a moving blood pressure wave resulting from heart pumping. Distension, a fundamental parameter measured by quality arterial stiffness software, is the difference between systolic and diastolic diameters. The pressure and distension values are used to calculate the stiffness parameters using the software[13]. In addition, this technique presents CIMT measurements at the micrometer level, which facilitates the acquisition of more precise and clearer results compared to other methods with millimeter accuracy[12].

We aimed to evaluate subclinical atherosclerosis using the US RF data technology in patients with PsA without clinically evident CVD or traditional CV risk factors.

METHODS

Study design and population

This cross-sectional study was conducted at the Diskapi Yildirim Beyazit Training and Research Hospital, Rheumatology and Radiology outpatient clinics between May 2019 and July 2019. This study included 29 PsA patients and 42 age- and sex-matched healthy controls. PsA patients fulfilled the classification criteria for the diagnosis of PsA (CASPAR)[14]. The control group consisted of healthy volunteers who applied to the rheumatology outpatient clinic and were not diagnosed with any rheumatological disease as a result of the evaluations. The age of PsA patients and controls were 18–60 years. The exclusion criteria for both groups were as follows: diabetes mellitus, arterial hypertension, obesity, dyslipidemia, smoking, primary cardiovascular or cerebrovascular disease, acute or chronic renal insufficiency, chronic obstructive pulmonary disease, and chronic infectious or inflammatory disease.

The study protocol was approved by the Clinical Trials Ethics Committee of our hospital (29.04.2019 – 62/03). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all PsA patients and controls before enrollment.

Clinical assessment of psoriatic arthritis

The physical examination included recording the number of tender and swollen joints using the 68 tender/66 swollen joint counts. Laboratory markers of disease activity included erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Disease activity was assessed using the Disease Activity Index for Psoriatic Arthritis (DAPSA) score[15]. The disease activity levels were defined, with disease remission as ≤4, low disease activity (LDA) as >4 to ≤14, moderate disease activity (MDA) as >14 to ≤28, and high disease activity (HDA) as >28.

Ultrasonographic assessment

Participants' details were recorded in a US device, which functioned on a MyLab 60 platform (Esaote SpA, Genoa, Italy) with a high-resolution 12-MHz linear sequence transducer (LA523). The device was equipped with the RF Quality Intima-Media Thickness Analysis and RF Quality Arterial Stiffness Analysis software, which worked using the RF method. All participants lied in the supine position with the head 45° up and horizontally 30° turned contralateral to the side being examined. The CIMT measurements were obtained from the B-mode examinations using the US RF monitoring technology from the distant common carotid arteries (CCAs) wall at a 10-mm distal segment, where appropriate images were obtained from the longitudinal plane and no plaque was visualized. After six cardiac cycles, the software calculated a real-time mean CIMT value and its standard deviation (Figure 1).

Using the RF Quality Arterial Stiffness Analysis software, arterial wall movements were monitored by RF signals at systolic and diastolic phases during six cardiac cycles in B-mode examinations. The RF Quality Arterial Stiffness Analysis technology provides a list of stiffness parameters calculated by measuring the arterial distension waveform combined with the brachial artery BP. These parameters are distensibility coefficient (DC), compliance coefficient (CC), α, β, and PWV. If the artery is stiffer, DC and CC will be lower, and α, β, and PWV will be higher.

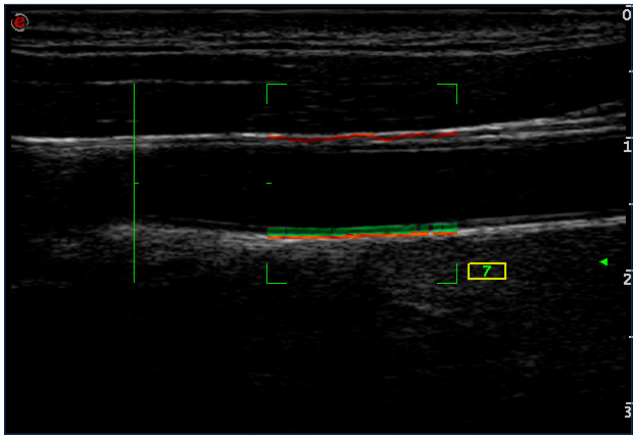

Figure 1. Left CCA quality intima-media thickness analysis. The orange line represents the RF signal following the anterior edge of the media-adventitia interface, and the green line represents the RF signal following the anterior edge of the lumen-intima interface.

Arterial stiffness parameters and CIMT measurements were made from the right and left carotid arteries of each participant, and their mean values were recorded.

