18F-FDG PET/CT in the follow-up of large-vessel vasculitis: a study of 37 consecutive patients

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F-FDG PET/CT in the follow-up of large-vessel vasculitis: a study of 37 consecutive patients.

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Abbreviations

$^{18}$F-FDG : $^{18}$F-Fluorodeoxiglucose

CRP : C-reactive protein

CT : computed tomography

ESR : erythrocyte sedimentation rate

GCA : giant cell arteritis

IQR : interquartile range

LVV : large-vessel vasculitis

PMR : polymyalgia rheumatica

PET/CT : positron emission tomography/computed tomography

TBR : target-to-background ratio

SD : standard deviation

SUVmax : maximum standardized uptake value
Abstract

**Objective.** $^{18}$F-FDG PET/CT has proved to be of potential value for early diagnosis of large-vessel vasculitis (LVV), which frequently involves the aorta. However, its role in the follow-up of these patients has not been well established. Our aim was to evaluate the contribution of $^{18}$F-FDG PET/CT in this clinical situation.

**Methods.** This study included 37 consecutive patients (28 women, 66.5±9.9 y.) with an initial $^{18}$F-FDG PET/CT positive for LVV and a mean±standard deviation follow-up PET/CT of 7.5±2.9 months after the initial scan. A semiquantitative analysis of aortic wall uptake was performed calculating the target-to-background ratio (TBR: aortic wall uptake divided by blood pool uptake). The initial and follow-up TBR as well as the clinical and laboratory outcome were compared.

**Results.** Overall, the mean TBR decreased from 1.7±0.5 at the initial scan to 1.5±0.3 at the time of follow-up ($p=0.0001$). In the 21 patients who experienced clinical improvement following therapy the TBR also decreased from 1.8±0.6 to 1.5±0.3 ($p=0.0002$). However, in the other 16 patients, in whom the treating physician considered that there was no clinical improvement following therapy, no statistically significant differences in TBR were found when data from the first and the follow-up PET/CT scans were compared (1.6±0.3 vs. 1.5±0.3, $p=0.1416$). Patients who experienced clinical improvement following therapy showed a non-statistically significant higher TBR at the time of disease diagnosis (1.8±0.6 versus 1.6±0.3; $p=0.12$).

**Conclusions.** $^{18}$F-FDG PET/CT appears to be useful in the follow-up of LVV.

**Keywords:** Large vessel vasculitis; aortitis, giant cell arteritis; $^{18}$F-FDG PET/CT; positron emission tomography.
Introduction

Large-vessel vasculitis (LVV) typically involves the aorta and its major branches [1]. Giant cell arteritis (GCA) and Takayasu arteritis are the most common types of LVV [2, 3]. Nevertheless, non-infectious LVV may occur in the context of autoimmune and inflammatory diseases such as systemic lupus erythematosus, Sjögren’s syndrome, rheumatoid arthritis, spondyloarthropathies, ulcerative colitis, sarcoidosis, other systemic vasculitis and polymyalgia rheumatica (PMR) [4, 5, 6].

Patients with LVV often show non-specific clinical manifestations, including back or chest pain, malaise, weakness, weight loss, fever and increased levels of laboratory inflammatory parameters (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]). In some cases, structural imaging techniques may yield negative results in patients with early stages of the disease. In this context, a tool that may help us to make an early diagnosis of LVV could be of great relevance for clinicians.

$^{18}$F-FDG PET/CT was found to be of potential value to make an early diagnosis of large and medium vessels inflammation, even before the development of vascular structural changes [6-10]. It was also useful to establish the presence and extend of extracranial vasculitis in patients with GCA [7-11]. In this context, aortic involvement has been described in more than 50% of $^{18}$F-FDG PET/CT scans performed in patients with GCA [7, 8, 12, 13] and a positive PET/CT has been associated with a significantly higher risk of complications such as aneurysms, stenosis and aortic dissection [14]. In these patients an early and adequate therapy (including glucocorticoids with/without immunosuppressive drugs) and close follow-up is important to prevent these severe complications [2, 3].

