Evidence for uncoupling of clinical and ^{18}-FDG activity of PET/CT scan improvement in tocilizumab-treated patients with large-vessel giant cell arteritis

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ABSTRACT

Objective. *Clinical improvement following tocilizumab (TCZ) therapy in patients with large-vessel (LVV) giant cell arteritis (GCA) is well established. However, information on TCZ effect on imaging vascular activity is limited. We aimed to determine if clinical improvement correlated with reduction of vascular ^{18}F-fluorodeoxyglucose (^{18}F-FDG) uptake in positron emission tomography (PET/CT) scans.*

Methods. *Observational study of patients with refractory LVV-GCA treated with TCZ who had a baseline and a follow-up ^{18}F-FDG-PET/CT scan. For the visual analysis of ^{18}F-FDG vascular uptake, a total vascular score (TVS) was defined, ranging from 0 to 15. Besides, a semiquantitative analysis was performed as a target to background ratio (TBR)= SUVmax thoracic aorta wall/SUVmax aortic vascular pool. The baseline and follow-up TVS and TBR were compared. Clinical and laboratory outcomes were also assessed.*

Results. *We included 30 patients (24 women/6 men); mean age±standard deviation 65.7±9.8 years. Baseline PET/CT scans were performed due to active disease at a median [interquartile range-IQR] of 1.5 [0.0–4.0] months before TCZ onset. Following TCZ therapy, 25 (83.33%) patients achieved clinical remission and reduction of ^{18}F-FDG vascular uptake was also observed after a mean ± standard deviation of 10.8±3.7 months. TBR decreased from 1.70 ± 0.52 to 1.48 ± 0.25 (p=0.005) and TVS from 4.97±2.62 to 3.13±1.89 (p< 0.001). However, only 9 (30.0%) patients showed complete normalisation of TBR and only 3 (10%) normalisation of TVS. TBR and TVS showed a good correlation (r=0.576).*

Conclusion. *Although most LVV-GCA patients achieve clinical remission after TCZ therapy, less than one-third show normalisation of ^{18}F-FDG vascular uptake.*

Introduction

Giant cell arteritis (GCA) is a large-vessel vasculitis (LVV) that mainly affects individuals older than 50 years from Europe and North America (1). Classically, GCA affects cranial arteries derived from the external carotid artery. However, it can also involve extracranial large vessels, such as the aorta and its main branches. In this regard, the advent of new imaging techniques has been of great help to identify the presence of extracranial LVV in patients who did not complain of cranial ischaemic manifestations (2, 3).

Some imaging techniques, such as computed tomography angiography (CT-A) or magnetic resonance imaging angiography (MRI-A), may yield negative results in early stages of vascular affection. In contrast, ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) has shown high sensitivity in detecting the presence of LVV during the earliest stages of the disease, even before the development of structural changes (4-7).

Extracranial LVV involvement is more commonly found in GCA patients than previously expected. It has been widely reported that over 50% of GCA patients who undergo a PET/CT scan show aortic involvement (8, 9). This technique often discloses the presence of LVV in patients presenting with polymyalgia rheumatica (PMR) features (2, 3). In addition, PET/CT scan has also shown to be useful to monitor disease activity during follow-up in patients with LVV-

GCA (10, 11). A positive result for LVV in PET/CT scan may have clinical and prognostic implications. In this regard, patients with LVV involvement have higher risk for developing severe complications, such as aneurysms, stenosis and aortic dissection (12). Therefore, as recently highlighted by Felicetti *et al*. (13), an early and adequate therapy and close follow-up is needed in LVV-GCA patients to prevent life-threating consequences.

Glucocorticoids are the cornerstone of GCA treatment. However, adjuvant therapy is usually required due to a high rate of relapses and the development of side-effects related to glucocorticoids. Nowadays, Tocilizumab (TCZ) is the only approved agent by the European Medicine Agency (EMA) and the Food and Drug Administration (FDA) for the treatment of GCA. TCZ is a monoclonal anti-interleukin 6 (IL-6) receptor which has proved to be effective to induce remission, prevent relapses and decrease the cumulative prednisone dose in patients with GCA in both clinical trials and real-life studies (14-17). However, it remains unclear if TCZ also leads to a complete resolution of the vessel inflammation confirmed by imaging techniques.

