The Relationship of Carotid Intima-Media Thickness with Cell Adhesion Molecules and Pentraxin-3 in Patients with Psoriatic Arthritis

Die Relation der Karotis-Intima-Media-Dicke zu Zelladhäsionsmolekülen und Pentraxin-3 bei Patienten mit Psoriasis-Arthritis

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Keywords

psoriatic arthritis, aterosclerosis, carotid intima–media thickness, cell adhesion molecules, pentraxin 3

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ABSTRACT

Aim Cardiovascular morbidity is increased in patients with psoriatic arthritis (PsA) compared to the general population. Several recent studies have indicated that pentraxin 3 (PTX-3) and cell adhesion molecules (CAMs) might be independent biomarkers of subclinical atherosclerosis. In this study, we aimed to determine the relationship of CAMs and PTX-3 with carotid intima media thickness (CIMT) in patients with PsA and to compare CIMT and serum levels of these biomarkers in patients with healthy controls (HCs).

Method PsA patients fulfilling the CASPAR (Classification criteria for Psoriatic Arthritis) criteria without traditional cardiovascular (CV) comorbidity and HCs without autoimmune and/or CV disease were included in this cross-sectional study. Carotid artery Doppler ultrasound examinations were conducted by a single radiologist blinded to the participants' clinical characteristics. Serum vascular adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1), E-selectin, and PTX-3 concentrations were analized.

Results 43 PsA patients (27 females, mean age 42.49 ± 11.70 years, and a mean disease duration of 9.37 ± 7.96 years) and 37 HCs (28 females, mean age 42.16 ± 11.38 years) were included. In regression analyses, age and PTX-3 were found to be the best predictors of CIMT in patients with PsA. CIMT was significantly higher in PsA patients compared with HCs (0.63 ± 0.18 vs.

0.49 ± 0.10 mm, p < 0.01). In te PsA group, serum levels of PTX-3, ICAM-1, and VCAM-1 were also significantly higher than HCs. CIMT correlated positively with age, disease duration, PTX-3, ICAM-1, and VCAM-1 (p < 0.05).

Conclusion In our study, age and serum level of PTX-3 were found to be the predictors of CIMT in patients with PsA without CV comorbidity. This outcome highlights the importance of monitoring CIMT and serum level of PTX-3 as CV risk factors in PsA patients.

Introduction

Psoriatic arthritis (PsA) is an inflammatory disease characterized not only by joint and skin involvement, but also by an higher prevalence of cardiovascular (CV) risk factors and a greater risk of subsequent cardiovascular disease (CVD) compared to the general population [1]. CVD is responsible for 20–56 % of all deaths in these patients [2]. Conventional CV risk factors such as obesity, hypertension (HT), impaired fasting glucose, and hyperlipidemia have been shown to be more common in patients with PsA [3]. However, the increase in CV morbidity and mortality cannot be fully explained by traditional risk factors. Chronic inflammation is also an important factor accelerating atherosclerosis in PsA patients with no known risk of CVD [4]. Due to increased CV morbidity and mortality, all rheumatologists should be aware of the need for accurate CV risk estimation and CVD detection, even in subclinical stages of atherosclerosis.

Carotid ultrasound is a non-invasive, well-validated and reproducible imaging modality that determines subclinical vascular disease and ultimately CVD risk. An increased carotid intima-media thickness (CIMT) as an early predictor of atherosclerosis have been demonstrated previously in PsA patients with no known risk of CVD [4]. In addition, it has been suggested that many biomarkers of the ongoing low-grade systemic inflammation during the development of atherosclerosis may be useful in determining CV risk in these patients [3].

