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ORIGINAL ARTICLE

Association of aortic vascular uptake of ^{18}FDG by PET/CT and aortic wall thickness by MRI in psoriasis: a prospective observational study

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Abstract

Background The contribution of inflammation to the incidence of cardiovascular disease (CVD) has been increasingly recognized in recent years. We investigated the relationship of aortic vascular uptake of 18F-FDG by PET/CT and aortic wall thickness (AWT) by MRI in psoriasis, a chronic inflammatory disease with increased incidence of CVD. One hundred sixty-five patients with plaque psoriasis participated in an ongoing longitudinal cohort study. Subclinical atherosclerosis was assessed as aortic uptake of 18F-FDG by PET/CT reported as target-to-background ratio (TBR) and AWT by MRI reported as maximal thickness.

Results Patients with psoriasis were middle aged, predominantly male, and had mild CV risk by traditional risk factors. Psoriasis severity as measured by PASI score was a notable determinant of AWT ($\rho = 0.20$, $p = 0.01$). Moreover, aortic vascular uptake of 18F-FDG associated with AWT by MRI at baseline in unadjusted analysis ($\beta = 0.27$ $p = 0.001$) and following adjustment for traditional cardiovascular risk factors, waist-to-hip ratio, and statin use ($\beta = 0.21$ $p = 0.01$). Finally, following 1 year of psoriasis treatment, a decrease in aortic vascular uptake of 18F-FDG was associated with a reduction in AWT in fully adjusted models ($\beta = 0.33$, $p = 0.02$).

Conclusion In conclusion, we demonstrate that psoriasis severity and aortic vascular uptake of 18F-FDG in the aorta were associated with AWT. Following treatment of psoriasis, a decrease in aortic vascular uptake of 18F-FDG was associated with a reduction in AWT at 1 year. These findings suggest that aortic vascular uptake of 18F-FDG is associated with early evidence of vascular disease assessed by aortic wall thickness. Prospective studies in larger populations including other inflammatory diseases are warranted.

Keywords Psoriasis · Inflammation · Atherosclerosis · Thoracic MRI · ^{18}FDG PET/CT

Abbreviations

AWT	Aortic wall thickness
MRI	Magnetic resonance imaging
^{18}FDG PET/CT	18Fluorodeoxyglucose positron emission tomography computed tomography
TBR	Target-to-background ratio
PASI	Psoriasis area severity index

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Background

The contribution of inflammation to the progression and morbidity of atherosclerosis has been increasingly recognized in recent years [1, 2]. In addition to disease associated with age, sex, dyslipidemia, and other traditional risk factors, patients with elevated inflammatory levels as measured by high-sensitivity C-reactive protein are also at increased risk of adverse cardiovascular events [3]. Indeed, the recent CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcome Study) trial demonstrated that this residual inflammatory risk can be at least partially ameliorated via treatment with medications which reduce systemic inflammation [2]. However, given the high cost and relatively high number needed to treat for all-comers with both elevated cardiovascular risk and elevated inflammatory markers, further investigation is needed to elicit which individuals may benefit the most from these biologic anti-inflammatory drugs [4].

Non-invasive imaging can be effectively used to monitor treatment response and evaluate cardiovascular risk over time [5–8]. Metabolic imaging modalities, such as ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F-FDG PET/CT), have a documented capability to assess vascular disease over time by detecting vascular uptake of ^{18}F-FDG by PET/CT [6, 9–12]. This uptake is directly associated with coronary artery disease [9], increased risk of future cardiovascular events [6], and is sensitive to modulation of risk factors with preventive strategies such as lifestyle changes, statin therapy, and biologic treatment [10–12]. Changes in anatomic imaging modalities in response to biologic treatment have been limited to carotid intima-media thickness with few studies on aortic wall thickness (AWT) by magnetic resonance imaging (MRI) [13, 14]. Thoracic MRI can be used to reliably determine AWT, with good correlation to pathological specimens [15]. AWT, in turn, was associated with increased risk of future cardiovascular events in the Dallas Heart Study (hazard ratio 1.28 per 1 standard deviation, or per 0.33 mm increase) [16]. Previously published data from the Multi-Ethnic Study of Atherosclerosis as well as the Dallas Heart Study showed age, hypertension, male sex, blood glucose, body mass index (BMI), smoking status, cholesterol, and triglyceride levels to be associated with AWT [17–19]. Estimated average annual rates of change in mean AWT ranges from 0.014 to 0.032 mm per year [20, 21].