Although vascular imaging techniques have been shown to play a relevant role in the evaluation of disease activity in LVV (18), information on imaging outcomes in patients with LVV-GCA diagnosis in response to immunosuppressive therapy is scarce. Blockmans *et al*. conducted a prospective study on 35 patients with LVV-GCA under glucocorticoid therapy who underwent serial PET/CT scans at 3 and 6 months. They found that FDG uptake decreased in response to glucocorticoids, but a sizable proportion of patients showed evidence of persistent subclinical vascular inflammation (19). The prognostic meaning of ongoing FDG vascular uptake was recently assessed by Grayson *et al*. (20) who found that the persistence of vascular activity in PET/CT scan in patients during clinical remission was associated with a higher risk for future clinical relapse. These insights suggest that glucocorticoids may not completely suppress the inflammatory response at the vessel wall. In this regard, we wondered if ongoing vascular inflammation may also occur in patients with LLV-GCA under TCZ therapy.

Taking all these considerations into account, the aim of this study was to assess if the achievement of clinical remission in patients with LVV-GCA treated with TCZ correlated with the normalisation of vascular ^{18}F-FDG uptake in PET/CT scans.

Patients and methods

Patients and study design

We conducted a single-centre observational study on patients diagnosed with LVV-GCA treated with TCZ who underwent a baseline and follow-up ^{18}F-FDG PET/CT scan from February 2012 to December 2019. All patients fulfilled the revised criteria for GCA defined in the protocol of GiACTA trial (21, 22) and exhibited LVV involvement confirmed by ^{18}F-FDG PET/CT.

Clinical assessment and definitions of disease activity

Disease activity was evaluated based on clinical features and laboratory parameters. Clinical symptoms included for assessment were headache, visual manifestations, polymyalgia rheumatica (PMR), constitutional symptoms, fever and limb claudication. Headache was considered to be present if it was of recent onset or had different characteristics than usual. Visual manifestations included blurred vision, diplopia, amaurosis fugax, unilateral or bilateral hemianopsia and permanent unilateral or bilateral blindness. PMR was based on EULAR/ACR 2012 classification criteria for PMR (23). Constitutional symptoms included asthenia, anorexia and weight loss greater than 5% of the normal body weight over the last 6 months. Fever was considered if temperature was ≥38ºC. Limb claudication was defined when the patient complained of muscle pain in the arms and/or legs on mild exertion.

Normalisation of acute phase reactants was considered if C-Reactive Protein (CRP) ≤0.5 mg/dL and/or erythrocyte sedimentation rate (ESR) ≤20 mm/1st hour.

Remission was defined if the patients were free of symptoms and had normalisation of the acute phase reactants (CRP and ESR).

^{18}F-FDG PET/CT imaging

Baseline PET/CT scans were performed due to active disease at a median [interquartile range-IQR] of 1.5 [0.0-4.0] months before TCZ onset. The time to perform a follow-up PET/CT scan was based on the attending physician decision.

Patients fasted for at least 6 hours before ^{18}F-FDG administration. The serum glucose level was lower than 160 mg/dL in all patients (FreeStyle Optimum glucose meter, Abbott, UK). Whole-body PET/CT including lower extremities was acquired 180 min after intravenous injection of 7 MBq/kg of ^{18}F-FDG. A Biograph LSO Pico 3D from Siemens Healthcare Molecular Imaging (Hoffman Estates, Illinois, USA) was used. First, we obtained a low dose CT scan without contrast enhancement for attenuation correction and anatomic localisation, followed by a PET scan, acquiring 250 sec per bed position. Reconstructed images were displayed in coronal, sagittal, and axial planes.

Imaging evaluation

Both visual and semiquantitative imaging evaluation was performed following the European Association of Nuclear Medicine/Society of Nuclear Medicine and Molecular Imaging (EANM/SNMMI) recommendations for LVV assessment by ^{18}F-FDG PET/CT (24). Images were evaluated in the same session by two experienced nuclear medicine physicians and the differences were solved by consensus. CT images were carefully analysed together with PET images in order to exclude the presence of atherosclerotic plaques that could show a focal FDG uptake.

For the visual analysis, ^{18}F-FDG uptake at the vessel wall was visually graded compared to liver uptake (0: no uptake, 1: less than liver, 2: equal to liver, 3: greater than liver). In addition, we defined for each patient a total vascular score for visual assessment considering 5 vascular regions (supra aortic trunks, thoracic aorta, abdominal aorta, iliac ar-

Table I. Baseline features at tocilizumab (TCZ) onset of the 30 patients with GCA included in the study.

