

ONLINE FIRST

Systemic and Vascular Inflammation in Patients With Moderate to Severe Psoriasis as Measured by [18F]-Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography (FDG-PET/CT)

A Pilot Study

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Objective: To evaluate the feasibility of using [18F]-fluorodeoxyglucose positron emission tomography–computed tomography (FDG-PET/CT) to detect and quantify systemic inflammation in patients with psoriasis.

Design: Case series with a nested case-control study.

Setting: Referral dermatology and preventive cardiology practices.

Participants: Six patients with psoriasis affecting more than 10% of their body surface area and 4 controls age and sex matched to 4 of the patients with psoriasis for a nested case-control study.

Main Outcome Measures: The FDG uptake in the liver, musculoskeletal structures, and aorta measured by mean standardized uptake value, a measure of FDG tracer uptake by macrophages and other inflammatory cells.

Results: FDG-PET/CT identified numerous foci of inflammation in 6 patients with psoriasis within the skin, liver, joints, tendons, and aorta. Inflammation in the joints

was observed in a patient with psoriatic arthritis as well as in 1 patient with no history of joint disease or joint symptoms. In a nested case-control study, FDG-PET/CT imaging demonstrated increased vascular inflammation in multiple segments of the aorta compared with controls. These findings persisted after adjustment for traditional cardiovascular risk factors in multivariate analysis (mean $\beta=0.33$; $P<.001$). Patients with psoriasis further demonstrated increased hepatic inflammation after adjusting for cardiovascular risk factors ($\beta=0.18$; $P<.001$), but the association was no longer significant when adjusted for alcohol intake ($\beta=-0.25$; $P=.07$).

Conclusion: FDG-PET/CT is a sensitive tool for identifying inflammation and can be used to identify clinically observed inflammation in the skin and subclinical inflammation in the blood vessels, joints, and liver of patients with psoriasis.

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PSORIASIS IS A CHRONIC INFLAMMATORY disease affecting 2% to 3% of the adult population.^{1,2} It is associated with an inflammatory arthritis (psoriatic arthritis) in about 10% of patients, with much higher frequencies in patients with more extensive skin disease.³ Psoriasis is also associated with increases in markers of inflammation in the skin and blood and increasingly is thought to be a systemic inflammatory disease and risk factor for incident diabetes mellitus, myocardial infarction, stroke, and premature cardiovascular (CV) death.⁴⁻¹⁸ The mechanism behind these associated comorbidities,

however, remains unknown. It has been widely suggested that a possible common pathway linking psoriasis to metabolic and CV disease is chronic inflammation mediated by T_H17 and T_H1 cells.¹⁹⁻²³ Yet, despite evidence of systemic inflammation in psoriasis, few techniques have been successfully used to identify and quantify locations of inflammation in vivo in these patients. Because traditional markers of systemic inflammation, such as high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate, only modestly correlate with psoriasis severity and do not provide regional information about disease involvement, novel assessments of

inflammation *in vivo* are particularly important in understanding the impact of psoriasis on systemic inflammation and systemic comorbidities.²⁴

The development of [18F]-fluorodeoxyglucose positron emission tomography–computed tomography (FDG-PET/CT), a validated technique used extensively in cancer and neuroimaging, enables highly precise, novel measurements of inflammatory activity, including vascular, visceral, and whole-body inflammation *in vivo*.²⁵ Previous studies using animal models and immunohistochemical analysis in humans indicate that FDG-PET/CT is exquisitely sensitive for detecting macrophage activity, an important source of cellular inflammation in numerous tissues, including early stages of atherosclerosis in vessel walls.^{26–30} The high sensitivity of FDG-PET/CT to detect early, subclinical inflammation with minimal error from operator dependence, demonstrated in studies of vasculitis,^{29,30} atherosclerosis,^{31–34} and joint disease,^{35–37} has expanded its use as a novel investigative tool to detect regional inflammatory disease. Importantly, observational studies indicate that aortic and carotid inflammation measured by FDG-PET/CT are strong predictors of future major vascular events.^{34,38,39} Furthermore, randomized controlled trials demonstrate that statin and therapeutic lifestyle interventions improve vascular inflammation as measured by FDG-PET/CT within 12 weeks and 16 months, respectively.^{40,41}

FDG-PET/CT therefore represents an innovative approach to studying systemic inflammation in a manner that is sensitive, quantifiable, and anatomically localizable. Furthermore, inflammation detected by FDG-PET/CT has been shown to be responsive to modulation by anti-inflammatory medical treatments and predictive of future vascular events. Such a tool could therefore be valuable in further defining systemic inflammation in patients with psoriasis. We therefore conducted a proof-of-principle study to describe FDG tracer uptake consistent with inflammation in the skin, liver, blood vessels, and joints in a series of patients with moderate to severe psoriasis. The second part of the pilot study attempted to determine if FDG-PET/CT can discriminate systemic inflammation in a subset of our patients with psoriasis compared with healthy controls using a nested case-control design.

METHODS

We conducted a proof-of-principle study (in 6 patients) evaluating the role of FDG-PET/CT in psoriasis to detect sites of inflammation. This study enrolled patients 18 to 70 years old with psoriasis involving a body surface area (BSA) greater than 10%. Because this study was designed to demonstrate the feasibility of applying FDG-PET/CT to this novel population, we allowed inclusion of treated patients with psoriasis to ensure a broad range of patients and improve the generalizability of our experience. Therefore, patients with psoriasis undergoing active light therapy, topical therapy, or being treated with stable doses (not changed within 12 weeks of study enrollment) of oral systemic medications (eg, methotrexate) or biologic agents were eligible. We excluded individuals with diabetes mellitus, tobacco use, history of CV disease, uncontrolled hypertension (defined as systolic blood pressure >180 mm Hg or diastolic

blood pressure >95 mm Hg), warfarin sodium use, coagulopathy, pregnancy or lactation, regular use of alcoholic beverages (>2 drinks per day), nonskin malignant disease within 5 years, positive status for human immunodeficiency virus, major surgery within 3 months of imaging, history of intravenous drug use within the past year, research drug study participation in the 6 weeks prior to imaging, or active infection within preceding 72 hours or other serious medical or psychiatric conditions.