Statistical analysis

The data were evaluated using the SPSS (Statistical Package for Social Sciences) program for Windows 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean (standard deviation), frequency, and percentage. χ^2 test was used to evaluate categorical variables. Visual (histograms and probability diagrams) and analytical methods (Shapiro-Wilk test) were used to check whether or not the variables were normally distributed. For normally distributed variables, Student's t-test was used to measure any statistically significant differences between two independent groups. As a statistical method for variables without a normal distribution, Mann-Whitney U test was used to measure the statistical significance between two independent groups. The relationships between variables were analyzed using Spearman's correlation coefficients. A p-value of <0.05 was considered statistically significant.

RESULTS

There was no significant difference between the groups in terms of demographic, clinical, and laboratory characteristics (p>0.05), except for ESR and CRP levels (p<0.05) (Table 1).

The mean symptom duration of the patient group was 4.5±2.9 (1–15) years, and the mean duration of diagnosis and treatment was 3.3±2.4 (1–12) years. All of the patients were using disease-modifying antirheumatic drug (DMARD) therapy and 4 (13.8%) patients were using anti-tumor necrosis factor (TNF)-alpha treatment in addition to the DMARD therapy. The mean DAPSA score of patients was 9.3±6.5 (2.3–22.2). In terms of DAPSA scores, 12 patients (41.4%) were in remission, 10 patients (34.5%) were in LDA, and 7 patients (24.1%) were in MDA periods.

In PsA patients, the mean CIMT, α and β stiffness indices, and PWV values were significantly higher than those in the controls (p<0.05). The mean DC and CC values of the patient group were significantly lower than those of the control group (p<0.05) (Table 2).

There was no statistically significant difference between DAPSA groups in terms of carotid artery hemodynamic parameters (CIMT, DC, CC, PWV, and α and β stiffness indices) (p>0.05).

Table 1. Demographic, clinical, and laboratory characteristics of PsA patients and healthy controls.

	PsA Patients (n=29)	Controls (n=42)	p-value
	Mean (SD)	Mean (SD)	
Age (years)	40.3 (9.6)	38.2 (7.9)	0.325[a]
Gender (Female:male)	18:11	26:16	0.989[b]
Glucose (mg/dL)	84.3 (7.9)	83.8 (6.2)	0.782[a]
Total Cholesterol (mg/dL)	179.5 (16.2)	172.4 (18.7)	0.109[c]
LDL (mg/dL)	123.4 (17.6)	114.7 (22.5)	0.112[c]
HDL (mg/dL)	50.6 (12.8)	47.9 (12.7)	0.383[a]
Triglycerides (mg/dL)	117.4 (41.4)	108.9 (33.7)	0.348[a]
ESR (mm/h)	17.5 (14.6)	10.2 (6.1)	0.03[c]
CRP (mg/L)	6.3 (5.8)	3.3 (2.1)	0.006[c]
BMI (kg/m^2)	26 (2.2)	25.4 (2.1)	0.082[c]
BMI categories (n, %)			
<18.5 (underweight)	0 (0)	0 (0)	0.075[b]
18.5–24.9 (normal weight)	9 (31)	22 (52.4)	
25–29.9 (overweight)	20 (69)	20 (47.6)	
≥30 (obesity)	0 (0)	0 (0)	
SBP (mm Hg)	123.6 (3.8)	122.4 (3.3)	0.206[c]
DBP (mm Hg)	81.6 (3.2)	80.2 (3.9)	0.252[c]
Pulse (beats/min)	77.7 (6.8)	77.5 (6.4)	0.876[a]

PsA: psoriatic arthritis; SD: standard deviation; LDL: low-density lipoprotein; HDL: high-density lipoprotein; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure. [a]Student's t-test, [b]χ^2 test, [c]Mann-Whitney U test.

Table 2. Distribution of carotid artery hemodynamic parameters between PsA patients and healthy controls.

	PsA Patients (n=29)	Controls (n=42)	p-value
	Mean (SD)	Mean (SD)	
*Mean-CIMT (μm)	542.3 (81.3)	487.9 (64.1)	0.002[a]
*Mean-DC (1/kPa)	0.014 (0.01)	0.03 (0.01)	<0.001[b]
*Mean-CC (mm^2/kPa)	0.57 (0.33)	1.02 (0.4)	<0.001[b]
*Mean-α Stiffness Index	9.3 (6.3)	3.9 (0.1)	<0.001[b]
*Mean-β Stiffness Index	18.7 (17.7)	8.04 (4.2)	<0.001[b]
*Mean-PWV (m/s)	10.2 (3.8)	6.4 (1.5)	<0.001[b]

PsA: psoriatic arthritis; SD: standard deviation; CIMT: carotid intima-media thickness; DC: distensibility coefficient; CC: compliance coefficient; PWV: pulsed wave velocity. [a]Student's t-test, [b]Mann-Whitney U test. *Values were given as the mean of right and left carotid artery hemodynamic parameters.

