European Journal of Internal Medicine 126 (2024) 69–76

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

# Prognostic value of 18 FDG-PET at diagnosis and follow-up in giant cell arteritis: An observational restrospective study

Anne-Claire Billet [a], Thomas Thibault [b], Éric Liozon [c], Hubert De Boysson [d], Laurent Perard [e], Olivier Espitia [f], Aurélie Daumas [g], Quentin Gomes De Pinho [h], Cécile-Audrey Durel [e], Arnaud Hot [i], Boris Bienvenu [j], Sébastien Humbert [k], Claude Bachmeyer [l], Sabine Mainbourg [m], Thomas Sené [n], Hervé Devilliers [b], Bastien Durand Bailloud [o], Hélène Greigert [a,p], Alexandre Cochet [o], Bernard Bonnotte [a,p], Jean-Louis Alberini [o], Maxime Samson [a,p,*], for the French Study Group for Large Vessel Vasculitis (GEFA)

[a] *Department of Internal Medicine and Clinical Immunology, Referral Center for Rare Systemic Autoimmune and Autoinflammatory Diseases (MAIS), Dijon Bourgogne University Hospital, Dijon, France*
[b] *Department of internal medicine and systemic diseases, Dijon Bourgogne University Hospital, Dijon, France*
[c] *Department of Internal Medicine, University Hospital, Limoges, France*
[d] *Department of Internal Medicine, University Hospital, Caen*
[e] *Department of Internal Medicine, Saint Joseph Saint Luc Hospital, Lyon, France*
[f] *Nantes University, CHU Nantes, Department of Internal and Vascular Medicine, l'institut du thorax, INSERM UMR1087/CNRS UMR 6291, Team III Vascular & Pulmonary diseases, F-44000 Nantes, France*
[g] *Department of Internal Medicine, Geriatric and Therapeutic, La Timone, APHM, C2VN, Aix-Marseille University, France*
[h] *Department of Internal Medicine, NORD hospital, APHM, C2VN, Aix-Marseille University*
[i] *Department of Internal Medicine, Edouard Herriot Hospital, Hospices Civils de Lyon, France*
[j] *Department of Internal Medicine, Saint Joseph Hospital, Marseille, France*
[k] *Department of Internal Medicine, University Hospital, Besancon, France*
[l] *Department of Internal Medicine, Tenon, Paris University Hospital, France*
[m] *Department of Internal and Vascular Medicine, South University Hospital, Hospices Civils de Lyon, France*
[n] *Department of Internal Medicine, Rothschild Hospital Foundation, Paris, France*
[o] *Laboratoire ICMUB, CNRS UMR 6302, Université de Bourgogne, Dijon, France*
[p] *INSERM, EFS BFC, UMR 1098, RIGHT Graft-Host-Tumor Interactions/Cellular and Genetic Engineering, Bourgogne Franche-Comté University, Dijon, France*

ARTICLE INFO

*Keywords:*
PET/CT
Giant cell arteritis
Large vessel vasculitis
Relapse

ABSTRACT

*Objectives:* To evaluate the ability of $^{18}$FDG PET/CT, at diagnosis of giant cell arteritis (GCA) and during follow-up, to predict occurrence of relapse in large-vessel GCA (LV-GCA).
*Methods:* We conducted a retrospective study using the French Study Group for Large-Vessel Vasculitis (GEFA) network. Data from patients with LV-GCA diagnosed by PET/CT and who had PET/CT in the following year were collected. For each PET/CT, PET vascular activity score (PETVAS) and total vascular score (TVS) were assessed, and their ability to predict the occurrence of subsequent relapse was assessed.
*Results:* A total of 65 LV-GCA patients were included, of whom 55 had undergone a follow-up PET/CT 3 to 12 months after the diagnosis of GCA. Patients for whom the second PET/CT (PET2) was performed during active GCA were excluded. PETVAS and TVS decreased between PET1 and PET2 in all patients ($p < 0.001$). There was no correlation between vascular activity scores in PET2 and time to prednisone taper. For relapse prediction, at PET1, the AUC of the TVS and PETVAS were respectively 51.9 and 41.9 at 6 months, 55.3 and 49.7 at 1 year, 55 and 55.7 at 2 years. For PET2, the AUC were respectively 46.1 and 46.7 at 6 months, 52.1 and 48.9 at 1 year, 58.4 and 52.3 at 2 years.
*Conclusion:* PET vascular activity scores at diagnosis and at follow-up PET/CT performed outside a period of GCA activity do not display high performance to predict the occurrence of subsequent relapse in LV-GCA patients.

* Corresponding author at: Service de Médecine Interne et Immunologie Clinique, CHU Dijon Bourgogne, 14 boulevard Gaffarel 21000 Dijon, France.
*E-mail address:* maxime.samson@u-bourgogne.fr (M. Samson).

https://doi.org/10.1016/j.ejim.2024.03.037
Received 17 December 2023; Received in revised form 12 March 2024; Accepted 15 March 2024
Available online 15 April 2024

## 1. Introduction

$^{18}$F-Fluorodeoxyglucose (FDG) positron emission tomography (PET), often co-registered with computerized tomography (PET/CT), can identify inflammatory vascular lesions and has shown very good sensitivity to diagnose giant cell arteritis (GCA) [1,2], particularly in cases with a large-vessel (LV) GCA phenotype [2,3].

Whereas its role in the diagnosis of GCA is well established, the appropriate role of PET/CT for monitoring LV-GCA activity has not yet been established [4]. After initiation of anti-inflammatory treatments (e.g., methotrexate, prednisone, and tocilizumab), previous studies have shown that basal FDG vascular uptake significantly decreased, especially after eight months of follow-up [5,6]. This metabolic regression is generally correlated with clinical and biological improvement [7,8]. However, other studies have observed the persistence of a vascular uptake in PET/CT performed in patients considered to be in remission, as defined by an absence of clinical signs and normal C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR) [9]. In their observational retrospective study, Prieto-Pena *et al.* reported on 30 patients with LV-GCA followed during 10.8 ± 3.7 months and demonstrated a significant reduction in vascular uptake after treatment. However, a complete normalization of vascular uptake was achieved in less than one third of patients [10]. It is hypothesized that the persistence of a low-grade vascular uptake could reflect smoldering inflammation or post-inflammatory vascular remodeling [11].