Inflammation is an important component of the atherosclerotic process and is characterized by leukocyte infiltration of the vascular endothelial wall. Binding of neutrophils to the endothelium leads to endothelial damage. Cell adhesion molecules (CAMs) are structural cell components that are presented on the cell surface with certain stimuli and play a role in the leukocyte-endothelial cell interaction in inflammation. There are four main groups of adhesion molecules: the integrin family, the immunoglobulin superfamily, selectins, and cadherins [5]. E-selectin plays a key role in leukocyte tethering and rolling on the endothelium. The members of the immunoglobulin superfamily including intercellular adhesion molecule 1 (ICAM-1) and vascular adhesion molecule 1 (VCAM-1) are responsible for endothelial adhesion and penetration of leukocytes. Proinflammatory cytokines and C-Reactive Protein (CRP) produced during acute and chronic inflammation promote endothelial expression of ICAM-1 and VCAM-1 [6]. The expression of VCAM-1, ICAM-1, and E-selectin are found to be related to the severity and prognosis of atherosclerosis in patients with known coronary artery disease [7].

Pentraxin 3 (PTX-3), from the same family as CRP (pentraxins), is another biomarker of CVD. PTX-3 has been shown to regulate the inflammatory response in atherosclerosis [8]. Data from animal models indicate that the inflammatory reaction of the vascular wall and macrophage accumulation in the plaque may be related to PTX-3 [9]. An association between elevated PTX-3 levels and increased CVD risk and mortality has been reported in the healthy population [10]. Cell adhesion molecules are believed to mediate the vascular effects of PTX-3 [11].

Angiogenesis and endothelial dysfunction are the major inflammatory pathways associated with atherosclerosis. Many biomarkers (PTX-3, E-selectin, angiopoietin, endothelial cell specific molecule 1, asymmetrical dimethylarginine, von Willebrand factor) can be used to evaluate endothelial dysfunction which is the earlier phase of vascular diseases [12]. An upregulation of CAMs is associated with increasing in angiogenesis. The expression of angiogenic factors (vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF) angiopoietins, and soluble CAMs) and anti-angiogenic factors (angiostatin, endostatin, PTX-3) is regulated by proinflammatory cytokines in rheumatic diseases, there by promoting angiogenesis in atherosclerotic plaques [13].

Angiogenesis is also an essential stage in the pathogenesis of PsA. In a clinical study comparing the joint microenvironments of patients with PsA and those with rheumatoid arthritis (RA), pro-angiogenic factors including VCAM-1, ICAM-1, E-Selectin were found to be significantly more expressed in the PsA synovial fibroblast culture (PsA SFC) than in the RA SFC [14]. Since neo-angiogenesis plays an important role in the progression of both atherosclerotic plaque and synovial inflammation, CAMs and PTX-3 may predict CVD in patients with PsA. The performance of PTX-3 and CAMs as candidate biomarkers of atherosclerosis has not previously been studied together in patients with PsA. The aim of this study was to determine the relationship between serum VCAM-1, ICAM-1, E-selectin, PTX-3 levels and CIMT in PsA patients without CV comorbidity.

Materials and Methods

Subjects

This cross-sectional study included 43 PsA patients who applied to the Manisa Celal Bayar University Hafsa Sultan Hospital rheumatology outpatient clinic between February 2019 and May 2020, and 37 healthy controls (HCs). The patients were classified as PsA according to the CASPAR (Classification criteria for Psoriatic Arthritis) criteria [15]. Patients with a history of CVD (myocardial infarction, coronary artery bypass graft surgery, coronary artery stenting), peripheral artery disease, and cerebrovascular disease were not included in the study. Patients diagnosed with diabetes mellitus (DM), HT, chronic kidney disease (CKD), and chronic liver disease were also excluded. Among the PsA patients who applied to the rheumatology outpatient clinic at that time, those who met the

study criteria and age-matched healthy individuals selected from our clinical staff were included in the study. The study protocol was approved by Manisa Celal Bayar University ethics committee (dated 29.08.2018, decision number 20.478.486). Informed consent forms were obtained from all participants before the study.

