

Clinical impact of ^{18}F -FDG-PET/CT in the extra cardiac work-up of patients with infective endocarditis

Ali Asmar^{1*}, Cengiz Özcan¹, Axel C.P. Diederichsen¹, Anders Thomassen², and Sabine Gill¹

¹Department of Cardiology, Odense University Hospital, Sdr Boulevard 29, 5000 Odense C, Denmark; and ²Department of Nuclear Medicine, Odense University Hospital, Sdr Boulevard 29, 5000 Odense C, Denmark

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Objective	The purpose of this study was to assess the clinical importance of ^{18}F -FDG-PET/CT used in the extra cardiac work-up of patients with infective endocarditis (IE).
Background	IE is a serious condition with a significant mortality. Besides the degree of valvular involvement, the prognosis relies crucially on the presence of systemic infectious embolism.
Methods	Seventy-two patients (71% males and mean age 63 ± 17 years) with IE were evaluated with ^{18}F -FDG-PET/CT in addition to standard work-up including patient history, physical examination, conventional imaging modalities, and weekly interdisciplinary conferences. When previous unknown lesions detected by ^{18}F -FDG-PET/CT were confirmed by succeeding examinations, they were considered <i>true positive new findings</i> and were further assessed for their <i>clinical importance</i> . Number needed to investigate was calculated as the number of patients who needed to undergo ^{18}F -FDG-PET/CT to find at least one <i>clinical important true positive new finding</i> , not identified by standard work-up prior to ^{18}F -FDG-PET/CT.
Results	^{18}F -FDG-PET/CT detected 114 lesions and 64 were <i>true positive</i> , of which 25 were new findings and detected in 17 patients. In 11 patients, the lesions were considered to have a clinical importance; osteomyelitis ($n = 7$), iliopsoas abscess ($n = 1$), gastrointestinal lesions ($n = 2$), and vascular prosthetic graft ($n = 1$). Number needed to investigate was 7 (11 of 72 patients).
Conclusions	^{18}F -FDG-PET/CT detected lesions of clinical importance in one of seven IE patients and may be a substantial imaging technique for tracing peripheral infectious embolism due to IE. Thus, ^{18}F -FDG-PET/CT may help to guide adequate therapy and thereby improve the prognosis of patients with IE.
Keywords	^{18}F -FDG-PET/CT • Clinical impact • Infective endocarditis • Extra cardiac work-up

Introduction

Infective endocarditis (IE) is a serious condition with a high mortality. The diagnosis of IE is established according to Dukes classification and modifications of these criteria suggested by European Society of Cardiology (ESC) and American Heart Association.^{1,2} Besides the degree of valvular pathology, the prognosis relies crucially on the presence of systemic infectious embolism. Embolic events have been reported to occur in 22–43% of patients with IE, and this occurs most frequently during the first 2 weeks after antibiotic

treatment is initiated.^{3,4} The extra cardiac infectious manifestations in patients with IE may involve several organs and are often difficult to distinguish from IE itself due to similarity of symptoms. However, silent/non-symptomatic embolism occurs in almost 20% of patients with IE.⁵ The prognosis of IE patients with prosthetic valves has been shown to be even worse.⁶

Patients with verified IE are routinely evaluated for the primary infectious origin and/or possible extra cardiac infectious manifestations. This process is tailored for each patient with IE and consists of clinical assessment, diagnostic microbiology, various imaging

* Corresponding author: Tel: +45 26282925; fax: +45 35313954, E-mail: aliasmar@sund.ku.dk

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techniques, and interdisciplinary conferences on a weekly basis. Early identification of these foci is very important for choosing the right type, dose, and duration of antibiotic treatment and indication for surgery.