This raises questions about the value of PET/CT in predicting the risk of subsequent relapse. In a recent prospective observational study, Grayson et al. analyzed 170 PET/CT performed in 56 LV-GCA patients. Using a semi-quantitative score adding the uptake grade of several vascular territories (PETVAS), the authors showed that a PETVAS ≥20 points in a PET/CT performed after the initiation of treatment was associated with an increased risk of relapse during a median follow-up of 15 months (55 vs 11 %) [12]. By contrast, PETVAS was not associated with subsequent relapses in the study of Galli *et al.* [11]. The fact that these studies contradict each other may be due to differing designs, small numbers of patients, relatively short follow-up and the use of different scores. We therefore set out to investigate the value of initial (PET1) and follow-up (PET2) PET/CT, analyzed using two scores (PETVAS and Total Vascular Score [TVS]), in predicting the risk of occurrence of subsequent relapse. By using the two most commonly used scores, our aim was to be able to compare our results with a large number of other studies and practices in nuclear medicine.

## 2. Patients and methods

### 2.1. Study population

We conducted an observational retrospective study in 12 French centers including 10 academic centers. The study was supported by the French Study Group for Large Vessel Vasculitis (GEFA). This study was conducted in accordance with good clinical practice and the principles of the Declaration of Helsinki. In accordance with French law, informed consent was not required for this study. Patients with LV-GCA were diagnosed between 2009 and 2020.

All patients fulfilled new ACR/EULAR classification criteria for GCA [13] and : i) were ≥50 years at diagnosis, ii) had a history of sedimentation rate ≥50 mm/h or CRP ≥10 mg/L, iii) had at least one clinical sign of GCA or polymyalgia rheumatica, iiii) and had proof of vasculitis (positive temporal artery biopsy [TAB] or evidence of large vessel vasculitis [aorta or supra-aortic trunks] by angio-CT, PET-CT and/or angio-MRI). All patients presented large-vessel vasculitis (LVV) on PET/CT at the time of diagnosis of GCA.

For all patients, PET/CT was performed at diagnosis (PET1), within 3 weeks of initiation of corticosteroid therapy, and during follow-up (PET2), 3 to 12 months after diagnosis, while GCA was in remission.

### 2.2. FDG-PET protocol

$^{18}$FDG PET/CT (diagnostic and follow-up) were performed according to usual conditions in each participating center. PET was coupled with a low-dose CT scan in patients with a plasma glucose level (glycemia < 7 mmol/L). The acquisition was performed 60 to 90 min after the $^{18}$FDG injection (3 MBq/kg). For examinations performed at the investigating center, the PET images were reconstructed using an OSEM algorithm and an attenuation correction mode.

Physicians performed a semi-quantitative assessment of FDG uptake by visual assessment of arterial territories, each scored on a visual scale of 0 to 3, based on established criteria [14], comparing arterial hypermetabolism with liver uptake: 0 = no uptake, 1 = low grade uptake (< liver uptake), 2 = intermediate grade uptake (= liver), 3 = high grade uptake (> liver). PET/CT was considered positive if at least one arterial segment had a grade ≥ 2 uptake.

Two vascular activity scores were assessed: 1 - the Total Vascular Score (TVS), the sum of the Meller score [7] composed of 14 arterial territories, ranging from 0 to 42 points, including carotid arteries [$n$ = 2], subclavian arteries [$n$ = 2], axillary arteries [$n$ = 2], ascending thoracic aorta, aortic arch, descending thoracic aorta, abdominal aorta, iliac arteries [$n$ = 2], and femoral arteries [$n$ = 2]) [14]; and 2 - the PET Vascular Activity Score (PETVAS), with 9 arterial territories, ranging from 0 to 27 points, including ascending aorta, aortic arch, descending aorta, abdominal aorta, brachiocephalic trunk, carotid arteries [$n$ = 2], and subclavian arteries [$n$ = 2] [12]. Contrary to TVS, PETVAS does not include the arteries of the lower limbs, for which the interpretation of uptake can be disturbed by atheroma [14].

### 2.3. Data collected and definition of relapse

Clinical, biological and therapeutic data were collected retrospectively by the investigators in each center using a standardized case report form (available in sup data), until the most recent follow-up.

Relapse was defined, after a remission period of at least 3 months, as the recurrence of clinical signs of GCA or polymyalgia rheumatica whatever the value of CRP, or an inflammatory syndrome (CRP >10 mg/L) for at least 2 consecutive weeks without any other cause than GCA and leading to an intensification of the treatment of GCA (prednisone, DMARDs (disease-modifying antirheumatic drugs) and/or biologics).

### 2.4. Statistical analysis

Continuous variables are expressed as medians (interquartile range) and categorical variables as numbers (%).

Analyses of relapse-free survival rates between diagnosis and first relapse, estimating the discriminatory power of PET1, were performed on the entire population. Survival analyses between the PET2 and the first relapse, estimating the discriminatory power of PET2, were performed after excluding patients who had relapsed before PET2. Survival curves estimating the relapse rate of GCA during follow-up were drawn using the Kaplan-Meier method from diagnosis to the first relapse and from PET2 to the first relapse. Time-dependent receiving-operating-characteristic (ROC) curves and area under the ROC curve (AUC) predicting GCA relapse by PET/CT scores (TVS and PETVAS) were estimated at different follow-up times from PET1 and from PET2. For the AUC predicting GCA relapse from PET2 by scores, the analyses were adjusted for steroid dose at the time of PET2 (in mg per day) and for delay from GCA diagnosis to PET2 (in days) using a Cox regression model. In addition, we measured the correlation between PET/CT scores (TVS and PETVAS) and the time to lower the steroid dose to the following threshold after PET2, defined as 15 mg/d, 10 mg/d, 7.5 mg/d, 5 mg/d and 0 mg/d, in order to highlight the possible prescribing bias induced by knowledge of PET/CT results when choosing how to taper the steroid dose. Statistical analyses were performed using R (version 4.1.1) and time-dependent ROC curves drawn with the *"timeROC"*

package [15].