In the PsA group, disease activity was assessed using the DAS28-CRP (Disease Activity Score) [16] and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) [17]. The functional status of patients was evaluated using the HAQ (Health Assessment Questionnaire) [18], BASFI (Bath Ankylosing Spondylitis Functional Index) [19], and BASMI (Bath Ankylosing Spondylitis Metrology Index) [20]. In addition, psoriasis (PsO) severity was evaluated using the PASI scoring system (Psoriasis Area and Severity Index) [21]. The relatively new criterion DAPSA (Disease Activity index for PSoriatic Arthritis) [22] and CPDAI (Composite Disease Activity Index) [23] were calculated in all patients. The quality of life was with the ASQoL (Ankylosing Spondylitis Quality of Life) [24] and DLQI (Dermatology Life Quality Index) [25].

Procedures and Measurements

Anthropometric measurements were performed on an empty stomach with the patients in standing position, lightly clothed and without shoes. Body weight was measured with an electronic scale sensitive to 0.1 kg and height was measured with a stadiometer sensitive to 0.1 cm. Waist circumference was measured with an inelastic measuring tape midway between the lowest rib and the iliac crest. Body mass index (BMI) was calculated by dividing body weight (kg) by height squared (m^2).

Blood samples were collected from both patients and HCs after 12 hours of fasting for routine biochemical tests including complete blood count, erythrocyte sedimentation rate (ESR), CRP, lipid profile consisting of triglycerides, total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels, fasting blood glucose, and kidney and liver function tests. Serum was separated from the venous blood samples and stored at − 80 °C until analysis. CAMs and PTX-3 analyses of all samples were performed at the same time. Serum VCAM-1, ICAM-1, E-selectin, and PTX-3 concentrations were measured using enzyme-linked immunoassays (ELISA) (BioTek Instruments Inc. Highland Park, Winooski, VT, USA). Kit sensitivities were 22 pg/mL for the PTX-3 ELISA kit (BioVendor, Czech Republic) and 0.6 ng/mL, 2.2 ng/mL, and 0.3 ng/mL for the ELISA kits of VCAM-1, ICAM-1, and E-Selectin (Thermofisher Scientific, Czech Republic), respectively.

Carotid artery doppler ultrasound examinations were conducted by a single experienced radiologist blinded to the participants' clinical characteristics. The right and left carotid arteries were visualized while the patients were in the supine position and the neck was extended. Measurements were obtained with a Toshiba Aplio 500 ultrasound device using a superficial linear 12 MHz probe. The CIMT was measured as the distance between the two echogenic lines belonging to the intima-lumen interface and the media-adventitia interface. For each participant, 3 measurements were taken from the distal common carotid artery (the arterial segment 1 cm proximal to the carotid bulb), bulb, and proximal internal carotid artery (the arterial segment 1 cm distal to the carotid bifurcation) on each side and the mean of these 6 measurements was calculated as the CIMT. Plaque was defined as a localized thickening > 1.2 mm [26]. Patients with maximum IMT > 0.9 mm and/or the presence of plaque were classified as subclinical atherosclerosis [27].

Statistical Analysis

The data were recorded and analyzed using IBM SPSS Statistics version 24.0 (IBM Corp, Armonk, NY, USA). In the statistical analysis of continuous data, normality of distribution was assessed using Kolmogorov-Smirnov test. Depending on the results of the normality test, numerical data were compared between independent groups using independent samples T-test or Mann-Whitney U test and categorical variables were compared using Pearson's chi-square or Fischer's exact test. A two-tailed p value less than 0.05 was accepted as significant for all tests. Relationships between variables were examined using Spearman correlation analysis (r value).

Multiple regression analysis was used to determine the most important predictors of CIMT. Automatic stepwise regression analyses were employed with the CIMT in all subjects and CIMT in patients with PsA as dependent variables and CAMs, PTX-3, age, BMI, CRP, smoking, ESR, and serum glucose, HDL-cholesterol, and triglyceride levels as explanatory variables. All regression analyses were checked for multicollinearity.