Case	Age/Sex	GCA features	Temporal artery biopsy	ESR/CRP at TCZ onset	Treatment before TCZ
1	65/F	Cranial and LVV-GCA	Positive	45/2.4	Prednisone, MTX
2	72/F	Cranial and LVV-GCA	Positive	63/1.1	Prednisone, MTX
3	73/F	Cranial and LVV-GCA	Positive	46/0.8	Prednisone, MTX
4	82/F	Cranial and LVV- GCA	Positive	68/4.4	Prednisone, MTX
5	70/F	Cranial and LVV- GCA	Negative	8/0.3	Prednisone, MTX
6	67/F	Cranial and LVV- GCA	Positive	44/1.9	Prednisone, MTX
7	68/F	Cranial and LVV- GCA	Positive	10/0.6	Prednisone, MTX
8	65/F	LVV-GCA	Negative	39/2.3	Prednisone, MTX
9	65/F	LVV- GCA	Negative	51/1.1	Prednisone, MTX
10	60/F	LVV- GCA	Negative	89/3.0	Prednisone, MTX
11	55/F	LVV- GCA	Not performed	13/0.6	Prednisone, MTX
12	55/F	LVV- GCA	Not performed	39/0.2	Prednisone, MTX
13	48/F	LVV- GCA	Not performed	49/0.6	Prednisone, MTX
14	64/F	LVV- GCA	Not performed	15/0.5	Prednisone, MTX
15	72/M	LVV- GCA	Not performed	27/0.5	Prednisone, MTX
16	73/F	LVV- GCA	Negative	87/3.4	Prednisone, MTX
17	69/F	LVV- GCA	Negative	6/0.1	Prednisone, MTX
18	60/M	LVV- GCA	Not performed	7/1.4	Prednisone
19	85/F	LVV- GCA	Not performed	11/1.5	Prednisone, MTX
20	49/M	LVV- GCA	Not performed	10/1.0	Prednisone
21	65/F	LVV- GCA	Not performed	10/2.7	Prednisone, MTX
22	53/F	LVV- GCA	Not performed	2/0.1	Prednisone, MTX
23	65/F	LVV- GCA	Not performed	9/0.2	Prednisone, MTX
24	70/F	LVV- GCA	Negative	68/2.4	Prednisone, MTX
25	78/M	LVV- GCA	Negative	59/6.4	Prednisone, MTX
26	57/M	LVV- GCA	Negative	69/1.0	Prednisone, MTX
27	77/F	LVV- GCA	Negative	11/0.1	Prednisone, MTX
28	79/F	LVV-GCA	Not performed	21/4.2	Prednisone
29	48/M	LVV-GCA	Not performed	2/0.1	Prednisone
30	61/F	LVV-GCA	Not performed	4/1.2	Prednisone, MTX

CRP: C-reactive protein, expressed in mg/dl; ESR: erythrocyte sedimentation rate, expressed in mm/1st hour; F: female; GCA: giant cell arteritis; LVV: large-vessel vasculitis; M: male; MTX: methotrexate; TCZ: tocilizumab.

teries and, femorotibial arteries). Total vascular score ranged from 0 to 15 with higher scores indicating more intense and extensive vascular inflammation. Complete visual normalisation in follow-up PET/CT scans was considered when total vascular score= 0. We decided to analyse a more limited number of regions compared to other authors to simplify the results of the visual analysis, considering that these 5 territories included all the vessels involved in other approaches. Semiquantitative analysis of ^{18}F-FDG uptake was assessed as a target-to-background ratio (TBR) at the thoracic aorta. We have selected the thoracic aorta for this analysis as the most frequently involved vessel whose diameter and location allows an easily reproducible delimitation of the areas of interest. The aorta was checked and the region with the greatest intensity of uptake was considered for measuring the thoracic aorta wall maximum standardised uptake value (SUVmax). The TBR was obtained by dividing the thoracic aorta wall maximum standardised uptake value (SUVmax) by the blood pool SUVmax (25). Complete quantitative normalisation of 18F-FDG vascular uptake was considered when TBR at the thoracic aorta < 1.34, which is the cut-off established in a previous study including a control population (25).