## 3. Results

### 3.1. Characteristics of the study population

We collected data for 87 patients with LV-GCA diagnosed by PET/CT between January 2009 and May 2020, of whom 22 were excluded (3 PET2 performed > 12 months after diagnosis and 19 patients for missing data). Therefore, 65 patients were included in the analysis to estimate the discriminatory power of PET1. We then excluded a further 10 patients (4 due to relapse before PET2, 6 because PET2 was performed during a relapse), leaving 55 patients to estimate the discriminatory power of PET2 (Fig. 1).

Characteristics of included patients are summarized in Table 1. All 65 patients met the 2022 ACR/EULAR criteria [13] with diagnostic PET evidence of LVV. The population was mainly women ($n = 50$; 77 %) with a median age of 69 years at diagnosis. At GCA diagnosis, the main cardiovascular risk factors were active smoking (26 %) and arterial hypertension (28 %). Common general signs included weight loss (55 %) and fever (32 %). One in two patients had cephalic symptoms including headache (48 %) and jaw claudication (25 %). Only five (8 %) patients described visual disorders (amaurosis [$n = 3$], acute anterior ischemic optic neuropathy [$n = 1$], diplopia [$n = 1$]). Temporal arterial biopsy was performed in 59 patients (91 %) and was positive in 53 % of cases. All patients received prednisone at a dose of 0.7 to 1 mg/kg/day at diagnosis and three patients received pulses of methylprednisolone.

At PET1, the median vascular activity scores were 24 (19 - 30) for TVS and 21 (16 - 26) for PETVAS. Vascular activity scores (TVS and PETVAS) decreased in all patients between PET1 and PET2 (**supplementary Figure 1**). At PET2, all 55 patients were free of clinical signs with a median CRP level of 5 mg/L (0–10) and a median prednisone dose of 9 mg/day (5 - 15). In addition to prednisone, 6 patients were receiving tocilizumab and 4 patients methotrexate.

### 3.2. Relapses

During the follow-up period of 42.5 months (19.3 −72.0 months), 28/65 (43 %) patients experienced at least one relapse. At the time of the first relapse, 24 patients were still receiving prednisone, 3 patients were treated with tocilizumab and one with methotrexate. Among the 55 patients for whom PET2 was available during remission of GCA, 18 relapsed during the subsequent follow-up. In this population, median survival from PET2 until the first relapse was not reached. After PET2, the probability of relapse was 30 % after 1 year and 41 % and 2 years of follow-up (Fig. 2).

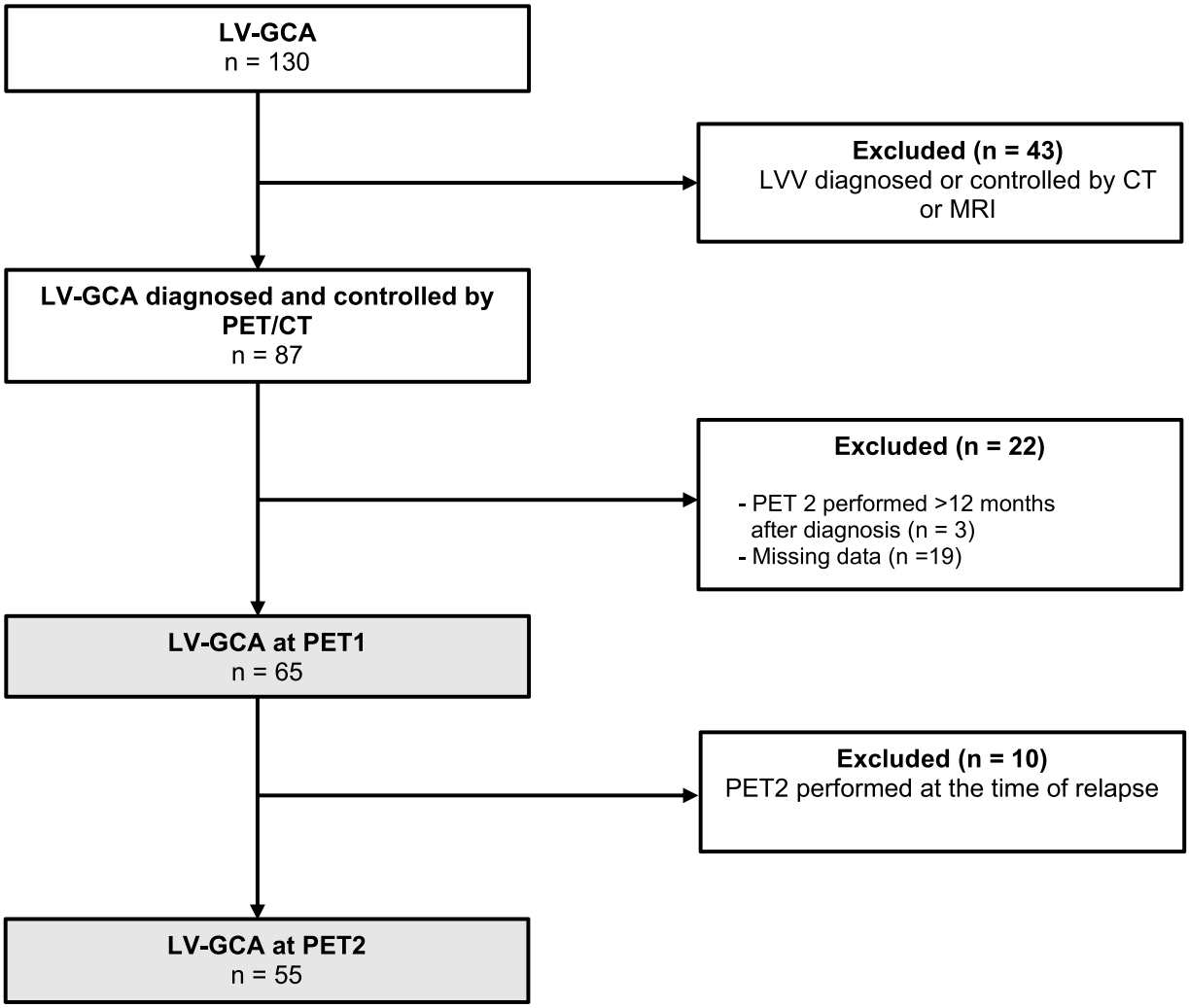


**Fig. 1.** Flow chart of the study
LVV: Large-vessel vasculitis; LV-GCA: Large-vessel giant cell arteritis; MRI: Magnetic resonance imaging.
CT: scanner; MRI: magnetic resonance imaging; PET: positron emission tomography; PET/CT: positron emission tomography/scanner.

