Positron Emission Tomography / Computerized Tomography in Newly Diagnosed Patients with Giant Cell Arteritis Who Are Taking Glucocorticoids

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ABSTRACT. ***Objective.*** Large vessel uptake on positron emission tomography/computerized tomography (PET/CT) supports the diagnosis of giant cell arteritis (GCA). Its value, however, in patients without arteritis on temporal artery biopsy and in those receiving glucocorticoids remains unknown. We compared PET/CT results in GCA patients with positive (TAB+) and negative temporal artery biopsies (TAB–), and controls.

Methods. Patients with new clinically diagnosed GCA starting treatment with glucocorticoids underwent temporal artery biopsy and PET/CT. Using a visual semiquantitative approach, 18F-fluorodeoxyglucose (FDG) uptake was scored in 8 vascular territories and summed overall to give a total score in patients and matched controls.

Results. Twenty-eight patients with GCA and 28 controls were enrolled. Eighteen patients with GCA were TAB+. Mean PET/CT scores after an average of 11.9 days of prednisone were higher in patients with GCA compared to controls, for both total uptake (10.34 ± 2.72 vs 7.73 ± 2.56; p = 0.001), and in 6 of 8 specific vascular territories. PET/CT scores were similar between TAB+ and TAB– patients with GCA. The optimal cutoff for distinguishing GCA cases from controls was a total PET/CT score of ≥ 9, with an area under the receiver-operating characteristic curve of 0.75, sensitivity 71.4%, and specificity 64.3%. Among patients with GCA, these measures correlated with greater total PET/CT scores: systemic symptoms (p = 0.015), lower hemoglobin (p = 0.009), and higher platelet count (p = 0.008).

Conclusion. Vascular FDG uptake scores were increased in most patients with GCA despite exposure to prednisone; however, the sensitivity and specificity of PET/CT in this setting were lower than those previously reported. (First Release September 15 2017; J Rheumatol 2017;44:1859–66; doi:10.3899/jrheum.170138)

Key Indexing Terms:
GIANT CELL ARTERITIS
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Giant cell arteritis (GCA) is the most common systemic vasculitis in patients over the age of 50 years, with an estimated incidence of 10/100,000[1]. It classically affects the temporal arteries[2], but involvement of the aorta and its major branches may be identified in up to 67.5% of patients at diagnosis using computerized tomography angiography (CTA)[3]. Autopsy data from patients with GCA also suggest that large-vessel involvement is present in most patients[4].

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Ultimately, GCA is a clinical diagnosis, supported by a positive temporal artery biopsy (TAB). Unfortunately, biopsy specimens may be falsely negative in between 15% and 42% of cases because of the patchy character of the disease[5,6,7,8], inadequate length of biopsy specimen, number of sections evaluated, or other sampling limitations. Missed diagnoses can lead to potentially catastrophic outcomes, such as permanent loss of vision, aortic dissection, and death[9], highlighting the ongoing need for additional diagnostic tests in GCA.

In cases of suspected GCA with negative TAB (TAB–), imaging studies may be used to support the diagnosis. While conventional angiography[6], CTA[3], and magnetic resonance angiography[10,11,12,13] may be used for diagnosis of large-vessel vasculitis, positron emission tomography combined with CT (PET/CT) offers the additional advantage of detecting active vessel wall inflammation. Studies of PET/CT in GCA have demonstrated large-vessel involvement in 50–80% of patients[10,14,15,16,17] with high sensitivity and specificity[10,14,15,18]. In addition, PET/CT may potentially identify patients at higher risk for future aortic complications[19,20]. Because of strong background 18F-fluorodeoxyglucose (FDG) uptake within the brain and the small diameter of the superficial temporal arteries, PET/CT cannot adequately distinguish inflammatory changes in these smaller vessels[14].

