Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in polymyalgia rheumatica: an observational study

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Abstract

Objective

Polymyalgia rheumatica (PMR) is an inflammatory disease with a diagnosis that is sometimes difficult to establish. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) might be helpful. We analysed the usefulness of ^{18}F-FDG PET/CT for the diagnosis of PMR.

Methods

This was an observational retrospective study of individuals with PMR who underwent ^{18}F-FDG PET/CT and a control group. We assessed clinical and ^{18}F-FDG PET/CT characteristics. Sixteen sites were studied. The number of sites with significant FDG uptake, the mean maximum standardised uptake value (SUVmax) and the highest SUVmax value were assessed for each patient.

Results

Data for 123 patients with PMR (37 with corticosteroids [CSTs] use) were analysed; 85 had new-onset PMR. As compared with the 75 controls, patients with new-onset PMR had higher mean ± SD number of sites with significant FDG uptake (11.3 ± 3.3 vs. 0.9 ± 1.1, p<0.001) and higher SUVmax scores (p<0.001). A cut-off of 5 hypermetabolic sites provided sensitivity of 96.5% and specificity 100%. For the total SUVmax score, a cut-off of 3 had the best sensitivity (92.6%) and specificity (86.1%). As compared with PMR patients using CSTs, those who were CST-naive had significantly higher CRP level (p<0.001), number of sites with significant FDG uptake (p<0.001) and SUVmax scores (p<0.01). In contrast, large-vessel vasculitis was more frequent in patients receiving CSTs than CST-naive patients (27% vs. 8%, p<0.01).

Conclusion

The number of hypermetabolic sites or SUVmax quantification might be useful for PMR diagnosis, and CSTs might affect the results of ^{18}F-FDG PET/CT.

Key words

polymyalgia rheumatica, ^{18}F-FDG PET/CT

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Introduction

Polymyalgia rheumatica (PMR) is an inflammatory disease affecting older people that is characterised by pain and stiffness of the shoulder and pelvic girdles (1). This pain is related to inflammation of articular and peri-articular structures, and acute phase reactants are generally increased in level. PMR can be associated with giant cell arteritis (GCA) in its cranial or extra-cranial form. Symptoms of PMR are non-specific, and other disorders mimicking PMR, such as rheumatoid arthritis or spondyloarthritis, need to be eliminated in the diagnosis. In the absence of specific diagnostic tests, the diagnosis of PMR can sometimes be difficult, but imaging might be helpful (2).

Ultrasonography of shoulders and hips is able to detect bursitis or synovitis of these joint sites (3, 4) and is included in the ACR/EULAR 2012 classification criteria for PMR (5). However, ultrasonography seems more useful for distinguishing PMR from mechanical disorders than an inflammatory disease such as rheumatoid arthritis (5). Recently, several studies have highlighted the usefulness of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for PMR diagnosis but also for detecting GCA (6-10). This imaging modality allows for whole-body analysis of hypermetabolic joints or vascular sites. However, although some diagnostic scores were proposed (8-10), ^{18}F-FDG PET/CT is not currently integrated in classification criteria. Moreover, the impact of corticosteroids (CSTs) use or associated large-vessel vasculitis (LVV) was not well studied.

In the present study, we analysed ^{18}F-FDG PET/CT findings in a large cohort of PMR patients in comparison to non-PMR controls and determined cut-offs for PMR diagnosis. We also studied the characteristics of patients according to the use of CSTs or LVV.

Materials and methods

Patients and study design

This was an observational retrospective study. Included patients were seen at the rheumatology department of a tertiary care centre (University Hospital of Bichat-Claude Bernard, Paris, France) during a 10-year period (2011-2021). Patients were referred to our unit by general practitioners or rheumatologists for suspected PMR (n=85) or suspected relapse/CSTs resistance (n=37) (Fig. 1).

To be included, patients needed to have a positive diagnosis of PMR according to the ACR/EULAR 2012 classification criteria for PMR (11) and that did not mimic other disorders such as rheumatoid arthritis as well as results of at least one ^{18}F-FDG PET/CT exam during the disease course. Exclusion criteria were age <50 years and previous diagnosis of GCA.