Patients with chronic inflammatory conditions such as psoriasis experience increased early cardiovascular mortality, even beyond adjustment for traditional risk factors, further suggesting shared mechanisms between skin disease involvement and presence of vascular disease [22, 23]. Moreover, we have previously demonstrated that psoriasis is associated with higher aortic vascular uptake of ^{18}F-FDG by PET/CT compared with age- and sex-matched healthy volunteers [24]. Moreover, this increase in vascular uptake of ^{18}F-FDG by PET/CT has been shown to be reduced following 1 year of biologic therapy [10]. While the relationship of aortic vascular uptake of ^{18}F-FDG with coronary artery disease has been previously demonstrated, vascular uptake of ^{18}F-FDG has not been linked directly to increase in AWT [10, 12].

Therefore, we sought to investigate the relationship between vascular uptake of ^{18}F-FDG and AWT at baseline and over time. We hypothesized that vascular uptake of ^{18}F-FDG by PET/CT will correlate with AWT by MRI at baseline. Furthermore, we hypothesized that, following 1 year of psoriasis therapy, a change in aortic uptake of ^{18}F-FDG would be associated with change in AWT beyond traditional risk factors. Finally, we sought to assess if vascular uptake of ^{18}F-FDG at baseline is associated with change in AWT over time.

Methods

Patient population

This was an observational longitudinal cohort study of patients with psoriasis. Patients were recruited at the National Institutes of Health Clinical Center in Bethesda, MD, USA, as described in Supplementary Figure 1. The study was approved by the National Institutes of Health Institutional Review Board. From January 1, 2013, to July 1, 2018, 291 patients with psoriasis were recruited consecutively and underwent a baseline physical exam and laboratory assessment. Of those, 165 underwent thoracic MRI scans at baseline and 88 at 1 year. All study protocols are in compliance with the Declaration of Helsinki. Strengthening the reporting of observational studies in epidemiology (STROBE) criteria was followed for reporting the findings of this observational study [25].

Patients were required to be greater than 18 years of age, with plaque psoriasis documented by a health care provider. Psoriasis severity was assessed by psoriasis area severity index (PASI) score, which is the most commonly cited measure of psoriasis severity and combines the severity of lesions and the area affected into a single score, considering erythema, induration, and desquamation within each lesion [26]. Participants were excluded if they had estimated glomerular filtration rate < 30 mL/min/1.73m^2, existing cardiovascular disease, any comorbid condition known to promote cardiovascular disease or systemic inflammation, such as uncontrolled hypertension, internal malignancy within 5 years, human immunodeficiency virus, active infection within the past 72 h of baseline, major surgery within the past 3 months, and pregnancy or lactation. All patients underwent a fasting blood draw, from which lipid panel, glucose, insulin, glycated hemoglobin, and high-sensitivity C-reactive protein were obtained. Systemic treatment was defined as methotrexate or systemic steroids, and biologic treatment was defined as

treatment with anti-tumor necrosis factor, anti-interleukin (IL) 12/23, or anti-IL 17.

Imaging studies

MRI was performed using a 3.0 T whole body MRI system (Siemens Healthcare, Erlangen, Germany). MRI of the aorta was performed to obtain two-dimensional T1-weighted black blood cardiac gated axial images from the pelvis through the lung apices. Fat suppression was performed using chemical saturation. Imaging parameters were repetition time (TR), 700–900 msec depending on R-R interval; echo time (TE), 25 msec; field of view, 36 cm; slice thickness, 5 mm; and matrix size, 256 × 256. Images of the descending aorta were contoured by a single, trained reader at the level of the right pulmonary artery using QPlaque (Medis, Leiden, The Netherlands) using at least three continuous slices. The reader was blinded to clinical information including date of visit, disease status, and treatment.