Although promising, several questions remain regarding the involvement of PET/CT in GCA. Specifically, the performance characteristics of PET/CT in patients receiving glucocorticoids may vary based on dose and duration of drug exposure[21,22,23,24], and its yield in TAB– patients is unclear[23,24]. In addition, there is no standardized approach to the diagnosis of large-vessel vasculitis with PET/CT and confounding with other diseases such as atherosclerosis may occur[25,26].

The primary objective of our study was to describe the distribution and intensity of large-vessel involvement on PET/CT scanning in a typical cohort of recent-onset clinically diagnosed (TAB+ and TAB–) and empirically treated patients with GCA and matched controls. The secondary objectives were to compare the imaging abnormalities of the TAB+ versus TAB– patients with GCA, and to examine the association of clinical variables (including patient demographics, GCA symptoms, glucocorticoid use, and laboratory variables) with imaging results.

MATERIALS AND METHODS

Patients. Patients being evaluated for a new diagnosis of GCA in the Division of Rheumatology at The Arthritis Centre at Queen Elizabeth II Health Sciences Centre and Dalhousie University, between June 2011 and October 2013 were considered for participation in our study. Consenting patients who met 1990 American College of Rheumatology (ACR) Classification Criteria for GCA[27] and who received a new clinical diagnosis of GCA (from their treating rheumatologist) were prospectively enrolled and treated empirically with high-dose prednisone (about 1 mg/kg/day, as per the treating physician's discretion). Patients were then classified as either biopsy-positive (TAB+) GCA or biopsy-negative (TAB–) GCA based on results of temporal artery specimens. Exclusion criteria included unwillingness to have a TAB or PET/CT scan, the use of > 10 mg/day of prednisone for > 1 month prior to the diagnosis, or an alternative diagnosis for the patient's presentation. Patients were also excluded if they had insulin-dependent diabetes, poorly controlled diabetes (defined as either glycosylated hemoglobin or fasting glucose > 8.0 mmol/l), or diabetes whose control was unknown, given the requirement to fast prior to imaging and the unknown effects of elevated blood glucose on FDG uptake. These variables were recorded using standardized forms: demographic (age, sex), clinical [weight, height, body mass index (BMI), blood pressure, clinical symptoms of vasculitis, duration of symptoms, and use of antiplatelet agents, statins, antihypertensives, and glucocorticoids], and laboratory [complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), creatinine]. Glucocorticoid use was recorded both as daily dose (mg) and total cumulative exposure prior to PET/CT acquisition and prior to TAB.

Controls. Control scans were obtained from a database of oncology patients who had previously undergone whole-body FDG PET/CT imaging for investigation of possible metastatic melanoma. PET/CT reports were reviewed first by nonradiology investigators, and those patients with evidence of malignancy were excluded to maintain blinding during scoring of the PET/CT scans. Control subjects with scans that did not identify metastases were then matched to GCA cases based on age and sex.

Biopsy procedure. All patients with a clinical diagnosis of GCA underwent a prompt TAB, performed by a vascular surgeon. Length of artery specimen was recorded. Histopathological evaluation was performed independently by 2 anatomical pathologists with a special interest in temporal arteritis, and disagreements were resolved by consensus. Specimens were classified as having features of either GCA (TAB+ group) or no arteritis on biopsy (TAB– group).

PET/CT acquisition and interpretation. All patients and controls underwent total body PET/CT scanning on a GE Discovery STE16 machine (GE Healthcare). Patients with GCA were scanned as soon as possible following their clinical diagnosis (mean 6.6 days after first visit), subject to scanner access. After 4 h of fasting, patients were injected with 10 mCi of FDG. Sixty minutes later, PET imaging was obtained from head to foot, in conjunction with a low-dose, nonenhanced CT, and interpreted using a visual, semiquantitative scoring system.

