Diagnostic yield of $^{18}$F-FDG PET/CT in suspected diagnosis of vascular graft infection: A prospective cohort study

Hans Bowles, MD, Juan Ambrosioni, MD, PhD, Gaspar Mestres, MD, PhD, Marta Hernández-Meneses, MD, Nuria Sánchez, MD, Jaime Llopis, MD, PhD, Xavier Yugueros, MD, Manel Almela, MD, Asunción Moreno, MD, PhD, Vicenç Rambau, MD, PhD, David Fuster, MD, PhD,Jose M. Miró, MD, PhD, and Hospital Clinic Endocarditis Study Group

a Nuclear Medicine Department, Hospital Clínic i Provincial de Barcelona, Barcelona, Spain
b Infectious Diseases Service, Hospital Clinic, Barcelona, Spain
c Cardiovascular Surgery Department, Hospital Clinic, Barcelona, Spain
d Statistics Department, Faculty of Biology, University of Barcelona, Barcelona, Spain
e Clinical Microbiology Department, Hospital Clínic, Barcelona, Spain
f Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain

Received Feb 23, 2018; accepted Jun 4, 2018
doi:10.1007/s12350-018-1337-1

Background. Prosthetic vascular graft infection (PVGI) is a severe complication associated with high morbidity and mortality. Clinical diagnosis is complex, requiring image testing such as CT angiography or leukocyte scintigraphy, which has considerable limitations. The aim of this study was to know the diagnostic yield of PET/CT with $^{18}$F-Fluorodeoxyglucose ($^{18}$F-FDG) in patients with suspected PVGI.

Methods. We performed a prospective cohort study including 49 patients with suspected PVGI, median age of 62 ± 14 years. Three uptake patterns were defined following published recommendations: (i) focal, (ii) patched (PVGI criteria), and (iii) diffuse (no PVGI criterion).

Results. Sensitivity, specificity, and positive and negative predictive values for $^{18}$F-FDG-PET/CT were 88%, 79%, 67%, and 93%, respectively. $^{18}$F-FDG-PET/CT identified 14/16 cases of PVGI showing a focal ($n = 10$) or patched pattern ($n = 4$), being true negative in 26/33 cases with either a diffuse pattern ($n = 16$) or without uptake ($n = 10$). Five of the seven false-positive cases (71%) showed a patched pattern and all coincided with the application of adhesives for PVG placement.

Conclusions. $^{18}$F-FDG-PET/CT is a useful technique for the diagnosis of PVGI. A patched pattern on PET/CT in patients in whom adhesives were applied for prosthetic vascular graft placement does not indicate infection. (J Nucl Cardiol 2020;27:294–302.)

Key Words: Fluorodeoxyglucose (FDG) • diagnostic and prognostic application • PET/CT imaging

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12350-018-1337-1) contains supplementary material, which is available to authorized users.

The authors of this article have provided a PowerPoint file, available for download at SpringerLink, which summarizes the contents of the paper and is free for re-use at meetings and presentations. Search for the article DOI on SpringerLink.com.

Members of the Hospital Clinic Endocarditis Study Group are listed in the “Acknowledgement”.

Funding This work was supported by AGAUR 2014 SGR 279. Jose M. Miró received a personal 80:20 research grant from the Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain during 2017–19. The European Regional Development Fund (ERDF) “A way to build Europe” also provided funding.

Hans Bowles and Juan Ambrosioni have equally contributed to this work.

Reprint requests: David Fuster, MD, PhD, Nuclear Medicine Department, Hospital Clínic i Provincial de Barcelona, Villarroel, 170, 08036 Barcelona, Spain; dfuster@clinic.cat
1071-3581/$34.00
Copyright © 2018 American Society of Nuclear Cardiology.
Five years according to the series.1,2 The risk of infection complications with mortality rates as high as 40% at diagnosis, and in some cases may lead to serious reconstructive surgery. It requires immediate accurate rate between 1% and 6%), which may develop following severe complication, albeit relatively rare (incidence and 100%, respectively.5

However, CT usually fails to differentiate changes in biological, and imaging results. Several studies with computed tomography (CT)1 have described very good diagnostic accuracy with this method in patients with advanced graft infection, reporting a sensitivity and specificity of around 94% and 85%, respectively.4 However, CT usually fails to differentiate changes in the early period post-surgery and to detect low-grade infection, having a sensitivity and specificity about 55% and 100%, respectively.5