We then conducted a substudy to evaluate the ability of this modality to discriminate inflammation with high sensitivity by comparing patients with psoriasis from our case series with healthy controls matched based on age, sex, and a restricted body mass index (BMI), calculated as weight in kilograms divided by height in meters squared, lower than 30. Of the 6 patients with psoriasis in our case series, 2 were excluded from this analysis: 1 had an existing diagnosis of psoriatic arthritis (a known cause of systemic inflammation), and the second had a BMI of 35.7 (obesity is associated with systemic inflammation). The substudy focused on quantification of subclinical vascular inflammation and hepatic inflammation in both groups to test the hypothesis that psoriasis is associated with increased inflammation *in vivo* compared with controls. To compare vascular inflammation assessed by FDG-PET/CT, we matched patients with psoriasis by age and sex to 3 prospectively recruited controls and a single historical control from another FDG-PET/CT study at our institution. The inclusion and exclusion criteria for controls were similar to those for our patients with psoriasis, except that controls were excluded if they had known chronic inflammatory diseases. All 4 patients with psoriasis included in this analysis would have otherwise qualified as healthy controls (if they did not have psoriasis) based on the criteria used.

All patients underwent a whole-body FDG-PET/CT scan using the standard protocol described herein. Patients fasted for 8 hours prior to the FDG-PET/CT scan. Fasting serum glucose levels were checked by fingerstick to assure glucose levels lower than 150 mg/dL prior to FDG administration. (To convert glucose to millimoles per liter, multiply by 0.0555.) Whole-body PET/CT image acquisition (Gemini TF; Philips Medical Systems, Bothell, Washington) commenced approximately 60 minutes after intravenous administration of 140 μ Ci/kg FDG. Axial, sagittal, and coronal PET reconstructions were interpreted with and without attenuation correction using noncontrast CT images for attenuation correction and anatomical correlation of FDG uptake. After qualitative review of PET and CT images, 2-dimensional (2D) circular regions of interests (ROIs) were manually placed on PET images around the external aortic contour, around the hepatic margin, and around articular spaces on all transverse slices passing through these structures using low-dose CT images for anatomic guidance. Mean standardized uptake values (SUVs) and areas of each ROI were measured for each slice using dedicated PET/CT image analysis software that autocalculates the SUV per slice within the specified ROI (Extended Brilliance Workstation; Philips Healthcare, Bothell, Washington). The total numbers of slices differ slightly from patient to patient depending on body habitus and anatomical variation, but these differences do not alter interpretation of regional data.³³ Details of this method have been published previously by our group and have been validated for the quantification of atherosclerosis, hepatic, and joint inflammation.^{33,37,42–45}

In our case series of 6 patients with psoriasis, our primary outcomes were defined as any finding on FDG-PET/CT consistent with inflammation, measured by SUV, the unit for FDG uptake, in the vasculature, viscera, and musculoskeletal system. Vascular SUVs were compared descriptively with expected norms based on age and sex from published literature.³¹ In the nested case-control substudy, our primary outcome

Table 1. Six Patients With Psoriasis Demonstrating Whole-Body Inflammation Detected by FDG-PET/CT

Patient/ Sex/Age, y	Cardiovascular History	Psoriasis History	Current Psoriasis Treatment (Within 3 mo)	Past Psoriasis Treatments (>3 mo prior)	Psoriatic Arthritis	FDG-PET/CT		
						Vascular, SUV, Mean (SD)	Liver, SUV, Mean (SD)	Musculoskeletal
1/M/41 ^a	No CV history HDL-C: 36 LDL-C: 106 BMI: 29.9 hsCRP: 2.9 Medications: fish oil	Duration: 20 y BSA: 13 PGA: 2 PASI: 7.2	NB UV-B (20 treatments)	Topical steroids NB UV-B Etanercept	No	AsA, 1.84 (0.08) Arch, 1.70 (0.06) TA, 1.59 (0.16) SRAA, 1.75 (0.15) IRAA, 1.61 (0.13)	2.28 (0.36)	None
2/M/40	Hyperlipidemia HDL-C: 33 LDL-C: 161 BMI: 36.7 hsCRP: 2.5 Medications: statin	Duration: 24 y BSA: 20 PGA: 2.66 PASI: 12.1	Methotrexate Abatacept	Topical steroids Infliximab Etanercept PUVA Laser	Yes	AsA, 1.67 (0.05) Arch, 1.53 (0.09) TA, 1.43 (0.14) SRAA, 1.50 (0.07) IRAA, 1.37 (0.13)	1.76 (0.19)	Inflammation of medial left knee (SUV _{max} , 3.3) Inflammation of posterior left tibiotalar joint Inflammation of muscle and subcutaneous fat within anterior planar aspects of feet and medial plantar aspects of toes Enthesitis of distal right quadriceps tendon (SUV _{max} , 1.7) Sclerosing mesenteritis noted in left mesentery.
3/M/56 ^a	Hyperlipidemia HDL-C: 52 LDL-C: 90 BMI: 29.1 hsCRP: 0.1 Medications: statin, aspirin, fish oil	Duration: 8 y BSA: 19 PGA: 3.3 PASI: 17	Topical steroids	Topical steroids	No	AsA, 1.51 (0.06) Arch, 1.40 (0.06) TA, 1.72 (0.10) SRAA, 1.40 (0.07) IRAA, 1.29 (0.15)	1.64 (0.23)	Inflammation lateral to left trochanter (SUV _{max} , 2.2) trochanteric bursitis or enthesitis Enthesitis of right quadriceps tendon (SUV _{max} , 1.7) Synovitis of knee joints bilaterally (right SUV _{max} , 3.0; left SUV _{max} , 2.2) Enthesitis of Achilles tendons (right SUV _{max} , 2.9; left SUV _{max} , 1.8) Inflammation of sinus tarsi bilaterally (right SUV _{max} , 1.5; left SUV _{max} , 2.2) Inflammation of right talonavicular joint (SUV _{max} , 2.0)
4/M/53	Hyperlipidemia, hypertension HDL-C: 36 LDL-C: 69 BMI: 35.7 hsCRP: 2.0 Medications: statin, diuretic, aspirin, fish oil	Duration: 25 y BSA: 15 PGA: 2.8 PASI: 10.1	Topical steroids	Topical steroids NB UV-B	No	AsA, 1.72 (0.04) Arch, 1.62 (0.10) TA, 1.45 (0.16) SRAA, 1.47 (0.05) IRAA, 1.50 (0.14)	1.56 (0.50)	None
5/F/58 ^a	No CV history HDL-C: 87 LDL-C: 104 BMI: 18.3 hsCRP: NA Medications: none	Duration: 2 y BSA: 11 PGA: 2 PASI: 9.6	Topical steroids	Topical steroids	No	AsA, 1.52 (0.04) Arch, 1.33 (0.08) TA, 1.41 (0.06) SRAA, 1.34 (0.05) IRAA, 1.47 (0.13)	1.80 (0.14)	None
6/M/44 ^a	No CV history HDL-C: 38 LDL-C: 165 BMI: 24.3 hsCRP: 8.4 Medications: none	Duration: 3 y BSA: 10.2 PGA: 2.3 PASI: 6.5	Topical steroids	Topical steroids	No	AsA, 1.40 (0.00) Arch, 1.42 (0.42) TA, 1.46 (0.08) SRAA, 1.36 (0.11) IRAA, 1.19 (0.18)	1.84 (0.26)	Focal inflammation of left posterior arm musculature (SUV _{max} , 2.1) Asymmetric inflammation in right knee joint (SUV _{max} , 2.2)

