Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

METHODS AND MATERIALS

Study Population, and Inclusion/Exclusion Criteria

Participants were >18 years of age; psoriasis patients were required to have a formal diagnosis of plaque psoriasis for study inclusion. A trained healthcare provider evaluated all patients with psoriasis for the assessment of psoriasis skin disease severity measured as a psoriasis area severity index (PASI) score. Exclusion criteria included estimated glomerular filtration rate <30 mL/minute/1.73 m^2, pregnancy, lactation in female patients and any comorbid condition known to promote cardiovascular disease or systemic inflammation; such as clinically diagnosed cardiovascular disease, uncontrolled hypertension, internal malignancy within 5 years, human immunodeficiency virus, active infection within the past 72 hours of baseline, and major surgery within 3 months.

Analysis of Aortic Vascular Inflammation by ^{18}FDG PET/CT

All patients underwent ^{18}FDG PET/CT scans. All scans were read in a blinded fashion to patient characteristics and imaging time point. Images were analyzed using a dedicated PET CT analysis program (Extended Brilliance Workspace; Phillips Healthcare) to quantify vascular inflammation (VI) measured as target-to-background ratio[1,2]. Patients underwent ^{18}FDG PET/CT scans following an overnight fast. Images were acquired approximately 60 minutes after administration of 10 mCi ^{18}FDG. Imaging was performed using a Siemens Biograph mCT PET/CT 64-slice scanner (Siemens Medical Solutions USA, Malvern, PA, USA). Standard bed positions of three minutes each, scanning cranially to caudally were obtained for each patient from the vertex to the toes. 1.5mm thick axial slices of aorta were used to measure uptake of ^{18}FDG in the aortic wall from its origin as ascending aorta from the aortic outflow tract to its bifurcation into iliac arteries. Two measures of metabolic activity, mean standardized uptake value and maximal standardized uptake value were obtained by placing regions of interest in the entire aorta. Similar regions of interest were placed on 10 contiguous superior vena cava slices, and an average of the mean standardized uptake values from these 10 slices was used as the blood activity which served as the background. Target-to-background ratio was derived from each aortic slice by dividing the maximal standardized uptake values by the average venous mean standardized uptake value and was then averaged over the total number of slices yielding a single value that was used as a measure of aortic VI in each patient. In this study, we present data only from the aorta. Data pertinent to other arteries will be reported separately.

Analysis of CCTA for CAD Indices including Coronary Plaque Burden, Luminal Stenoses and HRP characterization

Psoriasis patients who provided consent to undergo additional scans also underwent coronary computed tomography angiography (320-detector row volumetric scanner, Aquilion ONE ViSION or Genesis). All guidelines set forth by the National Institutes of Health Radiation Exposure Committee were followed for all imaging procedures. Scans were performed with a 100-120 kV tube voltage with tube current automatically selected based on the patient's attenuation from the scout images, with a gantry rotation time of 275 ms. Oral beta-blocker was administered if heart rate was greater than 70 beats per minute and nitrates were used to enhance coronary imaging. Image-acquisition characteristics included slice thickness of 0.5 mm and a slice interval of 0.25 mm. All CCTA scans were analyzed by two blinded readers. Coronary plaque burden adjusted for luminal attenuation was evaluated across each of the main coronary arteries using the dedicated software QAngio CT by previously described methods[3-5]. Semiautomated segmentation of each of the major coronary artery was performed. The need for manual adjustment was reviewed by assessing transverse reconstructed cross-sections at 0.5 mm increments. Total coronary plaque burden (TB) and non-calcified coronary plaque burden (NCB) indices, assessed as mm^2, were calculated by dividing total vessel plaque volume by total vessel length for standardization, and were attenuated for luminal intensity measures for accuracy.

