Comparison of early (60 min) and delayed (180 min) acquisition of $^{18}$F-FDG PET/CT in large vessel vasculitis


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**ABSTRACT**

**Purpose:** To compare the contribution of the $^{18}$F-FDG-PET/CT acquisition at 180 min and at 60 min in suspicion of large vessel vasculitis (LVV).

**Material and methods:** A prospective study including 23 patients was performed. PET/CT was acquired at 60 and 180 min (early and delayed scan) after $^{18}$F-FDG injection. A visual analysis was performed at the supra-aortic trunks (SAT), thoracic aorta (TA), abdominal aorta (AA), iliac arteries (IA) and femoral/tibioepineal arteries (FTA). Intensity (0–3) and uptake pattern (diffuse/linear) were assessed in the 115 vascular regions.

**Results:** There was no FDG uptake in the early and delayed acquisition in 20/115 vascular regions (17.4%). Of the 95 regions (82.6%) showing FDG uptake at the early, delayed or both acquisitions, intensity did not change in the delayed acquisition in 46 and changed in 49. Of the 49 regions in which the intensity changed, it decreased in 36 and increased in 13 (TA:8, SAT:5). AA, IA and FTA intensity did not increase in any of the cases. Uptake pattern at the TA in the early acquisition was diffuse in 16 patients. In 7, it changed to linear and in 9 the uptake disappeared. The early pattern was linear in 7 patients and 6 of them showed increased intensity in the delayed acquisition and in 1 remained the same.

**Conclusion:** The 180 min delayed FDG-PET/CT acquisition provides a more detailed visualization of the vessel wall, showing the washout of the blood pool activity. Therefore, it may contribute to a more accurate diagnosis of LVV.

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**PALABRAS CLAVE:**
$^{18}$F-FDG PET/CT
Tomografía por emisión de positrones
Vasculitis de grandes vasos
Arteritis de células gigantes

**RESUMEN**

**Objetivo:** Comparar la contribución de la adquisición con $^{18}$F-FDG-PET/TC a 180 min con la de 60 min en sospecha de vasculitis de grandes vasos (VGV).

**Material y métodos:** Este estudio prospectivo incluyó 23 pacientes. El estudio PET/TC fue adquirido a 60 y 180 min (precoz y tardío) tras la administración de $^{18}$F-FDG. Se realizó un análisis visual de las imágenes valorando los troncos supraauróicos (TSA), la aorta torácica (AT), la abdominal (AA), las arterias ilíacas (AI) y las femorales/tibioperoneas (AFT). En las 115 regiones vasculares se evaluó la intensidad (0-3) y el patrón de captación (difuso/lineal).

**Resultados:** En 20/115 regiones vasculares (17,4%) no hubo captación en la adquisición precoz y tardía. De las 95 regiones (82,6%) con captación en la adquisición precoz la intensidad no cambió en la tardía en 46 y cambió en 49. De esas 49 regiones en las que la intensidad cambió, esta disminuyó en 36 y aumentó en 13 (AT: 8, TSA: 5). En ningún caso la intensidad aumentó en la AA, las AI y las AFT. El patrón de captación en la AT fue difuso en la adquisición precoz en 16 pacientes, en 7 de ellos cambió a lineal en la tardía y desapareció en 9. El patrón precoz fue lineal en 7 pacientes, 6 de ellos mostraron un aumento de intensidad en la tardía y en uno permaneció igual.

**Conclusión:** La adquisición tardía de 180 min con FDG-PET/TC proporciona una más detallada visualización de la pared vascular, mostrando la desaparición de la actividad del pool vascular y contribuyendo a un más correcto diagnóstico de VGV.