^{18}F-FDG PET/CT was performed as previously published [12]. Patients underwent ^{18}F-FDG PET/CT scans following overnight fast. Images were obtained approximately 60 min after administration of a fixed 10 mCi dose of 18 FDG. All scans were completed using a 64-slice scanner (Siemens Biograph mCT PET/CT 64 slice scanner, Malvern, PA, USA) with 1.5 mm axial slices of the aorta obtained. We analyzed the uptake of 18 FDG within the aorta using a dedicated PET/CT image analysis program (Extended Brilliance Workspace, Phillips Healthcare, Andover, MA, USA) to measure vascular uptake of ^{18}F-FDG calculated as target-to-background ratio using blood as the background [10]. The reader was blinded to clinical information including date of visit, disease status, and treatment.

Statistical analysis

Normality of data was assessed using skewness and kurtosis. Statistical significance was assessed at 1 year using the paired Student's *t* test for normally distributed continuous variables, the Wilcoxon matched-pairs signed-ranks test for non-normally distributed continuous variables, and Pearson's χ^2 test for categorical variables. Patients with mild psoriasis at baseline, or PASI score ≤ 3, were compared with those with moderate to severe disease at baseline, or PASI score > 3. Comparisons were performed using Student's *t* test, the Wilcoxon rank-sum test, or Pearson's χ^2 test for continuous normal, continuous non-normal, and categorical variables, respectively, for baseline analysis. Spearman's test was used to assess correlations between baseline AWT and clinical variables. Univariate and multivariate linear regressions were performed to assess correlations between baseline AWT and other variables of interest at baseline and over 1 year. Natural logarithmic transformation was used for regressions of variables with skewness > 1.5. Analyses were performed using statistical software (STATA 12.0; Stata Corp, College Station, TX). A p value of < 0.05 was considered statistically significant.

Results

Baseline characteristics of the cohort

The psoriasis cohort was middle aged, predominantly male, and had low cardiovascular risk by Framingham 10-year risk score at baseline. Almost half of the cohort was diagnosed with hyperlipidemia, with 32% of the cohort on statin therapy. Participants had mild-moderate psoriasis disease severity (PASI score 5.3 (2.8–8.9)), with 27% of the cohort on systemic or biologic psoriasis therapy at baseline. On performing stratified analyses, patients with moderate to severe psoriasis at baseline were similar in demographics and clinical values when compared with mild disease. Aortic vascular uptake of ^{18}F-FDG by PET/CT was found to be greater in the group with moderate to severe psoriasis (TBR 1.72 ± 0.27 for moderate-severe vs. 1.61 ± 0.19 in mild disease, $p = 0.01$). Similar to aortic vascular uptake of ^{18}F-FDG by PET/CT, patients with moderate to severe psoriasis had a greater AWT (3.23 ± 0.55 mm, vs. 3.00 ± 0.61 mm, $p = 0.01$) compared with patients with mild disease (Table 1) (Fig. 1).

Determinants of AWT (relationship between aortic vascular uptake of ^{18}F-FDG by PET/CT and AWT by MRI, respectively)

Multiple variables were related to baseline AWT (Table 2). Variables with greatest magnitude of ρ for AWT were age ($\rho = 0.38$, $p < 0.001$), Framingham risk score ($\rho = 0.53$, $p < 0.001$), hypertension ($\rho = 0.18$, $p = 0.02$), hyperlipidemia ($\rho = 0.28$, $p < 0.001$), and body mass index ($\rho = 0.17$, $p = 0.03$). Other notable determinants of AWT include psoriasis severity as measured by PASI score ($\rho = 0.20$, $p = 0.01$). Interestingly, aortic vascular uptake of ^{18}F-FDG correlated with AWT at baseline in unadjusted analysis ($\beta = 0.27$ $p = 0.001$) as well as when adjusted for traditional cardiovascular risk factors, waist-to-hip ratio, and statin use ($\beta = 0.21$ $p = 0.01$).