The following data were collected from medical records: clinical and demographic characteristics, laboratory test results and ^{18}F-FDG PET/CT findings. Symptoms suggesting LVV were jaw claudication and ischaemic symptoms, headaches, temporal artery induration and loss of vision.

A total of 85 PMR patients had new-onset PMR, defined by no previous diagnosis of PMR and a delay between the ^{18}F-FDG PET/CT exam and introduction of CSTs <15 days. The remaining PMR patients had relapsing disease or CST resistance (CST dosage >7.5 mg/day). Among the whole population of PMR, 86 were naive to CSTs (Fig. 1). Among patients with new-onset PMR, only 7 received CSTs for <15 days and the 78 remaining were CST-naive.

The control group (n=75) corresponded to patients undergoing ^{18}F-FDG PET/CT for sarcoidosis (n=51), infectious disease (n=15) and cancer (n=9).

^{18}F-FDG PET/CT imaging protocol

After an overnight fast, ^{18}F-FDG 3.5 MBq/kg was injected in patients. PET images were acquired 60 min later by using a combined PET/CT scanner (Discovery 690; GE Healthcare, CT, France). Low-dose CT (100 keV and 140 mA with current modulation system) without contrast enhancement was acquired for anatomic correlation and attenuation correction of PET data. PET images were reconstructed by using 3-D time-of-flight ordered subset expectation maximisation with and without attenuation correction and re-

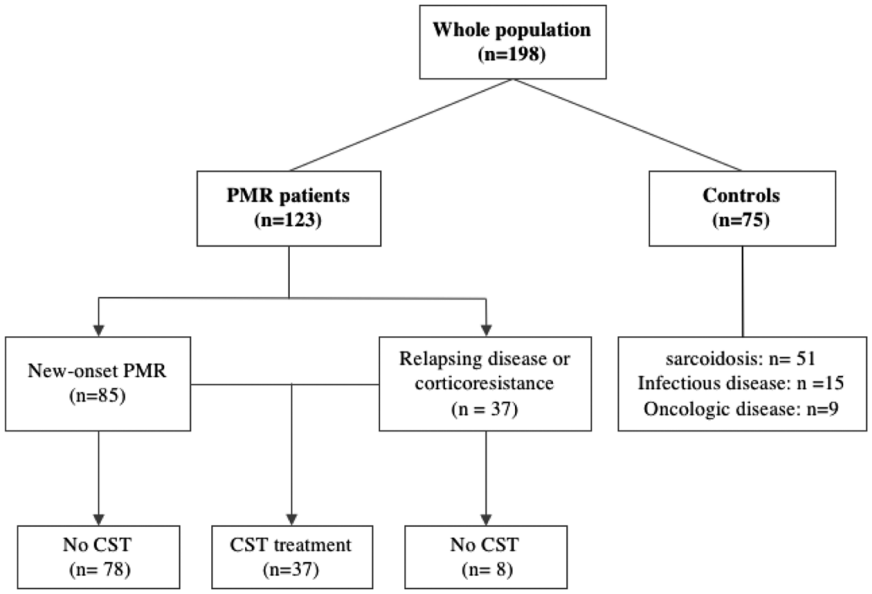

Fig. 1. Flow chart of the study
CST: corticosteroids

Table I. Baseline characteristics of patients with new onset polymyalgia rheumatica (PMR) and controls.