The use of radiolabeled leukocytes has been quite successful in detecting low-grade PVGIs, but low resolution hinders their ability to differentiate adjacent soft tissue infections.6 Preliminary studies found 18F-FDG-PET to be more accurate compared to contrast CT but showing potential high 18F-FDG uptake in non-infected vascular grafts requiring PET/CT findings to be interpreted with caution.7,8 Thereafter, other groups suggested the higher sensitivity and specificity of PET/CT using focal and diffuse patterns trying to differentiate infection from inflammatory and/or physiologic uptake.9,10 However, more recent studies have coincided in the need to define non homogenous or patched uptake patterns 11,12 and the degree of uptake13 necessary to establish a differential diagnosis of PVGI. Other relevant technical aspects to correctly interpret PET/CT findings include the progressive use of surgical adhesives which produce severe active inflammation surrounding the glue remnant and show increased heterogeneous 18F-FDG uptake making it difficult to distinguish between PVGI or inflammatory changes.3 In this context, a study by Guenther et al. showed a surprisingly low specificity for PET/CT in the diagnosis of infection of the proximal thoracic aorta.14 A case definition was recently proposed for aortic graft infections, with PET/CT being considered as a minor criterion.15

The primary aim of this study was to evaluate the diagnostic yield of PET/CT in patients with suspected PVGI. The secondary aims were to determine the usefulness of PET/CT to discriminate between PVGI and infectious processes of adjacent tissues and the influence of bioglu in 18F-FDG uptake.

See related editorial, pp. 303–304

INTRODUCTION

Prosthetic vascular graft infection (PVGI) is a severe complication, albeit relatively rare (incidence rate between 1% and 6%), which may develop following reconstructive surgery. It requires immediate accurate diagnosis, and in some cases may lead to serious complications with mortality rates as high as 40% at 5 years according to the series.1,2 The risk of infection varies according to the location of the prosthesis: aortic grafts limited to the abdomen have a risk of around 1% whereas the percentage varies from 1.5% to 2% in the aortofemoral and may be of up to 6% in the infringuinal arteries.3 Synthetic grafts are made of either Dacron or polytetrafluoroethylene (PTFE) and both materials may be used for endovascular implants and for open surgery. Dacron grafts are more susceptible to infections and are mainly used in large vessels in aortic and aortoiliac surgery, whereas PTFE peripheral implants are preferably used for medium and small vessels.3

The diagnosis of prosthetic infection is based on the presence of clinical manifestations, laboratory, microbiological, and imaging results. Several studies with computed tomography (CT)1 have described very good diagnostic accuracy with this method in patients with advanced graft infection, reporting a sensitivity and specificity of around 94% and 85%, respectively.4 However, CT usually fails to differentiate changes in the early period post-surgery and to detect low-grade infection, having a sensitivity and specificity about 55% and 100%, respectively.5

The use of radiolabeled leukocytes has been quite successful in detecting low-grade PVGIs, but low resolution hinders their ability to differentiate adjacent soft tissue infections.6 Preliminary studies found 18F-FDG-PET to be more accurate compared to contrast CT but showing potential high 18F-FDG uptake in non-infected vascular grafts requiring PET/CT findings to be interpreted with caution.7,8 Thereafter, other groups suggested the higher sensitivity and specificity of PET/CT using focal and diffuse patterns trying to differentiate infection from inflammatory and/or physiologic uptake.9,10 However, more recent studies have coincided in the need to define non homogenous or patched uptake patterns 11,12 and the degree of uptake13 necessary to establish a differential diagnosis of PVGI. Other relevant technical aspects to correctly interpret PET/CT findings include the progressive use of surgical adhesives which produce severe active inflammation surrounding the glue remnant and show increased heterogeneous 18F-FDG uptake making it difficult to distinguish between PVGI or inflammatory changes.3 In this context, a study by Guenther et al. showed a surprisingly low specificity for PET/CT in the diagnosis of infection of the proximal thoracic aorta.14 A case definition was recently proposed for aortic graft infections, with PET/CT being considered as a minor criterion.15

The primary aim of this study was to evaluate the diagnostic yield of PET/CT in patients with suspected PVGI. The secondary aims were to determine the usefulness of PET/CT to discriminate between PVGI and infectious processes of adjacent tissues and the influence of bioglu in 18F-FDG uptake.

MATERIALS AND METHODS

Patients and Design

We performed a prospective cohort study from 49 consecutive patients with suspected PVGI attended in an 850-bed university hospital from June 2014 to July 2016. Since 1979, all patients with PVGI attended at the Hospital Clinic of Barcelona have been managed by a multidisciplinary group which meets on a weekly basis. Patients were classified in line with the Samson Classification for vascular graft infection according to the depth of infection and degree of graft involvement.16 The study was approved by the Institutional Review Board and written informed consent to perform PET/CT was obtained from all the patients included.

