

## The Association of Psoriatic Arthritis with Carotid Intima-Media Thickness

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### Abstract

**Background:** Previous studies have showed that psoriatic arthritis increases the risk of cardiovascular disease and atherosclerosis. On the other hand, an increased carotid intima-media thickness can be associated with atherosclerosis. The present study aimed to evaluate the association between psoriatic arthritis and carotid intima-media thickness.

**Methods:** In this case-control study performed during 2018, 22 patients with psoriatic arthritis and 22 healthy controls matched for age and sex were participated. In all subjects, the carotid intima-media thickness was measured by ultrasonography. Systemic inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were assessed in psoriatic arthritis patients.

**Results:** The mean carotid intima-media thickness was  $56 \pm 0.10$  mm in the psoriatic arthritis patients and  $54 \pm 0.07$  mm in the control group with no significant difference ( $p=0.358$ ). According to the regression analysis, carotid intima-media thickness had no positive correlation with age, sex and body mass index. The carotid intima-media thickness increased in psoriatic arthritis patients with increasing the duration of arthritis, disease activity (DAS-28), CRP, and ESR, but the correlations were not statistically significant.

**Conclusion:** The study findings do not support the previous reports that claimed a potential correlation between mean carotid intima-media thickness and psoriatic arthritis.

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### Introduction

Psoriatic arthritis (PsA) is a rheumatoid-like arthritic disease characterized by inflammation, pain, and swelling in the joints of patients with psoriasis (1). This disorder occurs in

up to 42 % of patients suffering from psoriasis and affects approximately 0.1–1.0 % of the general population (2).

Previous studies have showed that psoriasis increases the risk of cardiovascular disease and atherosclerosis (3, 4).

Observational studies on patients with rheumatic diseases have shown a link between inflammation and atherosclerosis (5). Inflammation can promote atherosclerosis directly or affects cardiovascular risk factors, such as hypertension, serum cholesterol level, and insulin level (6).

Increased carotid intima-media thickness (CIMT) is associated with atherosclerosis (7). Systemic inflammation in patients with rheumatoid arthritis, systemic lupus erythematosus, psoriasis, and scleroderma is associated with an increase in CIMT. It can be used to assess the risk of coronary heart disease (8). CIMT greater than or equal to 75% (generally > 0.9 mm) is an indicative of increased cardiovascular disease risk and the need for medical interventions. Previous studies have shown that CIMT difference of 0.1 mm can increase the risk of ischemic heart attack up to 15% and the risk of stroke by 13% to 18% (9).

Cardiovascular damage (CVD) and atherosclerosis in patients with psoriatic arthritis can be caused by several mechanisms such as increase of the production of inflammation mediators (chemokines, cytokines, and adhesion molecules), anti-endothelial cell antibodies, genetic polymorphisms, shifting T lymphocyte subsets and oxidative stress. CVD is one of the leading causes of death in psoriatic arthritis patients (10).

The number of studies that evaluated the relationship between PsA and CIMT is low. Several studies have found increased CIMT in patients with psoriatic arthritis. In the study of Tam *et al.*, the mean CIMT was significantly higher among PsA patients than among healthy individuals (3). Balci *et al.* reported that the mean CIMT was significantly higher in the patients with PsA in comparison to healthy people (11). But, Yilmazer *et al.* (12) and Yiu *et al.* (10) did not report a significant difference between patients and control group in

CIMT. Therefore, further study can help to clarify contradictory findings. The present study was aimed to evaluate the association between psoriatic arthritis and carotid intima-media thickness.

