Clinical and Laboratory Studies

Dermatology

Dermatology 2009;218:110–113
DOI: 10.1159/000182256

Received: July 14, 2008
Accepted: September 24, 2008
Published online: December 6, 2008

Chronic Plaque Psoriasis Is Associated with Increased Arterial Stiffness

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Key Words
Chronic plaque psoriasis · Pulse wave velocity · Endothelial dysfunction

Abstract
Background: Patients with moderate to severe chronic plaque psoriasis have a higher prevalence of cardiovascular risk factors and atherosclerosis. Arterial stiffness is a measure of endothelial dysfunction and an independent predictor of cardiovascular events. ***Objectives:*** To investigate whether chronic plaque psoriasis is associated with an increased arterial stiffness. ***Methods:*** A cross-sectional study on 39 adult patients with moderate to severe chronic plaque psoriasis and 38 control patients with skin diseases other than psoriasis was conducted. Arterial stiffness was assessed by carotid-femoral and carotid-radial pulse wave velocity (PWVcf, PWVcr). ***Results:*** PWVcf was significantly higher in patients with psoriasis than in controls (means ± SD; 8.88 ± 1.96 vs. 7.57 ± 1.34 m/s; p = 0.001). Difference was still significant after adjustment for age, gender, smoking status, hypertension and body mass index (8.78 ± 1.98 vs. 7.78 ± 2.0 m/s; p = 0.03). There was a positive correlation between PWVcf and years of psoriasis duration (r = 0.58; p = 0.0001), but not with disease severity. ***Conclusion:*** Moderate to severe chronic plaque psoriasis may be independently associated with increased arterial stiffness. Psoriasis duration could be a risk factor for arterial stiffness and atherosclerosis.

Introduction

Patients with psoriasis have a higher prevalence of obesity, atherogenic dyslipidemia, diabetes, hypertension, hyperhomocysteinemia and metabolic syndrome, all of which may favor the development of atherosclerosis [1–5]. However, these factors alone do not explain excess vascular disease in psoriasis patients [6, 7]. Accumulating evidence indicates that moderate to severe chronic plaque psoriasis is an independent risk factor for cardiovascular diseases [6, 7]. Therefore, persistent skin inflammation in psoriasis patients may contribute to a premature atherosclerosis, as it occurs in rheumatoid arthritis [8] and systemic lupus erythematosus [9]. Endothelial dysfunction is the critical early step in the process of atherogenesis, and it is commonly investigated by measuring arterial stiffness [10]. In this study, we evaluated arterial stiffness by measuring pulse wave velocity (PWV) in patients with moderate to severe psoriasis. The aim of this study was to evaluate whether psoriasis patients could demonstrate higher PWV compared to controls.

Patients and Methods

Thirty-nine psoriasis patients (cases) and 38 patients with a diagnosis of a skin disease other than psoriasis (controls) with an age range of 30–60 years and BMI range of 20–30 were selected among those consecutively admitted to the outpatient clinic of the University Hospital of Verona. The source population of cases

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Table 1. Characteristics of the study populations

	Controls	Psoriasis	p
Number of patients	38	39	
Male/female ratio	19/19	19/19	
Age, years	51.5 ± 12.7	51.3 ± 13.4	0.94
Weight, kg	76.6 ± 15.1	80.5 ± 13.8	0.26
Height, cm	165.2 ± 25.4	170.8 ± 7.8	0.20
BMI	26.9 ± 4.2	26.4 ± 3.2	0.68
Current smokers	8 (21)	16 (41)	0.01
Blood pressure, mm Hg			
Systolic	126.0 ± 17.2	133.5 ± 16.4	0.06
Diastolic	82.0 ± 9.8	83.9 ± 10.8	0.43
Pulse pressure, mm Hg	44.1 ± 10.0	47.6 ± 13.6	0.14
Mean arterial pressure, mm Hg	100.4 ± 10.3	106.1 ± 11.3	0.22
Augmentation index, %	10.4 ± 18.4	10.8 ± 15.8	0.94
Homocysteine, μmol/l	11.3 ± 8.2	12.8 ± 4.9	0.15
CRP, mg/l	4.5 ± 3.4	4.4 ± 3.1	0.78
Glucose, mg/dl	96.5 ± 3.9	96.8 ± 4.9	0.86
Total cholesterol, mg/dl	199.3 ± 39.6	212.3 ± 38.5	0.15
Triglycerides, mg/dl	126.2 ± 41.5	140.9 ± 51.2	0.19