Clinical reads for the CCTA scans based on the American Heart Association proposed segmentation[6] and following the Society of Cardiovascular Computed Tomography guidelines[7] were utilized for analysis of luminal stenosis. Quantitative stenosis grading recommended in these guidelines was employed for categorization of stenosis severities. Furthermore, all coronary segments were analyzed for the presence of HRP, defined as a plaque with positive remodeling (PRP) (remodeling index ≥1.1) or presence of low-attenuation plaque (LAP) (<30 Hounsfield units)[8,9]. Positive remodeling was visually assessed in multiplanar reconstructed images in both long- and short-axis views. Outer vessel wall diameter was measured at the reader's discretion with PRP defined as remodeling index ≥1.1. If low-attenuation was visualized in a non-calcified plaque, 3 regions-of-interest (>0.5 mm^2) were placed and mean attenuation was calculated. LAP was defined by mean attenuation of <30 Hounsfield units. LAP and PRP scores were calculated for each artery by calculating the number of LAPs or PRPs present in that artery. HRP score was calculated by addition of LAP and PRP scores. All scores were confirmed by 2 separate, trained and blinded readers (ICC=94% for intraexaminer and ICC=93% for interexaminer analysis).

Analysis of Traditional Cardiovascular and Cardiometabolic Risk Factors, Psoriasis Treatments, and Inflammatory Biomarkers

All patients underwent fasting blood draws for the assessment of the lipid panel, including total, high- and low-density lipoprotein cholesterol, glucose, and high-sensitivity C-reactive protein levels at a certified clinical laboratory. Framingham 10-year risk score and homeostasis model assessment of insulin resistance (HOMA-IR) were calculated using online calculators based on published guidelines[10,11]. Baseline psoriasis treatment for the cohort was defined by up to 12 months of any of the following therapy before inclusion in the study: systemic or biologic therapy (steroids, methotrexate, adalimumab, etanercept, and ustekinumab), psoralen plus ultraviolet A (PUVA) or ultraviolet B (UVB), and topical treatments. Patients were asked to complete survey-based questionnaires regarding smoking, previous cardiovascular disease, family history of cardiovascular disease, and previous established diagnoses of

hypertension and diabetes. Patient responses were confirmed by interview with the study provider. Cardiovascular disease included acute coronary syndrome comprising both MI and unstable angina pectoris, stable angina pectoris, cerebrovascular event, transient ischemic attack, peripheral vascular disease and revascularization procedures that comprised of coronary artery bypass grafting and percutaneous interventional procedures. Diabetes and hypertension were defined either by an established diagnosis or by use of glucose lowering and blood pressure lowering drugs, respectively.

Statistical Analyses

Summary statistics were generated for patient groups. Continuous data were reported as mean±S.D. for parametric variables and as median with interquartile range for non-parametric variables, whereas categorical variables were reported as frequencies. Normality was assessed by skewness and kurtosis. Comparisons between stratified groups were performed using student's t-tests for parametric continuous data while non-parametric data was compared using Mann-Whitney U tests. Categorical variables were compared using Pearson's chi-squared tests. Multivariable linear regression analyses were performed to evaluate the association between VI by ^{18}FDG PET/CT derived target-to-background ratios and TB and NCB burden adjusting for confounding covariates. We also checked for homoscedasticity of residuals and found constant residual variance. Standardized beta co-efficient and p-values were reported for all linear regression analyses. Multivariable logistic regression analyses were implemented for analyzing the association between VI and presence of luminal stenoses as well as HRP. Finally, for the assessment of the association between various severities of luminal stenoses as well as HRP scores and HRP subtype scores and VI, ordered logistic regression was employed. Post-estimation tests such as likelihood-ratio testing and Brant test were used to confirm the proportional odds assumption for the ordered logistic regression analyses, and where the assumption was violated, generalized ordered logistic regression was performed. Odds ratio with 95% confidence intervals were reported for all logistic regression analyses.

We hypothesized an additional effect of 0.15 of VI in the adjusted R-squared for fully adjusted model assessing the association between VI and NCB. Thus, our sample size of 182 patients provided us a power greater than 90% to detect this association with statistical significance. Furthermore, for our secondary analyses encompassing the associations between luminal stenosis and VI as well as HRP and VI, our respective sample sizes of 171 and 169 patients were sufficient to detect these associations with >90% power for odds ratios between 2.0 and 4.0. All statistical analyses were performed using STATA version 12 (StataCorp, College Station, TX, USA), $p<0.05$ was considered for determining statistical significance.