Abbreviations: Arch, aortic arch; AsA, ascending aorta; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BSA, body surface area; CV, cardiovascular; FDG-PET/CT, [18F]-fluorodeoxyglucose positron emission tomography-computed tomography; HDL-C, high-density lipoprotein cholesterol, in milligrams per deciliter; hsCRP, high-sensitivity C-reactive protein level; IRAA, infrarenal abdominal aorta; LDL-C, low-density lipoprotein cholesterol, in milligrams per deciliter; NA, not available; NB-UV-B, narrowband UV-B therapy; PASI, Psoriasis Area Severity Index; PGA, physician's global assessment; PUVA, psoralen and UV-A light therapy; SRAA, suprarenal abdominal aorta; SUV_{max}, maximum standardized uptake value; TA, descending thoracic aorta.

^aPatient is included in the nested case-control study.

PSORIASIS AND DETECTION OF INCREASED FDG UPTAKE IN THE BODY BY FDG-PET/CT



Figure 1. [18F]-Fluorodeoxyglucose positron emission tomography-computed tomographic (FDG-PET/CT) imaging of skin correlates with observed skin inflammation. A, Photograph of a patient with psoriasis showing extensive multifocal plaques. B, Corresponding PET image from a FDG-PET/CT study in the same patient demonstrates skin inflammation in similar distribution (arrows).

was aortic mean SUV, defined as the average of all mean SUVs recorded from sequential 2D ROIs in the aorta. The mean aortic SUV was calculated for 5 segments of the aorta: ascending aorta, aortic arch, descending thoracic aorta, suprarenal abdominal aorta, and infrarenal abdominal aorta. These segments were defined to consider separately various regions of aortic disease that are associated with different clinical phenotypes (eg, aortic arch disease with stroke, abdominal aortic disease with abdominal aortic aneurysm). As a secondary analysis, we also examined hepatic SUV in psoriasis and controls. Unadjusted analyses were performed using 2-sided *t* tests and Mann-Whitney tests for continuous data and Fisher exact tests for dichotomous data. Linear regression was performed to adjust for known CV risk factors (age, sex, hypertension, low-density lipoprotein cholesterol [LDL-C] level, and BMI), with mean SUV as the outcome. Hypertension in our models was adjusted as a dichotomous variable; all other variables were continuous. To study the effect of psoriasis on hepatic inflammation, we adjusted for CV risk factors, including BMI, and further adjusted analysis for alcohol use in the multivariate regression model. Finally, to accommodate within-patient correlation of SUV, we performed random effects regression models. Given that we did not observe any difference in estimates for psoriasis, we present the β -coefficient from the linear regression models. All analyses were performed with Stata 11 statistical software (StataCorp, College Station, Texas). The study was approved by the institutional review board at the University of Pennsylvania, Philadelphia, and complies with the Declaration of Helsinki. Written informed consent was obtained from all study participants.

The characteristics and measurements of FDG uptake in the vasculature, liver, and musculoskeletal structures of all 6 patients with psoriasis in the case series are shown in **Table 1**. Patients with psoriasis had the disease for a median of 14 years (interquartile range [IQR], 3-24) and had a median BSA of 14% (IQR, 11%-19%), median physician's global assessment of 2.5 (IQR, 2.0-2.7) and median Psoriasis Area Severity Index of 9.9 (IQR, 7.2-12.1) (Table 1). Current psoriasis therapies (within 3 months) included topical steroids (in 4 patients), combination treatment with methotrexate and abatacept (in 1 patient), and narrowband phototherapy (in 1 patient). Thus, 5 patients were not receiving systemic treatment or phototherapy at the time of the study. One patient (ie, the individual treated with methotrexate-abatacept) had a diagnosis of psoriatic arthritis established by rheumatologic testing that was clinically symptomatic, and another patient had a history of anterior cruciate ligament repair 12 months prior to the study and was asymptomatic. The remaining patients had no history of joint disease or joint symptoms. The CV risk factors are noted in Table 1, with 3 patients having diagnosed hyperlipidemia while prescribed statins and 1 having hypertension while prescribed a single agent.