Baseline characteristics	New-onset PMR (n=85)	Controls (n=75)	*p*-value
Age (years), mean ± SD	70.7 ± 8.6	65.2 ± 10.9	**< 0.001**
Sex, female	51 (61)	38 (51)	0.24
Patients with CST use	7 (8)	5 (7)	0.82
Controls' diagnosis			
Sarcoidosis	NA	51	-
Infectious disease	NA	15	-
Oncologic disease	NA	9	-
PET findings, mean ± SD			
Number of sites with significant FDG uptake (0-16)	11.3 ± 3.3	0.9 ± 1.1	**<0.001**
SUVmax score	3.9 ± 0.8	2.7 ± 0.4	**<0.001**
Highest SUVmax	5.4 ± 1.3	2.7 ± 0.4	**<0.001**
Sites with FDG uptake (score ≥2)			
Acromioclavicular joint	54/170 (32)	8/150 (5)	**<0.001**
Sternoclavicular joint	116/170 (68)	2/150 (1)	**<0.001**
Shoulders	150/170 (88)	20/150 (13)	**<0.001**
Cervical interspinous process	37/85 (44)	0/75 (0)	**<0.001**
Lumbar interspinous process	71/85 (84)	4/75 (5)	**<0.001**
Hips	151/170 (89)	9/150 (6)	**<0.001**
Greater trochanter	135/170 (79)	14/150 (9)	**<0.001**
Symphysis pubis	96/170 (56)	0/150 (0)	**<0.001**
Ischial tuberosity	149/170 (88)	7/150 (5)	**<0.001**
Wrists*	75/150 (50)	0/54 (0)	**<0.001**
LVV	6/85 (7)	1/75 (1)	0.12

Data are n (%) patients unless indicated.
PMR: polymyalgia rheumatica; SUV: standardised uptake value; LVV: large-vessel vasculitis; FDG: 18 fluorodeoxyglucose; PET: positron emission tomography; NA: not attributable.
*Some patients had no analysis of hands because of the patient's position during PET/CT.

oriented in axial, sagittal, and coronal slices (3-mm cross-section thickness and 256×256 matrix for a visual field of view of 70 cm). Reconstructed images were displayed on an Advantage Workstation (GE Healthcare) for visual analysis (Fig. 2).

FDG uptake was first evaluated by using semiquantitative analysis with a previously described score (12): 0, no FDG uptake; 1, slight uptake, less than to liver; 2, moderate uptake equal to liver, 3, intense uptake higher to liver. Significant FDG uptake was defined by a score ≥2.

A total of 16 sites were assessed: two acromioclavicular and sternoclavicular joints, two hips, two shoulders, two greater trochanters, two ischial tuberosities, two symphysis pubis enthesis, and cervical and lumbar interspinous processes. We calculated a total score (0–16), corresponding to the sum of all sites with significant FDG uptake, for each patient. Peripheral involvement included the following locations: elbows, hands, feet and knees.

A quantitative analysis of FDG uptake involved the maximum standardised uptake value (SUVmax). We measured the SUVmax for each site with significant FDG uptake and calculated the mean SUVmax score and the highest SUVmax score for each patient.

Analysis of large vessels involved the same method as for the musculoskeletal system.

Ethics statement

This observational study was retrospective and did not require ethical approval according to standards currently applied in France. All patients gave their informed consent for the [18]F-FDG PET/CT exams.

Statistical analysis

Data are presented as median (interquartile range [IQR]), mean±SD, or number (%). To compare quantitative variables, we used the chi-squared test or Fisher exact test. Statistical analyses for continuous data involved the Student *t*-test, Wilcoxon test or Mann-Whitney U-test. Two-sided $p<0.05$ was considered statistically significant. Statistical tests were performed with pvalue.io (https://www.pvalue.io). Receiver operating characteristic (ROC) curves were built for the number of sites, SUVmax score and highest SUVmax.

To identify items independently associated with the diagnosis of PMR, we used logistic regression with PMR diagnosis as the outcome variable and age as an explanatory variable. We selected the candidate covariates from