Figures in parentheses are percentages. CRP = C reactive protein.

and controls was the same. The inclusion criteria for the cases were a clinical diagnosis of moderate to severe chronic plaque psoriasis (i.e. body surface involvement >10% or Psoriasis Area and Severity Index, PASI, score >10) and the absence of systemic treatment for at least 2 months before study investigations. Inclusion criteria for controls were diagnosis of a skin disease other than psoriasis. Subjects with diabetes, psoriatic arthritis and/or a history of major cardiovascular events (i.e. myocardial infarction or stroke) were excluded. None of the subjects engaged in physical exercise more than once a week.

Anthropometric Measurements

While the subjects were wearing light indoor clothes and no shoes, their body weight was measured to the nearest 0.1 kg (Salus, Milan, Italy) and height to the nearest 0.5 cm with a stadiometer (Salus). BMI was calculated as body weight adjusted by stature squared (kg/m^2).

Smoking Status

Current smokers were defined as participants who smoked cigarettes daily or who had stopped smoking <5 years before the enrollment in the study. Nonsmokers were participants who had smoked <5 to 10 packs of cigarettes during their lifetime or who had stopped smoking >5 years before the enrollment.

Laboratory

Venous samples were taken after the subjects had fasted overnight. Plasma levels of total homocysteine were measured by high-performance liquid chromatography. Serum cholesterol, triglycerides, glucose and C reactive protein were measured with enzymatic procedures.

Blood Pressure and Arterial Stiffness Measurements

Non-invasive brachial blood pressure was measured thrice in a time frame of 15 min using a traditional sphygmomanometer in the left arm of the subject, in the supine position. The mean of 3 readings was considered as the real blood pressure. The blood pressure was recorded immediately prior to tonometric recording. Carotid-femoral (PWVcf) and carotid-radial (PWVcr) pulse wave velocity were measured noninvasively using a small portable tonometer (PulsePen; Diatecne, Milan, Italy). The software provides absolute arterial pressure values, assessment of arterial pulse wave contours, estimation of reflection waves and measurements of PWV [11].

Statistical Analysis

Analyses were made using SPSS version 12.0 (SPSS, Chicago, Ill., USA) and GraphPad version 4.0 (El Camino Real, San Diego, Calif., USA) software packages. Results are presented as means ± standard deviations (SD). Log transformation was performed for non-normal variables. Comparisons of anthropometric, metabolic and blood pressure variables between cases and controls were made by using an unpaired t test. Comparisons in arterial compliance variables between cases and controls were made with ANOVA. ANCOVA was then used to adjust for age, gender, smoking status, hypertension and body mass index. Backward multiple regression analyses were used to test the joint effects of sex, age, smoking habit, hypertension, psoriasis, hypercholesterolemia, hyperhomocysteinemia and mean arterial pressure on PWVcf. The Pearson test was used to analyze the correlation between PWVcf and years and extension of disease. The level of statistical significance was $p < 0.05$ for all the variables.

Results

Baseline Characteristic of the Study Population

Baseline characteristics of the study population are reported in table 1. There were not significant differences between psoriasis patients and controls concerning gender distribution, age, BMI, systolic and diastolic blood pressures, as well as serum values of homocysteine, C reactive protein, cholesterol and triglycerides. However, the prevalence of currents smokers was higher in psoriasis patients than in controls (41.0 vs. 21.0%; p = 0.01). The mean PASI value was 12.4 ± 4.7 (range, 5.9–21.4) and the median was 9.8. Psoriasis duration was 14.8 ± 12.7 years (range, 1.5–45) with a median of 12 years. Forty percent of controls were affected by chronic eczema (atopic and/or allergic contact dermatitis), 34% by chronic idiopathic urticaria and 26% by basal cell carcinomas.