The distribution of FDG uptake was recorded in each of 8 major vascular territories: the ascending aorta, aortic arch, descending thoracic aorta, abdominal aorta, and carotid, subclavian/axillary, iliac, and femoral arteries. A semiquantitative score based on the visual assessment of the intensity of FDG uptake in each of these territories relative to the liver was determined (0 = no uptake; 1 = minimal uptake, less than liver; 2 = moderate uptake, equal to that of the liver; 3 = high uptake, greater than that of the liver), as has previously been described[10]. All images were assessed independently by 2 nuclear medicine radiologists who were blinded to patient identification, and discrepancies between scores were resolved by consensus. Maximum scores for each vascular territory, and a total PET/CT uptake score (the sum of all 8 vascular territories, maximum score 24) was determined for each patient and control. Of note, positive PET/CT uptake was not required for diagnosis of patients with GCA who were TAB–.

Statistics. Patients with GCA were assigned to groups based on the presence or absence of arteritis on biopsy. Descriptive statistics were used to describe the TAB+ and TAB– groups. PET/CT scores (per vascular territory and summed total) between all patients with GCA and controls, and between TAB+ and TAB– patients with GCA were compared using nonparametric Wilcoxon rank sum 2-sample test. A secondary analysis, comparing PET/CT scores among all 3 groups (TAB+, TAB–, and controls) was also performed using the nonparametric Kruskal-Wallis exact test, with pairwise comparisons of the patient groups done using nonparametric Wilcoxon rank sum 2-sample test where Kruskal-Wallis was significant at $p < 0.025$. Continuous variables were correlated with total PET/CT uptake scores using Spearman correlation, and categorical variables were analyzed with nonparametric

Wilcoxon exact tests. The influence of daily dose of prednisone (categorized as < 20 mg/day, 21–50 mg/day, or > 50 mg/day) and cumulative prednisone exposure prior to PET/CT (categorized as < 500 mg, 500–1000 mg, or > 1000 mg) on total PET/CT uptake was analyzed using rank order analysis variance. The effect of prednisone on total PET/CT uptake was also evaluated after adjusting for patients' body weight (daily dose per kg of body weight and cumulative exposure per kg of body weight). Receiver-operating characteristic (ROC) curves were plotted for total PET/CT uptake score. A flexible graphics tool generated with an SAS macro was used to visualize the effect of changing the cutpoints of the total PET uptake. The optimal cutpoint in terms of sensitivity and specificity was selected to generate a dichotomized variable to be used in predictive screening. All analyses were carried out using SAS STAT software, version 9.3 (SAS Institute).

Ethics. This study was approved by the Research Ethics Board of the Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada (REB registration number 1004664).

RESULTS

Patients. Forty-one patients were screened between June 2011 and October 2013 for study inclusion. Ten patients were ineligible and 3 withdrew prior to PET/CT imaging, leaving 28 patients with newly diagnosed GCA, all of whom fulfilled 1990 ACR classification criteria[27]. Patients were predominantly female (61%), with a mean ± SD age of 70.4 ± 8.9 years, and all were treated empirically with prednisone. On histopathologic review, 18 patients with GCA (64.3%) had TAB+ arteritis and 10 were TAB–. Complete baseline demographic and clinical details of patients can be found in Table 1. At baseline, TAB+ patients with GCA were noted to be several years older on average, with lower hemoglobin levels, and higher platelet counts and CRP values compared to TAB– patients with GCA.

PET/CT uptake scores (total and per territory). Whole-body PET/CT images were obtained in all 28 patients with GCA after a mean of 11.9 days of treatment with high-dose prednisone (mean cumulative prednisone exposure 645 mg prior to PET/CT) and compared to 28 age- and sex-matched controls. Overall, the mean total PET/CT vascular uptake score was significantly higher in patients with GCA (10.3 ± 2.7) than controls (7.7 ± 2.6; p = 0.001). Illustrative examples are provided in Figure 1. When scores for individual vascular territories were compared, mean FDG uptake in 6 of the 8 vascular territories was significantly higher in patients with

Table 1. Baseline characteristics of giant cell arteritis study patients.

