Serum Calprotectin Level is Independently Associated with Carotid Plaque Presence in Patients with Psoriatic Arthritis

Cheng Isaac T
Prince of Wales Hospital
Huan Meng
Prince of Wales Hospital
Martin M Li
Prince of Wales Hospital
Edmund K Li
Prince of Wales Hospital
Priscilla C Wong
Prince of Wales Hospital
Byran P Yan
Prince of Wales Hospital
Alex PW Lee
Prince of Wales Hospital
Ho So
Prince of Wales Hospital
Lai-Shan Tam (lstam@cuhk.edu.hk)
Prince of Wales Hospital

Research Article

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Abstract

Background Whether calprotectin could play a role in augmenting cardiovascular (CV) risk in patients with psoriatic arthritis (PsA) remains uncertain. The aim of this study is to elucidate the association between serum calprotectin and subclinical atherosclerosis and arterial stiffness in patient with PsA.

Method Seventy-eight PsA patients (age: 52±10 years, 41 [52.6%] male) without CV disease were recruited into this cross-sectional study. Carotid intima-media thickness (cIMT) and the presence of plaque were determined by high-resolution ultrasound. Arterial stiffness was measured by brachial-ankle PWV (baPWV) and augmentation index (AIx) Calprotectin levels in serum were quantified by enzyme-linked immunosorbent assay. **Results** 29/78 (37.2%) of patient had carotid plaque (CP+ group). Serum calprotectin levels were significantly higher in the CP+ group (CP- group: 564.6 [329.3-910.5] ng/ml; CP+ group: 721.3 [329.3-910.5] ng/ml, P=0.005). Serum calprotectin level correlated with C-reactive protein (CRP) (r=0.244, P =0.033) and PsA disease duration (r=0.245, P =0.030). Using multivariate logistic regression analysis, the levels of Ln-calprotectin were significantly associated with the presence of CP (OR: 3.19, 95% confidence interval [CI]: [1.22, 8.38]; P=0.018), and mean cIMT (β: 0.35, 95% CI [0.02, 0.68]; P=0.038) after adjusting for baseline covariates. The optimal cut-offs for discriminating patients with and without CP were calprotectin >569ng/ml (AUC: 0.688; sensitivity: 79%; specificity: 51%; P=0.006) and FRS >9% (AUC: 0.645; sensitivity: 62%; specificity: 67%; P=0.033).

Conclusion Serum calprotectin level may be a good biomarker for CV risk stratification in PsA. Further studies are required to confirm whether this pathway is associated with CV events in PsA.

Introduction

Psoriatic arthritis (PsA) is a systemic inflammatory arthropathy associated with an increased cardiovascular disease (CVD) risk (1, 2).The incidence of traditional CV risk factors is higher in PsA patients when compared to the general population. (1, 3, 4). Nonetheless, traditional CV risk factors can only explain part of the elevated risk for myocardial infarction in PsA patients(1). Different types of inflammatory arthritis had no significant difference in the incidence and prevalence of major adverse cardiovascular events, indicating that inflammation per se may contribute to the CV risk rather than a specific disease (5).

We have demonstrated that the prevalence of subclinical coronary and carotid atherosclerosis was also increased in PsA(6, 7). The baseline carotid plaque independently predicted the risk of CVD even after adjusting to three traditional cardiovascular scores and inflammatory burden as reflected by the Disease Activity in Psoriatic Arthritis (DAPSA), with hazard ratio (HR) ranging from 2.35 to 3.42 (8). As all the CV risk scores underestimated the subclinical carotid atherosclerosis risk, and the European League Against Rheumatism (EULAR)-recommended modification only improved a moderate level considered to the sensitivity of the CV risk scores (9), soluble biomarkers which are associated with carotid atherosclerosis may be useful to guide physicians to whom carotid ultrasound should be considered.Biomarkers such as

soluble ST2, which acts as a decoy receptor for interleukin-33, were independently related with the presence of carotid plaques in PsA(10). However, the soluble ST2 level did not associate with inflammatory markers (10). Biomarkers that may be associated with metabolic abnormalities and dysregulated inflammatory pathways driving the atherosclerotic process in PsA would deserve further studies.