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**Introduction**

$^{18}$F-fluoro-2-deoxy-d-glucose (FDG) is the most common PET radiotracer used for cancer detection, as it is taken up by any tissue that is characterized by high glycolysis rate, like the malignant cells. In addition, cells involved in inflammatory and infectious diseases show FDG uptake and are considered the main source of...
false-positive findings in cancer patients.\textsuperscript{1–4} In recent years there have been an increasing number of studies specifically aimed to assess the usefulness of FDG PET and PET/CT in different inflammatory processes.\textsuperscript{5–9}

Large vessel vasculitis (LVV) is an inflammatory disease involving leukocytic infiltration of blood vessel wall, and giant cell arteritis is its most frequent form. Clinically, the diagnosis of LVV and assessment of the disease activity frequently remains a challenge, especially in patients with non-specific symptoms or indeterminate laboratory test, negative temporal artery biopsy and non-conclusive structural imaging. The contribution of FDG-PET in vasculitis was first described by Blockmans et al.\textsuperscript{10} in 1999. Ever since, several authors have reported FDG-PET and PET/CT as a helpful non-invasive tool in the diagnosis and management of LVV by providing a metabolic functional image of the inflammation of the vascular wall in large vessels.\textsuperscript{11–16} In a recently published interesting work, Fuchs et al.\textsuperscript{17} reported that FDG increases the overall diagnostic accuracy of vasculitis and has an impact on the medical management in a high proportion of patients. The main advantage of FDG imaging is that vessel wall inflammation can be detected early during the development of the disease before structural changes are seen.

In general, the acquisition protocol used by most authors is the same applied for oncological purposes, that is, at 60 min after FDG intravenous administration. However, at this time blood pool activity in the large vessels, mainly aorta, is frequently seen and, therefore, could overlap the vessel wall uptake.

Our aim was to evaluate the contribution of a 180 min delayed FDG-PET/CT acquisition to the early acquisition at 60 min in suspicion of LVV, hypothesizing that blood pool activity would decrease with time and vessel wall uptake would increase. To our knowledge, this is the first prospective study specifically aimed to evaluate the timing of the acquisition of the FDG scan in LVV.

Material and methods

Patients

This prospective study included 23 consecutive patients, 16 women and 7 men (mean age: 69.5 ± 15.1 years). Of these 23 patients, 15 were submitted for suspicion of LVV and 8 for assessment of disease activity of a LVV previously diagnosed. The mean ± SD erythrocyte sedimentation rate (ESR) was 53.3 ± 37.4 mm/h and the mean plasma C-reactive protein (CRP) level was 7.6 ± 18.9 mg/dL (normal < 0.5 mg/dL).

FDG PET/CT acquisition

Patients fasted for at least 6 h before the examination. The serum glucose level was lower than 160 mg/dL in all the patients. Whole-body FDG-PET/CT was acquired 60 and 180 min (early and delayed scan, respectively) after injection of 7 MBq/kg of \textsuperscript{18}F-FDG, using a Biograph LSD Pico 3D Siemens. A low dose CT scan was obtained first, and then, a PET scan was performed, acquired at 120 s/bed in the early scan and 250 s/bed in the delayed scan.

Analysis of FDG-PET/CT images

A visual analysis of the early and delayed FDG-PET/CT scans was performed by two experienced nuclear medicine specialists who were blinded to clinical and laboratory data. Five vascular regions were considered: supraaortic trunks (SAT), thoracic aorta (TA), abdominal aorta (AA), iliac arteries (IA) and femoral/tibioepioperoneal arteries (FTA). In total, 115 vascular regions were evaluated.

Table 1

<table>
<thead>
<tr>
<th>Uptake intensity</th>
<th>Vascular regions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No uptake in both scans</td>
<td>20 (17.4)</td>
</tr>
<tr>
<td>Uptake</td>
<td></td>
</tr>
<tr>
<td>No change in intensity</td>
<td>46 (40.0)</td>
</tr>
<tr>
<td>Change in intensity</td>
<td>49 (42.6)</td>
</tr>
<tr>
<td>Total</td>
<td>115 (100)</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Uptake intensity</th>
<th>Vascular regions (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA</td>
<td>SAT</td>
</tr>
<tr>
<td>Increased</td>
<td>8</td>
</tr>
<tr>
<td>Decreased</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
</tbody>
</table>

SAT, supraaortic trunk; TA, thoracic aorta; AA, abdominal aorta; IA, iliac arteries; FTA, femoral and tibioepioperoneal arteries.