Results

The study included 43 PsA patients without CV comorbidity and 37 HCs. Most PsA patients were women (62.8 %), with a mean age of 42.49 ± 11.70 years, and a mean disease duration of 9.37 ± 7.96 years. Age, gender distribution, body mass index, and smoking rates were similar between the groups. The comparison of demographic, clinical, and laboratory data between the groups and disease activity, functional, and quality of life parameters in the patient group are summarized in ▶ **Table 1**. Waist circumference was significantly increased in PsA patients compared to HCs.

In the PsA group, serum levels of PTX-3, ICAM-1, and VCAM-1 were significantly higher than HCs ($p < 0.05$ for all values) (▶ **Table 1**). Carotid ultrasound evaluation revealed carotid plaque in one of the PsA patients and subclinical atherosclerosis in a total of 3 (7 %) patients (two patients had CIMT > 0.9 mm). There was no plaque or subclinical atherosclerosis in the HCs group. CIMT was significantly higher in PsA patients compared with HCs (0.63 ± 0.18 vs. 0.49 ± 0.10 mm, $p < 0.01$).

In subgroup analyses, there was no difference between smokers (38 %) and non-smokers in terms of CAMs, PTX-3, or CIMT values ($p > 0.05$ for all values). The PsA group included 14 patients with predominantly axial involvement, 12 patients with predominantly peripheral involvement, and 17 patients with both peripheral and axial involvement. Serum CAMs and PTX-3 levels and CIMT were similar in these clinical subgroups ($p > 0.05$ for all values).

In the PsA group, 10 patients (23.8 %) were receiving corticosteroids (CS), 14 patients (33.3 %) were receiving nonsteroidal anti-inflammatory drugs (NSAIDs), and 39 patients (90.7 %) were receiving disease-modifying antirheumatic drugs (DMARDs) [methotrexate, leflunomide, anti-TNF agents, interleukin-17 (IL-17) inhibitors] . Serum CAMs and PTX-3 levels and CIMT values showed no significant difference in patients using CS or biologic agents compared to non-users ($p > 0.05$ for all).

▶ **Table 1** Demographic, clinical, and laboratory features of healthy controls and patients with psoriatic arthritis.

Variables	Psoriatic arthritis (n = 43)	Healthy controls (n = 37)	*p*
Age (year)	42.49 ± 11.70	42.16 ± 11.38	0.900
Sex (M/F) (%)	16/27 (37/63)	9/28 (24/76)	0.215
Smoking (%)	39.50	36.10	0.755
BMI (kg/m²)	29.29 ± 5.11	27.84 ± 3.25	0.141
Waist circumference (cm)	95.73 ± 13.96	89.95 ± 11.48	0.048
Disease duration (year)	9.37 ± 7.96	_	_
BASDAI	4.12 ± 2.68	_	_
BASFI	2.08 ± 2.23	_	_
BASMI	3.16 ± 0.94	_	_
HAQ	0.48 ± 0.21	_	_
DAS28CRP	3.34 ± 1.35	_	_
PASI	2.35 ± 2.26	_	_
CPDAI	1.71 ± 0.81	_	_
DAPSA	23.8 ± 8.76		
DLQI	4.33 ± 3.13	_	_
ASQoAL	6.23 ± 5.35	_	_
ESR (mm/h)	23.93 ± 17.19	18.53 ± 9.29	0.112
CRP (mg/L)	8.36 ± 11.58	2.95 ± 3.04	0.001
Fibrinogen (mg/dL)	385.50 ± 115.48	306.32 ± 69.28	0.007
Total cholesterol (mg/dL)	201.23 ± 45.21	205.17 ± 37.07	0.701
HDL cholesterol (mg/dL)	52.50 ± 11.60	58.86 ± 11.67	0.028
LDL cholesterol (mg/dL)	123.33 ± 38.00	124.24 ± 30.86	0.915
TG (mg/dL)	135.20 ± 87.09	119.24 ± 54.45	0.440
ICAM-1 (ng/mL)	425.32 ± 89.17	379.19 ± 111.15	0.048
VCAM-1 (ng/mL)	827.60 ± 229.06	621.12 ± 121.75	< 0.001
E-selectin (ng/mL)	62.74 ± 28.59	61.46 ± 15.43	0.397
PTX-3 (ng/mL)	3.49 ± 0.77	2.22 ± 0.66	< 0.001
CIMT (mm)	0.63 ± 0.18	0.49 ± 0.10	< 0.001

