

# Carotid intima-media thickness in patients with mild or moderate psoriasis

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## Abstract

**Introduction:** Psoriasis is a chronic inflammatory disease associated with a significantly higher morbidity and various comorbidities (obesity, metabolic syndrome, diabetes). Previous studies focused mainly on patients with severe psoriasis who were found to have increased markers of early atherosclerosis, higher intima-media thickness (IMT) values.

**Aim:** To evaluate the association between the severity or duration of psoriasis and carotid IMT in patients with mild and moderate psoriasis.

**Material and methods:** We studied seventy four patients with mild and moderate psoriasis. Clinical assessment and common carotid artery (CCA) IMT measurements were performed in all patients.

**Results:** The mean CCA IMT value was  $1.03 \pm 0.37$  mm, mean PASI score (psoriasis area severity index) was  $18.6 \pm 10.5$ . There was a significant association between PASI score and IMT values ( $r = 0.33$ ;  $p = 0.007$ ) adjusted for age, psoriasis duration, blood pressure and smoking. However, we found no correlations between carotid IMT and disease duration or other clinical variables.

**Conclusions:** The severity of psoriasis is associated with carotid IMT even in patients with mild and moderate psoriasis.

**Key words:** intima-media thickness, psoriasis, cardiovascular risk, atherosclerosis.

## Introduction

Psoriasis is a chronic inflammatory disease that affects 1–3% of the general population, which is about 800 000–1 000 000 people in Poland [1–4]. Although the exact etiology is unclear, major abnormality in the disease is an increased number of cell divisions in the basal layer of the epidermis as well as the accelerated and irregular cycle of maturation of keratocytes. Moreover, immunological activation observed in psoriasis and reported in prior studies shares some common pathways with vascular atherosclerosis [5, 6]. Available data suggest that psoriasis increase the risk of atherosclerosis and cardiovascular events [6–8]. The explanation is focused on similarities in the inflammatory process with the same cells and inflammatory mediators observed in both psoriasis and atherosclerosis. Moreover, some common pleio-

tropic genetic loci (PSOR2-4, CDKAL1 AOE4) may probably play also a role in the shared genetic susceptibility to both psoriasis and metabolic syndrome [1, 2, 5–7]. Sommer *et al.* demonstrated that patients with psoriasis have a significantly higher risk of metabolic syndrome [9, 10]. Love *et al.* confirmed this increased risk, regardless of age, gender, race, smoking and C-reactive protein (CRP) levels [11, 12]. Meta-analysis of more than 41 000 patients showed that the risk of metabolic syndrome is increased more than twice in patients with psoriasis [9, 13] and inversely, a high body mass index (BMI) and smoking predispose to the occurrence of psoriasis [11, 12]. Previous studies showed significantly increased carotid artery intima-media thickness (IMT) in patients with psoriatic arthritis and patients with severe exacerbation of skin lesions [10] with limited data among individuals with less severe disease.

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## Aim

Therefore, our aim was to assess carotid IMT in patients with mild to moderate psoriasis.

## Material and methods

The study included 74 patients with psoriasis (mean disease duration: 17.1 ±11.2 years) followed up in the Department of Dermatology at the Medical University of Silesia.

The precise assessment of psoriasis included a clinical examination with a past history of treatment and duration of psoriasis with the psoriasis area and severity index (PASI) score. The PASI score lower than 10 points was considered a mild form of the disease, 10–50 – a moderate and more than 50 – a severe disease [4, 7]. The main exclusion criteria included prior diagnosis or treatment of coronary or peripheral artery disease diagnosed on the basis of non-invasive tests or coronary angiography, acute coronary syndrome, heart failure, stroke or transient ischemic attack, significant liver or kidney dysfunction and severe hypertension.

Patients with mild hypertension and antihypertensive monotherapy (9%) were not excluded from the study. All the patients used topical agents and biological therapy was used only in 5 (7%) patients. None of the patients used any other cardiovascular pharmacotherapy.

Common carotid artery IMT was obtained as a mean value from serial manual measurements taken from both sides at the distal segments of common carotid artery (CCA). Atherosclerotic plaque was diagnosed with a carotid artery wall thickness exceeding 1.5 mm. We used the high-resolution ultrasonography with a linear probe

of 7.5 MHz (Toshiba Aplio). Carotid IMT was assessed by two independent investigators blinded to the patients' data. In addition, for each patient body weight, height, waist and hip circumference were measured.