The usefulness of ^{18}F -FDG-PET/CT has proved its worth in a spectrum of malignant conditions due to its ability to depict cells with enhanced glucose metabolism. Besides, ^{18}F -FDG-PET/CT has shown its potential in inflammation and infection.⁷ Several studies demonstrated the usefulness of ^{18}F -FDG-PET/CT as a diagnostic tool in patients with fever with unknown origin.^{7–10} In a previous study, we assessed the value of ^{18}F -FDG-PET/CT in the diagnostic work-up of extra cardiac infectious manifestations in patients with IE.¹¹ We found an overall sensitivity of 40%. When mainly excluding organs with high physiological FDG uptake (central nervous system, heart, urinary tracts, and dental region) sensitivity increased to 87%. ^{18}F -FDG-PET/CT was able to detect IE in 13 (18%) patients. Despite limited data, studies suggest ^{18}F -FDG-PET/CT as an important diagnostic tool for tracing extra cardiac infectious manifestations in IE patients. However, the clinical impact is unknown. Thus, we found it relevant to address the significance of hitherto unknown systemic infectious embolism detected by ^{18}F -FDG-PET/CT in the diagnostic work-up in patients with IE.

Methods

Study population

This retrospective, single-center study comprised 72 patients, previously described by Özcan et al.,¹¹ with definite IE according to Duke's modified criteria.¹ They were admitted to the Department of Cardiology, Odense University Hospital from January 2008 to December 2010 and underwent at least one ^{18}F -FDG-PET/CT scan. ^{18}F -FDG-PET/CT scans were booked at the discretion of the attending physician, when undetected infection was suspected. During the same time another 104 patients with IE were admitted to our department, without having an ^{18}F -FDG-PET/CT scan performed. The patients' condition varied from critically ill to less severe courses, treated surgically or conservatively. All the patients received treatment in accordance with the guidelines from the ESC. Two physicians (C.Ö. and A.A.) were responsible for gathering all relevant and pre-specified data from the medical records. Each case was discussed in the entire study group, and in cases with doubt about the clinical importance of a finding, final data were made up as a consensus decision.

^{18}F -FDG-PET/CT

Examinations were conducted on dedicated ^{18}F -FDG-PET/CT systems (GE Discovery VCT XT, GE Discovery RX or GE Discovery STE; GE Healthcare, Milwaukee, WI, USA). Patients were fasting 6 h (diabetes patients only 4 h) prior to injection and were given a weight adjusted dose of 4 MBq/kg (min. 200 MBq and max. 400 MBq) ^{18}F -FDG 60 min prior to image acquisition. The duration of the PET scan was at least 2.5 min per bed position increasing to 3.5 min in extremely overweight patients. Different CT protocols were used according to the type of disease. Contrast-enhanced CT (iopromide 370 mg iodine/mL) was performed when pathological conditions were suspected in the abdomen or in the head/neck region, whereas non-contrast-enhanced CT was performed when pathological conditions were suspected in other regions. The standard field of view for the ^{18}F -FDG-PET/CT imaging extended the base of the skull to the mid-thighs, unless it was specified differently. The analysis of the ^{18}F -FDG-PET/CT imaging for infection and inflammation relied on a visual assessment of the distribution and intensity of the

tracer. The ^{18}F -FDG-PET imaging was interpreted by two nuclear medicine physicians, and the contrast-enhanced CT by a radiologist. A mutual conclusion was achieved.

^{18}F -FDG-PET/CT vs. other modalities

Since no gold standard in the work-up of extra cardiac manifestations in IE exists, the result of each ^{18}F -FDG-PET/CT scan was compared with the results of the clinical standard work-up according to ESC Guidelines for IE, which at the same time served as the gold standard. Depending on the clinical setting, the work-up included patient history, physical examination (including examination by a dentist), laboratory tests, ultrasound, X-ray, CT, MRI, nuclear imaging techniques, histopathological studies, microbiological cultures, endoscopies, and clinical assistance from other specialities. All patient courses were reviewed weekly at a conference with participants from the departments of cardiology, thoracic surgery, anaesthesiology, infectious diseases, and microbiology with the purpose of optimizing patient treatment, diagnostics, and to consider the indication for surgery.