Images were evaluated according to the intensity of the FDG uptake compared with the hepatic uptake and were graded from 0 to 3 (grade 0: no uptake, grade 3: higher than liver uptake). In addition, the pattern uptake at the TA was classified as diffuse (when it was not possible to distinguish vessel wall uptake from blood pool activity) and lineal (when it involved only the vessel wall).

Results

Overall, out of the 115 vascular regions evaluated both acquisitions showed no FDG uptake in 20 (17.4%). In 95 regions (82.6%) there was uptake at the early, delayed or both acquisitions, in 46 (40%) the intensity of the uptake did not change and in 49 (42.6%) it changed (Table 1). Since the 49 regions where the intensity changed are the most interesting we show in Table 2 the distribution of the uptake change in each vascular region considered. In 13 regions the uptake increased in the delayed acquisition and they included 8 at the TA and 5 at the SAT. In none of the AA, IA and FTA the intensity increased. In 36 the intensity of the uptake decreased in the delayed acquisition, in 29 of them it happened at the AA, IA and FTA and only 7 involved TA and SAT (Table 2).

Regarding the pattern of uptake, all the 23 patients included showed FDG uptake at the TA region in the early acquisition. In 16 of them (69.6%) the early pattern was diffuse and in 7 (30.4%) was lineal. Of the 16 patients showing an early diffuse uptake, it disappeared in the delayed acquisition in 9 (39.1%) (Fig. 1), while in the remaining 7 patients (30.4%) the diffuse uptake changed into a lineal uptake by the vessel wall (Fig. 2).

The pattern of uptake in the early acquisition was lineal in 7 patients (30.4%) (Table 3). In 6 of them (26.2%) the intensity of the lineal uptake increased in the delayed acquisition (from grade 1 to grade 2 in 2 patients and from grade 2 to grade 3 in 4 patients) (Fig. 3). In 1 patient the uptake remained lineal with the same intensity (grade 2).

Table 3

| Pattern of uptake at the thoracic aorta in the early and delayed PET/CT scan. |
|------------------|------------------|------------------|------------------|------------------|------------------|
| Diffuse uptake | Lineal uptake | No uptake | Total |
| Early scan | 16 | 7 | – | 23 |
| Delayed scan | 0 | 14 | 9 | 23 |
Fig. 1. In this 68-year-old man the early FDG-PET/CT scan (A: sagittal and coronal views) shows a mild diffuse FDG uptake at the TA that decreases in the delayed scan at 180 min (B: sagittal and coronal views).

Fig. 2. A 56-year-old man submitted for suspicion of large vessel vasculitis. The early FDG-PET/CT scan (A: axial, sagittal and coronal views) shows a diffuse uptake in the TA territory. The delayed scan (B: axial, sagittal and coronal views) shows a decrease of blood pool activity and an increase of the vessel wall uptake, changing from diffuse to linear pattern.

Discussion

FDG-PET and PET/CT scans are generally acquired 60 minutes after FDG injection. However, the normal distribution pattern of FDG at this time includes activity in the mediastinum due to the vascular activity in the aorta territory.\(^1\) Regarding LVV, this activity could overlap the aorta wall uptake. Assuming that along time blood pool activity decreases and the wall uptake increases, a delayed acquisition would overcome this overlap and, therefore, the vessel wall uptake would be better visualized.