Besides limitations for the early diagnosis of LVV, the structural imaging techniques have in some cases limitations in monitoring the vascular inflammatory activity. This fact highlights the need of a non-invasive sensitive tool for the follow-up of these patients in the clinical setting. In this context, the role of $^{18}$F-FDG PET/CT has not
been well established and, up to now, only a few studies involving a limited number of patients have been published with promising preliminary results [8, 15-18]. A recent guideline recommended the use of $^{18}$F-FDG PET/CT for the diagnosis of LVV. However, the authors of this guideline recognized that the utility of PET/CT in monitoring anti-inflammatory therapy response is still unknown and requires further clarification [19].

Taking all these considerations into account, the purpose of the present study was to evaluate the contribution of $^{18}$F-FDG PET/CT in the follow-up of patients with LVV.
Methods

Patients

This study included 38 consecutive patients with LVV who were evaluated by $^{18}$F-FDG PET/CT scan and showed abnormal $^{18}$F-FDG uptake involving mainly the aorta. One patient was excluded due to technical problems and poor quality of PET/CT images. Therefore, we assessed 37 patients (28 women and 9 men, mean± standard deviation [SD] age: 66.5±9.9 y.). Table 1 summarizes the main characteristics of the patients, including the features that led to perform PET/CT scan to determine the presence of LVV and the medical treatment at the time of the initial PET/CT.

All patients included in this study had an initial $^{18}$F-FDG PET/CT scan positive for aortitis and a follow-up $^{18}$F-FDG PET/CT carried out 3-12 months after the initial scan (mean time± SD: 7.5±2.9 months).

Twelve of the 37 patients had a previous diagnosis of typical “isolated” PMR, 3 atypical PMR, 6 GCA, 1 retroperitoneal fibrosis, 1 panuveitis, 1 rheumatoid arthritis, and 1 psoriatic arthritis. For the diagnosis of GCA and PMR the American College of Rheumatology classification criteria [20], and the criteria proposed by Chuang et al [21] were used. Atypical PMR was defined when patients presented aches and pain resembling PMR and did not fulfill the quoted criteria. $^{18}$F-FDG PET/CT scan was requested in patients with PMR, inflammatory arthritis and autoimmune diseases to determine the presence of LVV if they had persistent fever, inflammatory low back pain, diffuse lower limb pain, constitutional symptoms, lack of improvement with low-medium dose oral glucocorticoids and/or unexplained increase of ESR and CRP. In patients with GCA a PET/CT scan was performed to demonstrate extracranial involvement due to poor clinical response to glucocorticoids, unexplained low back, upper or lower limb pain, persistently increased ESR and CRP levels or relapses of the disease.

In the remaining 12 patients a PET/CT scan was performed because of the presence of non-specific symptoms, mainly fever, asthenia, weight loss. In these cases
other conditions including autoimmune diseases and neoplasms had previously been excluded. In these 12 patients a diagnosis of “idiopathic” LVV vasculitis was made based on the PET/CT scan findings, the response to treatment and the clinical outcome over the extended follow-up.

Twenty-three out of the 37 patients (62.2%) were under long-term treatment (mean± SD: 42.6±35.5 months) at the time of the initial scan: 19 patients with glucocorticoid therapy (median: 10 of prednisone mg/day, interquartile range [IQR]: 4.5-12.5) with or without methotrexate (median: 10 mg/week, IQR: 10-15) or anti-IL6 receptor tocilizumab therapy (median: 8 mg/kg/iv/month), and 4 patients with less than two months of glucocorticoid therapy (median: 20 of prednisone mg/day, IQR: 12.5-50).

Clinical and laboratory (ESR and CRP) assessment of patients was performed at the time of first PET/CT scan and also at the time of the follow-up PET/CT scan.

Clinical improvement was assessed in each patient based on the information included in the medical records. The treating physician considered that the patient had improved when clinical symptoms such as polymyalgia features, cranial ischemic manifestations, constitutional symptoms or other manifestation related to the underlying disease improved following therapy.

The institutional review board has approved the study and all patients signed a written informed consent.