Characteristics	TAB+, n = 18	TAB–, n = 10	Overall, n = 28	p
Age, yrs	73.2 ± 8.1	65.4 ± 8.4	70.4 ± 8.9	0.024
Female, n (%)	12 (67)	5 (50)	17 (61)	0.39
Mean BMI, SD, kg/m^2	29.4 ± 18.1	28.1 ± 6.9	28.9 ± 15	0.83
Mean systolic BP, mm/hg	134 ± 13.6	128 ± 12.4	132 ± 13.3	0.27
Mean diastolic BP, mm/hg	73.5 ± 9.5	75.3 ± 9.3	74.1 ± 9.3	0.63
Symptoms, n (%)				
Fever	6 (33)	1 (10)	7 (25)	0.51
Weight loss	8 (44)	4 (40)	12 (43)	0.82
Polymyalgia rheumatica	8 (44)	3 (30)	11 (39)	0.45
Headache	13 (72)	9 (90)	22 (79)	0.27
Visual	7 (39)	7 (70)	14 (50)	0.11
Jaw claudication	11 (61)	4 (40)	15 (54)	0.28
Scalp tenderness	13 (72)	9 (90)	22 (79)	0.27
Chest pain	1 (6)	0 (0)	1 (4)	0.45
Limb claudication	2 (11)	0 (0)	2 (7)	0.27
Laboratory variables, mean				
WBC, × 10^9/l	10.2 ± 3.7	7.8 ± 3.2	9.3 ± 3.7	0.10
Hemoglobin, g/l	117 ± 18	132 ± 9.7	122 ± 17	0.022
Platelet, × 10^9/l	392 ± 160	278 ± 79	351 ± 146	0.046
ESR, mm/h	78 ± 42	47 ± 36	66 ± 42	0.06
CRP, mg/l	112 ± 95	35 ± 45	84 ± 88	0.024
Creatinine, mmol/l	85 ± 37	80 ± 17	83 ± 31	0.70
Length of biopsy specimen, cm	2.7 ± 1.0	2.1 ± 0.9	2.5 ± 1.0	0.12
Medications, n (%)				
Aspirin or clopidogrel	5 (28)	2 (20)	7 (25)	0.65
Statin	5 (28)	1 (10)	6 (21)	0.27
Antihypertensive	8 (44)	4 (40)	12 (43)	0.82
Prednisone	18 (100)	10 (100)	28 (100)	1.00
Daily dose prednisone, mg	55.6 ± 12	51.5 ± 13	54.1 ± 12	0.41
Cumulative prednisone, mg				
Prior to PET/CT	603 ± 515	720 ± 416	645 ± 477	0.54
Prior to biopsy	517 ± 438	892 ± 807	651 ± 610	0.12

All values presented reflect the mean values ± SD unless otherwise stated. TAB: temporal artery biopsy; BMI: body mass index; BP: blood pressure; WBC: white blood cells; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PET/CT: positron emission tomography/computerized tomography.