Data collection and ethics

Data regarding demographics, previous treatments, clinical outcomes, laboratory parameters and ^{18}F-FDG PET/CT imaging measurements were collected and gathered according to the agreed protocol. Information was stored in a computerised database. The study was approved by the Local Clinical Research Ethics Committee (no 2018.080). Our study also adhered to the tenets of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using SPSS Statistics for Windows, v. 18.0 (SPSS Inc, Chicago, IL, USA). All continuous variables were tested for normality, and results were expressed as mean ± standard deviation (SD) or as median and interquartile range (IQR) as appropriate. Student's t-test or Mann-Whitney U-test were used to compare continuous variables, and chi-squared test for categorical variables. The comparison of continuous variables among time periods was performed using the Wilcoxon signed rank test. A p-value <0.05 was considered as statistically significant in all the calculations.

Results

Baseline data prior to TCZ onset

We included 30 patients (24 women/6 men); mean ± SD age 65.7±9.8 years. Among them, 7 (23.3%) patients had both cranial and LVV-GCA features whereas 23 (76.7%) patients had only LVV-GCA findings. Temporal artery biopsy was performed in 16 patients, being positive in 6 of them. The median [IQR] time from GCA diagnosis to TCZ onset was 6.5 [2.0-20.0] months. Besides glucocorticoids and before TCZ, 26 (86.7%) patients had received methotrexate (MTX). The main base-

line demographic data of the 30 GCA patients who were treated with TCZ are shown in Table I.

Before TCZ onset, all patients had received high-dose glucocorticoids, and most of them (86.7%) also MTX. Glucocorticoids were administered at an initial dose of prednisone between 40 and 60 mg/day and gradually tapered. The dose of MTX prior to TCZ ranged from 7.5 to 25mg/SC or OS/week.

TCZ therapy

TCZ was started when refractory symptoms and/or severe adverse events to previous therapy occurred. Patients were treated with TCZ as monotherapy or combined with MTX. TCZ was administered IV at a standard dose (8 mg/kg/4 weeks) or SC (162 mg/week). A written informed consent was obtained in those patients in whom TCZ was prescribed off-label before being approved by the EMA and the FDA for the treatment of GCA.

TCZ was initially administered IV to 21 (70%) patients and SC to 9 (30%). 7 of 21 patients who initially received IV TCZ were switched to SC TCZ during follow-up according to a shared decision between the patient and the attending physician. The maintenance dose of TCZ ranged from 8 mg/IV/kg/4 weeks to 4 mg/IV/kg/8 weeks, and from 162 mg/SC/week to 162 mg/SC/2 weeks. Regardless of glucocorticoids, TCZ was prescribed as monotherapy to 16 (53.3%) patients and combined with MTX in 14 (46.7%).

PET/CT scan imaging outcomes

All patients underwent a follow-up PET scan over a mean ± SD follow-up period of 10.8±3.7 months. At baseline assessment, the visual analysis showed that the thoracic aorta was the most commonly involved area (n=30), followed by supra-aortic trunks (n=20), abdominal aorta (n=17), femorotibial arteries (n=12) and iliac arteries (n=8). Most patients (n=26; 86.7%) showed vascular inflammation at different vascular territories, except for 4 patients who exhibited isolated thoracic aorta involvement. Overall, a decrease of FDG vascular uptake was observed following TCZ therapy. The TBR at the thoracic aorta decreased from a mean of 1.70±0.52 to 1.48±0.25 (p=0.005) (Fig. 1) and TVS from a mean of 4.97±2.62 to 3.13±1.89 (p<0.001). We observed a positive correlation between TBR and TVS measurements (r=0.576).