Diagnosis of PVGI was confirmed by clinical/surgical, radiologic, and laboratory findings in the presence of a single major criterion (pus, exposed graft, fistula, peri-graft fluid or gas on CT, and organisms recovered from graft or peri-graft fluid), plus any other criterion major or minor (localized clinical features, fever, radiological suspicion of a related infection, positive blood cultures, and elevated inflammatory markers), as described in the literature by Lyons et al.15 PET/CT was not used for PVGI diagnosis to ensure that there was no influence on the outcomes. PVGI was ruled out by a combination of biochemical, clinical, and imaging parameters (other than PET/CT) and a minimum follow-up of 6 months.
PET/CT

Whole-body scans were performed using a hybrid PET/CT (SIEMENS Biograph mCT 64S). The patients underwent a 6-hour fast period with blood glucose levels less than 140 mg/dL prior to the intravenous administration of 0.11 mCi (4.07 MBq)/kg of 18F-FDG. During the acquisitions, patients were in supine position with their arms raised above their head. Whole-body PET data were acquired 1 h after 18F-FDG administration in 3D mode and for 3 minute per bed position. PET images were reconstructed using the ordered-subsets expectation maximization algorithm with and without CT data for attenuation correction. PET, CT, and fused PET/CT images were available for review and shown in axial, coronal, and sagittal planes.

Image Interpretation

Images were interpreted separately by two nuclear medicine specialists trained in infection and 18F-FDG-PET/CT. Disagreements were settled by consensus with a third nuclear medicine specialist. Foci of increased 18F-FDG uptake were recorded. Three uptake patterns were defined visually following published recommendations: (i) focal (one dominant area of uptake), (ii) inhomogeneous or patched (PVGI criteria), and (iii) diffuse or homogenous (no PVGI criterion). 9 18F-FDG uptake in the region of the vascular graft was evaluated with 3D and volume rendering image fusion using software based on the Unix system to visually establish the uptake pattern and if the 18F-FDG uptake corresponded to the vascular graft or to the adjacent tissues (Osirix, Pixmeo, Geneva, Switzerland).

Additionally, a semi-quantitative analysis was made using the maximum standardized uptake value (SUVmax) in a spherical volume of interest area of suspected infection. The mean standard uptake value (SUVmean) was obtained in the blood pool using superior cava vein uptake. A Maximum target-to-blood pool ratio (M-TBR) was calculated by dividing the SUVmax of the area of interest by the SUVmean of the blood pool.

Table 1. Demographic characteristics of the study group

| Characteristics                        | All cases (n = 49) | Confirmed PVGI (n = 16) | PVGI ruled out (n = 33) | P   |
|----------------------------------------|-------------------|-------------------------|-------------------------|-----|
| Mean age (years)                       | 62 ± 14           | 61 ± 14                 | 63 ± 13                 | 0.62|
| Sex, n (%)                             |                   |                         |                         |     |
| Female                                 | 7 (14%)           | 2 (12%)                 | 5 (15%)                 | 0.45|
| Male                                   | 42 (86%)          | 14 (88%)                | 28 (85%)                | 0.04|
| Vascular prosthesis                    |                   |                         |                         |     |
| Location                               |                   |                         |                         |     |
| Ascending aorta                        | 16                | 2                       | 14                      | 0.004|
| Axillofemoral                           | 4                 | 1                       | 3                       | 0.62|
| Aortobifemoral                         | 9                 | 3                       | 6                       | 0.51|
| Aortoiliac                             | 7                 | 1                       | 6                       | 0.12|
| Femoropopliteal                        | 6                 | 5                       | 1                       | 0.22|
| Others                                 | 7                 | 4                       | 3                       | 0.97|
| Material                               |                   |                         |                         |     |
| Dacron                                  | 23                | 6                       | 17                      | 0.007|
| PTFE                                    | 22                | 10                      | 12                      | 0.81|
| TAVI                                    | 4                 | -                       | 4                       | 0.125|
| Treatment option                       |                   |                         |                         |     |
| Open surgery                           | 39                | 14                      | 25                      | 0.56|
| Endovascular                           | 8                 | 2                       | 6                       | 0.10|
| Hybrid surgery                         | 2                 | 0                       | 2                       | 0.11|
| BioGlue                                | 12                | 4                       | 8                       | 0.39|
| Angio-CT                                | 24                | 8                       | 16                      | 0.15|
| Median time from vascular graft (IQR), months | 6 (2-22)   | 10.5 (4-31)            | 4 (1-20)                | 0.16|
| Antibiotics prior to PET/CT            |                   |                         |                         |     |
| Yes                                     | 44                | 15                      | 29                      | 0.52|
| Duration (days) (mean, SD)             | 14 ± 5            | 13 ± 4                  | 16 ± 7                  | 0.33|