\(^{18}\text{F-FDG PET/CT imaging}\)

Patients fasted for at least 6 hours before \(^{18}\text{F-FDG injection}. The serum glucose level was lower than 160 mg/dL in all patients (FreeStyle Optimum glucose meter, Abbott UK). There were no differences between the mean serum glucose level at the time of the first and at the time of the follow-up PET/CT scan (94.9±17.9 vs. 102.4±28.6, \(p=0.1937\)). 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 localization, followed by a PET scan, acquiring 250 sec per bed position. Reconstructed images were displayed in coronal, sagittal, and axial planes.

For image evaluation, a semiquantitative analysis of $^{18}$F-FDG uptake at the aortic wall was performed, calculating a target-to-background ratio (TBR) both for the initial and follow-up PET/CT scan. The TBR was obtained by dividing the aortic wall maximum standardized uptake value (SUVmax) by the blood pool SUVmax [22]. The entire aorta was checked and the area with the greatest intensity of uptake was considered for measuring the aortic wall SUVmax. CT images were carefully analyzed together with PET images in order to exclude the presence of atherosclerotic plaques that could show a focal FDG uptake. The initial and follow-up TBR and the clinical and biochemical outcome were compared.

Statistical analysis

All continuous data were expressed as mean± SD or median and IQR. The Mann-Whitney U test was applied to determine the significance of the differences (statistical significance was established at $p$ values <0.05). All the calculations were performed using AnalystSoft Biostat Version 2009 for Windows (AnalystSoft Inc., Vancouver, Canada).
Results

Overall, the mean± SD TBR decreased significantly from 1.7±0.5 in the initial PET/CT scan to 1.5±0.3 in the PET/CT scan follow-up (p=0.0001). Twenty-one of the 37 patients evaluated (56.8%) experienced clinical improvement after the initial PET/CT scan and 16 patients (43.2%) had no clinical improvement. In the 21 patients with clinical improvement the mean TBR decreased significantly from 1.8±0.6 to 1.5±0.3 (p=0.0002). However, in the other 16 patients, in whom the treating physician considered that there was no clinical improvement following therapy, no statistically significant differences in TBR were found when data from the first and the follow-up PET/CT scans were compared (1.6±0.3 vs. 1.5±0.3, p=0.1416) (Table 2).

In assessing inflammatory laboratory markers, the mean ESR was 40.3±35.8 mm/1st hour (normal: 1-20 mm/1st hour) at the time of the initial PET/CT scan and decreased to 23.9±22.2 mm/1st hour at the time of the follow-up scan (p=0.0591). The mean CRP was 2.5±4.9 mg/dL at the time of the initial PET/CT scan and 1.1±1.4 mg/dL at the time of the follow-up scan (normal: <0.5 mg/dL), p=0.3343.

We observed a reduction of ESR and/or CRP in 23 of the 37 patients (62.2%) during the follow-up. In these patients the mean TBR decreased significantly from 1.8±0.6 to 1.5±0.3 (p=0.0062). To our surprise, in the other 14 patients (37.8%) who did not show decrease of ESR and/or CRP at the time of the follow-up PET/CT scan, the TBR also decreased from 1.7±0.3 to 1.4±0.1 (p=0.0041).

Patients who experienced clinical improvement following therapy showed higher TBR at the time of disease diagnosis (1.8±0.6 versus 1.6±0.3) but the difference did not reach statistical significance (p=0.1291).

TBR at the time of the follow-up PET/CT scan decreased significantly from 1.7±0.2 to 1.5±0.3 in the 23 patients who were receiving medical treatment at the time of the first PET/CT scan assessment (p=0.0055). A TBR reduction at the time of the follow-up was also observed in the 14 patients who did not receive medical treatment.
when the first PET/CT scan was performed (1.8±0.7 to 1.4±0.3; \( p=0.0086 \)) (Table 3). Figure 1 shows the decrease of aortic wall \(^{18}\)F-FDG uptake after 12 months of glucocorticoid and methotrexate therapy in a representative patient who experienced good clinical and laboratory response.