## Statistical analysis

All results presented in the text, tables and figures are expressed as means ± standard deviation or number and percentage. The results' normal distribution was analyzed with the Kolmogorov-Smirnov test. Associations between parameters were assessed using Pearson or Spearman correlation analysis depending on the parametric or nonparametric variables. Multivariable logistic and linear regression was used to assess independent predictors of low-density lipoprotein (LDL)-cholesterol (LDL-C), LDL/high-density lipoprotein (HDL) ratio and lipid goals achievement. A value of  $p < 0.05$  was considered statistically significant. Statistical analysis was undertaken using MedCalc software.

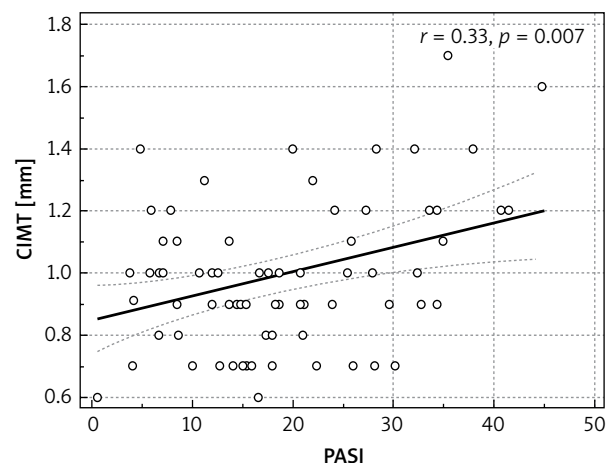
## Results

The study included 74 patients (F/M 47/27, mean age: 46 ±12 years old). Seven patients had mild hypertension (9%) and 27 (36%) were cigarette smokers, mean BMI was 27.8 ±5.2 kg/m<sup>2</sup>. The mean duration of psoriasis was 17.1 ±11.2 years, and the average severity of the disease using PASI score was 18.6 ±10. The study group included patients with mild and moderate psoriasis. The clinical characteristics of the study group is presented in Table 1.

The average value of carotid IMT in the study group was 1.03 ±0.37 mm. Carotid IMT adjusted for age, psoriasis duration, blood pressure and smoking was significantly associated with the PASI score ( $r = 0.33$ ;  $p = 0.007$ ) (Figure 1). There was no correlation between IMT and duration of psoriasis ( $r = 0.10$ ;  $p = 0.38$ ). Moreover, none of the anthropometric parameters were associated with the

**Table 1.** The baseline clinical characteristics of the study group

Parameter	Result
	Mean ± SD or n (%)
Age [years]	46.1 ±11.9
Females/males	47 (64)/27 (36)
Hypertension	7 (9)
Diabetes	0 (0)
Hyperlipidemia	0 (0)
Current smoking	27 (36)
Body mass index [kg/m <sup>2</sup> ]	27.8 ±5.2
Weight [kg]	81.2 ±15.9
Waist/hip ratio	0.92 ±0.08
Psoriasis [years]	17.1 ±11.2
Psoriasis area severity index score	18.7 ±10.6



**Figure 1.** Association between carotid intima-media thickness (CIMT) and psoriasis area severity index (PASI)

severity or duration of psoriasis. Mean blood pressure values were within normal limits and we did not find any associations with the duration of psoriasis or PASI score.

## Discussion

Our study showed that increased subclinical measures of atherosclerosis are observed even at the stage of mild and moderate psoriasis. A great majority of previous studies on the increased cardiovascular risk in psoriasis included only patients with psoriatic arthritis (PsA), which seems to be a logical analogy to an increased previously established cardiovascular risk in patients with other autoimmune diseases, such as rheumatoid arthritis (RA). Moreover, patients with PsA were reported to have an increased risk of obesity, hypertension, dyslipidemia, and insulin resistance, which may be associated with common pathways of inflammation [10]. A study by Tam *et al.* demonstrated that carotid IMT was significantly higher in the PsA group compared to healthy controls and remained significant when PsA patients were divided into subgroups with and without risk factors for cardiovascular disease (CVD) [10]. When the carotid IMT cut-off point of 95 percentile for age, gender and race was included with the presence of known CVD risk factors (obesity, smoking, hypertension), an increase in carotid IMT was associated with an increase in the 10-year risk of coronary artery disease by 14% [10, 14–16]. It suggests that psoriatic arthritis is an independent risk factor for atherosclerosis.