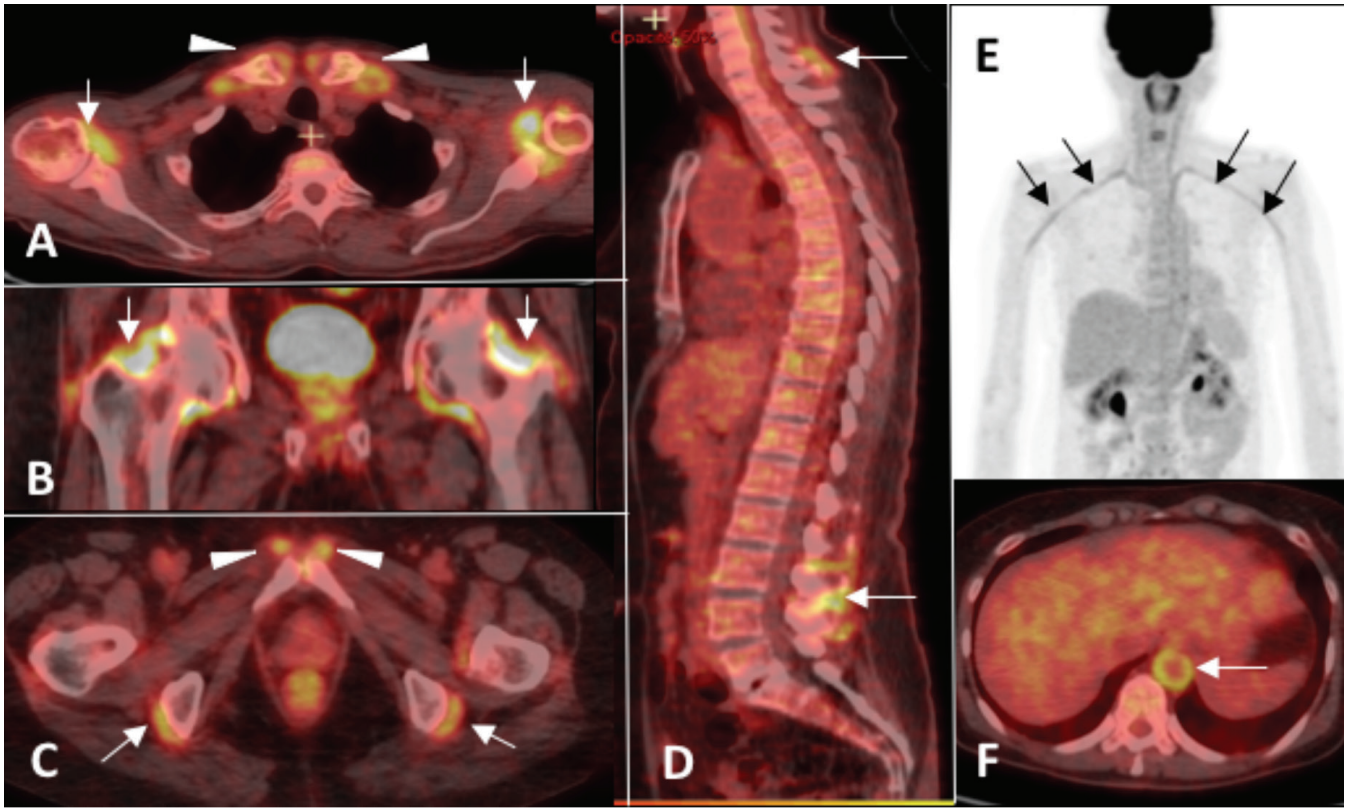

Fig. 2. [18]F-FDG PET/CT findings.
A: Fused [18]F-FDG PET/CT axial slice of the shoulder girdle showing focal high-tracer uptake of shoulders (white arrows) and sternoclavicular joints (white arrowheads).
B: Fused [18]F-FDG PET/CT coronal slice of the pelvis showing focal high-tracer uptake of hips capsules (white arrows).
C: Fused [18]F-FDG PET/CT axial slice of the pelvis showing focal high-tracer uptake of ischial tuberosities (white arrows) and symphysis pubis (white arrowheads).
D: Fused [18]F-FDG PET/CT sagittal slice of the spine showing focal high-tracer uptake of cervical and lumbar interspinous processes (white arrows).
E: [18]F-FDG PET showing FDG uptake of subclavicular vessels suggesting LVV (white arrows).
F: Fused [18]F-FDG PET/CT axial slice of the abdomen showing annular FDG uptake of aorta suggesting LVV (white arrows).
LVV: large-vessel vasculitis; [18]F-FDG PET/CT: fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography.

the set of collected variables so that less than 20% of patients had missing data or variables had less than 5% missing values. The covariates were *a priori* defined from the literature. The candidate covariates were included in a Least Absolute Shrinkage and Selection Operation (LASSO) penalised regression model. The penalty coefficient (lambda) was chosen to provide an estimation error <1 SD of the minimum error obtained by 10-fold cross-validation while being as parsimonious as possible. No variable had a coefficient different from 0 with this lambda coefficient. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated.