Whole-body FDG-PET/CT imaging revealed areas of systemic inflammation, including vascular, articular, periarticular, visceral, and skin territories, in patients with psoriasis. Focal areas of inflammation in the skin observed clinically as areas of plaque psoriasis corresponded to areas of skin inflammation observed on FDG-PET/CT (**Figure 1**). In addition, among the 5 patients without diagnosis or symptoms of psoriatic arthritis, vascular inflammation in all 5 aortic segments was increased compared with age-adjusted normal values (1.0-1.2 SUVs corrected for the scanner used).^{32,33} FDG-PET/CT imaging of the liver also demonstrated increased metabolic activity, likely indicative of increased hepatic inflammation. In addition, both clinical and subclinical joint inflammation were detected in the sample (Table 1). Of note, 1 patient without psoriatic arthritis, joint symptoms, or previous joint surgery demonstrated focal areas of FDG uptake on FDG-PET/CT in various tendons, entheses, and joint spaces, particularly in the knees (with maximum SUVs of 3.0 on the right and 2.2 on the left), consistent with inflammatory arthritis.³⁷ Similar findings of tendon, entheses, and joint inflammation were demonstrated on FDG-PET/CT for the patient with clinical psoriatic arthritis (Table 1).

A NESTED CASE-CONTROL STUDY SHOWING DIFFERENCES IN VASCULAR AND HEPATIC INFLAMMATION DETECTED BY FDG-PET/CT

We next matched controls to 4 patients from our psoriasis sample by age and sex. Patients in the substudy were restricted to those with a BMI lower than 30. The characteristics of this nested case-control study are shown in

Table 2. Demographic and Laboratory Results for Patients With Psoriasis and Controls^a

Variable	4 Patients With Psoriasis Median (IQR)	4 Controls, Median (IQR)	P Value	Normal Values
Age	50 (43-57)	49 (43-52)	.66	NA
Male, No. (%)	3 (75)	3 (75)	> .99	NA
BSA, %	12 (10.6-16)	NA	NA	NA
PGA	2.2 (2.0-2.8)	NA	NA	NA
PASI	8.4 (6.9-13.3)	NA	NA	NA
Diagnosed as having psoriatic arthritis, No. (%)	0	NA	NA	NA
Tobacco user, No. (%)	0	0	> .99	NA
BMI	26.9 (21.5-29.5)	29.7 (28.5-29.9)	.22	18.5-24.9
Fasting blood glucose, mg/dL	94 (89-107)	86 (72-96)	.23	70-99
Systolic BP, mm Hg	133 (123-142)	124 (118-134)	.48	90-140
Diastolic BP, mm Hg	81 (72-84)	73 (69-80)	.56	60-90
Diagnosed as having hypertension, No. (%)	1 (25)	1 (25)	> .99	NA
Antihypertensive therapy, No. (%)	0	1 (25)	> .99	NA
Cholesterol levels, mg/dL				
Total cholesterol	214 (182-225)	188 (186-206) ^b	.66	≤200
Triglycerides	120 (84-194)	262 (165-290) ^b	.15	≤150
HDL-C	45 (37-70)	50 (18-66) ^b	.66	≥40
LDL-C	105 (97-136)	118 (62-123) ^b	.58	≤100
Statin therapy, No. (%)	1 (25)	0	> .99	NA
hsCRP, mg/L	2.9 (0.1-8.4) ^b	1.5 (0.4-2.0)	.37	≤3.0
ALT, U/L	38 (18-68)	31 (22-51)	.73	17-63
AST, U/L	28 (19-43)	41 (23-62)	.50	15-41
Alkaline phosphatase, U/L	71 (56-92)	71 (57-95)	.91	32-91
Total bilirubin, mg/dL	0.8 (0.8-1.0)	0.8 (0.6-1.0)	.52	0.3-1.2
Alcohol consumption, No. (%)				
Nondrinker	2 (50)	3 (75)	> .99	NA
Social drinker, <7 drinks/wk	2 (50)	1 (25)	NA	NA

Abbreviations: ALT, alanine aminotransferase; AST, alkaline aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BSA, body surface area; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein level; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; NA, not available; PASI, Psoriasis Area Severity Index; PGA, physician's global assessment.

SI conversion factors: To convert ALT, AST, and alkaline phosphatase to microkatal per liter, multiply by 0.0167. To convert bilirubin to micromoles per liter, multiply by 17.104. To convert blood glucose to millimoles per liter, multiply by 0.0555. To convert total cholesterol, HDL-C, and LDL-C to millimoles per liter, multiply by 0.0259. To convert hsCRP to nanomoles per liter, multiply by 9.524. To convert triglycerides to millimoles per liter, multiply by 0.0113.

^aDiabetes mellitus, a traditional cardiovascular risk factor, is excluded from this table because it was an exclusion criterion in this study.

^bThree patients.

Table 2. The 4 patients with psoriasis (3 were male [75%]; mean age, 50 years [range, 43-57 years]) had similar, low-risk CV profiles compared with the 4 controls (3 were male [75%], mean age, 49 years [range, 43-52 years]) (Table 2). Both patients with psoriasis and controls also had a median BMI in the overweight category (26.9 [range, 21.5-29.5] vs 29.7 [28.5-29.9], respectively). We show an image from the PET component of a FDG-PET/CT study in a patient with psoriasis and an image from a control patient as an example of how the difference in inflammation detected between these 2 patients is visualized using FDG-PET/CT (**Figure 2**).