Differences in PWV between Cases and Controls

PWVcf was significantly higher in patients with psoriasis than in controls (8.88 ± 1.96 vs. 7.57 ± 1.34 m/s; p = 0.001), whereas PWVcr was not statistically different between the 2 groups (8.85 ± 5.70 vs. 8.91 ± 5.50 m/s;

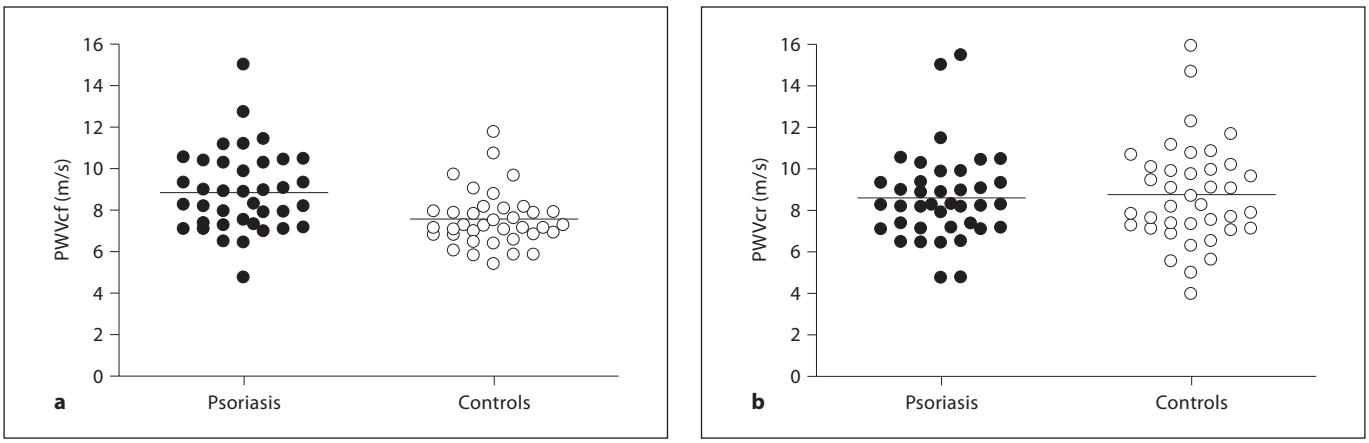

Fig. 1. a PWVcf was significantly higher in patients with psoriasis than in controls (p = 0.001). **b** PWVcr was not statistically different between the 2 groups (p = 0.8).

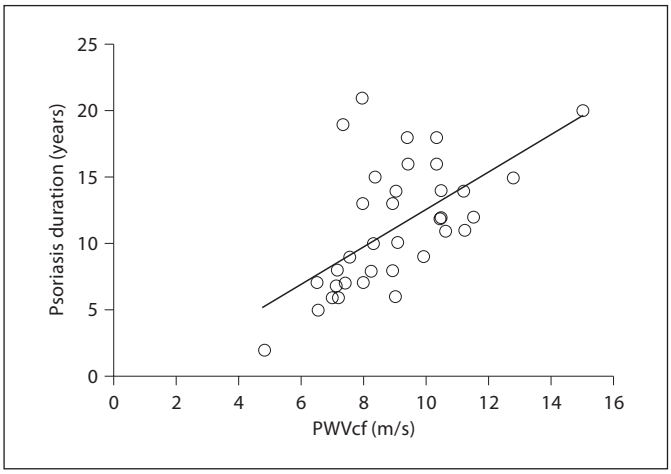

Fig. 2. PWVcf directly correlated with psoriasis duration according to the Pearson test (r = 0.58; p = 0.0001).