Results

Characteristics of the patients with new onset PMR and controls

Data for 123 patients with PMR were analysed (Supplementary Table); 85 patients had new-onset PMR. The characteristics of patients with new-onset PMR and controls are in Table I. PMR patients were slightly older than controls (70.7±8.6 *vs*. 65.2±10.9 years, $p<0.001$). All patients were negative for anti-citrullinated protein antibodies and rheumatoid factor.

As compared with controls, new-onset PMR patients had a higher mean number of sites with significant FDG uptake (11.3±3.3 *vs*. 0.9±1.1, $p<0.001$) and SUVmax score (3.9±0.8 *vs*. 2.7±0.4, $p<0.001$) and more elevated highest SUVmax (5.4±1.3 *vs*. 2.7±0.4, $p<0.001$).

The proportion of sites with significant FDG uptake was higher for PMR patients than controls for all sites except LVV. One control patient with sarcoidosis exhibited intense FDG uptake in vessels. The mostly hypermetabolic sites were hips, shoulders and ischial tuberosity, with 89%, 88% and 88% of FDG uptake, respectively. Acromioclavicular joints had the lowest percentage of FDG uptake (32%). Half of PMR patients had significant FDG uptake in wrists.

After adjustment by age, a diagnosis of new-onset PMR was associated with number of sites with significant FDG uptake (OR 2.6 [95% CI 1.8; 4.5], $p<0.001$), total SUVmax score (1.5 [1.3; 1.8], $p<0.001$) and highest SUVmax (1.5 [1.3; 1.9] $p<0.001$).

Determination of cut-offs for the diagnosis of new onset PMR

We next used ROC curve analysis to determine the optimal cut-offs to discriminate new-onset PMR and controls. A cut-off of 5 sites with significant FDG uptake provided a sensitivity of 96.5% and specificity 100%. For the total SUVmax score, a cut-off of 3 had the best sensitivity (92.6%) and specificity (86.1%). Finally, for the highest SUVmax, the optimal cut-off was 3.5,

Table II. Baseline characteristics of PMR patients according to CST use.

Baseline characteristics	Total (n=123)	No CST use (n=86)	CST use (n=37)	*p*-value
Age (years), mean ± SD	70.7 ± 8.8	71.0 ± 9.0	70.0 ± 8.6	0.56
Sex, female	82 (67)	54 (63)	28 (76)	0.16
Symptoms duration (weeks), median [IQR]	12 [5; 20]	12 [5; 16]	12 [5; 28]	0.66
Shoulder pain	121 (98)	84 (98)	37 (100)	1
Pelvis girdle pain	88 (72)	60 (70)	28 (76)	0.51
Neck pain	48 (39)	38 (44)	10 (27)	0.074
Peripheral involvement	58 (47)	48 (56)	10 (27)	**<0.01**
Constitutional symptoms	38 (31)	30 (35)	8 (22)	0.17
Symptoms suggesting LVV	20 (16)	10 (12)	10 (27)	**0.034**
CRP (mg/l) at PET/CT analysis, median [IQR]	47.0 ± 47.9	59.6 ± 50.3	17.6 ± 23.4	**<0.001**
Patients with CSTs use	37 (30)	0 (0)	37 (100)	-
Dosage of CSTs (mg/day), mean ± SD	16.5 ± 15	-	16.5 ± 15	-

Data are n (%) patients unless indicated.
PMR: polymyalgia rheumatica; IQR: interquartile range; LVV: large-vessel vasculitis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PET/CT: positron emission tomography/computed tomography; CST: corticosteroids.

Table III. FDG-PET/CT findings according to CST use.