Calprotectin (S100A8 and S100A9), the most-investigated S100 protein in rheumatic diseases by far, is recognized by toll-like receptor 4 on multiple inflammatory cell types which promote vascular plaque formation and destabilization through promoting inflammatory cytokine expression (11-13). Serum calprotectin levels have been reported to be associated with CV events (14), and to be an early and sensitive marker of patients with unstable angina (15). Thus, calprotectin might play a role in accelerating atherosclerotic disease secondary to systemic inflammation.

Rheumatoid arthritis and PsA patients had been reported to have higher serum calprotectin levels (16, 17). In a group of patients with inflammatory arthritis treated with anti-tumor necrosis factor- α (anti-TNF-α), calprotectin levels were associated with the progression in carotid intima-media thickness (cIMT) and aortic pulse wave velocity (baPWV) (16). Another study in patients with CVD (18) reported higher serum calprotectin levels in the carotid plaque (CP+) group. For the patients with PsA, whether serum calprotectin levels correlate with inflammatory burden and subclinical atherosclerosis would need to be addressed.

The objective of our study was to determine the relationship between the serum calprotectin, vascular parameters (including subclinical atherosclerosis as well as arterial stiffness), and inflammatory burden in PsA patients.

Methods

Study design and patients

Seventy-eight PsA patients were recruited consecutively for this cross-sectional study from the rheumatology clinic of The Prince of Wales Hospital. Details of patients in this study have been published before (10). Exclusion criteria were women who are pregnant and patients who had CV events previously. This study was approved by the Ethics Committee of The Chinese University of Hong Kong and conducted according to the ICH-GCP guidelines. All study participants signed an informed consent in accordance with the Declaration of Helsinki.

Clinical interview and laboratory tests

PsA disease features were recorded including pain, physician's and patient's global assessment, 68 tender joint count, 66 swollen joint count, the irreversibly 68 damaged joint count, the dactylitis counts, and the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES, range from 0 to 13) and Health Assessment Questionnaire Disability Index (HAQ-DI). Blood levels of C-reactive protein (CRP) and erythrocyte

sedimentation rate (ESR) were documented. Achievement of treatment target was defined by achieving minimal disease activity (criteria assessment were published before) (19) and joint and skindisease activity were assessed using the Psoriasis Activity and Severity Index (PASI) and DASPA respectively.

Cardiovascular assessments

The following anthropometric assessments were performed for all patients before the carotid ultrasound (US) exam: body height and weight,body mass index (BMI), and waist and hip circumferences. Current smoking and alcohol status, past clinical and medication use history, and family history were retrieved. Fasting blood glucose and lipid profile were also taken. Hypertension was defined as systolic blood pressure≥140mmHg or diastolic blood pressure ≥90mmHg with two consecutive records in the hospital, and/or current antihypertensive drugs use. A diagnosis of hyperlipidemia was considered if the total cholesterol was ≥6.2 or LDL-cholesterol was ≥4.13 or current statin use. Framingham risk score (FRS) was used for assessing 10-year CVD risk and was classified into three categories: low-risk <10%, intermediate-risk 10-19%, and high-risk ≥20%).

Subclinical atherosclerosis and arterial assessment

All participants had the cIMT and plaque assessment done at the PWH. Measurements of cIMT were carried out using a high-resolution B-mode US machine (Philips EPIQ7) as described previously (10) and were performed by an experienced sonographer blinded to all patients' information. Bilateral distal common carotid artery, bulb, and proximal internal carotid artery were assessed. The presence of plaque was detected and the mean /maximum cIMT of 6 arterial segments was computed accordingly. The reproducibility of cIMT in our center was 0.97 (18). As described before, CP criteria were defined as the focal protrusion of cIMT>1.2 mm that did not involve the whole lumen uniformly (19). Arterial stiffness were assessed by baPWV and augmentation index (AIx) (37). All the baPWV and AIx measurements were performed by the same experienced operator to ensure the consistency and reliability and measured as previously described (37). The intra-observer reliability was 0.86 (20).

Serum calprotectin measurement

Blood samples were collected in EDTA tubes, centrifuged within 30 min for 15 min, and the plasma was stored at -70°C. Calprotectin was analyzed by the QUANTA Lite Calprotectin Extended Range ELISA kit (INOVA Diagnostics, San Diego, CA, USA). All samples from each patient were studied in parallel on the same plate at the same time.