## Material and Methods

In this case-control study, 22 patients with PsA who referred to the Rheumatology clinic of Kashan University of Medical Sciences during 2018 and 22 healthy controls matched for age and sex were participated. The PsA patients who had CASPAR criteria (13) were included in the study. Exclusion criteria were hypertension (systolic blood pressure more than 140 mmHg and/or diastolic blood pressure more than 90 mmHg), diabetes mellitus (fasting blood glucose more than 110 mg/dL), hyperlipidemia (total cholesterol >200 mg/dL and/or triglyceride >160 in fasting plasma), renal disease (serum creatinine >1.3 mg/dL), obesity (body mass index  $\geq 25$  kg/m<sup>2</sup>), history of cardiovascular disease, smoking, pregnancy, history of chronic inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus and history of estrogen therapy. This study was approved by Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1398.038). All patients and healthy controls signed informed *consent* forms. Demographic data, including age, sex, and duration of skin psoriasis, duration of PsA, family history of psoriasis or PsA were collected from all patients, and blood samples were taken for the assessment of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). For all PsA patients, the number of swollen (SW28) and tender joints among 28 joints (T28), erythrocyte sedimentation rate, and Visual Analogue Scale (VAS) were calculated. Then,

disease activity was calculated using the Disease Activity Score in 28 joints (DAS 28) based on the following formula:

$$\text{DAS 28} = 0.56(\sqrt{T28}) + 0.28(\sqrt{SW28}) + 0.70 (\text{Ln ESR}) + 0.014 \text{ VAS}$$

The presence of atherosclerosis was determined by analyzing the carotid artery using ultrasound (US) examination performed by one radiologist in blinded conditions for all clinical information. The *CIMT* was calculated as a marker of atherosclerosis. The bilateral carotid ultrasonography performed with a 10-MHz linear-array transducer (Medison ultrasound V20, Seoul, Korea) on the subjects located in supine position.

### Statistical Analysis

All statistical analyses were performed using SPSS software 22 (SPSS Inc., Chicago, IL, USA). Data are represented as mean  $\pm$  standard deviation for continuous variables and frequencies. Categorical variables were compared using chi-square test. Student's t-test was used for comparison of the mean and maximum *CIMT* between PsA

patients and controls. Correlation of *CIMT* with variables was evaluated by regression analysis. A p-value below 0.05 was considered as statistically significant.

### Results

Demographic, clinical, and laboratory features of 22 patients with psoriatic arthritis and 22 matched controls have been summarized in Table 1. The mean age of PsA patients was 39.86 years, and 57.1% were male. The mean ( $\pm$ SD) of DAS28 score in PsA patients was 3.84 $\pm$ 1.03 (1.03-3.84). The mean of *CIMT* in the PsA patients and control group was 56 $\pm$ 0.10 and 54 $\pm$ 0.07 mm, respectively. Overall, the mean *CIMT* and maximum *CIMT* did not show significant differences between PsA patients and control group (p=0.358, p=0.689, respectively). The regression analysis did not show a significant correlation between *CIMT* and variables of age, sex and BMI (Table 2, p>0.05). The *CIMT* increased in PsA patients with increase of the duration of arthritis, DAS-28, CRP, and ESR, but the correlations were not statistically significant.

**Table 1.** Demographic, clinical, and laboratory features of the studied subjects

Characteristic	PsA patients (n=22)	Controls (n=22)	P value
Age (mean $\pm$ sd)	39.86 $\pm$ 8.28	41.8 $\pm$ 8.13	0.97
Sex (Male/Female)	8/14	8/14	1.00
Body mass index (kg/m <sup>2</sup> )	23.78 $\pm$ 0.94		
Duration of arthritis (years)	7.66 $\pm$ 8.77		
Duration of Psoriatic Skin (years)	11.59 $\pm$ 9.72		
DAS-28	3.84 $\pm$ 1.03		
ESR (mm/hr)	16.27 $\pm$ 12.03		
CRP (mg/dl)	3.86 $\pm$ 2.51		
Mean <i>CIMT</i> (mm)	0.56 $\pm$ 0.10	0.54 $\pm$ 0.07	0.358
Maximum <i>CIMT</i> (mm)	0.67 $\pm$ 0.09	0.69 $\pm$ 0.13	0.689

**Table 2.** Association of CIMT with variables in 22 patients with PsA

Parameter	r	P value
Age	0.251	0.101
Sex (Male/Female)	0.231	0.131
Body mass index (kg/m <sup>2</sup> )	0.186	0.408
Duration of arthritis (years)	0.205	0.361
DAS-28	0.067	0.767
ESR	0.001	0.995
CRP	0.174	0.439
PsA disease	0.930	0.358

## Discussion

Recently, it has been reported that PsA patients have a higher CIMT in comparison with the general population (3, 14, 15), but the result of the present study did not show a significant correlation between CIMT and PsA disease.