M male, *F* female, *BMI* body mass index, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *BASMI* Bath Ankylosing Spondylitis Metrology Index, *HAQ* Health Assessment Questionnaire, *DAS28* Disease Activity Score of 28 joints, *PASI* Psoriasis Area and Severity Index, *CPDAI* Composite Disease Activity Index, *DAPSA* Disease Activity index for Psoriatic Arthritis, *DLQI* Dermatology Life Quality Index, *ASQoAL* Ankylosing Spondylitis Quality of Life, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *TG* triglycerides, *ICAM-1* intercellular cell adhesion molecule-1, *VCAM-1* vascular cell adhesion molecule-1, *PTX-3* pentraxin-3, *CIMT* carotid intima-media thickness; Note: Data are presented as mean ± SD.

Correlation analysis in the PsA patient group showed that CIMT was positively correlated with age, disease duration, ICAM-1, VCAM-1, and PTX-3, and negatively correlated with GFR and albumin (▶ **Table 2**, ▶ **Fig. 1**). Age was positively correlated with ICAM-1 ($r = 0.452$, $p = 0.002$), VCAM-1 ($r = 0.393$, $p = 0.009$), and PTX-3 ($r = 0.491$, $p = 0.001$). In the patient group, PTX-3 was positively correlated with ICAM-1 ($r = 0.391$, $p = 0.010$) and VCAM-1 ($r = 0.401$, $p = 0.008$). Disease activity (assessed by BASDAI, DAS28-CRP, DAPSA and CPDAI) and functional capacity (assessed by BASFI, BASMI, HAQ) showed no significant correlation with CAMs, PTX-3, or CIMT ($p > 0.05$ for all values).

Best predictors of carotid intima-media thickness

To examine which markers best predicted CIMT, we performed automatic stepwise regression analyses with CIMT as the dependent variable and selected laboratory and demographic data as explanatory variables both for all subjects and for patients with PsA (▶ **Table 3**). Regression model 1 (all subjects) showed that 34.5 % of the variance in CIMT is explained by age. Introducing the other

▶ **Table 2** Correlation of CIMT with demographic and clinical disease variables in psoriatic arthritis patients.

Variables	r	p
Age (year)	0.582	<0.001
Disease duration (year)	0.416	0.005
BMI (kg/m²)	0.073	0.643
Waist circumference (cm)	0.115	0.309
ESR (mm/h)	0.031	0.844
CRP (mg/L)	0.108	0.490
GFR ml/min/1.73 m²	-0.524	<0.001
Glucose (mg/dL)	0.274	0.076
Albumin (g/dL)	−0.370	0.019
HDL cholesterol (mg/dL)	−0.040	0.804
LDL cholesterol (mg/dL)	0.110	0.501
TG (mg/dL)	0.027	0.867
ICAM-1 (ng/mL)	0.433	0.004
VCAM-1 (ng/mL)	0.491	0.001
E-selectin (ng/mL)	−0.113	0.471
PTX-3 (ng/mL)	0.690	<0.001

BMI body mass index, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *GFR* glomerular filtration rate, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *TG* triglycerides, *ICAM-1* intercellular cell adhesion molecule-1, *VCAM-1* vascular cell adhesion molecule-1, *PTX-3* pentraxin-3

biomarkers in the automatic analysis shows a better solution with all subjects (57.3 % of the variance explained) using age, PTX-3, and VCAM-1. In patients with PsA, regression model 2 shows that 52.1 % of the variance in CIMT is explained by age and PTX-3. BMI, CRP, smoking, ESR, and serum ICAM-1, E-selectin, glucose, HDL-cholesterol, and triglyceride levels were not significant in this regression.