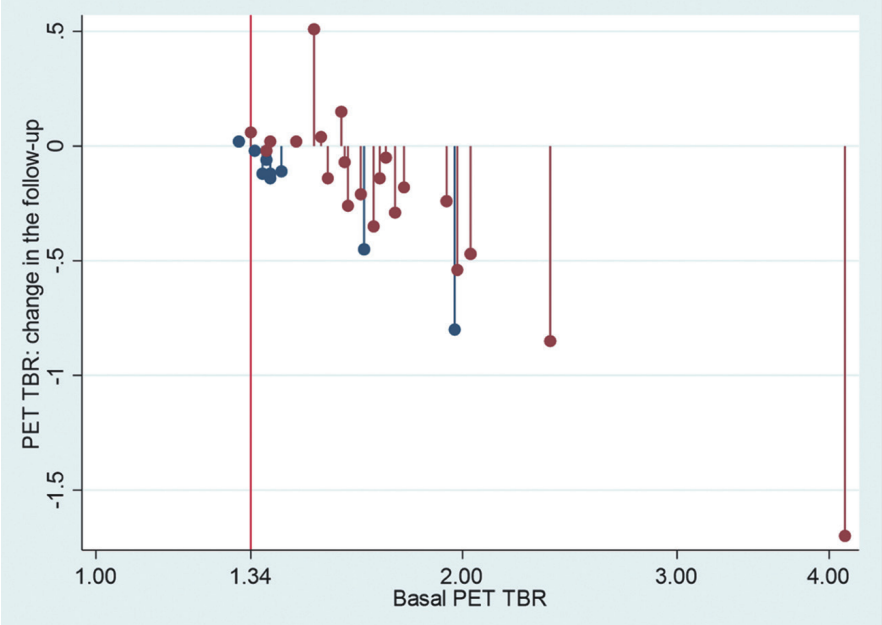

Fig. 1. Baseline values for PET TBR are represented in the x-axis. The change of PET TBR in the follow-up is represented in the y-axis. Blue points represent patients who normalised TBR (TBR < 1.34) after TCZ therapy, whereas, red points represent patients who did not.

Table II. Clinical, laboratory and ^{18}F-FDG vascular uptake improvement in the 30 patients with LVV-GCA diagnosis after TCZ onset.

	Baseline (n=30)	Follow-up (n=30)	*p*
Clinical improvement			
Remission, *n (%)*		25 (83.3)	
Laboratory markers			
ESR (mm/1st hour), *median [IQR]*	24.0 [10.0-53.0]	2.0 [2.0-3.0]	< 0.001
CRP (mg/dL), *median [IQR]*	1.0 [0.5-2.4]	0.1 [0.1-0.1]	< 0.001
Glucocorticoid therapy			
Prednisone dose (mg/day), *median [IQR]*	7.5 [5.0-10.0]	2.0 [0.0-5.0]	< 0.001
^{18}F-FDG vascular uptake			
Thoracic TBR, *mean ± SD*	1.70 ± 0.52	1.48 ± 0.25	0.005
Total vascular score, *mean ± SD*	4.97 ± 2.62	3.13 ± 1.89	< 0.001
Normalisation of TBR*, n (%)		9 (30)	
Normalisation of TVS**, n (%)		3 (10)	

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TBR: target-to-background ratio.
*Normalisation of TBR was considered when TBR <1.34.
**Normalisation of TVS was considered when TVS=0.

3 (10 %) patients had normalisation of TVS (Table II).

Figures 2 and 3 show various examples of PET/CT scans from patients who experienced complete normalisation of FDG vascular uptake in response to TCZ, in comparison to patients who exhibited persistent FDG vascular uptake despite the achievement of clinical remission after TCZ onset.

Correlation between clinical and PET/CT scan imaging outcomes

At the end of the follow-up period, 83.3% of patients achieved clinical remission. Conversely, only 9 of 30 patients (30%) showed normalisation of the TBR at the thoracic aorta and only