From these patients, we analyzed a total of 386 slices of the aorta in patients with psoriasis and compared them with 317 slices of the aorta in controls. We also performed quantitative analysis of the liver using 161 slices for patients with psoriasis and compared them with 154 slices for controls. FDG-PET/CT imaging detected greater inflammation in the aorta in patients with psoriasis compared with controls ($P < .001$). After stratifying analysis to specific segments of the aorta, we report that the SUVs within each aortic segment were notably higher in patients with psoriasis compared with controls (**Table 3**). In multivariable regression, psoriasis remained highly associated with SUV in

each aortic segment after adjusting for traditional CV factors and BMI compared with controls, and we show the β coefficient for psoriasis in the multivariate model (**Table 4**). Finally, compared with controls, patients with psoriasis demonstrated increased hepatic inflammation in multivariate analysis adjusting for known confounders and risk factors for liver disease, including age, sex, plasma triglycerides level, and BMI ($\beta = 0.18$; $P < .001$). However, when the model was further adjusted for alcohol use ($\beta = 0.76$; $P < .001$), the relationship between hepatic inflammation and psoriasis was no longer significant ($\beta = -0.25$; $P = .07$).

COMMENT

To our knowledge, this is the first description of in vivo whole-body inflammation in psoriasis detected by FDG-PET/CT simultaneously in 3 tissues: viscera, vasculature, and musculoskeletal structures. We demonstrate that FDG-PET/CT, a technique validated to assess vascular inflammation, can be used in patients with psoriasis to visualize and quantify anatomic regions of inflammation.^{33,42-44,46,47} In our case series, FDG-PET/CT detected numerous areas of inflammation in patients with psoriasis, including in-



Figure 2. [18F]-Fluorodeoxyglucose positron emission tomography-computed tomographic (FDG-PET/CT) imaging. A, Multifocal inflammation on PET image from an FDG-PET/CT study in a patient with psoriasis. B, FDG-PET image from a control patient is shown for comparison. In the control patient, FDG uptake is noted within the myocardium (top arrow) within the range of normal variation and also seen in the kidneys and bladder (bottom arrow), where FDG is excreted. *FDG uptake in the right knee joint (standardized uptake value [SUV], 3.0) and distal right quadriceps tendon, left trochanteric bursa, and left ankle in asymptomatic patient with psoriasis. †Moderately diffusely increased FDG uptake throughout the liver (SUV, 1.64) consistent with increased hepatic inflammation. ‡Diffuse FDG uptake in the aortic wall (SUV, 1.29-1.72) and in the femoral arterial tree, consistent with vascular inflammation. §Focal areas of FDG uptake in skin consistent with inflammation in thick plaques in lower extremities.

creased inflammation in the blood vessels, in the liver, in articular and periarticular structures, and in the skin. Interestingly, all of these findings occurred in patients with psoriasis who otherwise felt well (only 1 patient who had an established diagnosis of psoriatic arthritis had joint symptoms) and had no clinically significant abnormalities in their laboratory data, except for 1 patient (patient 6) who had an elevated hsCRP level of 8.4 mg/L. (To convert hsCRP to nanomoles per liter, multiply by 9.524.) These foci of inflammatory activity were observed with levels of inflammation far exceeding the reference range for joint, liver, and vascular inflammation despite a lack of evidence of clinical disease.⁴⁵

In our nested case-control study, FDG-PET/CT imaging revealed vascular inflammation more severe than in age-

Table 3. Association of Psoriasis With Vascular Inflammation in the Aorta

Region	Vascular Inflammation, SUV, Mean (SD) ^a		P Value ^b
	Patients With Psoriasis	Controls	
Ascending aorta	1.56 (0.16)	1.49 (0.08)	.02
Aortic arch	1.45 (0.15)	1.38 (0.14)	.09
Descending thoracic aorta	1.54 (0.16)	1.43 (0.14)	<.001
Suprarenal abdominal aorta	1.46 (0.20)	1.37 (0.09)	.002
Infrarenal abdominal aorta	1.40 (0.22)	1.29 (0.15)	<.001

Abbreviation: SUV, standardized uptake value.

^aVascular inflammation for each region was calculated by the weighted average of mean SUV per slice in the specified aortic segment. Mean SUV indicates the average degree of [18F]-fluorodeoxyglucose uptake per slice and measures the degree of inflammatory activity.

^bP values are reported for a 2-sided *t* test.

and sex-matched controls. The corresponding magnitude of SUV difference observed between patients with psoriasis and controls (0.20) in multiple segments of the aorta is equivalent to the magnitude of vascular inflammation observed over 2 additional decades of aging.³³ Furthermore, FDG-PET/CT imaging of patients with psoriasis demonstrated high-risk findings,^{48,49} including diffusely increased vascular inflammation in each segment of the aorta that remained significant after adjusting for traditional CV risk factors and BMI. We also observed that psoriasis was associated with increased hepatic inflammation in multivariate analysis adjusting for confounders and risk factors for liver disease, including plasma triglycerides level and BMI. This relationship, however, was no longer significant when adjusted for alcohol intake, suggesting that either patients underreported their alcohol use, because inclusion in the study permitted only light drinking (<2 drinks per day), or that patients with psoriasis may be more susceptible to liver dysfunction in the face of alcohol use. Despite this observation, this degree of hepatic inflammation is similar to that seen in patients with hepatic steatosis or chronic active hepatitis.⁴³ This finding warrants careful follow-up and further study and may present a compelling opportunity to explore the concept of the “psoriatic liver.” Finally, our observations of musculoskeletal inflammation are consistent with those of previous studies using conventional imaging techniques to demonstrate findings consistent with psoriatic arthritis, such as articular inflammation and enthesitis in patients with psoriasis.⁵⁰⁻⁵² In particular, the diffuse distribution of subclinical articular and periarticular involvement observed on imaging suggests that FDG-PET/CT may be a more feasible approach for detecting *subclinical* psoriatic arthritis than traditional imaging modalities such as ultrasonography or magnetic resonance imaging.