Statistical analysis

Baseline anthropomorphic assessments were described as mean ± SD, median (interquartile range) or percentage (%) according to the presence of CP (CP+ vs CP-). Comparisons and correlation analysis were performed using the independent samples t-test, Mann-Whitney U test and Pearson's correlation for continuous variables and Chi-squared or Fisher's exact test and Spearman's correlation for categorical variables according to the distribution of data. Explanatory variables associated with vascular

(subclinical atherosclerosis and arterial stiffness) parameters were analyzed using multivariate logistic or linear regression models with adjustment for potential confounding variables listed in table 1. The risks for a 0.1 mm increment in the mean cIMT were estimated. Potential explanatory variables associated with vascular parameters from the univariate analyses with a *P* value less than 0.1, were then put into a further multivariate model. Serum calprotectin levels were log-transformed (Ln-calprotectin) before inclusion in the logistic and linear regression models. The receiver operating characteristics (ROC) curve was performed to evaluate the ability of serum calprotectin and FRS models in discriminating the presence of carotid plaque. Cut-off values of these two models were determined by the Youden index which was the maximum obtained value calculated by the formula: sensitivity + specificity -1. Two-sided *P* values <0.05 were considered to indicate statistically significant and were analyzed by SPSS software (IBM Corp, version 24).

Results

Baseline characteristics of PsA patients

We followed 78 (41 male, 52.6%) PsA patients totally. Table 1 showed the baseline characteristics and disease-related features of all the participants. The mean age was 52±10 years, and the mean PsA disease duration was 14.1±7.0 years. The mean of serum calprotectin was 778.3±567.8 ng/ml (Table 1).

Serum calprotectin and inflammatory burden and CV risk

There is a positive correlation of serum calprotectin with PsA disease duration (rho=0.245, *P*=0.030), CRP levels (rho=0.244, *P*=0.033) and CP+ (rho=0.315, *P*=0.005).The relationship between calprotectin and ESR was not found to be significant (rho=0.189, *P*=0.099), although it was in a positive direction (Table 2). There were no associations between calprotectin levels and other disease-related parameters (data not shown).

Relationship between serum calprotectin and CP and cIMT

CP were identified in 29 (37.2%) patients (CP+ group). The CP+ patients were significantly older, had higher serum calprotectin levels (911.8 ±429.4 ng/ml vs 639.2 ±378.2 ng/ml, *P*<0.005) (Figure 1), a longer PsA disease duration, and a higher number of swollen joints. In the CP+ group, there was a trend suggestive of an increased CV risk as estimated by the FRS (*P*=0.094), and more patients were on statins (*P*=0.099) (Table 1).

Univariate analysis for exploring the association between clinical parameters and CP+, revealed that age, number of dactylitic digits, PsA disease duration, and Ln-calprotectin were related with CP+.After adjusting for these potential explanatory variables and the FRS, Ln-calprotectin (OR: 3.19, 95% confidence interval [CI] [1.22, 8.38]; *P*=0.018) and a longer PsA disease duration were independent explanatory variables related to CP+ (OR: 1.09, 95% CI [1.01, 1.17]; *P* =0.031) (Table 3).

In the univariate analysis, age, SBP and DBP, DASPA, the use of statin, fasting plasma glucose, FRS and Ln-calprotectin levels were positively associated with mean cIMT. We observed that FRS, and Ln-calprotectin, the independent explanatory variables significantly associated with higher mean cIMT included Ln-calprotectin after adjusting for DASPA, fasting plasma glucose, the use of statins (β: 0.35, 95% CI [0.02, 0.68]; *P*=0.038) and FRS (β: 0.04., 95% CI [0.02, 0.06]; *P*=0.002) (Table 4). Ln-calprotectin was not associated with the maximum cIMT, baPWV, and AIx, data was not shown.

The performance of calprotectin and FRS in predicting CP

The optimal cut-offs for discriminating the CP+ group from the CP- group were calprotectin 569 ng/ml and FRS 9%. The AUC of calprotectin model (calprotectin ≥ 569 ng/ml: AUC=0.688, *P*=0.006, sensitivity: 79%, specificity: 51%) was found to have higher discrimination than FRS model (FRS ≥ 9%: AUC=0.645, *P*=0.033, sensitivity: 62%, specificity: 67%). The performance of the FRS 20% model (indicating high CV risk) was poor in discriminating CP+ patients or not with low sensitivity of 14% and specificity of 89% (*P*>0.05) (Table 5).