FDG-PET/CT characteristics	Total (n=123)	No CST use (n=86)	CST use (n=37)	*p*-value
Sites with significant FDG uptake (0-16), mean ± SD	9.5 ± 4.5	11.1 ± 3.4	5.6 ± 4.4	**<0.001**
Total SUVmax score, median [IQR]	3.6 [3.1; 4.2]	3.8 [3.4; 4.3]	3.2 [2.9; 3.7]	**<0.01**
Highest SUVmax, median [IQR]	4.9 [4.1; 5.8]	5.2 [4.3; 6.1]	4.0 [3.5; 4.9]	**<0.001**
Sites with significant FDG uptake (score ≥2) at patient level				
Acromioclavicular joint	45 (47)	36 (42)	9 (24)	0.17
Sternoclavicular joint	80 (65)	68 (79)	12 (32)	**<0.001**
Shoulders	100 (81)	80 (93)	20 (54)	**<0.001**
Cervical interspinous process	46 (37)	39 (45)	7 (19)	**<0.01**
Lumbar interspinous process	89 (72)	69 (80)	20 (54)	**<0.01**
Hips	94 (76)	74 (86)	18 (49)	**<0.001**
Great trochanter	90 (73)	76 (88)	14 (38)	**<0.001**
Symphysis pubis	69 (56)	58 (67)	11 (30)	**<0.001**
Ischial tuberosity	100 (81)	76 (88)	24 (65)	**<0.01**
Hand	49/105 (47)	46 (53)	3 (8)	**<0.001**
LVV	17 (14)	7 (8)	10 (27)	**<0.01**
Grade LVV	3.9 [3.4; 4.5]	4.2 [3.7; 4.6]	3.7 [3.3; 4.1]	0.45
Location of LVV				
Aorta	11	5	6	-
Subclavicular arteries	10	4	6	-
Iliofemoral arteries	5	4	1	-
Carotids	11	4	7	-

Data are n (%) patients unless indicated.
PMR: polymyalgia rheumatica; IQR: interquartile range; LVV: large-vessel vasculitis; FDG PET/CT: fluorodeoxyglucose positron emission tomography/computed tomography; SUV: standardised uptake value; CST: corticosteroids.

providing a sensitivity of 95.1% and specificity 97.2%.

Characteristics of PMR patients according to CST intake

We next separated the whole population of PMR (n=123) according to CST intake before [18]F-FDG PET/CT assessment. A total of 86 PMR patients were naive of CST use and 37 received CSTs (mean dosage 16.5±15 mg/day) at the time of the [18]F-FDG PET/CT exam. Table II details the clinical and biological characteristics of those patients.

As compared with PMR patients who used CST, those who were CST-naive had significantly higher peripheral involvement (56% *vs*. 27%, $p<0.01$) and CRP level (59.6±50.3 *vs*. 17.6±23.4 mg/l, $p<0.001$).

[18]F-FDG PET/CT findings in PMR patients according to CST intake

As compared with PMR patients who used CST, those who were CST-naive had significantly higher mean number of sites with significant FDG uptake (11.1±3.4 *vs*. 5.6±4.4, $p<0.001$), median total SUVmax score (3.8 [IQR 3.4; 4.3] *vs*. 3.2 [2.9; 3.7], $p<0.01$) and more elevated median highest SUVmax (5.2 [IQR 4.3; 6.1] *vs*. 4.0 [3.5; 4.9], $p<0.001$) (Table III)

Except for acromioclavicular joints, for all musculoskeletal locations, significant FDG uptake was more frequent among CST-naive PMR patients than those using CSTs. In contrast, LVV was more frequent in PMR patients using than not using CSTs (27% *vs*. 8%, $p<0.01$).

[18]F-FDG PET/CT findings in PMR patients according to presence of LVV

Finally, we analysed the whole PMR population according to the presence of LVV. A total of 17 patients had LVV with involvement of carotids (n=11), aortas (n=11), and subclavicular (n=10) and ilofemoral (n=5) arteries (Table IV)

Logically, patients with than without LVV more frequently had clinical symptoms of LVV (53% *vs*. 10%, $p<0.001$). Moreover, patients with than without LVV more frequently used CSTs (59% *vs*. 25%, $p<0.01$) at a higher dosage (17.5 [IQR 15.0; 44.5] *vs*. 8.0 [5.0; 16.0] mg/day, $p<0.01$). In contrast, patients with than without LVV had lower peripheral involvement (18% *vs*. 52%, $p<0.01$) and number of sites with significant FDG uptake (3.0 [IQR 0; 7.0] *vs*. 11.0 [8.0; 13.0], $p<0.001$). The two groups did not differ in acute phase reactant levels, other clinical symptoms or SUVmax findings.