In a further step, we analyzed the clinical implication of the information shown in the first \(^{18}\)F-FDG PET/CT scan in the management of the 37 patients. Based on these data, clinicians in charge of the patients modified the treatment in 21 of the 23 patients who were on treatment at the time of the initial PET/CT scan. In 16 of the 21 patients the corticosteroid dose was increased and methotrexate was also added in 12 of them. In the remaining 5 patients, tocilizumab therapy was added to the glucocorticoid treatment. Figure 2 shows a representative patient with GCA initially treated with glucocorticoids who had aortic inflammation confirmed by the initial PET/CT. Due to refractory disease characterized by relapses when prednisone dose was tapered, methotrexate was added. However, no clinical improvement was achieved and in a second PET/CT scan a TBR increase was observed. In addition, the new PET/CT showed supraaortic trunks involvement (arrows). Because of that, intravenous tocilizumab therapy was prescribed with clinical improvement associated with decreased TBR (\(^{18}\)F-FDG uptake).

Following the first PET/CT scan medical treatment with glucocorticoids alone (n= 5) or associated with methotrexate (n= 6) or with methotrexate alone (n= 1) was started by the treating clinician in 12 of the 14 patients who had not been treated prior to the first PET/CT scan. These results indicate that a positive PET/CT scan had clinical implication to make a change in the treatment in most patients.

As shown in Table 4, the change in the therapy in 21 patients, characterized by increase in the dose of prednisone and/or the use of additional therapies such as methotrexate and/or tocilizumab, was associated with a significant reduction of TBR at the time of the PET/CT scan follow-up (1.5±0.3 versus 1.7±0.2 in the first study,
In addition, a statistically significant reduction of TBR following therapy was observed in those patients in whom therapy was started after the first PET/CT scan (1.5±0.3 versus 1.9±0.8, \(p=0.0094\)).

In assessing specifically the change of TBR for each patient, we observed that TBR decreased in the follow-up in 30 (81.1\%) of 37 patients. Among these 30 patients, the mean TBR decrease was significantly higher (\(p=0.0431\)) in the 19 patients who experienced clinical improvement (19.6±11.9\%) when compared with the 11 patients in whom the reduction of TBR was not associated with clinical improvement (11.8±12.9\%). Among the 7 patients without reduction of TBR in the follow-up PET/CT scan, the mean increase of the TBR in the 5 patients with clinical improvement was lower than in the 2 who did not show clinical improvement (TBR\% increase: 9.6±12.9\% vs. 12.4±9.4, \(p=0.4386\)).
Discussion

The role of $^{18}$F-FDG PET/CT scan in early diagnosis of LVV, evaluation of the extent of the disease [7, 8, 13] and also in the management of these patients [10, 23] has previously been established. In this regard, in a former report we emphasized the potential value of the semiquantitative analysis of $^{18}$F-FDG PET/CT images for the diagnosis of aortitis [11].

In the present study, we assessed the results obtained of the semiquantitative analysis of aortic $^{18}$F-FDG uptake because all of our patients had aortic inflammation demonstrated by PET/CT. We have also visually analyzed the $^{18}$F-FDG uptake in other vascular territories (not shown) and these results correlated well with those obtained for the aorta.

The results obtained in the present study support that $^{18}$F-FDG PET/CT may also be useful for monitoring the inflammatory activity in patients with LVV. In our series, the mean TBR decreased significantly during the follow-up in the group of patients who exhibited clinical improvement. However, in patients with poor clinical response no differences were found between the initial and the follow-up TBR results.

Previous studies have reported a decrease or even normalization of the vessel wall $^{18}$F-FDG uptake after treatment in relation to clinical and laboratory improvement. In a retrospective study based on a visual analysis of PET/CT images including a small number of patients, Bleeker-Rovers et al. reported the normalization of $^{18}$F-FDG vessel wall uptake in 5 patients with a follow-up PET/CT after therapy, which was in keeping with a good clinical and laboratory treatment response [15]. Meller et al. evaluated 6 patients with aortitis and PET/CT scan after starting immunosuppressive therapy. They described the normalization of $^{18}$F-FDG uptake in 80% of the regions with initial pathological uptake together with clinical improvement and normalization of the laboratory parameters and concluded that $^{18}$F-FDG PET/CT was more reliable than MRI for monitoring inflammatory activity [8]. Blockmans et al. evaluated 35 patients with GCA and reported a decrease of
18F-FDG uptake after 3 months of glucocorticoid therapy together with the disappearance of symptoms and the normalization of inflammatory parameters [16]. In another retrospective study, PET/CT scan and clinical and laboratory improvement was observed in 8 of 9 patients with LVV after 3 months of glucocorticoid treatment [17]. Henes et al. evaluated by PET/CT the response to cyclophosphamide in patients with refractory LVV and demonstrated a normalization of vascular 18F-FDG uptake in 9 of the 10 patients that was associated with good clinical and serological response, suggesting the usefulness of PET/CT as an additional tool for therapeutic decisions [25]. More recently, Bruls et al. performed a prospective study including 18 patients with aortitis and no previous glucocorticoid or immunosuppressive treatment. These authors described the disappearance of 18F-FDG uptake after surgery and/or immunosuppressive treatment along with clinical improvement in all patients [18].