For evaluating only the supplemental benefit of ^{18}F -FDG-PET/CT in the evaluation of IE patients, only lesions not previously detected by other modalities were evaluated, regardless of localization. Evaluation was based on a per-lesion analysis, potentially resulting in more than one lesion in each patient. A lesion was considered a *true positive new finding*, if the finding was confirmed by subsequent other modalities. Any lesion detected by ^{18}F -FDG-PET/CT was further evaluated for its *clinical importance*, and considered as a *clinical important finding* if resulting in any adjustment of the treatment course, whether medical or surgical.

Statistical analysis

Descriptive measures for continuous variables were presented as means \pm SD or as median values and range. Depending on the descriptive variables, unpaired *t*-test and Fisher's exact probability test were used for calculating the *P*-value (SigmaPlot 12, Systat Software, Inc., Chicago, IL, USA). Differences were considered statistically significant at values of $P < 0.05$.

Number needed to investigate was calculated by number of ^{18}F -FDG-PET/CT with clinical importance divided by the total number of ^{18}F -FDG-PET/CT performed.

Results

Patient characteristics

The mean age was 63 ± 17 years, the majority being males (71%). See Table 1 for baseline characteristics. Within 1 month from the onset of symptoms, 71% of patients were diagnosed with IE, and the ^{18}F -FDG-PET/CT was conducted at a median of 6 days (range; 5 days before to 58 days after) after the diagnosis was established. Left-sided IE was seen in the majority of cases, and staphylococci (40%) and streptococci (30%) were the most frequent bacterial species (Table 2). Forty-four per cent of the patients were treated surgically. Valvular regurgitation/destruction was the main indication for surgery (91%). In-hospital mortality was 15%. In our study, no indication of valve surgery was made on the basis of the ^{18}F -FDG-PET/CT findings. However, in one case with an abscess detected by ^{18}F -FDG-PET/CT surgery was done. With a median follow-up of >1 year (469 days, range; 25–1067 days), 6% had relapse, 3% reinfection, and long-term survival rate was 71%. Characteristics were similar between patients with and without findings at ^{18}F -FDG-PET/CT (positive and negative scans, respectively).

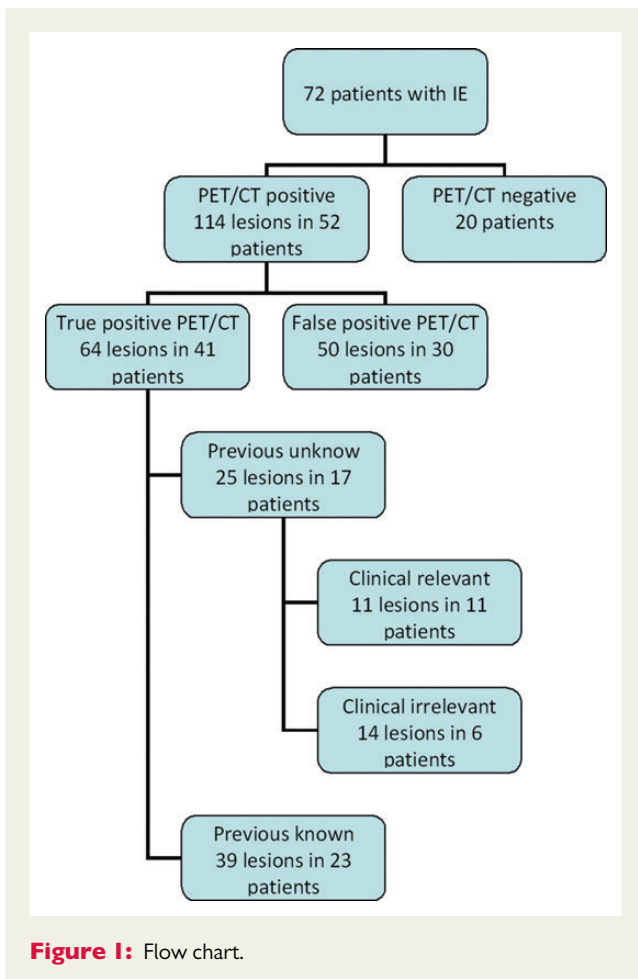
Variable	¹⁸ F-FDG-PET/CT all (n = 72)	¹⁸ F-FDG-PET/CT positive (n = 52)	¹⁸ F-FDG-PET/CT negative (n = 20)	P-value (positive vs. negative)
Age (years)	63 ± 17	64 ± 18	60 ± 13	0.40
Male	51 (71)	36 (70)	15 (75)	0.78
Diabetes mellitus	12 (17)	9 (17)	3 (15)	1.00
Hypertension	26 (36)	20 (38)	6 (30)	0.59
Presence or past tobacco use	42 (58)	34 (65)	8 (40)	0.06
Heart failure at admission (LVEF <50%) ^a	15 (22)	10 (19)	5 (25)	0.75
Haemodialysis	3 (4)	2 (4)	1 (5)	1.00
Immunosuppression	6 (8)	5 (10)	1 (5)	1.00
Current i.v. abuse	5 (7)	3 (6)	2 (10)	0.61
Congenital heart disease	6 (8)	4 (8)	2 (10)	0.67
Previous IE	9 (13)	7 (13)	2 (10)	1.00
Valve prosthesis	17 (24)	14 (27)	3 (15)	0.36
Native valve regurgitation/ stenosis	29 (40)	22 (42)	7 (35)	0.60