IQR interquartile range; PVGI, prosthetic vascular graft infection
Table 2. Clinical presentation, microbiological findings and outcome of the sixteen patients with confirmed diagnosis of PVGI

| Clinical and laboratory data | n (%) |
|-----------------------------|-------|
| Intermittent claudication   | 7 (44) |
| Traumatic vascular graft injury | 2 (12.5) |
| C-reactive protein, mg/dL (mean, SD) | 8.1 ± 9.1 |
| Erythrocyte sedimentation rate (mean, SD) | 42 ± 37 |
| Leukocytes, 10^9/L (mean, SD) | 6.5 ± 3.2 |
| Causal microorganisms |       |
| *Staphylococcus aureus* | 1 (6.25) |
| CoNS | 4 (25) |
| Polymicrobial | 4 (25) |
| GNR | 2 (12.5) |
| *Enterococcus faecalis* | 2 (12.5) |
| *Escherichia coli* | 2 (12.5) |
| Not identified | 1 (6.25) |
| Diagnosis criteria |       |
| Clinical/surgical |       |
| Pus | 2 (12.5) |
| Exposed graft | 2 (12.5) |
| Fistula | 3 (18.75) |
| Graft insertion in an infected site* | 4 (25) |
| Localized clinical features of PVGI* | 6 (38) |
| Fever ≥ 38 °C* | 8 (50) |
| Radiological |       |
| Peri-graft fluid (≥ 3 mo) or gas (≥ 7 mo) on CT | 4 (25) |
| Increase in peri-graft gas on serial imaging | - |
| Other suspicious signs on CT* | 7 (44) |
| Radiolabelled leukocyte uptake* | 1 (6.25) |
| Microbiological and laboratory |       |
| Organisms from explanted graft | 6 (38) |
| Organisms from intra-operative specimen | 4 (24) |
| Organisms from percutaneous peri-graft fluid | 2 (12.5) |
| Blood culture(s) positive* | 8 (50) |
| Elevated inflammatory markers* | 13 (81.25) |
| Vascular surgery | 10 (62) |
| Timing |       |
| Early (< 3 months) | 3 (18.75) |
| Late (≥ 3 months) | 13 (81.25) |
| Mortality related to PVGI episode | 3 (19) |

CoNS, coagulase-negative staphylococcus; GNR, gram-negative rods; PVGI, prosthetic vascular graft infection

*Minor criteria

**Statistical Analysis**

The statistical analyses were performed using the SPSS, version 22.0 (SPSS Inc.). The sensitivity and specificity, and the positive (PPV) and negative predictive values (NPV) were calculated. Inter-rater agreement with Kappa statistics was obtained. Areas under the receiver-operating characteristic curve (AUC) and total and sensitivity optimization thresholds were calculated. Differences in continuous and categorical variables on Table 1 were measured by Kruskal–Wallis test and by χ² test, respectively. A two-sided P value < 0.05 was considered significant.
RESULTS

Table 1 shows the baseline characteristics of the patients. The mean age ± standard deviation (SD) of the patients recruited (42 men and 7 women) was 62 ± 14 years. The median time span between PVG placement and PET/CT was six months (interquartile range [IQR] 2-36), and 44 patients (90%) received antibiotics before PET/CT. A final diagnosis of PVGI was established in 16 patients: with infection of the ascending aorta \((n=2)\), aortobifemoral \((n=3)\), aortoiliac \((n=1)\), axillofemoral \((n=1)\), femoral \((n=2)\), femoropopliteal \((n=5)\) and other locations \((n=2)\).

See Table 2. All 16 patients classified as PVGI had at least one major and one minor criterion based on the case definition by Lyons et al.\(^{15}\) Following Samson classification, nine out the 16 patients with confirmed PVGI were in group 4 \((n=5)\) or group 5 \((n=4)\). Eight patients were diagnosed with infection of adjacent tissues not related to the PVG. The causative microorganism was identified in 15 out of 16 infections, with \textit{coagulase-negative Staphylococci} \((n=4)\) and polymicrobial isolates \((n=4)\) being the most frequent (Table 2).