Regardless of ESR and CRP results, a significant association between clinical improvement and TBR decrease was observed in our patients during the follow-up. This finding highlights the potential use of PET/CT scan to monitor the clinical outcome of patients with LVV. Therefore, we feel that data retrieved from PET/CT scan evaluation may mirror more accurately the presence of LVV involvement and the inflammatory state than the acute phase reactants- ESR and CRP. Moreover, we also observed changes not only restricted to the intensity of 18F-FDG uptake but also in the extent of the vascular involvement that were associated with clinical improvement.

There are some methodological aspects that we followed at the time of performing 18F-FDG PET/CT to assess imaging vascular inflammation in our patients with LVV. In this regard, in contrast to the 1-hour standard protocol applied in oncology, we feel that a delayed acquisition of images 2-3 hours after 18F-FDG injection is more appropriate allowing better visualization of vessel wall uptake [26-28]. As described in the section of Methods, we followed this procedure in our assessment. Experts in the field have indicated that for PET/CT image evaluation qualitative methods is more specific than the semiquantitative ones but they have lower sensitivity [29]. Based on that and also in our
own experience, we decided to apply in our study a semiquantitative analysis that allowed us the detection of subtle changes of $^{18}$F-FDG uptake during the follow-up. In this context, it is mandatory that the acquisition and analysis of images may be rigorously carried out, using the same conditions for the initial and follow-up scan. All these factors were considered in our study and may contribute to a more accurate assessment of vascular inflammatory activity.

In our experience, a residual $^{18}$F-FDG vascular uptake is very frequently observed, even in patients with clinical improvement. Thus, the follow-up mean TBR for patients with and without clinical improvement was higher than the cutoff of 1.34 established in a previous study including a control population [22]. This observation is in accordance with previous reports in which a persistent $^{18}$F-FDG vascular uptake has been described, even up to 80% of cases at 6 months [30]. This uptake, even observed in asymptomatic patients with normal laboratory inflammatory parameters, has been attributed to persistent inflammatory activity, vessel wall remodeling or immune resistance and was not related to relapse [16, 30]. However, no studies have been conducted to analyze in depth this finding and the causes remain unclear.

Remarkably, we observed that the initial mean TBR was higher in patients who experienced clinical improvement following therapy when compared to the patients without clinical improvement although the difference was not significant. Based on this finding, we can hypothesize that a higher initial TBR, reflecting a more intense inflammatory process, seems to identify a subgroup of patients who may be more susceptible to reach clinical improvement following therapy. We acknowledge that this observation needs to be confirmed in larger series of patients.

There is still controversy on the routine monitoring and follow-up assessment of the patients by $^{18}$F-FDG PET/CT. With respect to this, Blockmans et al. consider that $^{18}$F-FDG PET/CT offers no additional advantage over the follow-up based on the clinical and laboratory monitoring of patients [31]. Nevertheless, our results indicate that $^{18}$F-FDG
PET/CT may be useful for the management of these patients. However, it must take into account that repeated PET/CT scans determine radiation exposure and expenses, so $^{18}$F-FDG PET/CT would be especially indicated in patients with poor clinical response or suspicion of relapse after the decrease or withdrawal of therapy.

Our study has several limitations that should be considered. In most patients the follow-up PET/CT scan was requested due to a poor clinical outcome, which introduces a selection bias. In addition, baseline situation of the patients was very heterogeneous as more than sixty percent of our patients were already undergoing therapy when the first PET/CT scan was requested. With respect to this, the variability in the therapy and the different timing of follow-up PET/CT scans were also potential limitations. Nevertheless, we consider that our results reflect the real scenario in a clinical setting.