Discussion

This analysis reports the CP+ group had significantly higher serum calprotectin levels, which were also significantly associated with the disease duration of PsA and CRP levels. Furthermore, we also demonstrated that serum calprotectin was independently associated with CP and mean cIMT in PsA patients after adjusting for FRS and inflammatory burden, suggesting that serum calprotectin levels could be used as an independent explanatory for subclinical atherosclerosis in these patients.

The association between PsA and increased CV risk is well established, however, only limited data investigated the actual mechanisms of this link. We are the first group to report elevated serum calprotectin levels in the group of CP+ compared to CP- in PsA patients. More importantly, serum calprotectin levels remained independently related with CP+ after adjusting for FRS and disease duration. The underlying mechanisms may involve platelet and endothelial cells activation. Indeed,calprotectin levels correlated with platelet aggregation and activation as well as serum thromboxane B2 level in stable coronary artery disease patients (21). Furthermore, calprotectin can bind to endothelial cells through carboxylated glycans and Toll-like receptor 4 (TLR4) leading to cell activation (22, 23), increase in permeability of endothelium with leukocyte extravasation (24), and trigger endothelial cell apoptosis (25), resulting in vascular and tissue damage. All these factors may subsequently lead to plaque formation.

The best-evaluated marker of the systemic inflammation burden in PsA remains uncertain, CRP and ESR levels, commonly used to value the acute inflammation, are usually in the normal range despite high disease activity (26). Serum calprotectin level has been reported as a more sensitive biomarker of joint disease and polymorphic disease manifestations in PsA than CRP (27). In the current study, serum calprotectin level correlated with the presence of CP as well as the cumulative inflammatory burden (as reflected by the disease duration). Notably, the PsA disease duration was also significantly associated with the CP+. While CRP and ESR were not significantly related with CP and disease duration (data were

not shown) indicating that serum calprotectin was more sensitive than CRP and ESR in reflecting the inflammatory and atherosclerotic burden in our study. Our results may provide new evidence between the inflammatory burden and subclinical atherosclerosis in PsA.

Increased aortic stiffness and mean cIMT have previously been shown to be related to inflammatory biomarkers and CVD in PsA patients (16, 28, 29). We have previously reported that increased cIMT was an independent explanatory variable related to CVD in PsA(30), similar to a meta-analysis study with overall estimates reporting an identical HR of 1.15 for every 0.01 mm increase in cIMT(31). In this scenario, we specifically addressed whether calprotectin could be associated with changes in mean cIMT and arterial stiffness parameters, such as baPWV and AIx, because of its association with both inflammatory activity and atherogenesis in inflammatory arthropathies (14, 32-35). In the present study, serum calprotectin levels were significantly associated with mean cIMT in both univariate and multivariable analysis adjusting for the FRS, DASPA, fasting glucose, and statin treatment, but not baPWV and AIx. In contrast, previous studies including RA, AS and PsA patientsfailed to find a positive correlation between circulating calprotectin and cIMT(16, 18), although calprotectin was associated with inflammatory biomarkers in SpA patients (36, 37). Further study should be performed to confirm or refute the relationship between calprotectin and subclinical atherosclerosis in PsA patients.

Traditional CV risk scores had moderate discriminating abilities to identify inflammatory arthritis patients with elevated CV risk (9, 38, 39). Based on the current study, the AUC of calprotectin in discriminating CP was higher than the FRS at 9% and FRS≥20%. Nonetheless, the AUC of a combined model including FRS>9% and calprotectin>569 ng/ml was lower than the AUC of calprotectin alone (detailed data not shown), suggesting that calprotectin levels may be able to replace FRS in discriminating patients at high CV risk as evidence by the presence of CP. This result is not surprising because atherosclerotic plaque formation is an inflammatory process (40). Proinflammatory cytokines also play a role in plaque remodeling and fibrous cap thinning, while most CV risk scores do not include inflammatory biomarkers. Whether calprotectin levels can predict future CV events in patients with PsA would need to be addressed in future prospective studies.

There are some potential limitations in this cross-sectional study. First, future prospective studies will be needed to assess the association between changes in calprotectin levels and progression of CP as well as arterial stiffness. Second, studies using 3D-US should be considered in the future to accurately assess the correlation between CP volume and calprotectin levels. Third, the association between serum calprotectin levels and TPA or plaque vulnerability would need to be addressed further. Last but not least, the majority of our patients had low disease activity (only six patients had moderate or high disease activity and the median value of DASPA was 2.5). Our results may not also be generally suitable for patients with moderate and high disease activity.