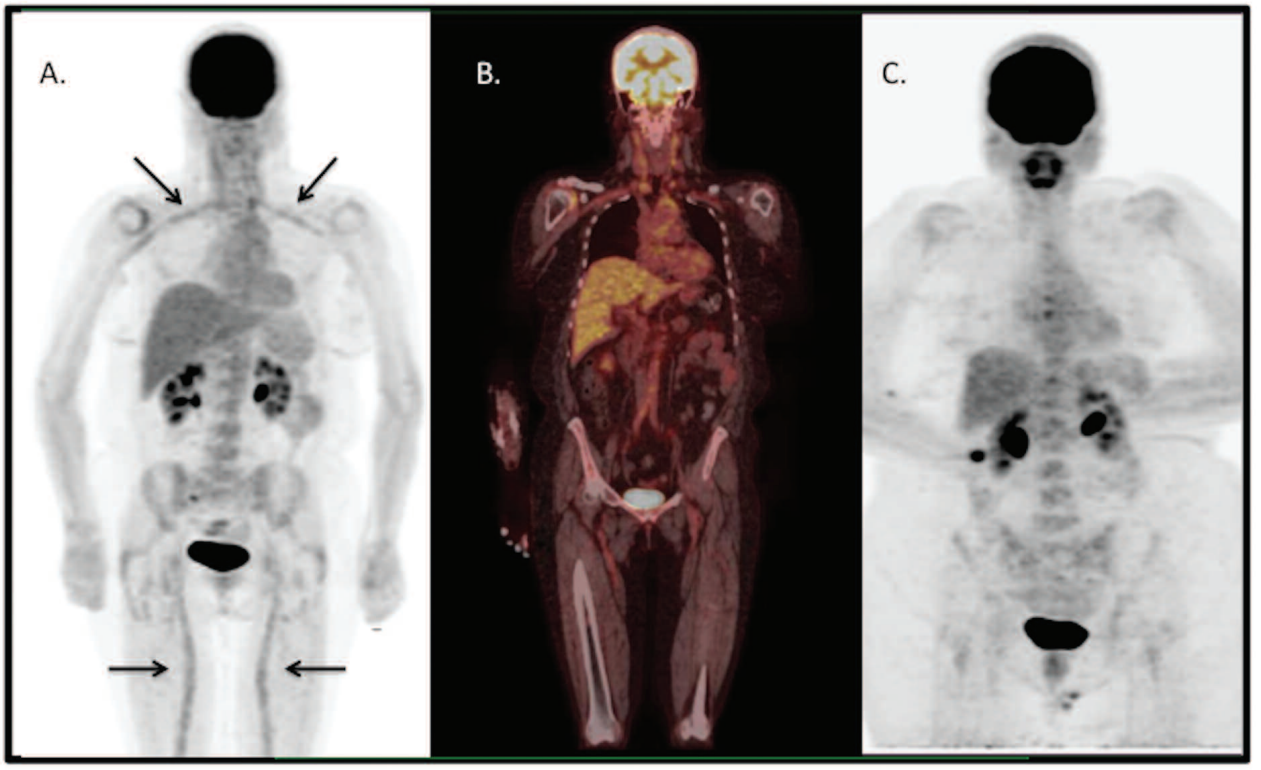

Figure 1. Acquired PET/CT images in patients with GCA and controls. A. A 3-D MIP PET image. Black arrows indicate areas of increased vascular FDG uptake. B. Coronal fused PET/CT image from a GCA patient with a vascular uptake score of 16.5/24. C. A 3-D MIP PET image from a control subject with a vascular uptake score of 2.5/24. PET/CT: positron emission tomography/computerized tomography; GCA: giant cell arteritis; MIP: maximum intensity projection; FDG: 18F-fluorodeoxyglucose.

GCA compared to controls (Table 2). Mean uptake scores in the ascending aorta and carotids did not differ significantly between cases and controls (1.43 ± 0.5 vs 1.14 ± 0.64 for ascending aorta, p = 0.12; and 1.07 ± 0.56 vs 0.8 ± 0.55 for carotids, p = 0.09, respectively).

When comparing PET/CT images of TAB+ to TAB– patients with GCA, there were no significant differences in either the mean total uptake scores (10.9 ± 2.6 vs 9.4 ± 2.8; p = 0.20), or in any of the 8 individual vascular territories (Table 3). When multiple comparisons of all 3 subgroups (TAB+, TAB– GCA, and controls) was performed, TAB+ patients had greater total uptake (p < 0.001) and uptake in 4 of 8 specific vascular territories compared to controls, but the difference in total PET/CT uptake scores between TAB– patients and controls was not statistically significant (p = 0.16; Supplementary Tables 1a and 1b have complete results, available with the online version of this article).

Using ROC curve, a total PET/CT uptake score of ≥ 9 provided the optimal cutoff for distinguishing GCA cases

Table 2. Mean PET/CT visual uptake scores per individual vascular territory in patients with GCA and controls. Values listed indicate visual scores ± SD.