Discussion

Clinical efficacy of TCZ for GCA has been widely reported. However, it re-

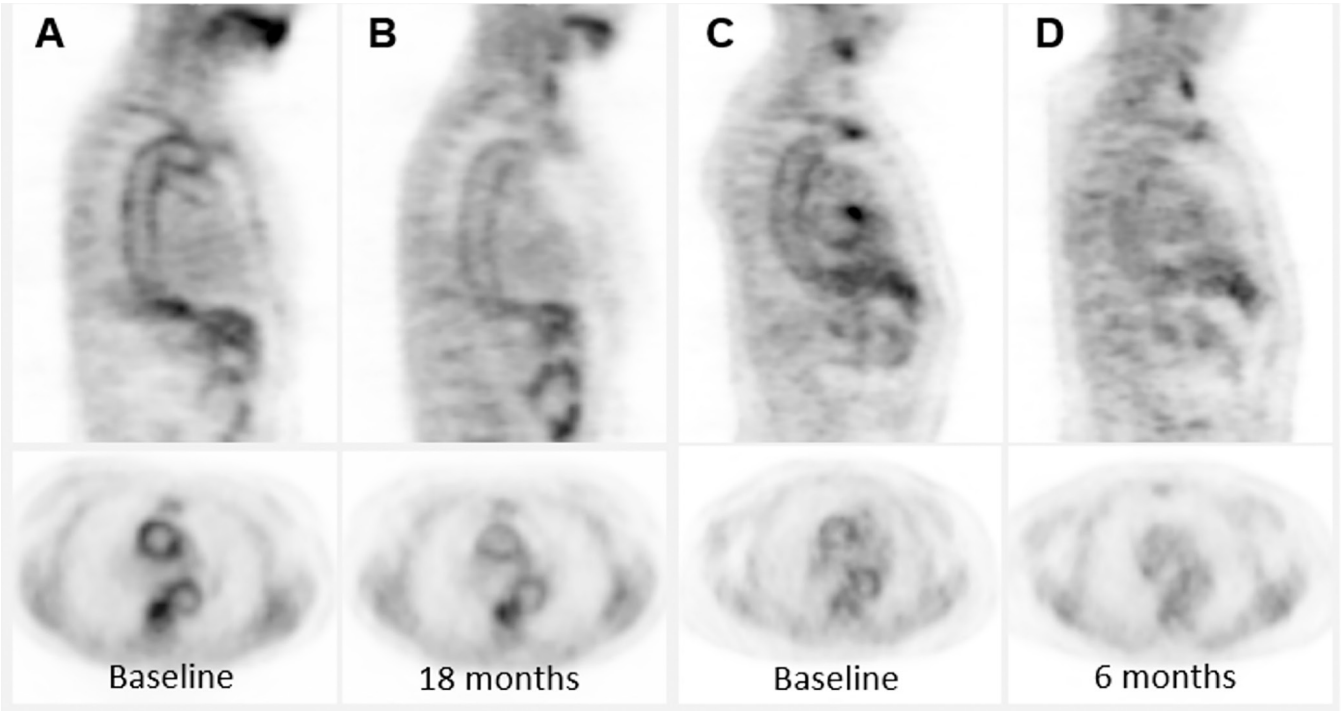

Fig. 2. **A**: PET images of a 64-year-old woman showed a baseline total vascular score (TVS) of 3 at the thoracic aorta and a TBR (target-to-background ratio) of 2.03. **B**: Both parameters decreased 18 months after treatment to 2 and 1.56, respectively. **C**: PET images of 67-year-old woman showed a baseline TVS of 3 at the thoracic aorta and a TBR of 1.97, **(D)** decreasing 6 months after treatment to a TVS of 0 and a TBR of 1.17. (Upper row: sagittal slices, lower row: axial slices).

mains to be unknown if TCZ also leads to a complete resolution of vascular inflammation in imaging techniques. In this regard, we present a series of 30 GCA patients under TCZ therapy in whom normalisation of vascular ^{18}F-FDG uptake was assessed by ^{18}F-FDG PET/CT scan. Overall, a decrease in vascular uptake was observed in line with clinical improvement. However, complete normalisation of vascular^{18}F-FDG uptake was only observed in about one third of the patients despite clinical remission.

Our results are in keeping with those from Grayson *et al*. (20), who observed in a prospective study involving 56 patients with LVV (30 with GCA and 26 with Takayasu's arteritis (TAK)) that follow-up FDG-PET/CT scans showed active vascular inflammation that often was not correlated with the clinical assessment. In this study, 58% of patients during clinical remission exhibited active vasculitis in the follow-up PET/CT scans. These patients were treated with glucocorticoids and, some of them, with immunosuppressive drugs.

In this line, Sammel *et al*. (26) reported persistence of grade 2 vascular uptake in at least one vascular territory in 5 of the 15 (33%) patients with GCA treated with glucocorticoids and immunosuppressive drugs. Our results showed a higher rate of persistent vascular uptake. This could be explained because we considered grade ≥1 vascular uptake as positive for active vasculitis in the follow-up PET/CT scans.

Recently, Banerjee *et al*. (11) also assessed the effect of immunosuppressive therapy on FDG vascular uptake in 52 patients with LVV (GCA=31 and TAK=21). Fourteen (82%) of 17 patients treated with TCZ experienced clinical remission while normalisation of visual vascular FDG uptake was only observed in 3 (18%) patients.