The findings of excess vascular, hepatic, musculoskeletal, and cutaneous inflammation on FDG-PET/CT are novel and suggest the potential of FDG-PET/CT technology to investigate systemic inflammation. The underlying inflammation linking chronic inflammatory disease states, such as atherosclerosis, metabolic syndrome, dia-

Table 4. Association of Psoriasis and Vascular and Hepatic Inflammation After Adjusting for Confounding Variables

Anatomic Region	Model, β -Coefficient for Psoriasis on Mean SUV ^a			
	Adjusted for Age, Sex, and BMI	Adjusted for Age, Sex, BMI, Hypertension, and LDL-C	Adjusted for Age, Sex, BMI, Triglycerides Level	Adjusted for Age, Sex, BMI, Triglycerides Level, and Alcohol
Ascending aorta	0.17	0.37		
Aortic arch	0.16 ^b	0.28		
Descending thoracic aorta	0.21	0.27		
Suprarenal abdominal aorta	0.25	0.40		
Infrarenal abdominal aorta	0.20 ^c	0.32		
Liver			0.28	-0.25 ^d

Abbreviations: BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; SUV, standardized uptake value.

^aBecause no patients in this study had diabetes mellitus or tobacco use, diabetes mellitus status and tobacco use were not included in the fully adjusted model.

$P < .001$ for all comparisons except where noted.

^b $P = .002$.

^c $P = .001$.

^d $P = .07$.

betes mellitus, and psoriatic arthritis, with psoriasis is captured in vivo by FDG-PET/CT, thereby providing a measurable phenotype (ie, biomarker) in a dynamic disease such as psoriasis. In this study, we demonstrate this novel application of FDG-PET/CT, which has exquisite sensitivity for detecting picomolar to nanomolar concentrations of glucose uptake with inflammatory cells. We further report a systematic approach to image analysis that can be used in future studies to regionally and globally quantify inflammation in the aorta, liver, and joints.

We note, however, that the findings we report are based on a pilot study that has important limitations, and thus additional studies are necessary to confirm and extend our findings. First, the small sample size and referral-based source of our patients may affect the generalizability of our results. However, our study is comparable in size and design with other landmark studies using FDG-PET/CT in inflammatory disease states.^{27,33,54} We also note that use of FDG-PET/CT is limited by the need for sophisticated hardware and software that may not be widely available, the need for patients to be willing to fast for 8 hours, and radiation exposure similar to that of a standard contrast-enhanced CT scan. As a result, patients may need to be highly motivated to enter studies using FDG-PET/CT, which may lead to particular challenges in recruiting healthy controls. In addition, in this pilot study patients were not required to undergo washout of topical or UV light treatments, and systemic treatments were permissible as long as the dose had been stable for 3 months. Thus, additional studies in patients with psoriasis who are treatment naïve or have washouts of psoriasis therapies will be necessary to further interpret our findings. Furthermore, the nested case-control study is subject to error introduced by selection bias and confounding. For example, it is possible that one group could have been more health conscious than the other (ie, through selection bias), although the laboratory and anthropometric data do not support this possibility as a potential source of error. We carefully adjusted for confounding variables for which we had detailed data; however, incomplete measurement of confounders, such as diet and exercise, could affect our measurement of as-

sociation. In addition, while our study attempted to adjust for LDL-C and hypertension, it is possible that incomplete adjustment for these confounders still exist, and we did not have LDL-C data for 1 of the controls. Finally, 3 patients with psoriasis in the case series and 1 patient with psoriasis in the nested case-control study were receiving active statin therapy. While statins may interfere with vascular inflammation, we would expect that they attenuate vascular inflammation, as demonstrated in a previously published clinical trial using FDG-PET/CT,⁴⁰ and therefore would bias our results toward the null. In addition, we note that none of the study participants had existing CV disease, and most CV risk prediction tools, such as the Framingham Risk Score, use current blood pressure and LDL-C measurements to assess CV risk without regard to medication usage because biometric data are more significantly correlated with CV outcomes.⁴⁹

In this study, we demonstrate that FDG-PET/CT represents a powerful molecular imaging modality to assess whole-body inflammation in association with psoriasis. Further studies are needed to (1) confirm and extend our results of increased vascular and hepatic inflammation in a larger series of patients, carefully selecting cases and controls and measuring confounding variables to determine if increased inflammation measured by FDG-PET/CT is due to psoriasis, its treatments, or other associated factors; (2) understand how to relate these findings to clinical prognosis; and (3) assess the effect of psoriasis treatment on the inflammation observed in various tissues.

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tion of data: Mehta, Yu, Saboury, Foroughi, Krishnamoorthy, Raper, Baer, Antigua, Van Voorhees, Torigian, Alavi, and Gelfand. *Analysis and interpretation of data:* Mehta, Yu, Saboury, Krishnamoorthy, Torigian, Alavi, and Gelfand. *Drafting of the manuscript:* Mehta, Yu, Foroughi, Krishnamoorthy, and Torigian. *Critical revision of the manuscript for important intellectual content:* Mehta, Yu, Saboury, Raper, Baer, Van Voorhees, Torigian, Alavi, and Gelfand. *Statistical analysis:* Mehta, Yu, Saboury, Foroughi, Krishnamoorthy, Torigian, and Gelfand. *Obtained funding:* Mehta, Yu, Torigian, Alavi, and Gelfand. *Administrative, technical, and material support:* Mehta, Yu, Krishnamoorthy, Raper, Baer, Antigua, Torigian, Alavi, and Gelfand. *Study supervision:* Mehta, Saboury, Baer, Torigian, Alavi, and Gelfand.