**Table 1**
Description of the studied population.

| Population at PET1 (GCA diagnosis) | $n = 65$ |
|---|---|
| Age (years), median (IQR) | 69 (64 –74) |
| Female sex, n (%) | 50 (77 %) |
| Cardiovascular risk factors, *n (%)* | |
| Active smoking | 17 (26 %) |
| Arterial hypertension | 18 (28 %) |
| Dyslipidemia | 10 (15 %) |
| Diabetes | 6 (9.2 %) |
| History of cardiovascular disease, *n (%)* | |
| Ischemic cardiopathy | 1 (1.5 %) |
| Peripheral arterial disease | 2 (3.1 %) |
| Stroke | 2 (3.1 %) |
| GCA symptoms, *n (%)* | |
| Weight loss | 36 (55 %) |
| Fever | 21 (32 %) |
| Cephalic signs | 34 (53%) |
| Headache | 31 (48 %) |
| Scalp tenderness | 13 (20 %) |
| Jaw claudication | 16 (25 %) |
| Visual signs | 5 (7.7 %) |
| Clinical abnormality of temporal artery | 16 (25 %) |
| Stroke | 3 (4.6 %) |
| Polymyalgia rheumatica | 23 (35 %) |
| Biology | |
| Hemoglobin (g/dL), median (IQR) | 11.2 (10.3 - 11.8) |
| CRP (mg/L), median (IQR) | 74 (42 - 106) |
| Temporal artery biopsy, n (%) | |
| Positive | 31/59 (53 %) |
| Doppler US-scan of temporal arteries | |
| Available data | 28/65 |
| Positive** | 15/28 |
| PET1 | |
| TVS, median (IQR) | 24 (19 - 30) |
| PETVAS, median (IQR) | 21 (17- 26) |
| **Population at PET2** | ***n* = 55** |
| Time between PET1 and PET2 (month), median (IQR) | 7 (5 - 9.6) |
| PET2 | |
| TVS, median (IQR) | 7 (2–14) |
| Delta TVS, median (IQR)*** | −15 (−20, −7) |
| PETVAS, median (IQR) | 6 (2–12) |
| Delta PETVAS, median (IQR)*** | −12 (−19, −6) |
| Prednisone dose (mg/day), median (IQR) | 9 (5 - 15) |
| CRP (mg/L), median (IQR) | 5 (0–10) |
| Occurrence of relapse after PET2, n (%) | 18 (33 %) |

*Positive temporal artery biopsy = *a* mononuclear inflammatory infiltrate of the media and/or intima.

** Positive doppler of temporal arteries = halo sign on at least one temporal artery.

*** Delta TVS and delta PETVAS are the differences of scores between PET1 and PET2 (a negative value indicates a lower score at TEP2).

PET: positron emission tomography; TVS: total vascular score; PETVAS: PET vascular activity score.

### 3.3. Value of PET/CT for predicting subsequent relapses

First, we studied the discriminatory power of PET1 to predict occurrence of relapse among our population of 65 patients. The AUC of the TVS was 51.9 at 6 months, 55.3 at 1 year, 55 at 2 years and 62.3 at 3 years. The AUC of the PETVAS was 41.9 at 6 months, 49.7 at 1 year, 55.7 at 2 years and 61.9 at 3 years. The ROC curves are shown in Fig. 3.

Second, the discriminatory power of PET2 to predict relapse was estimated in the 55 patients who had a follow-up PET/CT during a period of remission. The AUC was adjusted for the dose of prednisone (mg/day of prednisone equivalent) at the time of PET2 and for the delay from GCA diagnosis to the follow-up PET/CT (in days). The adjusted AUC of the TVS was 46.1 at 3 months, 52.1 at 6 months, 51.4 at 1 year and 58.4 at 2 years. The adjusted AUC of the PETVAS was 46.7 at 3 months, 48.9 at 6 months, 48.3 at 1 year and 52.3 at 2 years (Fig. 4).

Furthermore, we investigated the correlation between PET2 vascular activity scores (TVS and PETVAS) and time to prednisone taper after PET2. To this end, we analyzed regression lines and correlation

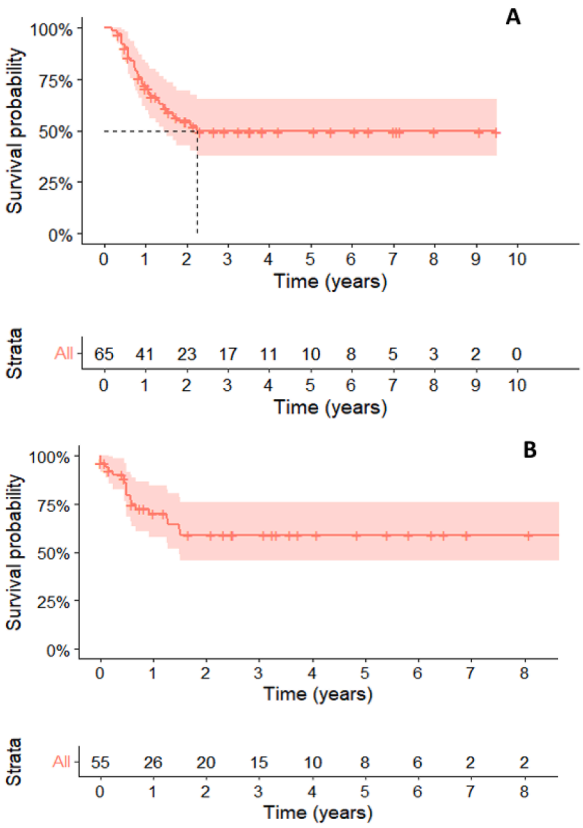


**Fig. 2.** Relapse-free survival curves
A: Time from diagnosis to first relapse; B: Time from control PET/CT (PET2) to first relapse.

coefficients between TVS and PETVAS scores and the time lapse before the prednisone dose was lowered to the next threshold, defined as 15 mg/d, 10 mg/d, 7.5 mg/d, 5 mg/d or 0 mg/d, in order to highlight the possible prescribing bias induced by knowledge of PET/CT results when establishing the course of prednisone dose tapering. We found no correlation between prednisone taper and PET/CT results for either TVS ($r = 0.259$, $p = 0.054$) or PETVAS ($r = 0.198$, $p = 0.14$), which suggests that clinicians did not significantly take the PET2 result into account when deciding whether to continue tapering prednisone or not (Fig. 5).