Discussion

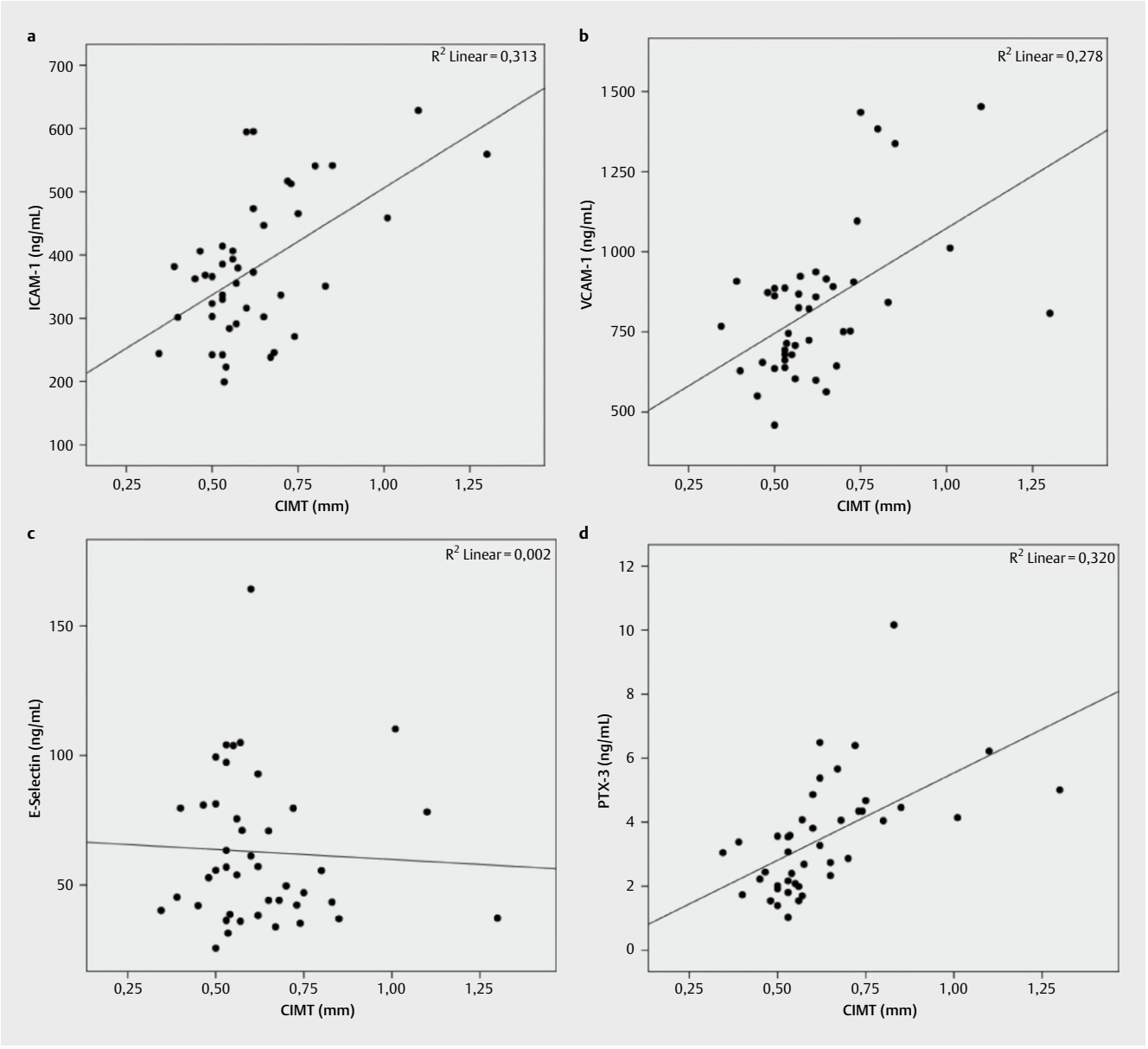
The main finding of the present study is that PsA is characterized by higher plasma levels of VCAM-1, ICAM-1, PTX-3, and increased CIMT as compared with HCs. There were significant positive correlations between CIMT and plasma levels of VCAM-1, ICAM-1, and PTX-3. In addition, in regression analyses, age and PTX-3 were found to be the best predictors of CIMT in patients with PsA.