In our series, \(^{18}\)F-FDG-PET/CT was able to identify 14/16 cases of PVGI (Figure 1) showing a focal \((n=1)\) or patched pattern \((n=4)\) and was true negative in 26/33 cases with either a diffuse pattern \((n=16)\) or without uptake \((n=1)\). The remaining 7/33 non infected cases were considered as false-positive results and showed a patched \((n=6)\) or focal \((n=1)\) uptake. The sensitivity, specificity, PPV, and NPV for \(^{18}\)F-FDG-PET/CT were 88%, 79%, 67%, and 93%, respectively. Two false negative cases were found in the ascending aorta and in the femoral PVG. The duration of antibiotic use in these two cases was 18 and 14 days, and the mean duration in PVGI group was 15 days (see Table 1). Five out of the 7 false-positive cases (71%) showed a patched pattern (2 cases in the anastomotic site and 3 cases throughout the vascular graft), coinciding with the application of adhesives for PVG placement (Figure 2). When these cases were excluded from the analysis, these PET/CT values rose to up to 88%, 93%, 87% and 93%, respectively. Additionally, PET/CT identified all the extra-prosthetic infections not identified by other procedures in the area surrounding the vascular graft: abscesses \((n=2)\), aneurysm \((n=3)\),

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Example of a diffuse uptake pattern (arrowheads) with a dominant area of focal uptake (arrows) with a SUVmax of 6.7, shown in transverse and coronal PET (A) and fused PET/CT (B) images and considered as PVGI of the aortic bifemoral bypass. The vascular graft was removed and explant cultures were positive for \textit{coagulase-negative staphylococcus}.
\end{figure}
infected hematoma \((n = 2)\), and sternal osteomyelitis \((n = 1)\). These cases represented 16\% of the total number of patients and PET/CT was determinant in establishing that the infection was not related to the PVG (Figure 3).

Quantitative analysis for PET/CT using AUC showed that the best thresholds to discriminate between infection and inflammatory and/or physiological uptake were a SUVmax = 4.2 (75\%, 78.79\%) and a M-TBR = 1.83 (93.75\%, 66.67\%) (Figure 4).

There was an agreement between the two observers to establish 18F-FDG uptake pattern as patched, focal, or diffuse in 38 of the 49 (78\%) cases. When considering only two categories as infected (patched and focal patterns) or not infected (diffuse pattern), the agreement rose to 45 out of 49 (92\%). Kappa statistics values using the same analysis to measure inter-rater agreement between operators were 0.618 (confidence interval [CI] 95\%; 0.420, 0.817) and 0.835 (CI 95\%; 0.681, 0.990), respectively. The Kappa coefficient was interpreted as having substantial agreement and almost perfect agreement, respectively.

**DISCUSSION**

In this cohort of suspected PVGI, the focal 18F-FDG uptake pattern on PET/CT was revealed as an accurate parameter for infection. However, the combination of inhomogeneous or patched pattern and the use of adhesives can be a source of false-positive results. PVGI is associated with high mortality and morbidity making early accurate diagnosis essential in order to provide the most appropriate treatment. Diagnosis of cardiovascular infections is currently dependent on the presence of certain clinical symptoms and echocardiographical and CT angiography findings. CT angiography is considered the gold standard modality in patients with suspected PVGI. However, the characteristic signs such as local peri-graft fluid retention and air bubbles are not always present in infected cases, and they cannot be interpreted as pathological in the early postoperative period (3 months).10 Although the sensitivity of angio-CT is relatively high at 85 to 100\%, it may decrease in low-grade infections.17 Other post-surgical complications such as infected hematomas or pseudoaneurysms

---

**Figure 2.** This is a case of suspected infection of a hybrid thoracic graft, consisting of open replacement of the ascending aorta and aortic arch, with bioglue, and endoprosthesis in the descending aorta. Fused PET/CT images show patched (arrows) 18F-FDG uptake (SUVmax = 8.3) predominantly at the proximal end of the vascular graft (A). 3D PET images and volume rendering fusion images clearly demonstrated intense uptake in the site where adhesives were deposited, indicating that the uptake was due to inflammatory changes (B). Patient follow-up confirmed the integrity of the vascular graft.
in the vicinity of the vascular graft may also make correct diagnosis difficult.

Several studies have shown that 18F-FDG may be a promising radiotracer for detecting cardiovascular infections.\textsuperscript{18,19} However, it should be noted that chronic aseptic inflammation in synthetic graft material also constitutes a potential base for 18F-FDG uptake, even long after surgery, which may potentially difficult the diagnosis of PVGI.\textsuperscript{8,13,20} In a previous study Wasselius et al. described 18F-FDG uptake in vascular grafts of a vast majority of patients without graft infection indicating the possible high risk of a false-positive diagnosis.\textsuperscript{8} Saleem et al. reported that 18F-FDG uptake can remain long after surgery, being especially dependent on the prosthetic material used, especially with Dacron.\textsuperscript{21} Accordingly to previous data, we detected diffuse 18F-FDG uptake in up to 69% of our cases.