## 4. Discussion

PET/CT plays an increasingly important role in the diagnosis of GCA, especially LV-GCA [4,16]. GCA activity is monitored through clinical signs and biological markers of inflammation, particularly CRP. However, the increasing use of tocilizumab for the treatment of GCA complicates the follow-up of these patients, since tocilizumab blocks the production of the main markers of inflammation (CRP, fibrinogen) and consequently interferes with the ESR [17,18]. As a result, the use of PET/CT to monitor GCA activity has increased dramatically in recent years. Therefore, it is important for clinicians to be able to analyze PET/CT images precisely and in more detail, using a semi-quantitative approach that allows scores to be assessed.

Two scores are currently used: the TVS and, more commonly, the PETVAS, the latter of which does not include the arteries of the lower limbs in the calculation of the score, as these are arterial segments often affected by atherosclerotic lesions that can lead to hypermetabolism on PET-CT without true vasculitis [12]. The value of these scores correlates well with the activity of the vasculitis. TVS [19,20] and PETVAS [11,12] are indeed higher at GCA diagnosis than when GCA is in remission under treatment. PETVAS is able to distinguish clinically active and inactive

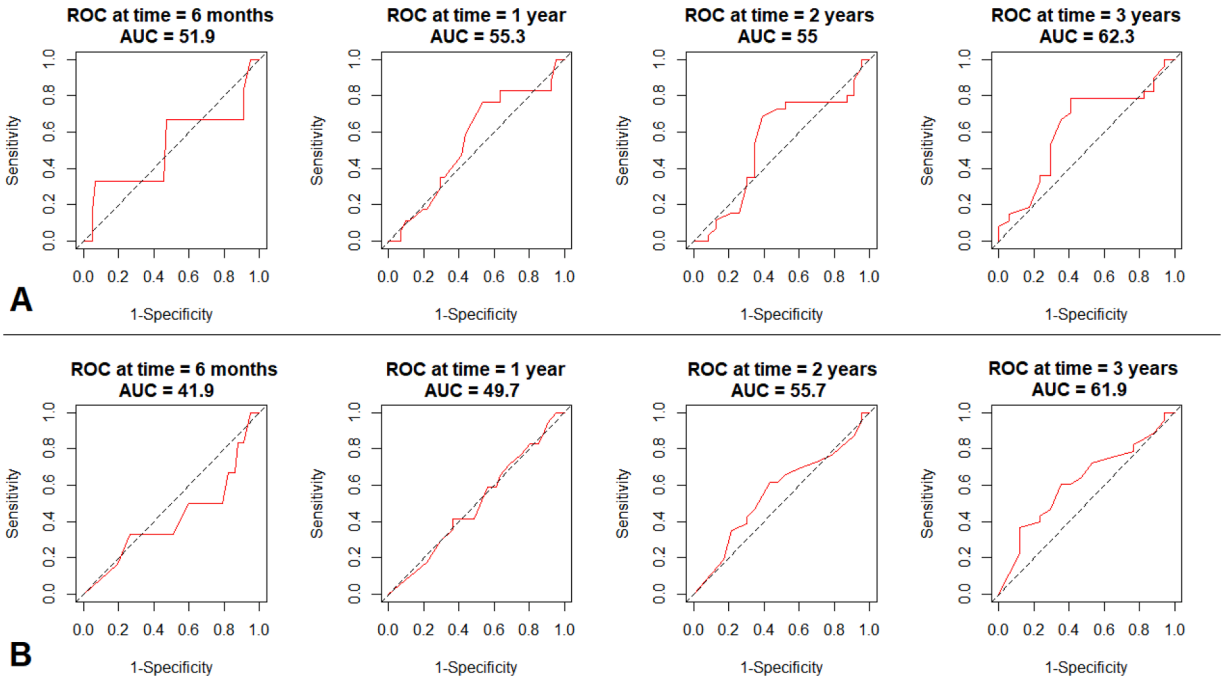


**Fig. 3.** AUC of TVS and PETVAS at PET1 for predicting relapses (A) AUC of the TVS. (B) AUC of the PETVAS.

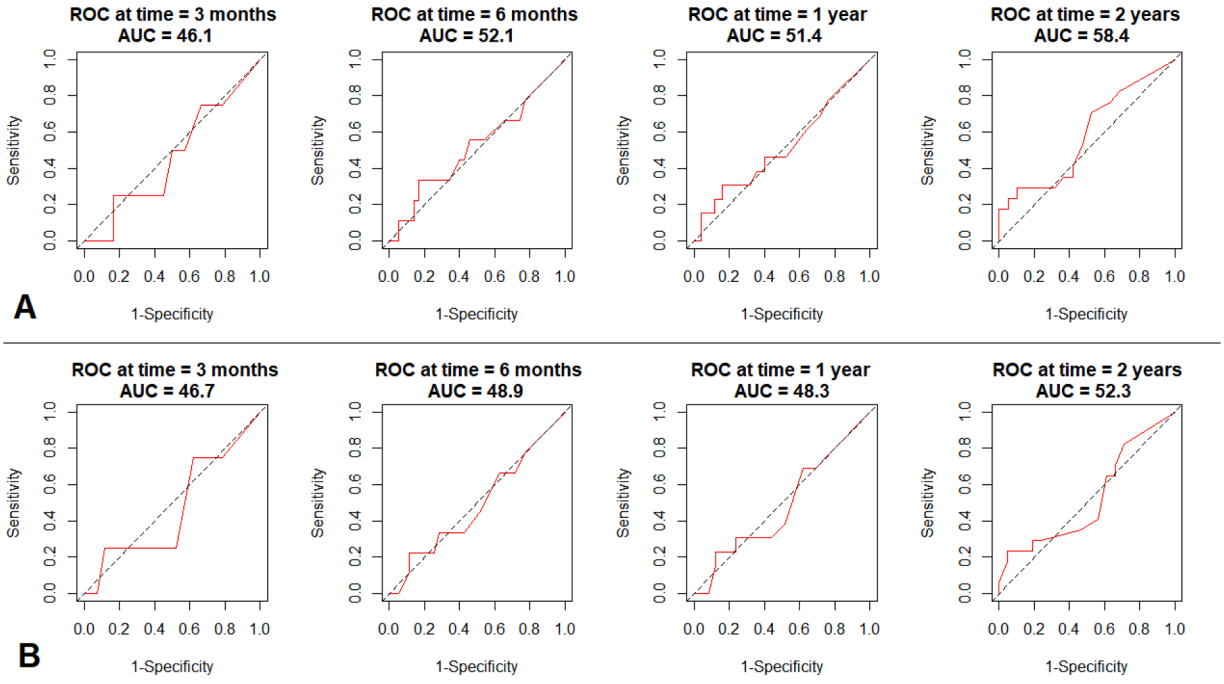


**Fig. 4.** AUC of TVS and PETVAS at PET2 for predicting relapses (A) AUC of the TVS. (B) AUC of the PETVAS.

LVV with a sensitivity of 60 % and a specificity of 80 %, with a PETVAS ≥10 threshold [11]. However, 80 % of patients with GCA in apparent remission retain hypermetabolic segments on PET-CT. This raises the question of the predictive value of this persistent hypermetabolism [21].

In the present study, our results demonstrate that neither PETVAS nor TVS was predictive of occurrence of subsequent relapse, with all AUCs close to 0.5 for both scores. This suggests that PET-CT may help clinicians to assess the activity of vasculitis at a given time, but not to predict its evolution in the medium or short term and therefore to adjust the follow-up or treatment of patients.

Our results are in line with those of other studies, which often included patients with GCA or Takayasu arteritis in both TVS [19,20] and PETVAS [11]. The study by Grayson et al. is one of the few to show that the value of PETVAS can predict the risk of relapse during subsequent follow-up [12]. They performed a prospective analysis of patients with Takayasu's arteritis ($n$ = 26) and GCA ($n$ = 30) who underwent serial PET/CT at 6-months interval during the course of the disease. After centralized review PET/CT, the risk of relapse was compared between patients with PETVAS < or ≥ 20 points thus showing that PETVAS ≥ 20 during follow-up was associated with an increased risk of relapse compared to patients with PETVAS < 20 points (55% vs 11 %, $p$ = 0.003). These differences between the results of the Grayson et al. study