^aData based on 67 patients.

Variable	¹⁸ F-FDG-PET/CT all (n = 72)	¹⁸ F-FDG-PET/CT positive (n = 52)	¹⁸ F-FDG-PET/CT negative (n = 20)	P-value (positive vs. negative)
IE type (%)				
Native valve	52 (72)	31 (60)	14 (70)	0.59
Prosthetic valve	12 (16)	12 (23)	2 (10)	0.32
Pacemaker/ICD	2 (3)	1 (2)	1 (5)	0.48
Vegetation negative	3 (4)	3 (6)	0	0.55
VSD	1 (1)	1 (2)	0	1.00
Other	2 (3)	2 (4)	0	1.00
Microbiology (%)				
<i>Staphylococcus aureus</i>	24 (33)	17 (33)	7 (35)	1.00
Coagulase-negative staphylococcus	5 (7)	5 (10)	0	0.31
Viridans group streptococci	9 (12)	6 (12)	3 (15)	0.70
<i>Streptococcus bovis</i>	0	0	0	1.00
Other streptococci	13 (18)	10 (19)	3 (15)	1.00
Enterococcus species	12 (17)	8 (15)	4 (20)	0.72
HACEK	1 (1)	1 (2)	0	1.00
Other bacteria	4 (6)	2 (4)	2 (10)	0.31
<i>Escherichia coli</i>	1 (1)	1 (2)	0	1.00
Negative culture findings	4 (6)	3 (6)	1 (5)	1.00

Positive ¹⁸F-FDG-PET/CT scans

prior to ¹⁸F-FDG-PET/CT) and were confirmed by a median of 3 (range 1–8) different modalities. Of these 25 findings 11 had clinical importance (Figure 1). Thus, the number needed to investigate—to find a clinically important lesion, that would change therapy—was 7 (11 divided by 72).



Clinical important findings

In eight cases, ^{18}F -FDG-PET/CT revealed a lesion suspicious for osteomyelitis (Figure 2). Seven were subsequently confirmed by MRI and one by bone scintigraphy. One of these patients was further diagnosed with an abscess located in the paravertebral muscle by ^{18}F -FDG-PET/CT. This was confirmed by MRI and subsequently treated with surgical drainage (Figure 3). ^{18}F -FDG-PET/CT identified one case with hitherto unknown gastrointestinal cancer and a case with acute cholecystitis, both being confirmed by endoscopic and ultrasonographic examinations. Finally, in one patient vascular graft infection, suggested by ^{18}F -FDG-PET/CT, was verified by contrast-enhanced CT (Figure 4).