Effect of psoriasis therapy on aortic vascular uptake of ^{18}F-FDG and AWT at 1 year

Of the 165 patients at baseline, 88 had 1 year data available in the form of both baseline and follow-up MRI scans. In general, modifiable cardiovascular risk factors were mildly improved at 1 year (Table 3). Psoriasis severity decreased by 44%, from median PASI score of 5.4 to a median of 3.0 at 1 year ($p < 0.001$). This was concurrent

Table 1 Comparison of baseline parameters in mild vs. moderate-severe psoriasis patients

Parameter	Mild psoriasis	Moderate to severe psoriasis	*p* value
Demographic and clinical characteristics	*N* = 46	*N* = 121	
Age (years)	49.9 ± 13.6	51.3 ± 12.6	0.27
Sex (male)	23 (50)	72 (61)	0.22
BMI (kg/m^2)	28.2 ± 5.0	29.5 ± 5.5	0.1
Current smoker	1 (2)	10 (8)	0.15
Hypertension	16 (35)	24 (20)	0.05
Diabetes	4 (9)	14 (12)	0.56
Hyperlipidemia	18 (39)	59 (50)	0.21
Statin treatment	15 (33)	37 (32)	0.88
Hypertensive treatment	13 (28)	28 (24)	0.55
Diabetic treatment	6 (13)	9 (8)	0.28
Clinical and lab values			
Systolic blood pressure (mm Hg)	124.4 ± 15.3	121.8 ± 14.9	0.17
Diastolic blood pressure (mm Hg)	71.9 ± 10.4	72.2 ± 9.5	0.44
HOMA-IR	2.4 (1.4–3.5)	3.0 (1.7–5.3)	0.09
Total cholesterol (mg/dL)	177.1 ± 32.7	184.5 ± 40.6	0.13
HDL cholesterol (mg/dL)	57.3 ± 20.1	54.5 ± 16.4	0.46
LDL cholesterol (mg/dL)	96.8 ± 24.6	105.5 ± 32.2	0.05
Triglycerides (mg/dL)	100 (76–133)	103 (79–142)	0.41
Glycated hemoglobin (%)	5.42 ± 0.66	5.6 ± 0.53	*0.03*
C-reactive protein (mg/dL)	1.3 (0.9–3.5)	2.3 (0.71–5.0)	0.13
Framingham risk score (%)	3.8 ± 3.9	4.2 ± 4.0	0.25
Psoriasis severity			
PASI score	1.7 (1.1–2.6)	7.1 (5.1–11.8)	*< 0.001*
Disease duration (years)	19.0 ± 12.8	21.2 ± 14.6	0.19
Systemic or biologic treatment	14 (31)	29 (25)	0.43
Vascular characteristics			
Aortic vascular uptake of FDG by PET/CT (TBR)	1.61 ± 0.19	1.72 ± 0.27	*0.01*
Aortic wall thickness by MRI, mm	3.00 ± 0.61	3.23 ± 0.55	*0.01*

Mild psoriasis defined as PASI score ≤ 3 at baseline. Moderate-severe psoriasis defines as PASI score > 3 at baseline. Values reported as mean ± SD for parametric variables, median (IQR) for nonparametric continuous variables, and *n* (%) for categorical variables. Statistical significance assessed by Student's *t* test for parametric variables, Wilcoxon rank-sum test for nonparametric continuous variables, and Pearson's χ^2 test for categorical variables. *BMI*, body mass index; *HOMA-IR*, homeostatic model assessment for insulin resistance; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *PASI*, psoriasis area severity index; *TBR*, target-to-background ratio

p-value <0.05 deemed significant

with a significant increase in the proportion of patients receiving systemic or biologic treatment from 25% at baseline to 50% at 1 year ($p < 0.001$). AWT decreased at 1 year (baseline 3.14 ± 0.48 mm vs. 2.95 ± 0.38 mm at