p = 0.8; fig. 1). Moreover, the difference in PWVcf between patients with psoriasis and controls was still statistically significant after adjustment for age, gender, smoking status, hypertension and body mass index (8.78 ± 1.98 vs. 7.78 ± 2.0 m/s; p = 0.03). A backward regression model procedure was then employed in which PWVcf was considered as the dependent variable, and sex, age, smoking habit, hypertension, psoriasis, hypercholesterolemia, hyperhomocysteinemia and mean arterial pressure were regarded as independent variables. The final model resulting from the selection procedure contained (among the independent variables) age, smoking status and psoriasis and explained 41.8% of the PWVcf variability. PWVcf values were directly correlated with psoriasis duration in years (r = 0.58; p = 0.0001; fig. 2). No significant correlations were found between PWVcf and PASI scores.

Discussion

Considerable evidence indicates a strong association between arterial stiffness and the risk of cardiovascular events, including coronary artery disease and stroke [12]. PWV is the gold standard measurement of arterial stiffness and is obtained by calculating the time taken for a pulse wave to travel between 2 sites in the arterial tree, most commonly, between the carotid and femoral peripheral artery sites [13]. It has been recently shown that PWVcf is a more precise indicator of atherosclerosis than either PWVcr or femoral-posterior tibial PWV [14]. PWVcf increases with age, blood pressure, diabetes, male gender, chronic renal diseases and chronic inflammatory autoimmune diseases [15–20]. In our study, we observed a significant difference between psoriasis patients and controls in PWVcf, but not in PWVcr. This finding suggests that psoriasis is associated with elastic artery stiffness, which is associated with higher cardiovascular risk. Our study shows that psoriasis is independently associated with increased arterial stiffness by age, gender, smoking status, hypertension and body mass index. Moreover, in the backward regression model (including all the cardiovascular risk factors as independent variables) psoriasis was one of the main independent predictors of PWVcf – explaining 41.8% of its variance with

gender, age and smoking habit. Endothelial function has been reported to also be significantly impaired in patients with psoriatic arthritis without clinically evident cardiovascular disease or risk factors [21]. Our results suggest that skin inflammation linked to chronic plaque psoriasis, even without articular involvement, could affect endothelial function and favor atherosclerosis. Interestingly enough, we found a positive association between PWVcf and years of psoriasis duration, but not disease severity. This may suggest that the persistence of skin inflammation rather than its severity is a more relevant risk factor for endothelial impairment. Cytokines evolve to impart their systemic metabolic effect at very low levels, such that even a minor degree of long-lasting and continuous elevation may be deleterious and promote accelerated atherogenesis. Indeed, psoriasis is associated with an increased production of cytokines (e.g. TNF-α, IFN-γ, IL-1β, IL-6 and IL-17) that generates a spectrum of proatherogenic changes, such as insulin resistance, dyslipidemia, prothrombotic effects, pro-oxidative stress and endothelial dysfunction [22]. In particular, TNF-α could mediate endothelial dysfunction via diminished expression of nitric oxide synthase and cycloxygenase-1 [23].

Our study has some limitations, including the sample size and the fact that patients had been treated in the past with systemic antipsoriatic drugs that could have altered endothelium. Moreover, the prevalence of current smokers was higher in the psoriasis group; nevertheless, the data have been adjusted for smoking status and PWVcf remained higher in psoriasis patients when excluding smokers.

Although there is not enough evidence to quantify the risk of cardiovascular events by the amount of elevation in PWVcf, this study suggests that PWVcf may be used for early recognition of endothelial dysfunction and assessment of cardiovascular risk in psoriasis patients also. In conclusion, our study shows that moderate to severe chronic plaque psoriasis may be independently associated with increased arterial stiffness; thus, psoriasis duration could be a risk factor for arterial stiffness and atherosclerosis.

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