**Conclusions**

In conclusion, $^{18}$F-FDG PET/CT appears to be useful in the follow-up of patients with large-vessel vasculitis, especially in cases with poor clinical treatment response or suspicion of relapse after the decrease or withdrawal of therapy, having relevant therapeutic implications.
Acknowledgements

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References


Figure legends

**Figure 1.** Initial (A) and follow-up (B) PET/CT scan showing a decrease of aortic uptake after treatment.

**Figure 2.** Sequential PET/CT scans in a patient at different times of treatment.
### Table 1. Main features of the 37 patients included in the study at the time of the initial PET/CT scan.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Previous diagnosis</th>
<th>Clinical indication to perform PET/CT scan</th>
<th>Temporal artery biopsy</th>
<th>ESR/CRP at the time of PET/CT</th>
<th>Treatment at the time of initial PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68/M</td>
<td>Atypical PMR</td>
<td>Gluteus and lower limbs pain. Poor treatment response.</td>
<td>NP</td>
<td>0.1/2</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>2</td>
<td>62/F</td>
<td>PMR</td>
<td>Thoracic aorta aneurysm.</td>
<td>NP</td>
<td>1.1/33</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>67/F</td>
<td>GCA</td>
<td>Persistently increased ESR/CRP. Low back and limbs pain.</td>
<td>Positive</td>
<td>0.4/5</td>
<td>MTX (chronic)</td>
</tr>
<tr>
<td>4</td>
<td>60/F</td>
<td>No*</td>
<td>Fever, headache, good treatment response. Increased ESR/CRP.</td>
<td>Negative</td>
<td>3.7/57</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>50/F</td>
<td>No*</td>
<td>Ischemic heart disease (stents), aortofemorale bypass. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.9/7</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>68/F</td>
<td>No*</td>
<td>Fever, headache, asthenia, weight loss, anemia. Increased ESR/CRP.</td>
<td>Negative</td>
<td>25.9/94</td>
<td>Prednisone (8 d)</td>
</tr>
<tr>
<td>7</td>
<td>81/F</td>
<td>No*</td>
<td>Chronic anemia, lower limbs ischemic lesions. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.7/62</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>63/F</td>
<td>GCA</td>
<td>Thoracic aorta aneurysm.</td>
<td>Positive</td>
<td>0.1/7</td>
<td>Prednisone+MTX+TCZ (chronic)</td>
</tr>
<tr>
<td>9</td>
<td>54/F</td>
<td>PMR</td>
<td>Pelvic girdle pain. Poor treatment response. Increased ESR/CRP.</td>
<td>NP</td>
<td>1.0/77</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>10</td>
<td>74/F</td>
<td>GCA</td>
<td>Constitutional symptoms, malaise. Relapse after decreasing treatment. Increased ESR/CRP.</td>
<td>Positive</td>
<td>1.2/32</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>11</td>
<td>72/F</td>
<td>PMR</td>
<td>Poor treatment response. Chronic anemia. Persistent increased ESR/CRP.</td>
<td>Negative</td>
<td>3.4/98</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>12</td>
<td>66/F</td>
<td>Atypical PMR</td>
<td>Scapular, low back and pelvic girdle pain. Poor treatment response. Increased ESR/CRP.</td>
<td>Negative</td>
<td>0.4/72</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>80/F</td>
<td>GCA</td>
<td>Fatigue, lower limbs pain. Increased ESR/CRP.</td>
<td>Positive</td>
<td>2.4/26</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>14</td>
<td>68/F</td>
<td>GCA</td>
<td>Weight loss. Increased ESR/CRP.</td>
<td>Positive</td>
<td>1.4/10</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>81/M</td>
<td>GCA</td>
<td>Lower limbs pain. Increased ESR/CRP.</td>
<td>Positive</td>
<td>1.7/15</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>16</td>
<td>68/F</td>
<td>No*</td>
<td>Scapular and pelvic girdle pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>4.3/95</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>62/F</td>