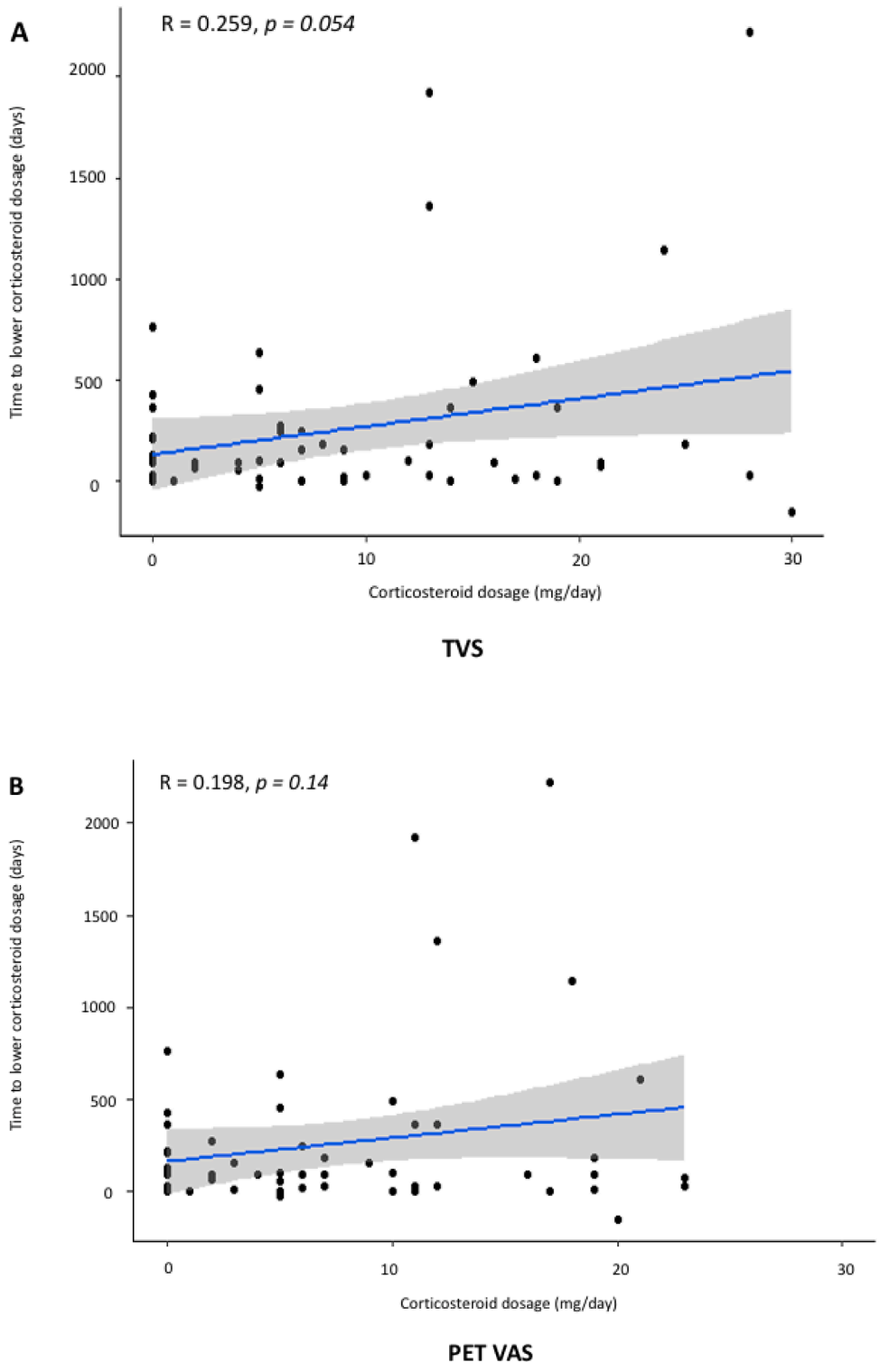


**Fig. 5.** Regression lines and correlation coefficients between TVS and PETVAS at PET2 and time to corticosteroid taper (15 mg / 10 mg / 7.5 mg / 5 mg / 0 mg).

and our study may be explained by several factors. First, the Grayson et al. study included patients with GCA and Takayasu's arteritis, whereas our study included only GCA. Secondly, the 26 patients with GCA in the Grayson et al. study had GCA for 2.6 +/- 2.7 years at the time of inclusion, whereas all patients in our study had their first PET-CT scan at the time of diagnosis of GCA. It is therefore possible that the patients included in the Grayson et al. study were more refractory than those in our study and therefore at greater risk of relapse. This may explain why some of them maintained a PETVAS of more than 20 points, which is relatively high. In fact, only 4/55 (7 %) patients in our study had a PETVAS > 20 points at the time of PET2.

In addition, a number of factors may affect the results of follow-up PET/CT and explain the heterogeneity of results in these studies [11, 12,19-21], including the treatment of GCA and the time elapsed between diagnosis and follow-up PET/CT. Some authors have indeed suggested that the metabolic response is greater with methotrexate and tocilizumab than with prednisone alone [8]. In our cohort, most patients were treated with prednisone, which did not allow us to identify a difference

between the two groups.

In most studies, the lack of association between the persistence of low vascular activity and an increased risk of relapse raises questions about the persistence of smoldering inflammation [11]. This could of course correspond to low-grade vascular inflammation, but the fact that it is not significantly associated with an increased risk of relapse suggests that this is not always the case. It is also possible that the semi-quantitative approach (grade 0–3) used to assess the TVS and PETVAS scores is not sensitive enough to discriminate precisely between patients with active and inactive disease. It would therefore probably be useful to have more quantitative approaches based on standard uptake values. We also hypothesized that glucose consumption detected by $^{18}$FDG PET/CT can be assumed by non-inflammatory cells involved in vascular remodeling, such as smooth muscle cells and myofibroblasts, which proliferate in the arterial wall and whose activation and proliferation is less controlled by treatments such as prednisone [22,23]. New tracers other than $^{18}$FDG could help to discriminate inflammation from vascular remodeling. Along this line, recent data have shown that $^{68}$Ga-DOTATATE PET/MRI, that specifically links to somatostatin receptors expressed by activated macrophages, had excellent sensitivity for detecting vascular inflammation in GCA and TAK [24]. Its ability to correlate better with GCA activity than $^{18}$FDG PET/CT, to predict risk of relapse or even to distinguish between inflammation and vascular remodeling has not yet been investigated but could lead to major advances in the coming years.