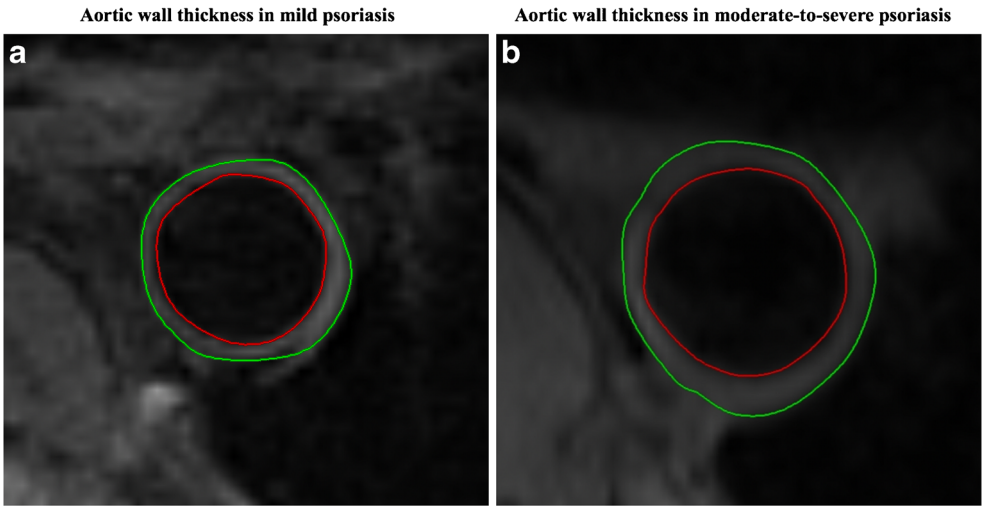

Fig. 1 Aortic wall thickness in mild and moderate to severe psoriasis patients. Transverse magnetic resonance imaging slices of a patient with mild psoriasis (**a**) at the level of descending aorta depicting lower aortic wall thickness when compared with moderate to severe psoriasis patient (**b**). The green and the red contour represent the outer and the inner border of the aortic wall respectively; QPlaque (Medis, Leiden, The Netherlands)

Table 2 Association of aortic wall thickness with cardiometabolic parameters

Parameter	Rho (*p* value)
Demographic and Clinical Characteristics ($n = 165$)	AWT
Age (years)	*0.38 (< 0.001)*
Sex (male)	0.07 (0.37)
BMI (kg/m^2)	*0.17 (0.03)*
Current smoker	− 0.04 (0.61)
Hypertension	*0.18 (0.02)*
Diabetes	0.05 (0.49)
Hyperlipidemia	*0.28 (< 0.001)*
Statin treatment	*0.19 (0.02)*
Hypertensive treatment	0.11 (0.15)
Diabetic treatment	0.04 (0.58)
Clinical and lab values	
Systolic blood pressure (mm Hg)	*0.21 (0.01)*
Diastolic blood pressure (mm Hg)	0.17 (0.03)
HOMA-IR	0.08 (0.31)
Total cholesterol (mg/dL)	0.005 (0.96)
HDL cholesterol (mg/dL)	0.03 (0.74)
LDL cholesterol (mg/dL)	− 0.01 (0.85)
Triglycerides (mg/dL)	0.04 (0.65)
Glycated hemoglobin (%)	0.08 (0.42)
C-reactive protein, mg/L	0.08 (0.31)
Framingham risk score	*0.53 (< 0.001)*
Psoriasis severity	
PASI score	*0.20 (0.01)*
Disease duration, years	0.02 (0.78)
Systemic or biologic Treatment	*− 0.24 (0.003)*
Vascular characteristics	
Aortic vascular uptake of FDG by PET/CT (TBR)	*0.27 (0.001)*