SUPPLEMENTARY RESULTS

Association of Aortic Vascular Inflammation and Non-calcified Coronary Plaque Burden with Traditional Cardiovascular Risk Factors

Univariable regression analyses for NCB demonstrated an association with male sex (ß=0.36, $p<0.001$), clinical history of hypertension (ß=0.20, $p<0.001$), BMI (ß=0.54, $p<0.001$), HOMA-IR (ß=0.19, $p<0.001$), ASCVD 10-year risk (ß=0.20, $p<0.001$), HDL cholesterol (ß=-0.35, $p<0.001$), and psoriasis severity measured by PASI (ß=0.16, $p<0.001$). Furthermore, similar analyses were performed for VI, which showed an association between VI and male sex

(ß=0.25, p<0.001), BMI (ß=0.56, p<0.001), ASCVD 10-year risk (ß=0.35, p<0.005), HDL (ß=-0.44, p<0.001), PASI (ß=0.17, p=0.02) and HOMA-IR (ß=0.31, p<0.001).

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SUPPLEMENTARY TABLES AND FIGURES

eTable 1: Baseline characteristics of the study cohort stratified by presence or absence of coronary artery stenoses.

Parameter	Stenosis absent (n=89)	Stenosis present (n=82)	p
Demographics and medical history			
Age, years	46.1±12.0	56.4±10.6	<0.001
Males	43 (48)	59 (72)	0.002
Ethnicity, Caucasians	68 (76)	70 (85)	0.48
Hypertension	16 (18)	33 (40)	0.001
Hyperlipidemia	39 (44)	46 (56)	0.11
Type 2 diabetes mellitus	7 (8)	10 (12)	0.34
Current tobacco use	6 (7)	6 (7)	0.88
Lipid treatment	20 (23)	38 (46)	0.001
Body mass index, kg/m^2	30.2±5.6	28.9±5.9	0.08
Clinical and laboratory values			
Systolic blood pressure, mm Hg	120.4±13.2	126.0±15.2	0.005
Total cholesterol, mg/dL	180.2±40.2	184.3±32.6	0.23
High-density Lipoprotein cholesterol, mg/dL	56.3±16.9	55.2±18.3	0.34
Low-density Lipoprotein cholesterol, mg/dL	103.2±29.6	100.9±31.9	0.32
Triglycerides, mg/dL	101 (73-140)	102 (79-138)	0.97
ASCVD 10-year risk	1.1 (0.3-2.2)	4.9 (2.1-8.9)	<0.001
HOMA-IR	2.6 (1.7-4.4)	2.8 (1.6-5.2)	0.38
High-sensitivity C-reactive protein, mg/L	2.4 (1.0-4.2)	1.2 (0.7-4.1)	0.09
Psoriasis Characterization			
Disease duration, years	19 (9-30)	20 (10-33)	0.28
Psoriasis area severity index score	5.5 (2.8-8.9)	8.7 (5.3-17.7)	0.001
Systemic or biologic treatment	34 (39)	27 (32)	0.41
Vascular Inflammation			
Aortic target-to-background ratio	1.65 ± 0.21	1.75 ± 0.28	0.007

Values reported as Mean ± SD or Median (IQR) for continuous data and N (%) for categorical data. P value less than 0.05 deemed significant. P values were calculated by using student's t-test or Mann-Whitney U test for continuous variables and Pearson's chi-squared test for categorical variables. ASCVD: atherosclerotic cardiovascular disease, HOMA-IR: homeostasis model assessment of insulin resistance.

eTable 2: Baseline characteristics of the study cohort stratified by presence or absence of high-risk plaque.

Parameter	HRP absent (n=112)	HRP present (n=57)	p
Demographics and medical history			
Age, years	46.8±11.4	58.3±11.0	<0.001
Males	57 (51)	43 (75)	0.002
Ethnicity, Caucasians	90 (80)	47 (82)	0.65
Hypertension	26 (23)	22 (39)	0.04
Hyperlipidemia	50 (45)	35 (61)	0.04
Type 2 diabetes mellitus	9 (8)	9 (16)	0.12
Current tobacco use	11 (10)	5 (9)	0.83
Lipid treatment	29 (26)	31 (54)	<0.001
Body mass index, kg/m^2	29.7±6.2	29.5±5.0	0.84
Clinical and laboratory values			
Systolic blood pressure, mm Hg	121.2±13.0	126.0±17.4	0.04
Total cholesterol, mg/dL	183.2±33.8	175.3±39.8	0.18
High-density Lipoprotein cholesterol, mg/dL	55.0±17.3	54.0±16.4	0.71
Low-density Lipoprotein cholesterol, mg/dL	103.2±29.1	97.4±31.0	0.24
Triglycerides, mg/dL	103 (74-142)	100 (78-140)	0.96
ASCVD 10-year risk	1.5 (0.4-3.3)	5.3 (2.6-10.1)	<0.001
HOMA-IR†	2.7 (1.7-5.2)	3.1 (1.8-4.3)	0.84
High-sensitivity C-reactive protein, mg/L	2.4 (1.0-5)	1 (0.6-2.4)	0.002
Psoriasis Characterization			
Disease duration, years	19 (9-27)	20 (10-33)	0.15
Psoriasis area severity index score	5.9 (3.2-10.1)	7.9 (4-17.7)	0.01
Systemic or biologic treatment	42 (38)	20 (35)	0.7
Vascular Inflammation			
Aortic target-to-background ratio	1.65±0.20	1.76±0.29	0.004