[18]F-FDG PET/CT findings in PMR patients according to CRP level

CRP levels were correlated with mean

Table IV. Characteristics of PMR patients by presence or not of large-vessel vasculitis

Baseline characteristics	no LVV (n=106)		LVV (n=17)		*p*-value
Age (years), median [IQR]	70.5	[64.3; 78.0]	73.1	[68.4; 77.1]	0.51
Sex, female	67	(63)	15	(88)	0.042
Symptoms duration (weeks), median [IQR]	12	[6; 17]	9	[4; 23]	0.54
Shoulder pain	104	(98)	17	(100)	1
Pelvis girdle pain	78	(74)	10	(59)	0.25
Neck pain	40	(38)	8	(47)	0.46
Peripheral involvement	55	(52)	3	(18)	**<0.01**
Constitutional symptoms	31	(29)	7	(44)	0.26
Symptoms suggesting LVV	11	(10)	9	(53)	**<0.001**
CRP at PET/CT analysis, median [IQR]	32.0	[10.2; 71.0]	30.0	[9.0; 55.0]	0.68
Patients with CSTs use	27	(25)	10	(59)	**<0.01**
Dosage of CSTs (mg/day), median [IQR]	8.0	[5.0; 16.0]	17.5	[15.0; 44.5]	**<0.01**
Sites with significant FDG uptake (0-18), median [IQR]	11.0	[8.0; 13.0]	3.0	[0; 7.0]	**<0.001**
Total SUVmax score, median [IQR]	3.64	[3.2; 4.2]	3.26	[3.0; 4.2]	0.32
Highest SUVmax, median [IQR]	4.95	[4.1; 5.8]	4.08	[3.6; 6.1]	0.66

Data are n (%) patients unless indicated.
LVV: large-vessel vasculitis; PMR: polymyalgia rheumatica; IQR: interquartile range; SUV: standardised uptake value; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PET/CT: positron emission tomography/computed tomography; CST: corticosteroids.

number of sites with significant FDG uptake (Pearson r=0.42, p<0.001), mean SUVmax score (r=0.39, p<0.001) and highest median SUVmax score (r=0.45, p<0.001).

Discussion

In the present study, we first aimed to determine the diagnostic performance of ^{18}F-FDG PET/CT for PMR. To our knowledge, our study is the largest to investigate this imaging modality in PMR. The number of sites with significant FDG uptake and the intensity of FDG uptake (mean and highest SUVmax values) were significantly higher for new-onset PMR patients than controls.

The main involved sites were hips, shoulders and ischial tuberosity, with a prevalence of almost 90%. These data are in line with previous studies by Henckaerts *et al*. and Yamashita *et al*., who found 85% and 96% with shoulder involvement, respectively (8, 13). The percentage was lower (58%) in the study by Sondag *et al*., probably because of a relatively high number of patients receiving CSTs (9). In contrast, acromioclavicular joints had the least percentage of FDG uptake (32%), which suggests that this location is not useful for PMR diagnosis. The most specific sites (>90%) were sternoclavicular joints, cervical interspinous process and symphysis pubis. This high specificity of interspinous bursitis was previously reported (8, 9, 14). As suggested by some studies (15, 16), the involvement of symphysis pubis enthesis had low sensitivity but was very suggestive of PMR. Thus, this location seems a site of interest when ^{18}F-FDG PET/CT is performed for PMR diagnosis.