The development of atherosclerosis is known to be associated with classical CV risk factors such as advanced age, increased BMI, elevated serum triglycerides, LDL-cholesterol, and total cholesterol levels [28]. PsA patients have a higher risk of developing CV risk factors, and a higher risk of presenting a CVD, compared to the general population. However, as in our study, the effect of systemic inflammation on the endothelium and its contribution to the atherosclerotic process can be better understood in patients without conventional CV risk factors and CV comorbidity. The mean CIMT value of the 43 PsA patients in our study (0.63 mm) was similar to that reported in previous studies and significantly higher than in the HCs group ($p < 0.001$) [29–31]. Although we found that this young patient population (mean age, 42 years) with no atherosclerotic disease burden had an increased waist circumference and low HDL-cholesterol levels compared to the HCs group, these findings were not correlated with CIMT.

Identification of biomarkers that can be used in determining subclinical atherosclerosis even years before clinical CVD is of great importance for predicting the CV morbidity and mortality risk. Homocysteine, CRP, IL-6, ICAM-1, fibrinogen, and uric acid were the markers shown to be associated with early atherosclerosis in PsA patients [4, 31]. In contrast to most studies, we did not find a correlation between CIMT and the commonly used acute phase reactants (CRP and ESR). This may be because most patients had normal or slightly elevated CRP and ESR values (8.36 ± 11.58 mg/L and 23.93 ± 17.19 mm/h, respectively). In addition, these parameters are acute phase markers and may not reflect a chronic inflammatory burden. Shen and colleagues reported no association with CIMT and PsO severity, PsA severity, or PsA treatment (NSAIDs, systemic steroids, and synthetic or biologic DMARDs) in line with our study [32]. Of the CAMs that mediate inflammation in both synovitis and atherosclerosis in PsA, ICAM-1 was shown to be associated with subclinical atherosclerosis [4, 31], whereas no such relationship has been previously reported for VCAM-1. However, in a recent study on patients undergoing coronary angiography, it was suggested that VCAM-1 may predict CVD risk due to its association with the prevalence of coronary lesions [33]. Dessein et al. [34] also reported that serum VCAM-1 levels were associated with CIMT and plaque formation in patients with RA. In our study, both ICAM-1 and VCAM-1 were positively correlated with CIMT.

The expression of PTX-3, another biomarker of CVD, was found to be increased in PsO patients compared to HCs and was associated with increased insulin resistance [35, 36]. Firstly, Sunar et al. reported that elevated PTX-3 was associated with increased CIMT in their study of 38 PsA patients [37]. Consistent with their results, we demonstrated a significant positive correlation between PTX-3 level and CIMT. Because we excluded patients with CV comorbidity, the relationship between PTX-3 and CIMT in our study is most likely a result of chronic inflammatory mechanisms associated with PsA. In addition, we showed for the first time that the most important predictors of CIMT in patients with PsA were age and PTX-3 level. Of the other variables included in the regression model, we found no significant correlation between CIMT and BMI, CRP, smoking, ESR, or serum ICAM-1, E-selectin, glucose, HDL-cholesterol, or triglyceride levels. In conclusion, PTX-3 seems to be an important biomarker for increased CIMT predicting the development of atherosclerosis in PsA patients, independent of classical risk factors such as obesity, hyperlipidemia, impaired fasting glucose, and smoking.