Values reported as standardized rho coefficient (*p* value). *BMI*, body mass index; *HOMA-IR*, homeostatic model assessment for insulin resistance; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *PASI*, psoriasis area severity index; *TBR*, target-to-background ratio

p-value <0.05 deemed significant

1 year, $p < 0.001$), in addition to results from our prior study which demonstrated a statistically significant decrease in aortic vascular uptake of ^{18}F-FDG [10] (baseline TBR 1.68 ± 0.25 vs. 1.60 ± 0.19 at 1 year, $p < 0.001$) following improvement in skin severity (baseline PASI score 5.4 (2.8–9.0) vs. 3.0 (1.8–5.3) at 1 year, $p < 0.001$). Furthermore, change in aortic vascular uptake of ^{18}F-FDG over time was associated with a reduction in AWT ($\beta = 0.31$, $p = 0.004$) even beyond adjustment for traditional risk factors, waist-to-hip ratio, and statin use ($\beta = 0.33$, $p = 0.02$). Finally, baseline value of aortic vascular uptake of ^{18}F-FDG was associated with a reduction in AWT ($\beta = 0.48$, $p < 0.001$) at 1 year in adjusted analyses.

Discussion

In a prospective observational study, we demonstrate determinants of wall thickness of the aorta in psoriasis. Second, we demonstrate a direct relationship between aortic vascular uptake of 18FDG by PET/CT and AWT by MRI within the same vessel in psoriasis. Third, following treatment of psoriasis, we observed that a reduction in vascular uptake of ^{18}F-FDG was associated with a decrease in AWT beyond adjustment for cardiovascular risk factors and statin use. Finally, the change in AWT was strongly related to the baseline value of aortic vascular uptake of ^{18}F-FDG.

Atherosclerosis has been demonstrated to be both an immune-mediated and lipid-associated process [27]. Furthermore, systemic inflammatory states such as psoriasis and rheumatoid arthritis have been associated with increased risk of cardiovascular disease [23, 28]. However, the effect of systemic inflammation on the arterial wall is poorly defined in human models of disease. Recently, the CANTOS trial demonstrated that treatment of residual inflammation with anti-inflammatory interleukin-1β inhibition had added benefit on cardiovascular risk reduction independent of lipid-level lowering [2]; however, additional investigation is needed to improve clinical decision-making.

Aortic vascular uptake of ^{18}F-FDG by PET/CT has been associated with subclinical vascular disease in systemic inflammatory diseases [10]. ^{18}F-FDG PET/CT uptake correlates with the accumulation of macrophages in the vasculature [29], is associated with cardiovascular disease biomarkers [30], modulates after treatment for cardiovascular risk factors [11], and is independently associated with future vascular events suggesting it represents a biomarker of vascular damage in retrospective studies [11]. While FDG uptake in the aortic wall is a good indicator of chronic low-grade vascular inflammation, other causes of FDG uptake should also be kept in mind including aortic aneurysm (thin walled), aortitis (including vasculitis syndromes like giant cell arteritis), aortic tumors (exceedingly rare, but sarcomas of the intima are most common), and sometime intramural hematoma in the aortic wall (especially when hemorrhaging of the aortic wall occurs in the absence of intimal disruption) [31]. Aneurysms appear enlarged and rounded and will have thin wall on low-dose CT; FDG uptake denotes an unstable lesion vs. a stable one where no uptake is usually seen. Aortitis and vasculitis in general have more intense FDG uptake with standardized uptake values reported two to three times higher than observed in chronic low-grade vascular inflammation such as psoriasis. Finally, atherosclerotic lesions which have not yet calcified avidly uptake FDG in a diffuse fashion whereas focal FDG uptake in the wall of the aorta can be seen in cases of intramural hematoma [31].