<td>Atypical PMR</td>
<td>Persistently increased ESR/CRP. Lower back and limbs pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.1/17</td>
<td>Prednisone+MTX (chronic)</td>
</tr>
<tr>
<td>18</td>
<td>56/M</td>
<td>PMR</td>
<td>Poor treatment response. Abdominal aorta aneurysm. Increased ESR/CRP.</td>
<td>Negative</td>
<td>0.7/22</td>
<td>Prednisone+MTX (chronic)</td>
</tr>
<tr>
<td>19</td>
<td>82/F</td>
<td>PMR</td>
<td>Poor treatment response. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.3/8</td>
<td>MTX (chronic)</td>
</tr>
<tr>
<td>20</td>
<td>65/F</td>
<td>PMR</td>
<td>Relapse after steroid withdrawal. Increased ESR/CRP.</td>
<td>NP</td>
<td>5.5/65</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>21</td>
<td>81/F</td>
<td>No*</td>
<td>Lower back and limbs pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.8/77</td>
<td>No</td>
</tr>
<tr>
<td>22</td>
<td>72/M</td>
<td>No*</td>
<td>Inflammatory cervical scapular, lower back and limbs pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>1.7/27</td>
<td>No</td>
</tr>
<tr>
<td>23</td>
<td>79/F</td>
<td>PMR</td>
<td>Pelvic girdle pain. Increased ESR/CRP.</td>
<td>Negative</td>
<td>1.4/66</td>
<td>No</td>
</tr>
<tr>
<td>24</td>
<td>58/M</td>
<td>No*</td>
<td>Vertebrobasilar stroke. Subclavian, axillary and right humeral artery occlusion. Upper limbs pain. Lower limbs pain. Claudication. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.1/2</td>
<td>No</td>
</tr>
<tr>
<td>25</td>
<td>54/F</td>
<td>Retropertioneal fibrosis</td>
<td>Increased ESR/CRP.</td>
<td>NP</td>
<td>0.7/37</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>26</td>
<td>55/F</td>
<td>No*</td>
<td>Lower back and limbs pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>0.1/9</td>
<td>No</td>
</tr>
<tr>
<td>27</td>
<td>65/F</td>
<td>Panarteritis</td>
<td>Lower back pain. Increased ESR/CRP.</td>
<td>Negative</td>
<td>2.0/102</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>28</td>
<td>65/F</td>
<td>PMR</td>
<td>Morning stiffness, scapular pain. Poor treatment response. Increased ESR/CRP.</td>
<td>Negative</td>
<td>0.1/19</td>
<td>Prednisone (14 d)</td>
</tr>
<tr>
<td>29</td>
<td>56/M</td>
<td>PMR</td>
<td>Neck, shoulders, hips and lower limbs pain. Increased ESR/CRP.</td>
<td>NP</td>
<td>3.5/33</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>30</td>
<td>66/F</td>
<td>PMR</td>
<td>Scapular and hips pain. Poor treatment response. Relapse after decreasing therapy. Increased ESR/CRP.</td>
<td>NP</td>
<td>1.1/15</td>
<td>Prednisone+MTX (chronic)</td>
</tr>
<tr>
<td>31</td>
<td>78/F</td>
<td>No*</td>
<td>Constitutional symptoms, fever, chronic anemia, weight loss. Increased ESR/CRP.</td>
<td>NP</td>
<td>10.5/120</td>
<td>No</td>
</tr>
<tr>
<td>32</td>
<td>67/F</td>
<td>RA</td>
<td>Low back pain, thoracic aorta aneurysm. Permanently increased ESR/CRP.</td>
<td>NP</td>
<td>0.7/11</td>
<td>Prednisone+MTX (14 d)</td>
</tr>
<tr>
<td>33</td>
<td>55/M</td>
<td>No*</td>
<td>Constitutional symptoms, scapular pain. Good steroid response.</td>
<td>NP</td>
<td>0.1/2</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>34</td>
<td>50/F</td>
<td>No*</td>
<td>Malaise, fatigue, chest pain. CT angiography: iliac/femoral arteries stenosis.</td>
<td>NP</td>
<td>0.2/15</td>
<td>No</td>
</tr>
<tr>
<td>35</td>
<td>59/F</td>
<td>PMR</td>
<td>Scapular, shoulders, pelvic girdle, lower limbs pain. Increased ESR/CRP.</td>
<td>Negative</td>
<td>13.9/110</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>36</td>
<td>66/M</td>
<td>Psoriatic arthritis</td>
<td>Scapular and chest pain. Poor treatment response.</td>
<td>NP</td>
<td>0.3/23</td>
<td>Prednisone (chronic)</td>
</tr>
<tr>
<td>37</td>
<td>89/M</td>
<td>PMR</td>
<td>Joint pain and stiffness. Poor treatment response.</td>
<td>Negative</td>
<td>0.1/19</td>
<td>Prednisone (59 d)</td>
</tr>
</tbody>
</table>