No significant correlation was found between carotid artery hemodynamic parameters and symptom duration, duration of diagnosis and treatment, DAPSA scores, ESR, and CRP levels (p>0.05).

DISCUSSION

The evidence for increased CVD burden and CV risk in patients with inflammatory rheumatic diseases is well recognized[16]. Inflammation is associated with endothelial dysfunction and atherosclerosis. Endothelial dysfunction, characterized by reduced nitric oxide (NO) bioavailability, is an early stage in the pathogenesis of atherosclerosis. The circulating inflammation mediators such as CRP can directly alter endothelial NO bioavailability[17]. PsA is associated with reduced levels of endothelial progenitor cells (EPCs) and impaired EPC function, leading to decreased release of NO[18]. Inflammatory cytokines such as TNF, interleukin (IL)-6, and IL-17 are implicated in the pathogenesis of endothelial dysfunction and atherogenesis. Inflammation leads to alterations in coagulation, increased vasoconstriction and impaired vasodilatation, and the formation of reactive oxygen species[16]. Inflammatory cells such as macrophages and polymorphonuclear neutrophils produce a variety of matrix metalloproteinases, which can alter the balance of elastin/collagen[18]. All these changes lead to subclinical and clinical atherosclerosis and adverse CV outcomes.

Early detection of subclinical atherosclerosis is important to reduce patients' CV risk[4]. Detection of increased arterial stiffness and CIMT measurement are the most commonly used methods for the diagnosis of subclinical atherosclerosis[4,7].

CIMT is a noninvasive measurement of the artery wall thickness and a surrogate marker for the presence and progression of atherosclerosis[7,8]. CIMT is used worldwide to evaluate the risk and incidence of CVD, because it can be simply, reproducibly, and noninvasively measured[7]. Similar to the results of our research, there are studies in which CIMT measurements were significantly higher in the PsA group than in the control group[19-24]. In a study by Bilgen et al., no significant difference was found between the PsA patients and control group in terms of CIMT values[25]. In our study, there was no significant correlation between CIMT values and symptom duration, duration of diagnosis and treatment, DAPSA score, CRP, and ESR levels. This result is thought to be due to the relatively small number of our patients. Similarly, Garg et al. reported that there was no correlation between CIMT and disease duration, ESR, CRP, disease activity score of 28 joints, and DAPSA scores[20]. In the other two studies, a significant correlation was found between CIMT and disease duration, ESR, and CRP levels[19,23].

There is a close relationship between arterial stiffness and atherosclerosis. Increased luminal pressure and shear stress due to arterial stiffening cause endothelial dysfunction, accelerate the formation of atheroma, and stimulate excessive collagen production and deposition in the arterial wall, leading to the progression of atherosclerosis[4]. PWV is a noninvasive method to measure arterial stiffness and is a strong predictor of future CV events and CV mortality[16]. Similar to our results, in a previous study, PWV measurements were significantly higher in PsA patients than in the control group[18]. In our study, no significant correlation was found between PWV measurements and symptom duration, duration of diagnosis and treatment, DAPSA scores, ESR, and CRP levels. Shen et al. showed that there was a significant correlation between PWV and cumulative-ESR but not cumulative CRP levels[18].

In our results, there was no statistically significant difference between DAPSA groups (remission, LDA, and MDA) in terms of carotid artery hemodynamic parameters, which might be due to the low number of patients in DAPSA groups.

The obvious limitation of this study was the relatively small number of patients in the sample. The exclusion criteria of our study were the most important reason for this limitation. On the contrary, the strongest aspect of our study was our exclusion criteria. Thus, we evaluated the relationship of our main variables with PsA.

CONCLUSION

In the results of our study, evidence of subclinical atherosclerosis has been detected in PsA patients without clinically evident CVD or traditional CV risk factors. To the best of our knowledge, this is the first study that detected subclinical atherosclerosis in PsA patients using US RF data technology. This ultrasonographic method is an easy, reproducible, noninvasive, sonographic technique that provides more precise and clear findings of subclinical atherosclerosis.

AUTHORS' CONTRIBUTIONS

CO: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, writing – original draft, writing – review and editing. **HK:** Conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft, writing – review and editing. **SCS:** Data curation, formal analysis, writing – original draft, writing – review and editing. **ZO:** Data curation, formal analysis, software, writing – original draft, writing – review and editing.

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