To augment soft tissue definition, MRI has recently gained interest. MRI can accurately assess aortic wall thickness, which has been shown to be predictive of future

Table 3 Characteristics of patients at baseline and at 1 year

Parameter	Baseline	1 year	*p* value
Demographic and clinical characteristics	*N* = 88	*N* = 88	
Age (years)	50.3 ± 12.6	51.3 ± 12.9	–
Sex (male)	43 (49)	43 (49)	–
BMI (kg/m^2)	28.8 ± 5.2	28.2 ± 5.3	*0.01*
Current smoker	4 (5)	2 (2)	0.16
Hypertension	23 (26)	22 (26)	0.71
Diabetes	10 (11)	9 (11)	0.32
Hyperlipidemia	38 (43)	41 (48)	0.32
Statin treatment	24 (38)	25 (29)	0.71
Hypertensive treatment	21 (24)	23 (27)	0.41
Diabetic treatment	6 (7)	7 (8)	0.32
Clinical and lab values			
Systolic blood pressure (mm Hg)	123.4 ± 15.8	116.4 ± 15.1	< *0.001*
Diastolic blood pressure (mm Hg)	73.6 ± 9.7	68.7 ± 9.4	< *0.001*
HOMA-IR	2.7 (1.8–4.6)	2.8 (1.7–5.2)	0.49
Total cholesterol (mg/dL)	185.6 ± 38.9	182.0 ± 35.7	0.16
HDL cholesterol (mg/dL)	56.8 ± 18.3	58.5 ± 19.2	0.09
LDL cholesterol (mg/dL)	102 ± 30	96 ± 29	*0.03*
Triglycerides (mg/dL)	100 (77–137)	105 (79–152)	0.06
Glycated hemoglobin (%)	5.5 (5.1–5.7)	5.4 (5.0–5.7)	*0.01*
C-reactive protein (mg/dL)	2.1 (0.9–4.4)	1.3 (0.7–3.4)	*0.05*
Framingham risk score (%)	2 (1–5)	1 (1–5)	0.07
Psoriasis severity			
PASI score	5.4 (2.8–9.0)	3.0 (1.8–5.3)	< *0.001*
Disease duration (years)	21.3 ± 15.0	21.9 ± 15.2	< *0.001*
Systemic or biologic treatment	25 (29)	50 (61)	< *0.001*
Vascular characteristics			
Aortic vascular uptake of FDG by PET/CT (TBR)	1.68 ± 0.25	1.60 ± 0.19	< *0.001*
Aortic wall thickness by MRI, mm	3.14 ± 0.48	2.95 ± 0.38	< *0.001*

Values reported as mean ± SD for parametric variables, median (IQR) for nonparametric continuous variables, and n (%) for categorical variables. Statistical significance assessed by paired *t* test for parametric variables, Wilcoxon signed-rank test for nonparametric continuous variables, and Pearson's χ^2 for categorical variables. *BMI*, body mass index; *HOMA-IR*, homeostatic model assessment for insulin resistance; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *PASI*, psoriasis area severity index; *TBR*, target-to-background ratio

p-value <0.05 deemed significant

cardiovascular events [17, 20]. Furthermore, a small study demonstrated that aortic pulse wave velocity, measured by tonometry, is associated with vascular uptake of ^{18}F-FDG; though PWV is a functional rather than anatomic imaging modality. This further suggests that aortic vascular uptake of ^{18}F-FDG may mark a diseased vessel wall [32].

We demonstrate that psoriasis severity as well as vascular uptake of ^{18}F-FDG in the aorta is associated with wall thickness of the aorta by MRI. Specifically, increased vascular uptake of ^{18}F-FDG related to greater wall thickness in the aorta after adjusting for known cardiovascular disease risk factors. Previous investigations have demonstrated that increases in vascular uptake and/or AWT either predict cardiovascular disease or relate to its severity [6, 7, 16]. Previous natural history studies have demonstrated an annual increase in AWT ranging from 0.014 to 0.032 mm per year; in this context, a decrease of 0.19 mm seen by us (max AWT) is striking [20, 21]. Cardiovascular risk factors and emerging disease states associated with accelerated cardiovascular disease demonstrate an increase in vascular uptake [24]. ^{18}F-FDG PET/CT-defined vascular uptake therefore may lead to increasing thickness of the vessel wall due to direct effects; however, this needs to be better defined by future studies. Additionally, the effect of systemic or biologic medication on baseline AWT also adds to the evidence that these therapies may modulate atherosclerosis [2]. Finally, change in aortic vascular uptake of ^{18}F-FDG over time as well as baseline aortic vascular uptake of ^{18}F-FDG was associated with a reduction in AWT prospectively, suggesting