Interestingly, in agreement with our findings, Reichenbach *et al*. (27) conducted a randomised controlled trial that included 9 patients with GCA treated with TCZ and glucocorticoids and 4 patients who only received glucocorticoids. Although clinical remission was achieved in all patients who received TCZ, magnetic resonance angiography (MRA) only disclosed 3 patients (33%) showing normalisation of vessel wall signals after 52 weeks of treatment. In the group of patients who only received glucocorticoids, only 1 of the 4 patients showed normalisation of MRA findings. Since histological specimens of the aortic wall in patients with LVV are seldom available, it remains to be known whether the persistent increase in FDG uptake in the vessel wall in patients who are in clinical remission corresponds to subclinical vasculitis, vascular remodelling, or a combination of both. In this regard, Grayson *et al*. (20), found that subclinical vascular inflammation is likely to be a major contributor to the persistent FDG vascular uptake observed during clinical remission since a higher risk for clinical relapse over a median follow-up of 15 months was observed in these patients. In contrast, Sammel *et al*. (26) reported that ongoing FDG vascular uptake was not predictive for clinical relapse in the subsequent 6 months. However, this study involved a smaller number of patients (only 5 patients showed persistent vascular uptake) and the follow-up period was shorter.

Interestingly, Rubbert-Roth *et al*. (28) found evidence of histopathologic residual inflammation in patients with LVV diagnosis during TCZ therapy. They reported 3 patients with LVV-GCA diagnosis receiving TCZ therapy who underwent surgery due to aortic