Values reported as Mean ± SD or Median (IQR) for continuous data and N (%) for categorical data. P value less than 0.05 deemed significant. P values were calculated by using student's t-test or Mann-Whitney U test for continuous variables and Pearson's chi-squared test for categorical variables. ASCVD: atherosclerotic cardiovascular disease, HOMA-IR: homeostasis model assessment of insulin resistance.

eTable 3: Association between luminal stenoses by coronary computed tomography angiography and aortic vascular inflammation

Model	Values	Presence of luminal stenosis	Severity of luminal stenoses
Unadjusted	Odds ratio (95% CI)	3.63 (1.71-7.70)	4.03 (1.90-8.55)
	p	0.001	<0.001
	Change in odds per 1 SD increase in TBR	1.38	1.42
Adjusted for age, sex, BMI, diabetes, hypertension, hyperlipidemia, smoking, hsCRP, statins, systemic/biologic psoriasis treatment	Odds ratio (95% CI)	3.40 (1.40-8.24)	3.38 (1.42-8.07)
	p	0.007	0.006
	Change in odds per 1 SD increase in TBR	1.36	1.36

Association for presence of luminal stenoses was assessed by logistic regression, whereas the association for severity was assessed by ordered logistic regression. CI: confidence interval, SD: standard deviation, TBR: target-to-background ratio, BMI: body mass index, hsCRP: high-sensitivity C-reactive protein. Luminal stenoses severities were categorized as: minimal (0-24%) or no stenosis as 0, mild (25-49%) as 1, moderate (50-69%) as 2, and severe (≥70%) as 3. There were no vessels with complete occlusion.