We acknowledge that our study has some limitations. First, patients were included in different centers from 2009 to 2020 with various PET techniques and resolutions. Systematic centralized double reading of all PET/CT was not possible due to the retrospective nature of our study. However, all PET/CT were interpreted by at least one nuclear physician, including a standardized semi-quantitative evaluation [25]. In addition, PET1 were performed within 3 weeks of initiation of corticosteroid therapy, a period during which the sensitivity of PET/CT could be reduced by the treatment. Another limitation is that the clinician prescribing the PET2 was aware of the imaging results, which may have influenced therapeutic decision making and therefore the risk of relapse.

In conclusion, our study in patients with evidence of LVV in PET/CT at the time of diagnosis shows that the extent of vascular hypermetabolism measured by FDG PET/CT at the diagnosis of GCA or during follow-up within 3 to 12 months, whether assessed by PETVAS or TVS, is not sufficiently discriminatory to assess the risk of relapse or to guide therapy.

## CRediT authorship contribution statement

**Anne-Claire Billet:** Methodology, Project administration, Writing – original draft. **Thomas Thibault:** Formalanalysis, Writing – original draft. **Éric Liozon:** Investigation. **Hubert De Boysson:** Investigation. **Laurent Perard:** Investigation. **Olivier Espitia:** Investigation. **Aurélie Daumas:** Investigation. **Cécile-Audrey Durel:** Investigation. **Arnaud Hot:** Investigation. **Boris Bienvenu:** Investigation. **SébastienHumbert:** Investigation. **Claude Bachmeyer:** Investigation. **Sabine Mainbourg:** Investigation. **Thomas Sené:** Investigation. **Hervé Devilliers:** Investigation. **Bastien Durand Bailloud:** Formal analysis. **Hélène Greigert:** Investigation. **Alexandre Cochet:** Formal analysis. **Bernard Bonnotte:** Methodology, Project administration,Investigation. **Jean-Louis Alberini:** Methodology, Project administration, Formal analysis. **Maxime Samson:** Methodology, Project administration, Investigation, Writing – original draft.

## Disclosures

**Maxime Samson**: Argenx (consulting), Boerhinger Ingelheim (consulting), Chugai (consulting), CSL Vifor (consulting), Fresenius Kabi (consulting), GSK (consulting), Novartis (consulting and research grant)

## Acknowledgements

We thank Thibault Maillet, Cécile Straub, and Eric Monard for their help with data collection. We thank Suzanne Rankin for her help in reviewing the manuscript.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2024.03.037.