Conclusion

This study showed serum calprotectin levels may be a useful biomarker associated with a high inflammatory burden and the presence of subclinical carotid atherosclerosis in patients with PsA

Abbreviations

PsA: Psoriatic arthritis

CVD: Cardiovascular disease

DAPSA: Disease Activity in Psoriatic Arthritis

HR: Hazard ratio

EULAR: European League Against Rheumatism

anti-TNF-α: Anti-tumor necrosis factor-α

cIMT: Carotid intima-media thickness

baPWV: Brachial-ankle pulse wave velocity

CP+: Carotid plaque (),

MASES: Maastricht Ankylosing Spondylitis Enthesitis Score

HAQ-DI: Health Assessment Questionnaire Disability Index

BMI: Body mass index

CRP: C-reactive protein

ESR: Erythrocyte sedimentation rate

PASI: Psoriasis Activity and Severity Index

US: Ultrasound

FRS: Framingham risk score

AIx: Augmentation index

ROC: Receiver operating characteristics

Declarations

Ethical Approval and Consent to participate

The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee written informed consents were obtained from all patients according to the Declaration of Helsinki. The ethical approval number is 2017.683.

Consent for publication

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Availability of data and matertials

No data are available.

Competing interests

None to declare.

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Authors' contributions:

All authors were involved in drafting the article or revising it for important intellectual content, and all authors approved the final version to be submitted for publication. Specific roles included: study design (LST, IC), data collection (LST, EKL, ML, APL, BPY, WP, HS). Data analysis (IC, HM), drafting of manuscript (HM, IC, LST).

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Tables

Table 1. Anthropometric and clinical characteristics of PsA patients with or without carotid plaque.

		Carotid plaque		
	All (N=78)	**No (n=49)**	**Yes (n=29)**	***P* value**
Male gender, n (%)	41 (52.6%)	22 (44.9%)	19 (65.5%)	0.078
Age, (years)	**52±10**	**50±11**	**56±8**	**0.024**
PsA characteristics				
PsA disease duration, (years)	**14.1±7.0**	**12.4±7.0**	**17.0±6.3**	**0.005**
Tender joint count, (0-68)	0.5 (0-3)	1 (0-3)	0 (0-3)	0.825
Swollen joint count, (0-66)	**0 (0-2)**	**0 (0-1)**	**1 (0-2)**	**0.044**
Damaged joint count, (0-68)	2 (0-6)	0 (0-5)	1 (0-8)	0.437
Dactylitis. (0-20)	0 (0-1)	0 (0-0)	0 (0-0)	0.091
MASES enthesitis, (0-13)	0 (0-11)	0 (0-1)	0 (0-0)	0.467
VAS Pain, (0-100)	30 (14-50)	30 (20-50)	30 (10-60)	0.654
Patients' global assessment, (0-100)	40 (20-60)	35 (20-55)	50 (30-60)	0.129
Physicians' global assessment, (0-100)	20 (6-40)	15 (6-35)	20 (10-40)	0.427
PASI, (0-72)	2 (0.5-5.9)	2 (0.7-5.8)	1.8 (0.5-5.4)	0.922
HAQ, (0-3)	0.5 (0-0.63)	0.13 (0-0.38)	0.38 (0-0.88)	0.149
MDA, n (%)	13 (16.7%)	10 (20.4%)	3 (10.3%)	0.249
DAPSA, (0-164)	2.5 (1.0-6.0)	2.2 (1.0-6.8)	2.8 (1.2-5.1)	0.722
ESR, (mm/1sthr)	16 (7-30.5)	14.5 (7-29)	21 (7-32)	0.991
CRP, (mg/dl)	3.0 (1.0-6.0)	2.8 (1.0-5.3)	3.3 (1.1-8.3)	0.506
CV traditional risk factors				
Body weight, (kg)	67.2±13.1	67.9±13.7	66.1±12.35	0.562
BMI, (kg/m^2)	25.2±4.1	25.6±4.2	24.6±3.9	0.314
Waist-to-hip ratio	0.9±0.1	0.9±0.1	0.9±0.1	0.544
Current smoker, n (%)	8 (10.2%)	5 (10.2%)	3 (10.3%)	0.248
Current drinker, n (%)	24 (30.8%)	16 (32.6%)	8 (27.6%)	0.622