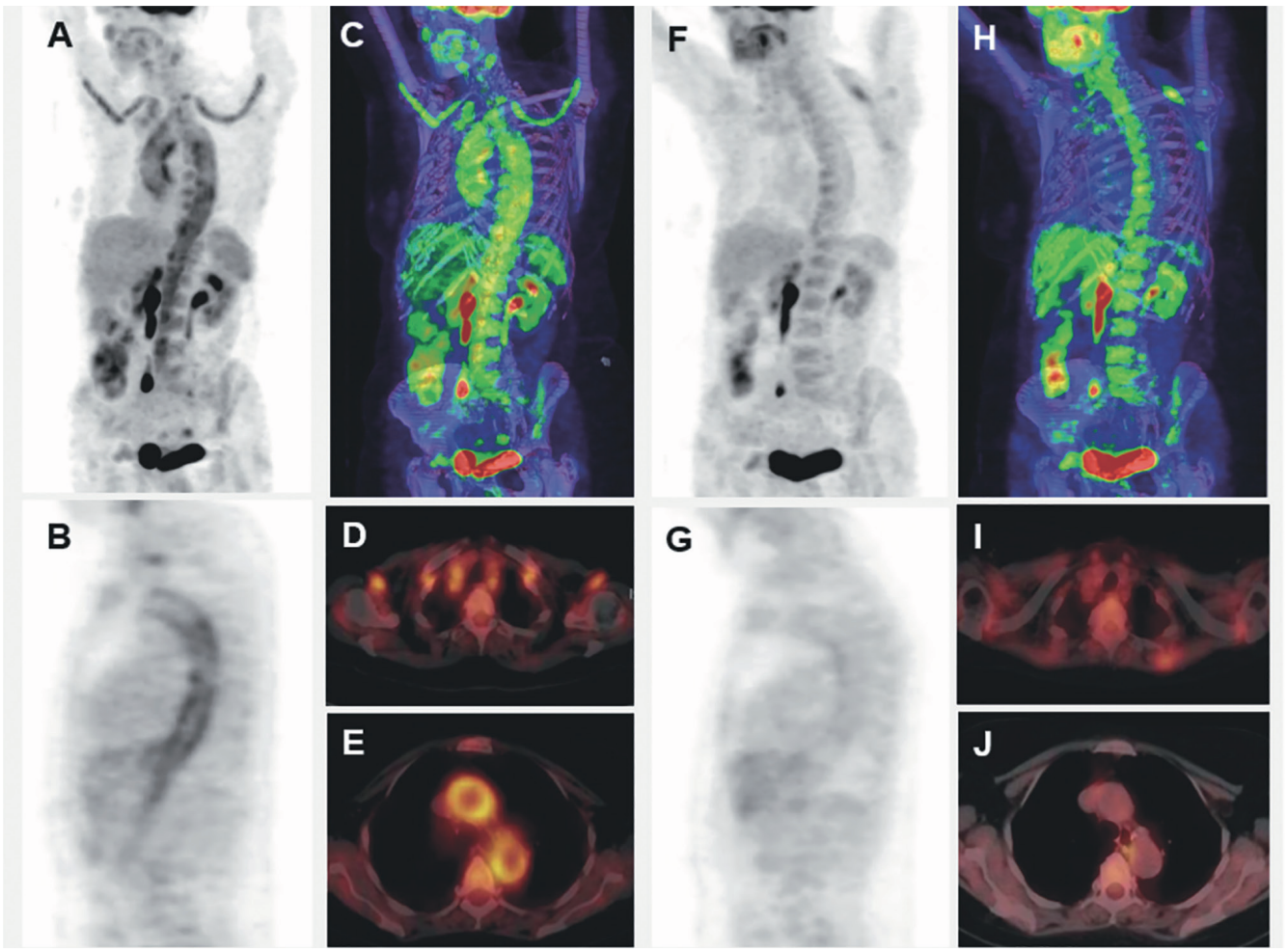

Fig. 3. Baseline PET (**A**, **B**) and fused PET/CT images (**C**-**E**) of a 71 year-old-woman, showed an intense FDG uptake along the thoracic and abdominal aorta, brachiocephalic trunk, subclavian and axillary arteries (TVS: 3; TBR at the thoracic aorta: 2.36). Follow-up PET (**F**, **G**) and fused PET/CT images (**H**-**J**) performed 24 months after tocilizumab showed the disappearance of uptake at the brachiocephalic trunk, subclavian and axillary arteries and an important decrease of aortic uptake (TVS: 1; TBR: 1.37). (TBR: target-to-background ratio; TVS: total vascular score).

complications (2 aortic aneurysm, 1 aortic dissection). At the time of surgery, laboratory markers were normal and imaging techniques (MRI and PET/CT) showed remission. However, the histopathological assessment of the aortic wall revealed persistent lymphoplasmacellular infiltrates and giant cells. These findings are in line with former autopsy studies. With respect to this, Unizony *et al*. described persistent vascular inflammation involving the brachiocephalic, subclavian, carotid, vertebral, and femoral arteries at autopsy of a patient with GCA diagnosis who experienced substantial clinical response to TCZ (29).

These insights indicate that the persistent FDG uptake observed in PET/CT scans may reflect subclinical active vascular inflammation. The complex pathophysiology of GCA can explain these findings. GCA pathogenesis is characterised by a predominance of T helper (Th) 17 cells secreting IL-17 and Th1 cells secreting interferon-γ (IFN-γ) over regulatory T cells (Treg). Initial Th17 response is believed to lead to the glucocorticoid-sensitive systemic inflammatory features of GCA. While, in late phases, Th1 response produce IFN-y that seems to be responsible of the glucocorticoid resistant ischaemic manifestations (30-31). TCZ through IL-6 receptor blockage restores the physiological Treg/Th17 balance, which explains substantial proportion of its clinical efficacy. However, Th1 response and consequently IFN-y production is only partially blocked by TCZ therapy. This could explain the persistence of subclinical vascular inflammation in patients with GCA treated with TCZ.

The main limitation of our study is related to its retrospective nature. However, there are also several strengths that are worth mentioning. The most important are the monocentric design of the study with the inclusion of LVV-GCA patients homogeneously evaluated and the careful analysis of the imaging by dedicated nuclear medicine physicians. Because of that, we excluded patients with a diagnosis of TAK or other LVV-associated diseases who could yield different responses to TCZ. Moreover, nuclear medicine physicians were blinded to clinical outcomes to avoid risk of bias. Both visual and semiquantitative imaging assessment was performed to double-confirm large-vessel activity. In addition, since strict criteria to establish the presence of normalisation in the visual analysis were applied, we only considered as normal if there was a complete absence of vascular uptake.

In conclusion, our results confirm that

there is a discordance between clinical and imaging activity assessment by PET/CT scan in patients with LVV-GCA undergoing TCZ therapy. Most patients showed persistent vascular activity in PET/CT scans despite clinical remission. These findings raise important questions on whether TCZ leads to a real suppressive effect on the underlying pathophysiology of GCA.

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Competing interests

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