In a study of 33 patients with an aortic graft, Fukuchi et al. found one-third to be infected, with false-positive results as high as 36%.\textsuperscript{7} This also coincides with our series in which almost half of the non infected vascular grafts showed a diffuse uptake pattern (16 out of 33 cases). Keidar et al. analyzed 18F-FDG uptake in non infected PVGs in 107 cases. They found 18F-FGDG uptake in 92% of patients, although none presented a focal pattern, supporting the concept that focal uptake is a strong indicator of graft infection.\textsuperscript{11} Nonetheless, we do not agree with these authors since the sensitivity in our study was 88% with a lower specificity of 79% for PVGI when either focal or patched uptake patterns of infection were present. As other authors\textsuperscript{12,21,22} we did not find additional value of SUVmax or M-TBR to establish a threshold to discriminate inflammation from infection because of the rather low specificities with best optimal thresholds of SUVmax = 4.2 (75%, 78.79\%) and M-TBR = 1.83 (93.75\%, 66.67\%), respectively.

Spacek et al. were the first to report non homogeneous FDG uptake in 18.8\% of cases, and of these 61\% were infected and 39\% were not. They therefore concluded that non homogeneous FDG uptake hampered the accuracy of PET/CT and must be considered as a non diagnostic result.\textsuperscript{12} These findings are crucial as focal and patched patterns can be difficult to differentiate as occurred in our series when the images were analyzed by two nuclear medicine specialists. This is important considering that the patched pattern can manifest as an inflammatory reaction and may not be due to an infectious process, especially in cases in which adhesives are necessary such as in open access for aortic root grafts, and some cases of endovascular aortic repair can show intense heterogeneous uptake.\textsuperscript{7,23} Taking this into account, positive PET/CT findings in patients with

**Figure 3.** Planimetry in the PET/CT coronal (A) and axial (B) axes shows a focal uptake suggestive of PVGI of a femoropopliteal by pass (arrows), which can be precisely located adjacent to the vascular graft after volume rendering image fusion (C) corresponding to an infected hematoma (SUVmax = 5.2).
Aortic root prosthesis should be interpreted with caution and monitoring with angio-CT is recommended. Our results in terms of specificity for 18F-FDG-PET/CT significantly improved from 79% to 93% after excluding patients in whom adhesives had been applied for PVG placement from the analysis. There were only two false-positive cases, one showing a patched and one a focal uptake pattern, which were indistinguishable from PVGI. An interesting case report by Ruiz-Zafra et al. concludes that false-positive 18F-FDG uptake as a result of a foreign body reaction can occur at any time during the follow-up period after lung cancer resection due to surgical adhesives. For all these reasons, we believe that surgical reports should detail the materials employed and the area(s) where they were used.

Combined PET/CT with volume render 3D images has also proved useful to discriminate between neighboring structures and allows the best resolution images to be obtained. This may be an interesting option to apply in the field of suspected PVGI to rule out infected pseudoaneurysms or hematomas close to the vascular graft. Indeed, we confirmed infection in the adjacent soft tissues of the suspected infected vascular graft showing a focal or heterogeneous uptake pattern in eight cases of our series, representing a non negligible 16% of the cases. In all these cases, PET/CT was determinant in establishing if infection was related to the prosthetic graft as shown in Figure 3. Other authors have reported similar difficulties in interpreting these findings, and this is important since inaccurate diagnosis may lead to the administration of inadequate treatment with a substantial potential morbi-mortality derived from unneed PVG extractions. The use of antibiotics prior to PET/CT negative results may be induced by scanning during or directly after antibiotic therapy if all signs and symptoms have abated, as is initially reported by Scholtens et al. in a recent case report. However, the mean duration of antibiotherapy in the two false negative patients was no significantly longer than in the remaining cases of PVGI.

This study has several limitations. Firstly, patients with PVGI represent a heterogeneous population with different causal microorganisms, different prosthetic materials, and different localizations of infection. Secondly, most of the patients in this series underwent antibiotic therapy prior to PET/CT and this may have influenced 18F-FDG uptake and may be a cause of lower sensitivities, so prospective randomized larger series should be performed to analyze its effect.