Hypertension observed in psoriatic patients may result from the treatment of psoriasis (steroids, cyclosporine). Three patients in our study (4%) required hypotensive monotherapy during the treatment of psoriasis (calcium channel blockers or diuretics). Carotid IMT was also associated with serum levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and blood pressure but not with lipid levels in patients with PsA [17]. Balci *et al.* demonstrated increased carotid IMT in patients with psoriasis, but in moderate and severe stages of disease compared to the control group. Moreover, carotid IMT was also associated with the PASI score ( $r = 0.5$ ;  $p < 0.01$ ). However, the same study did not confirm the relationship between carotid IMT and BMI [15]. Another study showed significant associations among PASI, carotid IMT and BMI in a group of fairly young patients (mean age: 39) [18]. Still, Kimhi *et al.* demonstrated that BMI was associated with disease activity only in patients with mild disease (mean PASI:  $8.6 \pm 2$ ) [19]. On the other hand, Kimhi *et al.* in their study did not show any correlation between IMT and PASI [19]. Inconclusive findings may result from the course of the disease. Psoriasis has periods of exacerbation and remissions with variable PASI score. The effectiveness of the treatment of both classical disease-modifying drugs and biological drug therapy should be also taken into account. Hence, a considerable variation in disease

activity (PASI) along the time/over time makes it difficult to demonstrate the relationship with the presence of subclinical markers of atherosclerosis such as carotid IMT [20–23]. On the other hand, even patients with mild psoriasis and low PASI values are at an increased risk of cardiovascular diseases. Wu *et al.* demonstrated in their retrospective analysis of more than 10 thousand patients with mild psoriasis and more than 50 thousand healthy controls, a significantly higher risk of heart attack in a group of psoriasis (HR = 1.3) [24].

In our study, the mean carotid IMT indicated an increased risk of CVD even in patients with slight disease activity, but also correlated with the severity of psoriatic disease. This may confirm the hypothesis that one of the causes of the increased risk and premature development of atherosclerosis in these patients is a common inflammatory pathway of both diseases. The share of the same inflammatory mediators and similar cellular response in both cases, leading to the endothelial dysfunction, angiogenesis, oxidative stress and additionally genetic predisposition allows to search for common methods of prevention and treatment.

The correlation between TNF- $\alpha$  and carotid IMT seems to be a very interesting issue. Several studies have confirmed that psoriasis treatment with TNF- $\alpha$  inhibitors is associated with a reduction in the CVD risk and a significant reduction of markers of subclinical atherosclerosis such as IMT and improvement of endothelial dysfunction [25]. The time in which the effect persists, varies according to different authors. Some of them believe that it disappears after 8 weeks [26], according to others it persists still 6 months after the treatment with adalimumab, infliximab, or etanercept [27]. In addition, previous studies showed that TNF- $\alpha$  inhibitor therapy is associated with a significant reduction in the risk of myocardial infarction as compared to the conventional treatment. Methotrexate therapy and phototherapy were also associated with a significant reduction in the cardiovascular risk [28–30]. Other studies point to the benefits of therapy in reducing the CVD risk, but did not confirm the impact of this treatment on IMT thickness [31]. It was also shown that the enhancement of the skin condition by treatment of the general and local inflammation may be responsible for improving HDL function without affecting lipid levels in these patients [28]. The effect of pharmacotherapy on the decrease in the CVD risk certainly requires a multicenter prospective study of a large group of patients because it may open a new way of treating atherosclerosis in its early stages in extremely endangered patients with psoriasis.

The main limitation in our study is the lack of a matched control group and the sample size. However, it provides new results in a subgroup of psoriatic patients with very limited data. We showed that even mild and moderate psoriasis is associated with an increased cardiovascular risk. Further studies should search for early markers of atherosclerosis in these patients in order to

identify individuals with a higher risk requiring optimal pharmacotherapy.

### Conflict of interest

The authors declare no conflict of interest.

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