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REFERENCES

- Gelfand JM, Weinstein R, Porter SB, Neimann AL, Berlin JA, Margolis DJ. Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. *Arch Dermatol.* 2005;141(12):1537-1541.
- Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. *J Am Acad Dermatol.* 2009;60(2):218-224.
- Gelfand JM, Gladman DD, Mease PJ, et al. Epidemiology of psoriatic arthritis in the population of the United States. *J Am Acad Dermatol.* 2005;53(4):573.
- Qureshi AA, Choi HK, Setty AR, Curhan GC. Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses. *Arch Dermatol.* 2009;145(4):379-382.
- Brauchli YB, Jick SS, Meier CR. Psoriasis and the risk of incident diabetes mellitus: a population-based study. *Br J Dermatol.* 2008;159(6):1331-1337.
- El-Mongy S, Fathy H, Abdelaziz A, et al. Subclinical atherosclerosis in patients with chronic psoriasis: a potential association. *J Eur Acad Dermatol Venereol.* 2010;24(6):661-666.
- Brauchli YB, Jick SS, Miret M, Meier CR. Psoriasis and risk of incident myocardial infarction, stroke or transient ischaemic attack: an inception cohort study with a nested case-control analysis. *Br J Dermatol.* 2009;160(5):1048-1056.
- Balci DD, Balci A, Karazincir S, et al. Increased carotid artery intima-media thickness and impaired endothelial function in psoriasis. *J Eur Acad Dermatol Venereol.* 2009;23(1):1-6.
- Davidovici BB, Sattar N, Prinz JC, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. *J Invest Dermatol.* 2010;130(7):1785-1796.
- Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. *JAMA.* 2006;296(14):1735-1741.
- Mehta NN, Azfar RS, Shin DB, Neimann AL, Troxel AB, Gelfand JM. Patients with severe psoriasis are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database. *Eur Heart J.* 2010;31(8):1000-1006.
- Prodanovich S, Kirsner RS, Kravetz JD, Ma F, Martinez L, Federman DG. Association of psoriasis with coronary artery, cerebrovascular, and peripheral vascular diseases and mortality. *Arch Dermatol.* 2009;145(6):700-703.
- Gelfand JM, Dommasch ED, Shin DB, et al. The risk of stroke in patients with psoriasis. *J Invest Dermatol.* 2009;129(10):2411-2418.
- Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol.* 2006;55(5):829-835.
- Ludwig RJ, Herzog C, Rostock A, et al. Psoriasis: a possible risk factor for development of coronary artery calcification. *Br J Dermatol.* 2007;156(2):271-276.
- Azfar RS, Gelfand JM. Psoriasis and metabolic disease: epidemiology and pathophysiology. *Curr Opin Rheumatol.* 2008;20(4):416-422.
- Gisoni P, Girolomoni G. Psoriasis and atherothrombotic diseases: disease-specific and non-disease-specific risk factors. *Semin Thromb Hemost.* 2009;35(3):313-324.
- Cohen AD, Sherf M, Vidavsky L, Vardy DA, Shapiro J, Meyerovitch J. Association between psoriasis and the metabolic syndrome. A cross-sectional study. *Dermatol.* 2008;216(2):152-155.
- Libby P. Inflammation in atherosclerosis. *Nature.* 2002;420(6917):868-874.
- Nishibu A, Han GW, Iwatsuki K, et al. Overexpression of monocyte-derived cytokines in active psoriasis: a relation to coexistent arthropathy. *J Dermatol Sci.* 1999;21(1):63-70.
- Alexandroff AB, Pauriah M, Camp RD, Lang CC, Struthers AD, Armstrong DJ. More than skin deep: atherosclerosis as a systemic manifestation of psoriasis. *Br J Dermatol.* 2009;161(1):1-7.
- Zaba LC, Fuentes-Duculan J, Eungdamrong NJ, et al. Psoriasis is characterized by accumulation of immunostimulatory and Th1/Th17 cell-polarizing myeloid dendritic cells. *J Invest Dermatol.* 2009;129(1):79-88.
- Kagami S, Rizzo HL, Lee JJ, Koguchi Y, Blauvelt A. Circulating Th17, Th22, and Th1 cells are increased in psoriasis. *J Invest Dermatol.* 2010;130(5):1373-1383.
- Ridker PM. Psoriasis, inflammation, and vascular risk: a problem more than skin deep? *Eur Heart J.* 2010;31(8):902-904.
- Basu S, Zaidi H, Houseni M, et al. Novel quantitative techniques for assessing regional and global function and structure based on modern imaging modalities: implications for normal variation, aging and diseased states. *Semin Nucl Med.* 2007;37(3):223-239.
- Yun M, Yeh D, Araujo LI, Jang S, Newberg A, Alavi A. F-18 FDG uptake in the large arteries: a new observation. *Clin Nucl Med.* 2001;26(4):314-319.
- Rudd JHF, Warburton EA, Fryer TD, et al. Imaging atherosclerotic plaque inflammation with [18F]-fluorodeoxyglucose positron emission tomography. *Circulation.* 2002;105(23):2708-2711.
- Tawakol A, Migrino RQ, Bashian GG, et al. In vivo 18F-fluorodeoxyglucose positron emission tomography imaging provides a noninvasive measure of carotid plaque inflammation in patients. *J Am Coll Cardiol.* 2006;48(9):1818-1824.
- Wassélius JA, Larsson SA, Jacobsson H. FDG-accumulating atherosclerotic plaques identified with ¹⁸F-FDG-PET/CT in 141 patients. *Mol Imaging Biol.* 2009;11(6):455-459.
- Ogawa M, Ishino S, Mukai T, et al. (18)F-FDG accumulation in atherosclerotic plaques: immunohistochemical and PET imaging study. *J Nucl Med.* 2004;45(7):1245-1250.
- Worthley SG, Zhang ZY, Machac J, et al. In vivo non-invasive serial monitoring of FDG-PET progression and regression in a rabbit model of atherosclerosis. *Int J Cardiovasc Imaging.* 2009;25(3):251-257.
- Bural GG, Torigian DA, Botvinick E, et al. A pilot study of changes in (18)F-FDG uptake, calcification and global metabolic activity of the aorta with aging. *Hell J Nucl Med.* 2009;12(2):123-128.
- Bural GG, Torigian DA, Chamroonrat W, et al. FDG-PET is an effective imaging modality to detect and quantify age-related atherosclerosis in large arteries. *Eur J Nucl Med Mol Imaging.* 2008;35(3):562-569.
- Aziz K, Berger K, Claycombe K, Huang R, Patel R, Abela GS. Noninvasive detection and localization of vulnerable plaque and arterial thrombosis with computed tomography angiography/positron emission tomography. *Circulation.* 2008;117(16):2061-2070.