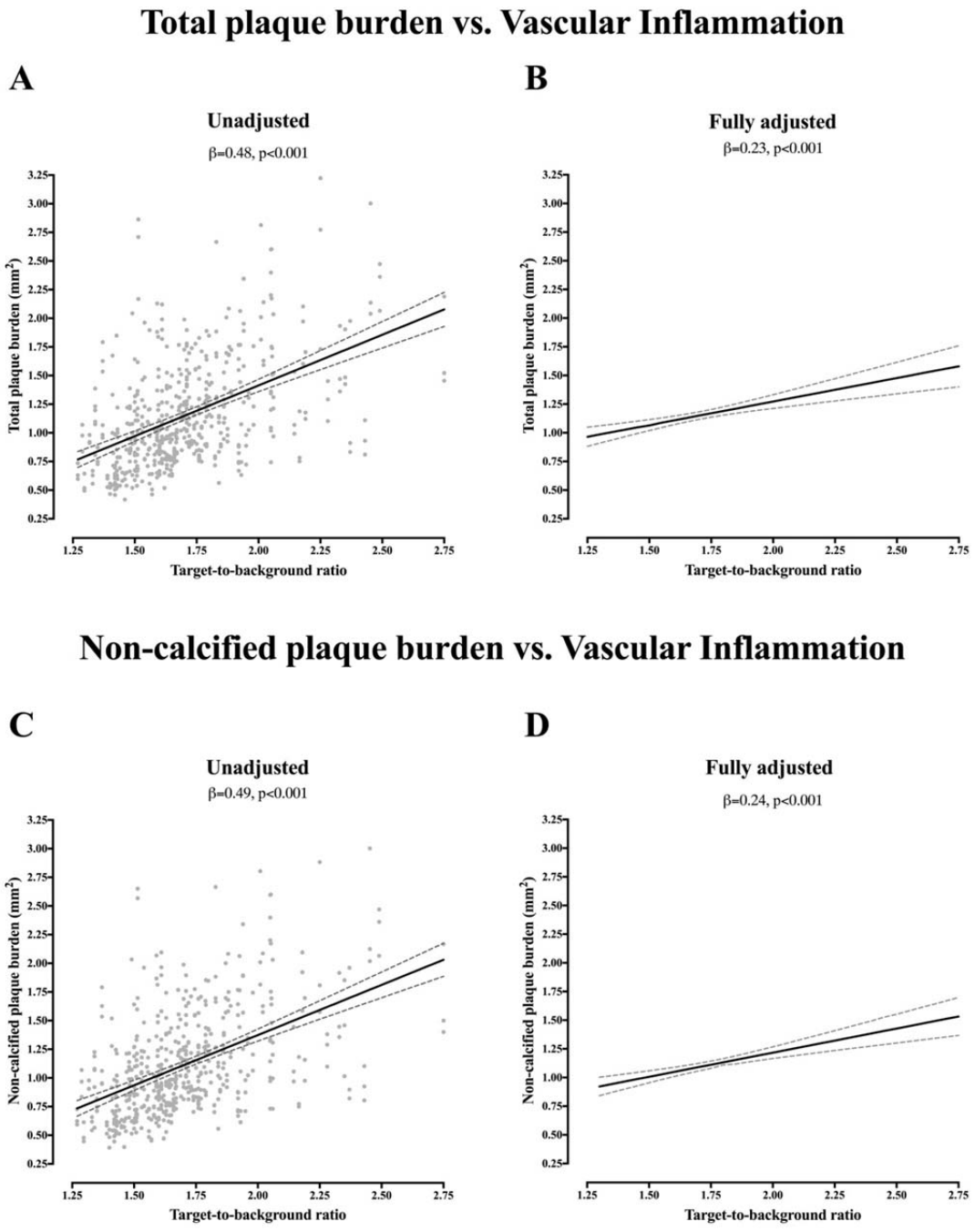
eTable 4: Association between presence of high-risk plaque, various high-risk plaque scores and aortic vascular inflammation

Model	Values	HRP presence	HRP score	LAP score	PRP score
Unadjusted	Odds ratio (95% CI)	3.05 (1.48-6.29)	3.03 (1.42-6.47)	5.63 (1.96-16.19)	1.51 (0.64-3.58)
	p	0.002	0.004	0.001	0.35
	Change in odds per 1 SD increase in TBR	1.34	1.33	1.57	1.11
Adjusted for age, sex, BMI, diabetes, hypertension, hyperlipidemia, smoking, hsCRP, statins, systemic/biologic psoriasis treatment	Odds ratio (95% CI)	2.72 (1.08-6.83)	2.95 (1.21-7.18)	6.33 (1.88-21.28)	1.22 (0.45-3.30)
	p	0.03	0.02	0.003	0.7
	Change in odds per 1 SD increase in TBR	1.3	1.32	1.61	1.05

Association for HRP presence was assessed by logistic regression, whereas the association for different HRP scores was assessed by ordered logistic regression. HRP: high-risk plaque, LAP: low-attenuation plaque, PRP: positively remodeled plaque, CI: confidence interval, SD: standard deviation, TBR: target-to-background ratio, BMI: body mass index, hsCRP: high-sensitivity C-reactive protein. LAP score and PRP score were calculated for each artery as the total number of LAP and PRP in that artery. HRP score was calculated for each artery by adding LAP score and PRP score.

eFigure 1: Aortic Vascular inflammation by ^{18}FDG PET/CT is associated with total and non-calcified coronary plaque burden.

Legend: The figure demonstrates unadjusted and adjusted regression plots for association between aortic vascular inflammation and total as well as non-calcified coronary plaque burden. A&B- unadjusted and fully adjusted regression plots for total plaque burden vs. aortic vascular inflammation; C&D- unadjusted and fully adjusted regression plots for non-calcified plaque burden vs. aortic vascular inflammation.



eFigure 2. Regression plot reveals no association between aortic vascular inflammation and dense-calcified coronary plaque burden

Legend: The figure demonstrates unadjusted regression plots for association between aortic vascular inflammation and dense-calcified coronary plaque burden.