NEW KNOWLEDGE GAINED

This is to our knowledge the first study with series of patients raising that PET/CT does not allow to distinguish between inflammation and infection in vascular grafts with surgical use of adhesives. Furthermore, our findings provide valuable guidelines regarding the interpretation of the different patterns of PET/CT uptake in the clinical management of PVGI.

CONCLUSIONS

PET/CT with 18F-FDG is recommended for the diagnosis of suspected PVGI which can be well characterized based on focal and diffuse uptake patterns to distinguish between inflammation and PVGI. The use of adhesives can mimic a heterogeneous patched uptake of 18F-FDG on PET/CT and consequently, these cases should be interpreted with caution as this pattern may also indicate the presence of inflammation. PET/CT can be recommended to ascertain PVG involvement vs soft tissue infection adjacent to the vascular graft, especially to exclude infected pseudoaneurysms or hematomas.
Acknowledgement

Investigators of the Hospital Clinic Infective Endocarditis Study Group: Jose M. Miró, Juan Ambrosioni, Juan M. Péricas, Adrian Téllez, Marta Hernandez-Meneses, Asunción Moreno (Infectious Diseases Service); Cristina Garcia de la María, Javier Garcia-Gonzalez (Experimental Endocarditis Laboratory); Francesc Marco, Manel Almela, Jordi Vila (Microbiology Service); Eduard Quintana, Elena Sandoval, Juan C. Paré, Carlos Falces, Daniel Pereda, Ramon Caraña, Salvador Ninot, Manel Aczetu, Marta Sitges, Barbara Vidal, José L. Pomar, Manuel Castella, José M. Tolosana, José Ortiz (Cardiovascular Institute); Guillermina Fita, Irene Rovira (Anesthesiology Department); David Fuster (Nuclear Medicine Service); Jose Ramírez, (Pathology Department); Mercè Brunet (Toxicology Service); Dolores Soy (Pharmacy Service); Pedro Castro (Intensive Care Unit), and Jaume Llopis (Department of Statistics, Faculty of Biology, University of Barcelona).

Disclosure

Potential financial conflicts of interest: Jose M. Miró has received consulting honoraria and/or research grants from Genentech, Gilead Sciences, Novartis, Pfizer, Contrafect, Cubist, Merck Sharp & Dohme, ViIV Healthcare, and Janssen-Cilag. All other authors: none to declare.