Several studies have found increased CIMT as an evidence for atherosclerosis (3, 14, 16). The present study revealed that PsA patients had slightly higher IMT ( $0.56 \pm 0.10$  mm) compared with controls ( $0.54 \pm 0.07$  mm), but this difference was not statistically significant ( $p=0.358$ ). The number of studies conducted on PsA and CIMT is low. In Yilmazer *et al.* study, CIMT in PsA patients and healthy subjects has been  $0.611 \pm 0.08$  mm and  $0.596 \pm 0.08$  mm, respectively and compatible with our results, they have not reported a significant association between PsA and CIMT (12). Similarly, no significant difference was found in maximum IMT results between PsA patients and healthy group ( $0.753 \pm 0.113$  versus  $0.743 \pm 0.09$ , respectively;  $p > 0.05$ ) in one of the other previous studies (14). In the study of Yiu *et al.*, CIMT was not significantly greater in PsA patients without cardiovascular disease risk factors than in control groups ( $0.71 \pm 0.11$  mm vs.  $0.67 \pm 0.08$  mm,  $P=0.08$ ) (10). In contrast, in the study of Tam *et al.* (3), the mean CIMT was  $0.740 \pm 0.126$  mm among PsA

patients and  $0.626 \pm 0.074$  mm among healthy controls, that this difference was significant ( $p < 0.001$ ). Balci *et al.*, reported that the mean CIMT was significantly higher in the patients with PsA in comparison to healthy individuals ( $0.609 \pm 0.146$  mm vs.  $0.526 \pm 0.104$  mm, respectively,  $P=0.003$ ) (11). Several other studies also have found a positive association between increased mean CIMT and PsA disease (5, 6). Participation of PsA patients with shorter duration of disease in the current study compared with the mentioned studies can be a reason for the contradictory results. In addition, sample size has been varied in different studies. However, results obtained in the present study cannot show the lack of association between PsA disease and atherosclerosis. Although CIMT is considered as an indicator for atherosclerosis in PsA disease, other markers that were not determined in this study such as flow-mediated endothelial-dependent vasodilatation (FMD) can be more sensitive than IMT (11).

In the current study, we did not find any correlation between CIMT and variables of age, sex, BMI, duration of disease, DAS-28, ESR and CRP level which is similar to the results of Mazlan *et al.* study (17). Yiu and colleagues also have not reported an association of increased CIMT with BMI, duration of disease, Psoriasis Area and Severity Index (10). In

study of Kimhi *et al.*, the mean of IMT significantly associated with age, BMI, duration of PsA and ESR (16). Eder *et al.*, too, found a correlation of PsA with ESR and CRP (14), but according to another study, the levels of acute-phase proteins (CRP and ESR) were not reliably increased in PsA patients even in active inflammation (4). Contessa and colleagues reported that IMT increase is associated with age, BMI, age at PsA onset, disease duration and activity, but not with CRP (18). Contradictions observed between the results of the current study and others may be due to the small sample size in our study and differences in some parameters such as age of patients, disease severity and disease duration among different studies. The exclusion of patients with high lipid profile, high BP and metabolic syndrome was a reason for no association between psoriatic arthritis and thickness of carotid intima media.

### Conclusion

This study findings do not support the previous reports claiming a potential correlation between mean CIMT and PsA. Future studies with large sample size are required.

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### Limitations

The small sample size was a limitation for this study.

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### Ethics approval and consent to participate

This study was approved by Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1398.038). Each subject signed an informed written consent form.

### Competing interests

The authors declare that they have no competing interests.

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