Findings without therapeutic consequences

The remaining six patients comprised pulmonary infections, polyp of the respiratory airway, unspecific gastrointestinal lesions, diverticulosis, and small liver as well as spleen abscesses, respectively. One patient had ultrasonographical signs of infection surrounding the long biceps tendon. None of these conditions had any influence on the ongoing treatment.

Discussion

In the present study, we assessed the clinical importance of previously unknown lesions, detected by ^{18}F -FDG-PET/CT, in patients with

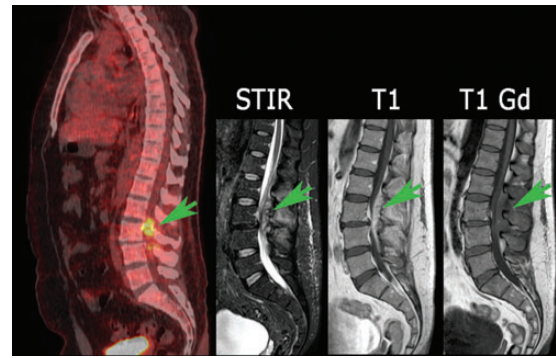


Figure 2: Osteomyelitis, a patient with a mitral valve endocarditis. He had a history of infection of the elbow and back pain. Sagittal ^{18}F -FDG-PET/CT image demonstrated fluorodeoxyglucose (FDG) accumulation in the lumbar vertebral canal suggestive of infection (green arrows). Magnetic resonance imaging (MRI) demonstrated epidural phlegmonous empyema at level L2–L4 with involvement of the paravertebral musculature. Short inversion time inversion recovery (STIR) sequences and T1-weighted MRI before (T1) and after gadolinium enhancement (T1 Gd).

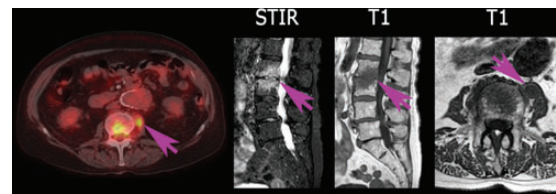


Figure 3: Spondylodiscitis and paravertebral muscle abscess, this patient had an infected artificial aortic stent valve. She had a history of coronary artery bypass grafting 4 years earlier. She had a FDG avid intervertebral disc and vertebral corpora at level L2/L3. ^{18}F -FDG-PET/CT was also suggestive of a small paravertebral abscess (transaxial images). Both spondylodiscitis and paravertebral abscess was confirmed by MRI (STIR and T1-weighted sagittal and transaxial images shown) (purple arrows). Abbreviations as in Figure 2.

definite IE. ^{18}F -FDG-PET/CT identified 11 out of 72 patients, who had clinical important lesions not detected by conventional work-up, most frequently axial osteomyelitis.

The diagnosis of IE is a challenge, especially due to extra cardiac infectious manifestations even in patients without suspicion.¹² These are severe complications, which may prolong and complicate the clinical course, thereby having impact on the therapeutic treatment of IE, in terms of choice of antibiotics, duration of treatment and optimal timing for surgical intervention.^{5,13,14}

The diagnostic role of ^{18}F -FDG-PET/CT has been investigated extensively in cancers as well as in cardiac and neurological disorders.^{15–17} However, in the past decade increasing numbers of studies have shown promising results in management of patients with infection^{7–10} possibly because ^{18}F -FDG-PET/CT has some