Territory	GCA, n = 28	Controls, n = 28	p
Ascending aorta	1.43 ± 0.5	1.14 ± 0.64	0.119
Aortic arch	1.63 ± 0.38	1.23 ± 0.46	0.001
Descending aorta	1.16 ± 0.58	0.89 ± 0.46	0.050
Carotids	1.07 ± 0.56	0.8 ± 0.55	0.089
Subclavians/axillaries	1.25 ± 0.46	0.84 ± 0.41	< 0.001
Abdominal aorta	1.11 ± 0.55	0.75 ± 0.4	0.007
Iliacs	1.09 ± 0.49	0.79 ± 0.52	0.027
Femorals	1.61 ± 0.57	1.29 ± 0.48	0.033

PET/CT: positron emission tomography/computerized tomography; GCA: giant cell arteritis.

Table 3. Mean PET/CT uptake scores per individual vascular territory in TAB+ and TAB– patients with GCA. Values listed indicate visual uptake scores ± SD.

Territory	TAB+, n = 18	TAB–, n = 10	p
Ascending aorta	1.47 ± 0.53	1.35 ± 0.47	0.604
Aortic arch	1.67 ± 0.34	1.55 ± 0.44	0.582
Descending aorta	1.25 ± 0.65	1.00 ± 0.41	0.369
Carotids	1.06 ± 0.51	1.1 ± 0.66	0.869
Subclavian/axillaries	1.36 ± 0.48	1.05 ± 0.37	0.137
Abdominal aorta	1.22 ± 0.62	0.9 ± 0.32	0.283
Iliacs	1.14 ± 0.54	1.0 ± 0.41	0.608
Femorals	1.69 ± 0.42	1.45 ± 0.76	0.132

PET/CT: positron emission tomography/computerized tomography; GCA: giant cell arteritis; TAB: temporal artery biopsy.

from controls. The area under the curve (AUC) was 0.745, with sensitivity of 71.4% and specificity of 64.3%.

Correlation of total PET/CT uptake with clinical variables in patients with GCA. Of the continuous variables examined, only lower hemoglobin (–0.48; p = 0.009), and higher platelets (0.490; p = 0.008) correlated significantly with greater mean PET/CT total uptake score. There was no significant association with age (–0.056; p = 0.78), BMI (–0.36; p = 0.06), white blood cell count (0.15; p = 0.46), ESR (0.38; p = 0.06), or CRP (0.34; p = 0.08).

For categorical variables, the presence of any systemic symptom (fever, weight loss, or polymyalgia rheumatica) correlated significantly with increased mean total PET/CT uptake scores (11.4 vs 8.2; p = 0.002). These variables were not significantly associated: female sex (10.6 vs 9.9; p = 0.79), the presence of vascular symptoms (headache, scalp tenderness, jaw claudication, visual change, chest pain, or limb claudication, 10.2 vs 13.5; p = 0.29), use of antiplatelet agents (10.6 vs 10.2; p = 0.91), and statins (10.0 vs 10.4; p = 0.61).

No statistically significant association could be detected between mean rank–ordered total PET/CT uptake and daily dose of prednisone used (< 20 mg/day, 21–50 mg/day, or > 50 mg/day; p = 0.56) or the cumulative exposure to prednisone prior to PET/CT acquisition (< 500 mg, 501–1000 mg, or > 1000 mg; p = 0.65). After adjustment of prednisone use according to patients' body weight, a higher daily dose of prednisone was significantly associated with increased mean total PET/CT uptake score (0.40; p = 0.03.) Cumulative exposure to prednisone per kg body weight prior to scanning remained nonsignificant (–0.47; p = 0.82).

Analysis of PET/CT uptake scores, excluding nonsignificant vascular territories. When the 2 nonstatistically significant vascular territories (ascending aorta and carotids) were excluded from the analysis, mean total PET/CT uptake scores remained significantly different between patients with GCA and controls (total score 8.9 ± 2.4 vs 6.6 ± 2.1; p = 0.001) and nonsignificant between TAB+ and TAB– patients with GCA (9.4 ± 2.5 vs 8.1 ± 2.5; p = 0.16.) In this analysis, lower hemoglobin level (–0.48; p = 0.009), higher platelet count (0.49; p = 0.008), the presence of any systemic symptom (9.7 vs 7.2; p = 0.005), and higher daily dose of prednisone per kg body weight (0.38; p = 0.04) were still significantly correlated with greater total FDG uptake.