References

1. Baddour L, Bettmann M, Bolger A, Epstein AE, Ferrieri P, Gerber MA, et al. Nonvalvular cardiovascular device-related infections. Circulation. 2003;108:2015–31.
2. Chiesa R, Astore D, Frigerio S, Garruboli L, Piccolo G, Castellano R, et al. Vascular prosthetic graft infection: Epidemiology, bacteriology, pathogenesis and treatment. Acta Chir Belg. 2002;102:238–47.
3. Schouten LR, Verberne HJ, Bouma BJ, van Eck-Smit BL, Mulder BJ. Surgical glue for repair of the aortic root as a possible explanation for increased F-18 FDG uptake. J Nucl Cardiol. 2008;15:146–7.
4. Orton D, LeVeen R, Saigh J, Culp WC, Fidler JL, Lynch TJ, et all. Aortic prosthetic graft infections: Radiologic manifestations and implications for management. Radiographics. 2000;20:977–93.
5. Low R, Wall S, Jeffrey R, Sollitto RA, Reilly LM, Tierney LJM. Aortoenteric fistula and perigraft infection evaluation with CT. Radiology. 1990;175:157–62.
6. Erba PA, Leo G, Sollini M, Tascini C, Boni R, Berchichili RN, et al. Radiolabeled leucocyte scintigraphy versus conventional radiological imaging for the management of late, low-grade vascular prosthetic infections. Eur J Nucl Med Mol Imaging. 2014;41:357–68.
7. Fukuchi Ishida Y, Higashi M, Tsunekawa T, Tsunekawa T, Ogino H, Minatoya K, et al. Detection of aortic prosthetic graft infection by fluorodeoxyglucose positron emission tomography: comparison with computed tomographic findings. J Vasc Surg. 2005;42:919–25.
8. Wasselius J, Malmstedt J, Kainil, Larsson S, Sundin A, Hedén U, et al. High 18F-FDG Uptake in symptomatic aortic vascular grafts on PET/CT in symptomatic and asymptomatic patients. J Nucl Med. 2008;49:1601–5.
9. Keidar Z, Engel A, Hoffman A, Israel O, Nitecki S. Prosthetic vascular graft infection: the role of 18F-FDG PET/CT. J Nucl Med. 2007;48:1230–6.
10. Bruggin JL, Glaudemans AW, Saleem BR, Meerwaldt R, Alkefaj H, Prins TR, et al. Accuracy of FDG-PET-CT in the diagnostic work-up of vascular prosthetic graft infection. Eur J Vasc Endovasc Surg. 2010;40:348–54.
11. Keidar Z, Pirmisashvili N, Leiderman M, Nitecki S, Israel O. 18F-FDG uptake in noninfected prosthetic vascular grafts: Incidence, patterns, and changes over time. J Nucl Med. 2014;55:392–5.
12. Spacek M, Belohlawek O, Votruba J, Sebesta P, Stadler P. Diagnostics of ‘‘non-acute’’ vascular prostheses infection using 18F-FDG PET/CT: our experience with 96 prostheses. Eur J Nucl Med Mol Imaging. 2009;36:850–8.
13. Berger P, Vaartjes I, Scholtens A, Moll FL, De Borst GJ, De Keizer B, et al. Differential FDG-PET uptake patterns in uninfected and infected central prosthetic vascular grafts. Eur J Vasc Endovasc Surg. 2015;50:776–83.
14. Guenther SP, Cyran CC, Rominger A, Saam T, Kazmierzczak PM, Bagaee E, et al. The relevance of 18F-fluorodeoxyglucose positron emission tomography/computed tomography imaging in diagnosing prosthetic graft infections post cardiac and proximal thoracic aortic surgery. Interact Cardiovasc Thorac Surg. 2015;21:450–8.
15. Lyons OT, Baguneid M, Barwick TD, Bell RE, Foster N, Homer-Vanniasinkam S, et al. Diagnosis of Aortic Graft infection: A case definition by the management of aortic graft infection collaboration (MAGIC). Eur J Vasc Endovasc Surg. 2016;52:758–63.
16. Samson RH, Veith FJ, Janko GS, Gupta SK, Scher LA. A modified classification and approach to the management of infections involving peripheral arterial prosthetic grafts. J Vasc Surg. 1988;8:147–53.
17. Sah B, Husmann L, Mayer D, Scherrera A, Rancic Z, Puippe G, et al. Diagnostic performance of 18F-FDG-PET/CT in vascular graft infections. Eur J Vasc Endovasc Surg. 2015;49:455–64.
18. Granados U, Fuster D, Pericas JM, Llopis JL, Ninot S, Quintana E, et al. Diagnostic accuracy of 18F-FDG PET/CT in infective endocarditis and implantable cardiac electronic device infection: A cross-sectional study. J Nucl Med. 2016;57:1726–32.
19. Fernández-López R, de-Bonilla-Damiá A, Acevedo-Bañez I, Luque-Márquez R, Borrego-Dorado I. Usefulness of 18F-FDG PET/CT in a case of suspected vascular graft infection. Rev Esp Med Nucl Imagen Mol. 2017;36:185–8.
20. Jamar Buscombe J, Chiti A, Christian PE, Christian PE, Delbeke D, Donohoe KJ, et al. EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. J Nucl Med. 2013;54:647–58.
21. Saleem BR, Pol RA, Slart RH, Reijnen MM, Zeebregts CJ. 18F-Fluorodeoxyglucose positron emission tomography/CT scanning in diagnosing vascular prosthetic graft infection. Biomed Res Int. 2014;2014:471971.
22. Abidov A, D’agnolo A, Hayes SW, Berman DS, Waxman AD. Uptake of FDG in the area of a recently implanted bioprosthetic mitral valve. Clin Nucl Med. 2004;29:948.
23. Pizzi MN, Roque A, Cuellar-Calabria H, Fernández-Hidalgo N, Ferreira-González I, González-Alujas MT, et al. 18F-FDG-PET/CTA of prosthetic cardiac valves and valve-tribe grafts: infective versus inflammatory patterns. JACC Cardiovasc Imaging. 2016;9:1224–7.
24. Ruiz-Zafría J, Rodríguez-Fernández A, Sánchez-Palencia A, Cueto A. Surgical adhesive may cause false positives in integrated positron emission tomography and computed tomography after lung cancer resection. Eur J Cardiothorac Surg. 2013;43:1251–3.
25. Bowles H, Sánchez N, Tapia A, Paredes P, Campos F, Blumenel C, et al. Radioguided surgery and the GOSTT concept: From preoperative image and intraoperative navigation to image-assisted excision. Rev Esp Med Nucl Imagen Mol. 2017;36:175–84.
26. Scholtens AM, van Aarnhem E, Budde RP. Effect of antibiotics on FDG-PET/CT imaging of prosthetic heart valve endocarditis. Eur Heart J Cardiovasc Imaging. 2015;16:1223.