An increase in CIMT was also detected in vasculitides such as giant cell arteritis (GCA) [38]. Systemic inflammatory response markers including IL-6, IL-1, IL-17, IL-23, VEGF, von Willebrand factor, ICAM-1, and PTX-3 are responsible from chronic inflammation and an increase in CIMT in patients with GCA [39]. Theoretically, secukinumab (IL-17 inhibitor), which have been shown to be effective in the treatment of GCA [40] and PsA [41] are likely to prevent the increase in CIMT and thus subclinical atherosclerosis in PsA patients. Further studies are needed in this regard.



▶ **Fig. 1** Correlation between CIMT and (a) ICAM-1, (b) VCAM-1, (c) E-Selectin, and (d) PTX-3 in PsA patients. *CIMT* carotid intima-media thickness, *ICAM-1* intercellular cell adhesion molecule-1, *VCAM-1* vascular cell adhesion molecule-1, *PTX-3* pentraxin 3, *PsA* psoriatic arthritis.

The strengths of our study are the relatively large number of patients, the simultaneous assessment of ICAM-1, VCAM-1, E-selectin, and PTX-3 in the serum of PsA patients, and the careful exclusion of diseases that could interfere with the results. A potential limitation of the current study was including patients with other traditional cardiovascular risk factors such as smoking and obesity. However, we observed no significant relationship between CIMT and variables associated with these factors in our correlation and regression analyses. Another limitation of our study was that all patients were using CS, conventional and/or biologic DMARDs. Blood levels of biomarkers and even CIMT may be affected by the medications used and the duration of use. It is well known that the use of NSAIDs and CS are associated with increased cardiac risk in the general population and in rheumatic patients. On the other hand, there has been increasing evidence in recent years that treatment with biological DMARDs is associated with a reduced risk of developing CVD in patients with PsO and PsA. However, our results indicated that CIMT and levels of CAMs and PTX-3 were not associated with the use of CS or biologic agents.

This is the first study analyzing the relationship between the CAM profile together with PTX-3 and CIMT, in PsA patients. Our results demonstrated that PsA is characterized by increased CIMT and high levels of VCAM-1, ICAM-1, and PTX-3. Although there was a correlation between adhesion molecules and CIMT in this study, we found PTX-3 to be the best predictive biomarker of vascular structural damage in patients with PsA. Therapeutic strategies targeting PTX-3 and cell adhesion molecules, which are overexpressed during inflammation, may be effective in managing the disease and

▶ **Table 3** Results of automatic stepwise multiple regression analysis with carotid intima-media thickness (CIMT) in all subjects and CIMT in patients with psoriatic arthritis (PsA) as dependent variables.

Dependent variables	Explanatory variables	β	t	*p*	F model	*df*	*p*	R^2 (%)
CIMT in all subjects								
#1	Age	0.596	5.980	<0.001	30.759	1/65	<0.001	34.5
#2	Age	0.486	5.455	<0.001	30.372	2/64	<0.001	51.0
	PTX-3	0.427	4.788	<0.001				
#3	Age	0.421	4.911	<0.001	30.521	3/63	<0.001	57.3
	PTX-3	0.310	3.409	0.001				
	VCAM-1	0.299	3.227	0.002				
CIMT in patients with PsA								
#1	Age	0.673	5.457	<0.001	29.779	1/36	<0.001	43.8
#2	Age	0.527	4.182	<0.001	21.107	2/35	<0.001	52.1
	PTX-3	0.340	2.694	0.011				

CIMT carotid intima-media thickness, *PsA* psoriatic arthritis, *PTX-3* pentraxin-3, *VCAM-1* vascular cell adhesion molecule-1

atherosclerosis caused by chronic inflammation. However, more studies are needed to verify the causality among these factors, as well as their associations with different aspects of disease activity and atherosclerosis.

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Main Points

1) Age and PTX-3 were found to be the best predictors of CIMT in patients with PsA.
2) PsA is characterized by higher plasma levels of VCAM-1, ICAM-1, PTX-3, and increased CIMT as compared with HCs.
3) There were significant positive correlations between CIMT and plasma levels of VCAM-1, ICAM-1, and PTX-3.

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Conflict of interest

The authors declare that they have no conflict of interest.

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