DISCUSSION

PET/CT is an emerging modality whose strength is its ability to provide not only structural details of vascular anatomy (e.g., stenoses and aneurysms), but also functional information about the vessel wall. The distribution and uptake of 18F-FDG mimics that of glucose within the body[28], providing a unique opportunity to image the inflammatory activity of the entire vasculature, and potentially allowing for identification of vasculitis at an earlier stage, before structural vessel damage has occurred[29]. In our study, we used a semiquantitative visual scoring system to evaluate large vessel PET/CT uptake both overall (total scores) and in individual vascular territories in consecutive, newly diagnosed and treated patients with GCA (TAB+ and TAB–) and controls. As expected, we found the mean total vascular PET/CT uptake was significantly greater in patients with GCA compared to controls, with no statistically significant differences between biopsy-positive and biopsy-negative patients. The calculated optimal total PET/CT cutoff score of 9 resulted in AUC of 0.75, with moderate sensitivity and specificity of 71.4% and 64.3% for the diagnosis of GCA, respectively.

Although still statistically significant, our reported test characteristics (in particular, specificity) are lower than those previously reported for PET/CT in GCA. For example, prior studies using visual scoring methods describe PET/CT sensitivities of up to 84% and very high specificities of 98–99% for the detection of increased large vessel uptake in this disease[15,16,17,21]. Studies using quantitative maximum standardized uptake values report sensitivities of 81–89% and specificities of 79–95%[22,30]. Discrepancies in our results may be due in part to differences in the methods used for interpretation of vascular uptake, including the use of summed total vascular scores. Indeed, the lack of a standardized approach to vascular PET/CT interpretation is a major limitation to its use in patients with large-vessel vasculitis[31,32,33]. In addition to differences in image interpretation, variability in the acquisition of PET/CT images has also been described. Although usual practice in most centers is to image 60 min following FDG injection (as was done in our study), some studies have described better delineation of large vessel wall FDG uptake by delaying imaging by 180 min[34,35]. Our results also very likely reflect differences in the patients themselves, most notably our inclusion of TAB– patients and those receiving prednisone.

Glucocorticoid use is known to result in rapid improvement in the inflammatory response, and may inhibit peripheral glucose uptake by reducing expression of glut transporters[36]. In addition, glucocorticoids may increase hepatic FDG uptake, potentially producing lower visual uptake ratios[22,33,37]. The sensitivity of PET/CT has been previously reported to fall from 99.6% to 52.9% in patients with GCA receiving immunosuppression[21]. The effect of specific doses and duration of glucocorticoid use on PET/CT, however, is not yet well understood. This is an important issue, because PET/CT may be difficult to obtain rapidly in clinical practice (outside of a research protocol) and it is not ethical to withhold glucocorticoid treatment in patients with suspected GCA. Although good sensitivity and specificity (80% and 79%, respectively) have been reported for PET/CT in patients with GCA receiving < 3 days of steroid therapy[22], a marked reduction in test characteristics occurs after 3 to 12 months of treatment[15,23,24,38,39]. In our study, patients

received treatment for an average of 11.9 days prior to PET/CT. Statistical analyses did not confirm any relationship between steroid dose or duration with PET/CT uptake in our patients, other than between higher daily dose/kg body weight and increased vascular uptake. We believe this association likely reflects the treating physician's impression of greater disease severity in these patients. Our inability to determine a suppressive effect of prednisone may be due to the small number of patients evaluated, and the fact that nearly all patients with GCA scanned were receiving similar high doses of prednisone. Interestingly, only 1 of our patients with GCA had vascular uptake scores of 3 ("greater than the liver") — a patient who underwent imaging on the day of diagnosis, prior to starting steroid therapy. It is also worth noting that, unlike previous studies[16,22], no positive associations between ESR and CRP and PET/CT uptake were identified in our study, also likely a result of moderate glucocorticoid exposure. Although difficult to execute in clinical practice, it may be that to obtain optimal diagnostic yield, PET/CT scans should be obtained within fewer than 12 days of initiation of glucocorticoid therapy. The influence of glucocorticoid use on FDG uptake requires further study.