35. Tateishi U, Imagawa T, Kanezawa N, et al. PET assessment of disease activity in children with juvenile idiopathic arthritis. *Pediatr Radiol*. 2010;40(11):1781-1788.
36. Taniguchi Y, Arai K, Kumon Y, et al. Positron emission tomography/computed tomography: a clinical tool for evaluation of enthesitis in patients with spondyloarthritis. *Rheumatology (Oxford)*. 2010;49(2):348-354.
37. Kubota K, Ito K, Morooka M, et al. Whole-body FDG-PET/CT on rheumatoid arthritis of large joints. *Ann Nucl Med*. 2009;23(9):783-791.
38. Paulmier B, Duet M, Khayat R, et al. Arterial wall uptake of fluorodeoxyglucose on PET imaging in stable cancer disease patients indicates higher risk for cardiovascular events. *J Nucl Cardiol*. 2008;15(2):209-217.
39. Rominger A, Saam T, Wolpers S, et al. 18F-FDG PET/CT identifies patients at risk for future vascular events in an otherwise asymptomatic cohort with neoplastic disease. *J Nucl Med*. 2009;50(10):1611-1620.
40. Tahara N, Kai H, Ishibashi M, et al. Simvastatin attenuates plaque inflammation: evaluation by fluorodeoxyglucose positron emission tomography. *J Am Coll Cardiol*. 2006;48(9):1825-1831.
41. Lee SJ, On YK, Lee EJ, Choi JY, Kim BT, Lee KH. Reversal of vascular 18F-FDG uptake with plasma high-density lipoprotein elevation by atherogenic risk reduction. *J Nucl Med*. 2008;49(8):1277-1282.
42. Bural GG, Torigian DA, Chamroonrat W, et al. Quantitative assessment of the atherosclerotic burden of the aorta by combined FDG-PET and CT image analysis: a new concept. *Nucl Med Biol*. 2006;33(8):1037-1043.
43. Bural GG, Torigian DA, Burke A, et al. Quantitative assessment of the hepatic metabolic volume product in patients with diffuse hepatic steatosis and normal controls through use of FDG-PET and MR imaging: a novel concept. *Mol Imaging Biol*. 2010;12(3):233-239.
44. Basu S, Zhuang H, Torigian DA, Rosenbaum J, Chen W, Alavi A. Functional imaging of inflammatory diseases using nuclear medicine techniques. *Semin Nucl Med*. 2009;39(2):124-145.
45. Beckers C, Ribbens C, André B, et al. Assessment of disease activity in rheumatoid arthritis with (18)F-FDG PET. *J Nucl Med*. 2004;45(6):956-964.
46. Rudd JHF, Narula J, Strauss HW, et al. Imaging atherosclerotic plaque inflammation by fluorodeoxyglucose with positron emission tomography: ready for prime time? *J Am Coll Cardiol*. 2010;55(23):2527-2535.
47. Wehrli NE, Bural G, Houseni M, Alkhalaf K, Alavi A, Torigian DA. Determination of age-related changes in structure and function of skin, adipose tissue, and skeletal muscle with computed tomography, magnetic resonance imaging, and positron emission tomography. *Semin Nucl Med*. 2007;37(3):195-205.
48. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*. 2001;285(19):2486-2497.
49. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97(18):1837-1847.
50. Gutierrez M, Filippucci E, De Angelis R, et al. Subclinical enthesal involvement in patients with psoriasis: an ultrasound study. *Semin Arthritis Rheum*. 2011;40(5):407-412.
51. Coates LC, McGonagle DM, Hodgson R, et al. Imaging in psoriasis and psoriatic arthritis: GRAPPA 2008. *J Rheumatol*. 2010;37(2):448-452.
52. Offidani A, Cellini A, Valeri G, Giovagnoni A. Subclinical joint involvement in psoriasis: magnetic resonance imaging and X-ray findings. *Acta Derm Venereol*. 1998;78(6):463-465.
53. Kobayashi Y, Ishii K, Oda K, et al. Aortic wall inflammation due to Takayasu arteritis imaged with 18F-FDG PET coregistered with enhanced CT. *J Nucl Med*. 2005;46(6):917-922.
54. Andrews J, Al-Nahhas A, Pennell DJ, et al. Non-invasive imaging in the diagnosis and management of Takayasu's arteritis. *Ann Rheum Dis*. 2004;63(8):995-1000.

Call for Papers

Comparative Effectiveness Research

Comparative effectiveness research expands the scope of clinical research to compare different therapies against one another as a means to improve delivery of value-based health care. Typically, outcomes analysis of quality of life, disability, and death are used to compare the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor dermatologic conditions.¹ Traditional efficacy research, used for approval of pharmaceuticals or devices, compares 1 or more treatment alternatives with placebo in a carefully selected population cared for in an ideal setting, thus answering the question of whether the intervention is effective and safe for human use.

In contrast, comparative effectiveness research seeks to answer a different set of questions including: (1) when to use the treatment (appropriate time), and (2) who should receive the intervention (proper patient selection). This research also considers patients from populations that are under less than ideal conditions. Thus, comparative effectiveness research seeks to replace the physician's informed intuition of case management with data-driven, scientifically derived, "best-treatment" protocols. We at the *Archives* are interested in comparative effectiveness research using observational and clinical trial methods comparing different strategies provided by dermatologists in heterogeneous patient populations and heterogeneous health care settings.

The *Archives of Dermatology*, along with *JAMA* and other *Archives Journals*, will publish a theme issue devoted to comparative effectiveness research in early 2012. Priority will be given to studies using rigorous methodological designs that are generalizable beyond a single institution. Authors should consult the Instructions for Authors at <http://www.archdermatol.com> for guidelines on manuscript preparation and submission. Manuscripts must be received before October 1, 2011, to allow for appropriate consideration.

June K. Robinson, MD
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1. Institute of Medicine of the National Academies Web site. Initial National Priorities for Comparative Effectiveness Research. June 30, 2009. <http://www.iom.edu/Reports/2009/ComparativeEffectivenessResearchPriorities.aspx>. Accessed January 24, 2011.