With regard to the study of the atheroma plaque, time point for imaging using also FDG was a topic previously addressed by some of the groups. Most of the authors recommend performing imaging at 3 h\(^1,2\) others reported that there is no advantage in acquiring a delayed image at 3 h.\(^3\) Likewise, Wu et al.\(^4\) reported, also in atherosclerotic population, that although the lesion-to-background contrast was better in the delayed images, the abnormal FDG uptake could be identified as well in the early images. However, when it applies to the study of LVV the topic did not deserve such interest. As there is no doubt that the mediastinum activity is seen at 60 min after injection and there are no reports prospectively designed to compare specifically the early and delayed acquisition in patients with LVV, we decided to design this prospective study to address this issue. In a preliminary study including a small number of patients with LVV we suggested a valuable contribution of the delayed acquisition.\(^5\)

It could be argued that 180 min uptake time would be too long due to the impact of \(^18\)F decay on the counting statistics and, therefore, on the poor quality of the image obtained. Taking this into account, we doubled the acquisition time (250 s compared to 120 in the early acquisition). Accordingly, the dose used was 7 MBq/kg of body weight instead of the most often used standard fixed dose of 370 MBq (10 mCi), which may provide adequate counting statistics for an average 70 kg weight and 60 min uptake time.

The first parameter evaluated in our study was the intensity of the uptake in the 115 vascular regions considered, both in the early and the delayed acquisition. Our results show that in 49 (42.6%) of the vascular regions the intensity of the uptake changed from the early to the delayed acquisition, and this is the most interesting subgroup of regions as in the other 66 the intensity did not change. In 13 out of these 49 regions the intensity increased in the delayed acquisition, all of them corresponding to the TA (8 patients) and the SAT (5 patients), and none to the AA, IA or FTA regions.
Fig. 3. A 73-year-old woman with biopsy-proven giant cell arteritis diagnosed 8 years ago and submitted for assessment of disease activity. In both the early and delayed FDG-PET/CT scans (A: early scan, axial, coronal and sagittal views; B: delayed scan, axial, coronal and sagittal views, respectively) the pattern of uptake at the TA was linear by the vessel wall. However, the delayed scan shows an increase in the intensity of uptake at the TA, and also at the SAT and AA, and the decrease of the blood pool activity.

The second and most interesting parameter evaluated was the pattern of uptake at the TA. The pattern of uptake in the early acquisition was diffuse in most patients (16/23 patients) and in all of them the diffuse uptake in the territory of the TA was washed out in the delayed acquisition, changing to lineal uptake in the vessel wall in 7. In the other 7 patients the early pattern of uptake was lineal along the vessel wall, in 6 of them, the intensity of the uptake increased in the delayed scan and in 1 it remain the same.

The contribution of the delayed image was more relevant at the TA region, because of its larger diameter, and in patients in whom the early scan could not distinguish the vessel wall uptake from the blood pool activity, showing a diffuse pattern of uptake at the TA similar to that reported as the normal pattern in the mediastinum.

However, in narrow vessels (SAT, IA and FTA, and even the AA) it is not possible to distinguish FDG uptake in the vessel wall and blood pool activity in the lumen due to the small diameter of this arteries. In this case, the contribution of the delayed images was showing an increase in the intensity of uptake at the SAT in some patients and, on the other hand, showing the wash out of blood pool activity especially in lower extremities, in a large number of patients who otherwise would be considered as with LVV.

Interestingly, previous studies have shown a reduced specificity in the evaluation of vessel wall uptake in the lower extremities. Thus, Blockmans et al.10 acquiring images at 60 min, reported FDG uptake in a control population in the lower limb arteries suggesting that it could be due to atherosclerosis. On the other hand, a mild uptake in the lower extremities vessels in patients without vasculitis was also observed by Papanathanasiou et al.25 also acquiring images at 60 min, suggesting that could be related to smooth muscle activity and also to atherosclerotic changes. However, and taking into account our results, it seems that the blood pool activity at 60 min after FDG injection could be a more likely explanation of the uptake since it frequently disappears in the delayed images.

In conclusion, and according to our results, the contribution of a delayed FDG-PET/CT acquisition is different depending on the vascular territory considered. At the TA the most interesting finding was the wash out of the blood pool activity and the better visualization of the lineal uptake by the vessel wall. At the small diameter vessels, the most significant findings were the wash out of the uptake due to blood pool activity, mainly in the lower extremities, in a large number of patients. These findings may contribute to a more accurate diagnosis of LVV.

Conflicts of interest

The authors state that there are no conflicts of interest to declare.

References