## References

[1] Lariviere D, Benali K, Coustet B, Pasi N, Hyafil F, Klein I, et al. Positron emission tomography and computed tomography angiography for the diagnosis of giant cell arteritis: a real-life prospective study. Med (Baltimore) 2016;95:e4146.
[2] Sammel AM, Hsiao E, Schembri G, Nguyen K, Brewer J, Schrieber L, et al. Diagnostic accuracy of positron emission tomography/computed tomography of the head, neck, and chest for giant cell arteritis: a prospective, double-blind, cross-sectional study. Arthritis Rheumatol 2019;71:1319–28.
[3] Fuchs M, Briel M, Daikeler T, Walker UA, Rasch H, Berg S, et al. The impact of 18F-FDG PET on the management of patients with suspected large vessel vasculitis. Eur J Nucl Med Mol Imaging 2012;39:344–53.
[4] Dejaco C, Ramiro S, Bond M, Bosch P, Ponte C, Mackie SL, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice: 2023 update. Ann Rheum Dis 2023.
[5] Quinn KA, Dashora H, Novakovich E, Ahlman MA, Grayson PC. Use of 18F-fluorodeoxyglucose positron emission tomography to monitor tocilizumab effect on vascular inflammation in giant cell arteritis. Rheumatol (Oxford) 2021;60:4384–9.
[6] Sebastian A, Kayani A, Prieto-Pena D, Tomelleri A, Whitlock M, Mo J, et al. Efficacy and safety of tocilizumab in giant cell arteritis: a single centre NHS experience using imaging (ultrasound and PET-CT) as a diagnostic and monitoring tool. RMD Open 2020;6.
[7] Meller J, Strutz F, Siefker U, Scheel A, Sahlmann CO, Lehmann K, et al. Early diagnosis and follow-up of aortitis with [(18)F]FDG PET and MRI. Eur J Nucl Med Mol Imaging 2003;30:730–6.
[8] Schonau V, Roth J, Tascilar K, Corte G, Manger B, Rech J, et al. Resolution of vascular inflammation in patients with new-onset giant cell arteritis: data from the RIGA study. Rheumatol (Oxford) 2021;60:3851–61.
[9] de Boysson H, Liozon E, Lambert M, Parienti JJ, Artigues N, Geffray L, et al. 18F-fluorodeoxyglucose positron emission tomography and the risk of subsequent aortic complications in giant-cell arteritis: a multicenter cohort of 130 patients. Med (Baltimore) 2016;95:e3851.
[10] Prieto Pena D, Martinez-Rodriguez I, Atienza-Mateo B, Calderon-Goercke M, Banzo I, Gonzalez-Vela MC, et al. Evidence for uncoupling of clinical and 18-FDG activity of PET/CT scan improvement in tocilizumab-treated patients with large-vessel giant cell arteritis. Clin Exp Rheumatol 2021;39(Suppl 129):69–75.
[11] Galli E, Muratore F, Mancuso P, Boiardi L, Marvisi C, Besutti G, et al. The role of PET/CT in disease activity assessment in patients with large vessel vasculitis. Rheumatol (Oxford) 2022;61:4809–16.
[12] Grayson PC, Alehashemi S, Bagheri AA, Civelek AC, Cupps TR, Kaplan MJ, et al. (18) F-Fluorodeoxyglucose-positron emission tomography as an imaging biomarker in a prospective, longitudinal cohort of patients with large vessel vasculitis. Arthritis Rheumatol 2018;70:439–49.
[13] Ponte C, Grayson PC, Robson JC, Suppiah R, Gribbons KB, Judge A, et al. 2022 American college of rheumatology/EULAR classification criteria for giant cell arteritis. Ann Rheum Dis 2022;81:1647–53.
[14] Slart R. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging 2018;45:1250–69.
[15] Blanche P, Dartigues JF. Jacqmin-Gadda H. Estimating and comparing time-dependent areas under receiver operating characteristic curves for censored event times with competing risks. Stat Med 2013;32:5381–97.
[16] Bardi M, Diamantopoulos AP. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice summary. Radiol Med 2019;124:965–72.
[17] Maz M, Chung SA, Abril A, Langford CA, Gorelik M, Guyatt G, et al. 2021 American college of rheumatology/vasculitis foundation guideline for the management of giant cell arteritis and takayasu arteritis. Arthritis Rheumatol 2021;73:1349–65.
[18] Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2020;79:19–30.
[19] Blockmans D, de Ceuninck L, Vanderschueren S, Knockaert D, Mortelmans L, Bobbaers H. Repetitive 18F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: a prospective study of 35 patients. Arthritis Rheum 2006;55:131–7.
[20] Sammel AM, Hsiao E, Schembri G, Bailey E, Nguyen K, Brewer J, et al. Cranial and large vessel activity on positron emission tomography scan at diagnosis and 6 months in giant cell arteritis. Int J Rheum Dis 2020;23:582–8.
[21] de Boysson H, Aide N, Liozon E, Lambert M, Parienti JJ, Monteil J, et al. Repetitive (18)F-FDG-PET/CT in patients with large-vessel giant-cell arteritis and controlled disease. Eur J Intern Med 2017;46:66–70.

[22] Corbera-Bellalta M, Garcia-Martinez A, Lozano E, Planas-Rigol E, Tavera-Bahillo I, Alba MA, et al. Changes in biomarkers after therapeutic intervention in temporal arteries cultured in Matrigel: a new model for preclinical studies in giant-cell arteritis. Ann Rheum Dis 2014;73:616–23.
[23] Greigert H, Genet C, Ramon A, Bonnotte B, Samson M. New Insights into the Pathogenesis of Giant Cell Arteritis: mechanisms Involved in Maintaining Vascular Inflammation. J Clin Med 2022;11.
[24] Corovic A, Wall C, Nus M, Gopalan D, Huang Y, Imaz M, et al. Somatostatin Receptor PET/MR Imaging of Inflammation in Patients With Large Vessel Vasculitis and Atherosclerosis. J Am Coll Cardiol 2023;81:336–54.
[25] Puppo C, Massollo M, Paparo F, Camellino D, Piccardo A, Shoushtari Zadeh Naseri M, et al. Giant cell arteritis: a systematic review of the qualitative and semiquantitative methods to assess vasculitis with 18F-fluorodeoxyglucose positron emission tomography. Biomed Res Int 2014;2014:574248.