On ROC curve analysis, ≥5 hypermetabolic sites provided sensitivity of 96.5% and specificity 100%. We also performed a quantitative analysis of FDG uptake by using SUVmax values. A SUVmax value ≥3.5 provided sensitivity of 95% and specificity 97%. This measure is easy to obtain in clinical practice, and the combined analysis of the number of hypermetabolic sites and calculation of the highest SUVmax might represent a good diagnostic tool for PMR. With a similar approach, Sondag *et al*. found a cut-off of ≥3 sites with sensitivity of 73% and specificity 79% (9), but the score used for defining significant FDG uptake differed. With different scoring systems, Henckaerts *et al*. found a cut-off >16 (8), and Flaus *et al*., by using machine learning, identified an optimal combination of two sites including interspinous bursitis (15). These discrepancies might be explained by use of different definitions of significant uptake and scoring system but also by the patient use of CSTs. Indeed, in two of the cited studies, a large number of patients (44–53%) received CSTs at the time of ^{18}F-FDG PET/CT analysis, which resulted in lower sensitivity for this imaging modality (9, 15). Our study also found this effect of CSTs on ^{18}F-FDG PET/CT. CST-naive PMR patients had a higher number of sites with significant FDG uptake and higher SUVmax score that those using CSTs. This finding agrees with previous studies finding decreased FDG uptake in CST users (9, 17). In contrast, use of non-steroidal anti-inflammatory drugs did not modify ^{18}F-FDG PET/CT results (18). This negative effect of CSTs on ^{18}F-FDG PET/CT findings might be explained by an increase in glycemia leading to decreased FDG uptake. However, the strict protocol for ^{18}F-FDG PET/CT assessment limits this interference. Another explanation might be the decreased activations of granulocytes by CSTs. In a mice model, after CST administration, the contribution of inflammatory cells to the ^{18}F-FDG uptake was less important in mice treated with chemotherapy alone (19). Moreover, there is a decrease of levels of acute-phase reactants with CST intake. PET/CT abnormalities can be decreased under CST therapy or tocilizumab (10, 20). Our findings showed that CRP level was strongly decreased among patients receiving CSTs. Otherwise, in line with a previous study (9), we also observed CRP level correlated with the number of sites with significant FDG uptake and SUVmax scores. These data confirm that ^{18}F-FDG PET/CT should be performed, if possible, before the introduction of CSTs.

Overall, 14% of all PMR patients had LVV, which agrees with two previous studies observing LVV in nearly 15% of PMR suspected cases, (8, 21) but the prevalence can be up to 40% (10, 22). LVV was more frequent in patients using than not using CSTs (37% *vs*. 8%). This finding is probably due to the fact that most PMR patients using CSTs had ^{18}F-FDG PET/CT for relapsing disease or CST resistance, which might lead to suspecting LVV in clinical practice. In PMR refractory to CSTs, Moya-Alvarado *et al*. observed an increase in LVV frequency in comparison to new-onset

PMR patients who were CST-naive (21), and the prevalence of LVV in CST-using patients can reach 61% (23). These data suggest that CST resistance is frequent in patients with underlying silent LVV.

Finally, regarding the search for neoplasms by ^{18}F-FDG PET/CT, only two of our patients had hypermetabolism of the colon leading to a diagnosis of neoplasm. Only one of 99 PMR patients had a diagnosis of a cancer neoplasm (8), whereas in another study, ^{18}F-FDG PET/CT helped to identify neoplasms in only three of the 103 PMR patients (21). These data suggest that the frequency of occult neoplasms is low in PMR patients.

Our study had some limitations. First, it was retrospective, which can limit the interpretation of the results. A bias of indication cannot be excluded because of the high prevalence of LVV in patients using CSTs. Indeed, ^{18}F-FDG PET/CT could have been performed for CST-resistant PMR in order to diagnose LVV. Moreover, our control patients did not include those with rheumatic disorders, although sarcoidosis patients might have joint or bone disease (24). Additionally, our ^{18}F-FDG PET/CT exams did not systematically assess wrists or knees, which limits the interpretation of peripheral involvement in our patients. Finally, we cannot exclude that ^{18}F-FDG PET/CT results were considered for PMR diagnosis, which could lead to overestimating the number of hypermetabolic sites or the SUVmax score.

In conclusion, our findings showed that ^{18}F-FDG PET/CT might be helpful for the diagnosis of PMR. An optimal cut-off of ≥5 hypermetabolic sites or high SUVmax score may distinguish PMR from other conditions. Our results also suggest that CST use might affect the ^{18}F-FDG PET/CT results by decreasing the number of involved sites and the SUVmax score. Finally, among PMR patients with CST resistance, ^{18}F-FDG PET/CT was able to identify LVV as an alternative diagnosis.

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