Systolic BP, (mmHg)	127±15	126.±15	128±15	0.765
Diastolic BP, (mmHg)	82±11	81±10	83±12	0.483
Total cholesterol, (mmol/l)	5.0±0.8	4.9±0.8	5.1±0.8	0.350
HDL cholesterol, (mmol/l)	1.4±0.4	1.4±0.3	1.5±0.5	0.481
LDL cholesterol, (mmol/l)	3.0±0.7	2.9±-0.7	3.1±0.7	0.206
Triglycerides, (mmol/l)	1.4±0.9	1.5±1.0	1.3±0.5	0.196
Fasting plasma glucose, (mmol/l)	5.5±1.5	5.7±1.8	5.1±0.7	0.155
Hypertension, n (%)	42 (53.8%)	27 (55.1%)	15 (51.7%)	0.772
Hyperlipidemia, n (%)	19 (24.3%)	9 (18.4%)	10 (34.5%)	0.109
Diabetes, n (%)	14 (17.9%)	9 (18.4%)	5 (17.2%)	0.900
FRS, (%)	10.7±8.4	9.2±8.5	12.7±7.8	0.094
Current medications, n (%)				
Anti-hypertensive	39 (50.0%)	26 (53.1%)	13 (44.8%)	0.482
Statins	12 (15.4%)	5 (10.2%)	7 (24.1%)	0.099
NASIDs	35 (44.9%)	23 (36.9%)	12 (41.4%)	0.633
csDMARDs	45 (57.7%)	30 (61.2%)	15 (51.7%)	0.412
bDMARDs	13 (16.7%)	8 (16.3%)	5 (17.2%)	0.917
Biomarker				
Calprotectin, (ng/ml)	**665.4 (415.0-947.0)**	**564.6 (329.3-910.5)**	**721.3 (574.1-1268.4)**	**0.005**

VAS: visual analogue scale; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; DAPSA: disease activity in psoriatic arthritis; MDA: minimal disease activity; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BMI: body mass index; BP: blood pressure; FRS: Framingham risk score; HDL: high-density lipoprotein; LDL: low-density lipoprotein; NSAID: nonsteroidal anti-inflammatory drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs. bDMARDs: biologics disease-modifying antirheumatic drugs. Values are the number (percentage) or median (interquatile range) or mean±SD. **Bold *P* value <0.05**.

Table 2. Correlation between serum calprotectin among inflammatory burden and CV risk parameters.

	r	*P* value
Age, (years)	0.199	0.261
Male gender, n (%)	-0.109	0.340
PsA disease duration, (years)	**0.245**	**0.030**
CRP, (mg/dl)	**0.244**	**0.033**
ESR, (mm/1st hr)	0.189	0.099
FRS, (%)	0.120	0.294
Presence of carotid plaque, n (%)	**0.315**	**0.005**

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; DAPSA: disease activity in psoriatic arthritis; FRS: Framingham risk score; **Bold *P* value <0.05.**

Table 3. Multivariate analysis for factors associated with presence of carotid plaque.

	Multivariate model		
	OR	95% CI	*P* value
Ln-calprotectin	**3.19**	**1.22-8.38**	**0.018**
PsA disease duration, (years)	**1.09**	**1.01-1.17**	**0.031**
FRS, (%)	1.03	0.97-1.09	0.348
Dactylitis, (0-20)	2.32	0.82-6.63	0.115

FRS: Framingham risk score; **Bold *P* value <0.05.**

Table 4. Multivariate linear regression analysis for the comparison between serum calprotectin (ln calprotectin) and mean cIMT.

	Multivariate model		
	β	**95% CI**	***P* value**
Ln-calprotectin	**0.35**	**0.02-0.68**	**0.038**
FRS, (%)	**0.04**	**0.02-0.06**	**0.002**
DASPA	0.04	-0.01-0.08	0.081
Use of statin, n (%)	0.50	-0.11-1.11	0.106
Fasting plasma glucose, mmol/l	0.07	-0.07-0.22	0.328

cIMT: carotid intima-media thickness; FRS: Framingham risk score; DAPSA: disease activity in psoriatic arthritis; **Bold *P* value <0.05.**

Table 5. Performance of serum calprotectin and Framingham risk scores in discriminating presence of carotid plaque.