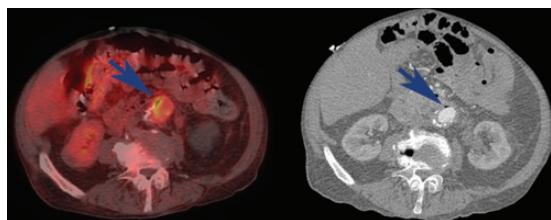


Figure 4: Vascular graft infection, the patient had an aortic valve endocarditis. By ^{18}F -FDG-PET/CT, an increased FDG uptake was seen focally in the abdominal aorta and there was suspicion of air in the aortic wall, which was difficult to evaluate by non-contrast-enhanced computed tomography. A subsequent contrast-enhanced computed tomography confirmed the air inside the aortic wall, suggestive of infection (blue arrows). Abbreviations as in Figure 2.

advantages compared with conventional nuclear imaging techniques like white blood cell scan; higher resolution and sensitivity together with detailed anatomic localization from the CT part of the examination. The latter, of course, is also possible in conventional nuclear imaging techniques with hybrid SPECT/CT scanners.

In our study, ^{18}F -FDG-PET/CT revealed lesions suspicious for osteomyelitis in eight patients, which prolonged the antibiotic treatment in each patient according to the guidelines from the ESC.¹ Seven episodes were subsequently confirmed by MRI and one by bone scintigraphy.

Bone scintigraphy has been utilized for years to evaluate patients with suspected osteomyelitis with a high sensitivity.¹⁸ Radiolabelled white blood cell scintigraphy is also used to detect osteomyelitis, as its specificity is higher than that of bone scintigraphy.¹⁸ However, treatment with antibiotics prior to radiolabelled white blood cell scintigraphy reduced sensitivity due to poor migration of the leucocytes.¹⁹ In addition, the sensitivity of radiolabelled white blood cell scintigraphy in the evaluation of chronic osteomyelitis in the axial skeleton is only 21% due to the poor contrast between the sites of infection and the surrounding red bone marrow.¹⁸ In our study, all episodes of osteomyelitis were located in the axial skeletons, although the ^{18}F -FDG-PET/CT was conducted after antibiotic treatment had been initiated.

^{18}F -FDG-PET/CT has shown to be highly sensitive for detecting chronic osteomyelitis, even in patients who have been treated with antibiotics prior to imaging,^{20–24} with a higher sensitivity and specificity compared with bone scintigraphy, radiolabelled white blood cell scintigraphy or MRI.^{18,24–27} Further, it has been observed, that FDG activity returned to normal after successful treatment of chronic osteomyelitis, whereas persistent abnormalities were seen with MRI.²⁸ This might be a relevant issue to distinguish between ongoing and past osteomyelitis prior to possible valve surgery to prevent relapse.

In one patient ^{18}F -FDG-PET/CT suggested vascular graft infection (Figure 4) and was verified by contrast-enhanced CT. The precise anatomic localization by ^{18}F -FDG-PET/CT enables accurate differentiation between graft and soft tissue infection. Fukuchi *et al.*²⁹ showed among 39 patients with suspected vascular graft infection, that ^{18}F -FDG-PET/CT had a sensitivity and specificity of 93 and

91%, respectively, on the basis of surgical, microbiological, and clinical follow-up findings.

By ^{18}F -FDG-PET/CT, Bonfiglioli *et al.*³⁰ found extra cardiac manifestations in 17 of 71 patients with suspected IE. Nonetheless, only 29 received a final clinical diagnosis of IE. Further, Saby *et al.*³¹ prospectively studied the value of ^{18}F -FDG-PET/CT for diagnosing prosthetic valve endocarditis (PVE) in 72 patients suspected of having IE. At the end of follow-up, only 30 patients were classified as having definite PVE. In this study, whole-body acquisition was performed to detect extra cardiac infectious foci, which was identified in eight patients (three splenic embolies and five cases of spondylodiscitis). Whether these lesions were previously unknown is not clear. However, the authors conclude that ^{18}F -FDG-PET/CT was useful for detecting infectious embolism. In the present study, all the patients were diagnosed with IE, which leaves a much more homogenous cohort to examine in a significantly larger number of patients.