Another unique feature of our study is the inclusion of both TAB+ and TAB– patients with GCA. Increased vascular FDG uptake has been observed previously in case reports and small series of biopsy-negative patients[15,20,21,32,33], and our results also indicate that large vessel uptake is similar in both groups of patients with GCA. When the PET/CT scans of all 3 groups were compared, however, only the TAB+ group had significantly greater uptake than controls. This may be due to a lack of statistical power owing to the small sample size or a lower inflammatory burden in biopsy-negative patients. Because clinical impression was used as the gold standard for diagnosis of GCA (as is done in clinical practice), misdiagnosis of TAB– patients with GCA is also possible.

Regarding FDG uptake in specific vascular beds, significantly greater uptake occurred in only 6 of the 8 territories in patients with GCA. Increased uptake in the aortic arch, descending thoracic aorta, and subclavian/axillary arteries was expected, because these vessels are well-known targets in GCA[15,17]. However, significantly greater uptake was also found in territories in which lesions are often presumed to be atherosclerotic, including the abdominal aorta, and iliac and femoral arteries. Our findings are supported by other studies showing frequent involvement of these arteries in GCA[15,22,40], and emphasize the importance of considering disease activity in every medium to large vessel. Interestingly, we did not find any difference in the FDG uptake in the ascending aorta and carotids of patients and controls, which was unexpected. Grade 2 ascending aorta uptake was noted in 6 of 28 controls (21%), suggesting that some uptake in this vessel may be a nonspecific finding. It seems likely that the amount of uptake seen in nonvasculitic vessels may vary by territory, because of individual vessels' susceptibility to atherosclerosis[41]; however, it should be noted that we did not specifically evaluate extent of atherosclerosis in our study. Further studies are needed comparing uptake in individual vascular territories in patients with GCA and controls.

There are limitations to our study. The total number of patients was small, and because nearly all patients with GCA received glucocorticoids at similar doses, we were unable to accurately determine the association between steroid use and FDG uptake. In GCA, involvement of specific vascular territories (cranial arteries, large vessels, or a combination of these) varies per individual, therefore we cannot be certain that the number of involved vascular structures in TAB+ and TAB– patients were equally distributed. In addition, use of oncology patients as controls is not ideal. Although efforts were made to preserve blinding by excluding those with metastatic disease, future studies should use control patients in whom the diagnosis of GCA was suspected, but ultimately ruled out. Our results are also likely influenced by our choice of visual scoring method. While many authors contend that visual scores are the simplest and most reliable method, the appropriate cutoff for positive uptake (equal to or greater than the liver) and the use of individual vascular territories versus summed scores continues to be studied[31,32]. Also, although most patients had normal renal function (mean creatinine 82.8 mmol/l), a few had mild to moderate dysfunction, which may theoretically increase the blood pool activity of FDG.

The major strengths of our study are the inclusion of patients with GCA representative of those encountered in clinical practice, and the study of individual vascular territories. We specifically included (1) patients who were clinically diagnosed, either with or without arteritis on TAB, and (2) those who were initiating treatment with glucocorticoids to see whether PET/CT would be of additional diagnostic value in this setting.

PET/CT uptake scores were significantly greater in patients with GCA receiving glucocorticoids (for average 11.9 days) compared to controls, with similar results in TAB+ and TAB– patients. The sensitivity and specificity of PET/CT for the diagnosis of GCA were lower than those reported in previous studies, likely because of glucocorticoid exposure. Future work evaluating the influence of specific steroid doses and duration on FDG uptake will be of great interest.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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