that high baseline vascular uptake of ^{18}F-FDG may be an important determinant of treatment response in psoriasis.

We acknowledge important limitations in our study. For small structures that approach the limitations of spatial resolution of PET imaging, change in size is known to follow with change in apparent uptake due to the partial volume effect [33]. Thus, further study is required to clarify how much of our observed change in uptake is due to a change in size or change in cellular FDG affinity (i.e., due to inflammation). Moreover, this is an observational study; it is possible that other treatment effects which were not controlled for may have confounded the results. Furthermore, patients were not randomized regarding the treatment they received. A significant number of patients elected to avoid undergoing MRI at follow-up due to the discomfort associated with the procedure, limiting the amount of data available for 1 year analysis. Finally, we have not studied hard cardiovascular events but instead used AWT and vascular uptake of ^{18}F-FDG to understand modulation of cardiovascular disease risk.

Conclusions

In conclusion, we demonstrate that psoriasis severity as well as aortic vascular uptake of ^{18}F-FDG is associated with AWT at baseline. Following treatment of psoriasis, decrease in aortic vascular uptake of ^{18}F-FDG was associated with AWT reduction at follow-up. These findings suggest that aortic vascular uptake of ^{18}F-FDG may provide an early window of future vascular disease development; however, prospective studies in larger populations are needed.

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Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions 1. Drs. Groenendyk, Dey, and Mehta had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

2. Concept and design: Dr. Mehta conceived the study concept and the study design was by Drs. Mehta and Gelfand.

3. Acquisition, analysis, or interpretation of data: Drs. Groenendyk, Dey, and Mehta acquired and analyzed the data.

4. Drafting of the manuscript: Drs. Groenendyk, Dey, and Mehta drafted the manuscript.

5. Critical revision of the manuscript for important intellectual content: All co-authors provided critical revisions of the manuscript.

6. Administrative, technical, or material support: Dr. Mehta provided technical guidance to Drs. Groenendyk and Dey during the study.

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Compliance with ethical standards

Ethics approval and consent to participate The study was approved by the National Institutes of Health Institutional Review Board. From January 1, 2013, to July 1, 2018, 291 patients with psoriasis were recruited consecutively and underwent a baseline physical exam and laboratory assessment. Informed consent was obtained from each patient prior to initiation of the study.

Consent for publication Not applicable.

Competing interests

1. NNM is a full-time US government employee and has served as a consultant for Amgen, Eli Lilly, and Leo Pharma receiving grants/other payments; as a principal investigator and/or investigator for AbbVie, Celgene, Janssen Pharmaceuticals, Inc., and Novartis receiving grants and/or research funding and as a principal investigator for the National Institute of Health receiving grants and/or research funding.
2. JMG was supported by an NIAMS grant (K24-AR-064310); Dr. Gelfand served as a consultant for BMS, Boehringer Ingelheim, GSK, Janssen Biologics, Menlo Therapeutics, Novartis Corp, Regeneron, Dr. Reddy's labs, UCB (DSMB), Sanofi and Pfizer Inc., receiving honoraria; and receives research grants (to the Trustees of the University of Pennsylvania) from Abbvie, Janssen, Novartis Corp, Sanofi, Celgene, Ortho Dermatologics, and Pfizer Inc.; and received payment for continuing medical education work related to psoriasis that was supported indirectly by Lilly and Ortho Dermatologics.
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