Although the European Medicines Agency has approved the use of ^{18}F -FDG-PET/CT in various infections, it is still not determined, whether ^{18}F -FDG-PET/CT should be included as a regular part of the extra cardiac work-up of IE patients.

Incomplete eradication of either the primary focus or secondary infectious embolism appears to be the most important contributor to a worse outcome and relapse of especially gram-positive bacteraemia.³² Therefore, it is appealing to have a sensitive whole-body scan, e.g. ^{18}F -FDG-PET/CT aimed to detect infectious embolism. Overall, ^{18}F -FDG-PET/CT was retrospectively proved to find relevant embolism in patients with bacteraemia, most of them with gram-positive bacteraemia,³³ despite the fact that three conventional imaging techniques had been performed prior to ^{18}F -FDG-PET/CT. This is similar to the present study in which one to eight imaging techniques were employed. Compared with ^{18}F -FDG-PET/CT, conventional imaging techniques would most often be performed partly as serial examinations rather than parallel examinations, which appears to be more time consuming and thereby at incremental costs. The question is whether a whole-body ^{18}F -FDG-PET/CT is able to substitute conventional imaging techniques. In a prospective study, Vos *et al.*³⁴ studied the value of ^{18}F -FDG-PET/CT performed in patients with gram-positive bacteraemia within 2 weeks after admission. The patients were matched regarding microorganism and risk profile for the presence of metastatic infectious foci with patients in whom ^{18}F -FDG-PET/CT was not performed. It was hypothesized that early detection and treatment of metastatic foci would be cost-effective due to less relapses or delayed cure. Not surprisingly, the number of patients with metastatic infectious foci was increased in the ^{18}F -FDG-PET/CT group, and the number of patients with IE was even doubled. Treatment of IE was the main cost driver. Despite the fact that ^{18}F -FDG-PET/CT resulted in increased costs due to more in-hospital treatment, the cost of prevented death was within the range accepted as efficient. However, confirmation of ^{18}F -FDG-PET/CT lesions should not be overestimated due to false positive lesions of ^{18}F -FDG-PET/CT. From the same patient cohort, we earlier reported 50 false positive lesions in 30 patients with IE. Further, we revealed that organs with high physiological uptake of FDG (central nervous system, heart, urinary tracts, and dental region) are not suitable for diagnostic approach by ^{18}F -FDG-PET/CT, and not surprisingly when excluded, the sensitivity of ^{18}F -FDG-PET/CT doubled (40–87%).¹¹ Thus, lesions located in

organs with a high physiological uptake need supplementary diagnostic modalities other than solely ^{18}F -FDG-PET/CT. Nevertheless, apart from detecting IE, ^{18}F -FDG-PET/CT's negative predictive value is considered high.¹¹

Finally, what would be the optimal timing to assess extra cardiac infectious foci in patients with IE? In the present study, ^{18}F -FDG-PET/CT was conducted at a median of 6 days (range; 5 days before to 58 days after) after the diagnosis was established. Thus, a certain number of ^{18}F -FDG-PET/CT scans were conducted relatively late from the onset of antibiotic treatment. Whether this has a clinical importance remains unclear. Embolic events occur most frequently during the first 2 weeks after antibiotic treatment is initiated.^{3,4} However, we demonstrated earlier that the sensitivity of ^{18}F -FDG-PET/CT in the diagnostic work-up of extra cardiac infectious foci increased from 79% when conducted early (<6 days from diagnosis of IE) to 91% when conducted late (>6 days from diagnosis of IE).¹¹ Nevertheless, the optimal timing for performing ^{18}F -FDG-PET/CT should be determined in future studies.