M: male; F: female; PMR: polymyalgia rheumatica; GCA: giant cell arteritis; RA: rheumatoid arthritis; ESR: erythrocyte sedimentation rate (mm/1° hour); CRP: C-reactive protein (mg/dL); NP: not performed; MTX: methotrexate; TCZ: Tocilizumab. * Diagnosed later as having “idiopathic” large-vessel vasculitis.
Table 2. Overall target-to-background ratio (TBR) and according to the clinical and laboratory outcome.

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Initial TBR</th>
<th>Follow-up TBR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>37</td>
<td>1.7±0.5 (1.2-4.1)</td>
<td>1.5±0.3 (1.1-2.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>With clinical improvement</td>
<td>21</td>
<td>1.8±0.6 (1.4-4.1)</td>
<td>1.5±0.3 (1.1-2.5)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Without clinical improvement</td>
<td>16</td>
<td>1.6±0.3 (1.2-1.9)</td>
<td>1.5±0.3 (1.1-2.2)</td>
<td>0.1416</td>
</tr>
<tr>
<td>With ESR and/or CRP decrease</td>
<td>23</td>
<td>1.8±0.6 (1.2-4.1)</td>
<td>1.5±0.3 (1.1-2.5)</td>
<td>0.0062</td>
</tr>
<tr>
<td>Without ESR and/or CRP</td>
<td>14</td>
<td>1.7±0.3 (1.3-2.5)</td>
<td>1.4±0.1 (1.1-1.7)</td>
<td>0.0041</td>
</tr>
</tbody>
</table>

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein (mg/dL); TBR: target-to-background ratio.

Table 3. Target-to-background ratio (TBR) in patients with and without treatment at the time of the initial PET/CT scan.

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Initial TBR</th>
<th>Follow-up TBR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undergoing treatment</td>
<td>23</td>
<td>1.7±0.2 (1.4-2.0)</td>
<td>1.5±0.3 (1.1-2.2)</td>
<td>0.0055</td>
</tr>
<tr>
<td>Without treatment</td>
<td>14</td>
<td>1.8±0.7 (1.2-4.1)</td>
<td>1.4±0.3 (1.1-2.5)</td>
<td>0.0088</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.9376</td>
<td>0.3014</td>
<td></td>
</tr>
</tbody>
</table>

TBR: target-to-background ratio.
Table 4. Target-to-background ratio (TBR) at the initial and follow-up PET/CT scan according to the therapeutic management of the patients.

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Initial TBR</th>
<th>Follow-up TBR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>On treatment at the initial PET/CT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in the therapy*</td>
<td>21</td>
<td>1.7±0.2</td>
<td>1.5±0.3</td>
<td>0.0092</td>
</tr>
<tr>
<td>No change</td>
<td>2</td>
<td>1.6±0.3</td>
<td>1.4±0.2</td>
<td>-</td>
</tr>
<tr>
<td>Without treatment at the initial PET/CT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Started treatment*</td>
<td>12</td>
<td>1.9±0.8</td>
<td>1.5±0.3</td>
<td>0.0094</td>
</tr>
<tr>
<td>No treatment</td>
<td>2</td>
<td>1.4±0.2</td>
<td>1.2±0.2</td>
<td>-</td>
</tr>
</tbody>
</table>

TBR: target-to-background ratio.
* Based on the clinician judgment including information yielded in the PET/CT scan study.
GCS: glucocorticoids; MTX: methotrexate.