	AUC	*P* value	Cut-off	Sensitivity (%)	Specificity (%)
Biomarker					
Calprotectin (ng/ml)	**0.688**	**0.006**	**569 (ng/ml)**	**79**	**51**
FRS					
FRS	**0.645**	**0.033**	**9%**	**62**	**67**
FRS high risk (FRS ≥20%)	0.508	0.909	20%	14	89

FRS: Framingham risk score; **Bold *P* value <0.05.**

Figures

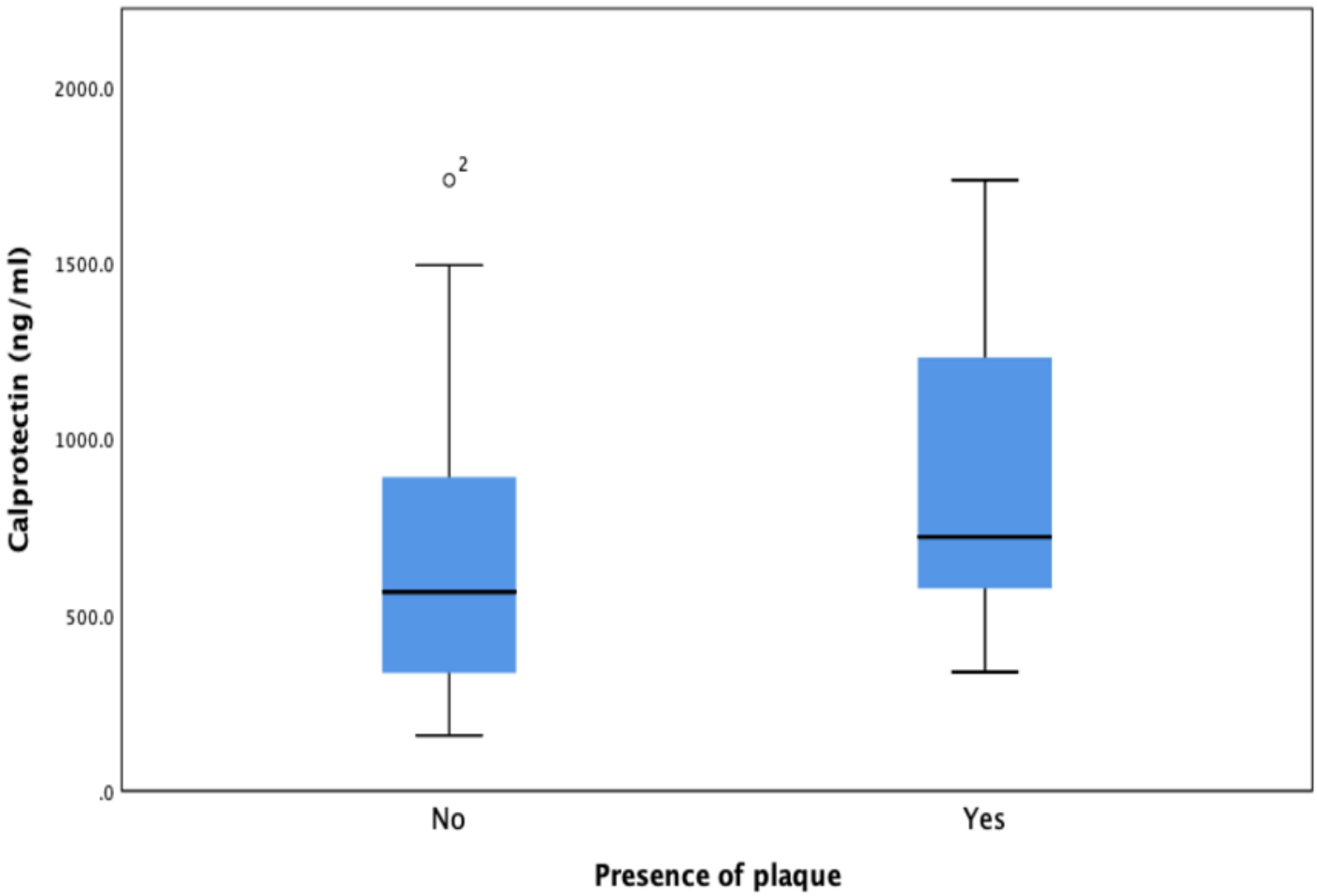

Figure 1

Caption not included with this version.