In our study, 11 patients had a significant clinical impact of the ^{18}F -FDG-PET/CT scan, which we interpreted as a number needed to investigate of ~7. To our knowledge, only one prospective study exists primarily assessing the diagnostic role of ^{18}F -FDG-PET/CT for early extra cardiac infectious manifestations.³⁵ In this study, 24 patients underwent an ^{18}F -FDG-PET/CT within 2 weeks after the diagnosis of IE. In 28% of patients, extra cardiac manifestations were detected early giving therapeutic impact. Our findings are in accordance with the findings in this study.

Limitations

The present study was conducted retrospectively, resulting in methodological difficulties concerning the comparison of ^{18}F -FDG-PET/CT results with the standard work-up. Since infection is a dynamic process, a head-to-head comparison between ^{18}F -FDG-PET/CT and other imaging modalities is more likely to resemble daily clinical practice. Further, the retrospective nature and referral of patients with IE to an ^{18}F -FDG-PET/CT scan by physician's clinical suspicion is not an optimal setting to study the true frequency of significant extra cardiac and needs a prospective assessment. However, due to the retrospective nature of the present study a significant follow-up was allowed.

The reference standard in the present study was other imaging modalities, e.g. X-ray, ultrasound which were obviously inferior to a whole-body ^{18}F -FDG-PET/CT. Potentially, this may underestimate the number of clinical important findings revealed in the present study. Further, we were not able to distinguish, whether any lesion detected by ^{18}F -FDG-PET/CT was to be considered as a primary source of IE or being a secondary infectious embolism. Though, the clinical consequences of this differentiation seem of minor importance only, as both types of infection need to be treated.

Finally, the number of patients in our study is limited. Though, this is the largest study published so far concerning the same issue, larger studies are needed to confirm our results.

Conclusion

In 11 of 72 patients, ^{18}F -FDG-PET/CT detected extra cardiac lesions with significant clinical importance, not detected by the standard work-up. Thus, the number needed to investigate was 7. Prospective

studies evaluating the role of ^{18}F -FDG-PET/CT in the clinical management of patients with IE are needed. However, at present we suggest that ^{18}F -FDG-PET/CT should be performed without significant time delay from the day of definite diagnosis together with other relevant diagnostic modalities.

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Conflict of interest: none declared.

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IMAGE FOCUS

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Brain drain causing severe tricuspid regurgitation

Satyendra Tewari, Srivatsa Nadig, and Aditya Kapoor*

Department of Cardiology, Sanjay Gandhi PGIMS, Lucknow 226014, India

* Corresponding author. Tel: +91 522 2494220/+91 9839008893; Fax: +91 522 2668073, Email: akapoor65@gmail.com

An adult male with breathlessness and audible tricuspid regurgitation (TR) had right atrial (RA) enlargement on chest X-ray (Panel A). Transthoracic echocardiography with 3D reconstruction revealed dilated RA, severe TR, normal right ventricular function, and a mobile, tubular structure in the RA seemingly traversing the superior vena cava (SVC; Panel B and see Supplementary data online, Videos S1 and S2). The mobile tubular structure was confirmed on transoesophageal echocardiography, traversing from the SVC, into the RA (see Supplementary data online, Video S3 and Panel C); thrombus or spontaneous echo contrast was absent.

Although the patient denied any previous cardiac intervention, a scar mark was visible in the neck (Panel D). He volunteered a history of ventriculo-atrial shunt 20 years ago for obstructive hydrocephalus. The intracardiac shunt catheter had caused functional TR secondary to malcoaptation, reminiscent of pacing lead-induced TR. In most such cases, TR is usually mild to moderate and severe TR is quite rare; moreover, malcoaptation as the sole mechanism of severe TR is rather unusual.

A ventriculo-atrial shunt meant for decompressing hydrocephalus (prompting the term 'brain drain') leading to severe TR is as yet an unreported entity. The patient improved following initiation of diuretics. Careful clinical examination and detailed transthoracic (with 3D reconstruction) and transoesophageal echocardiography were helpful in making the diagnosis in this unusual case.

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

