^{18}F-FDG positron emission tomography/ computed tomography in infective endocarditis

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Background. **The diagnosis of infective endocarditis (IE), especially the diagnosis of prosthetic valve endocarditis (PVE) is challenging since echocardiographic findings are often scarce in the early phase of the disease. We studied the use of 2-[^{18}F]fluoro-2-deoxy-*D*-glucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) in IE.**

Methods. **Sixteen patients with suspected PVE and 7 patients with NVE underwent visual evaluation of ^{18}F-FDG-PET/CT. ^{18}F-FDG uptake was measured also semiquantitatively as maximum standardized uptake value (SUV_{max}) and target-to-background ratio (TBR). The modified Duke criteria were used as a reference.**

Results. **There was strong, focal ^{18}F-FDG uptake in the area of the affected valve in all 6 cases of definite PVE, in 3 of 5 possible PVE cases, and in 2 of 5 rejected cases. In all patients with definite PVE, SUV_{max} of the affected valve was higher than 4 and TBR higher than 1.8. In contrast to PVE, only 1 of 7 patients with NVE had uptake of ^{18}F-FDG by PET/CT in the valve area. Embolic infectious foci were detected in 58% of the patients with definite IE.**

Conclusions. **^{18}F-FDG-PET/CT appears to be a sensitive method for the detection of paravalvular infection associated with PVE. Instead, the sensitivity of PET/CT is limited in NVE. (J Nucl Cardiol 2017;24:195–206.)**

Key Words: Infective endocarditis • prosthetic valve endocarditis • echocardiography • positron emission tomography • ^{18}F-fluorodeoxyglucose

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Abbreviations	
IE	Infective endocarditis
PVE	Prosthetic valve endocarditis
NVE	Native valve endocarditis
PET/CT	Positron emission tomography/ computed tomography
^{18}F-FDG	2[^{18}F]fluoro-2-deoxy-*D*-glucose
SUV_{max}	Maximum standardized uptake value
TBR	Target-to-background ratio
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

INTRODUCTION

Infective endocarditis (IE) is a life-threatening disease.[1-5] Despite developments in both imaging and microbiological techniques, the diagnosis of IE is challenging, especially the diagnosis of prosthetic valve endocarditis (PVE). The current standard of clinical assessment is the modified Duke criteria.[6,7] According to the modified Duke criteria, definite diagnosis of IE is mainly based on positive blood cultures with a typical micro-organism and/or evidence of IE by echocardiography. Sensitivity of transthoracic echocardiography (TTE) for endocarditis ranges from 20% to 65% and that of transesophageal echocardiography (TEE) from 70% to 90%.[8-10] Sensitivity can be improved by doing repeated examinations.[8,11] However, identification of IE vegetation in the presence of pre-existing valve lesions and differential diagnosis between IE vegetation and other pathologies, such as thrombosis can be difficult.[12] Furthermore, the sensitivity of echocardiography for diagnosing PVE is lower compared to diagnosing native valve infective endocarditis (NVE).[8,13] Rapid diagnosis of IE is important as early initiation of effective antimicrobial treatment prevents complications requiring valve surgery.[7] Therefore, new more sensitive methods to detect IE are needed.

Positron emission tomography (PET) with the glucose analogue 2-[^{18}F]fluoro-2-deoxy-*D*-glucose (^{18}F-FDG) has been used to detect inflammation and infection based on high glucose uptake of leukocytes. Recent studies have indicated that ^{18}F-FDG-PET/CT may be useful in IE, especially in the detection of extracardiac infectious foci.[14-16] However, less is known about the ability of ^{18}F-FDG-PET/CT to visualize directly heart valve infection in NVE or PVE. Therefore, we wanted to study the diagnostic value of ^{18}F-FDG-PET/CT imaging of valvular infection in patients with suspected PVE or NVE.

METHODS

Patients

This prospective study evaluated 23 consecutive patients admitted to Turku University Hospital, Turku, Finland between September 2011 and September 2014 due to suspected NVE or PVE. Patients with hemodynamic instability or need for urgent surgery were excluded. The hospital is a tertiary-care center for the south-west part of the country. Seven of the patients had suspected NVE and 16 of the patients had suspected PVE. The study was approved by the institutional ethical review board, and all participants signed an informed consent.

On admission and during hospital stay, clinical history and findings as well as data on blood culture findings and serum markers of inflammation (C-reactive protein and procalcitonin) were collected. Times from the onset of symptoms, onset of antimicrobial treatment, and valvular surgery to PET/CT were recorded. TEE was done in all except one patient who had tricuspid valve vegetation visible on TTE. Histological and microbiological findings of the tissue specimens taken during the operation were evaluated when available. Follow-up after hospital discharge was conducted for a mean of 19 months (range 2-33 months).

The clinical diagnosis of IE was done by expert team according to the modified Duke criteria[7] and based on all available clinical and microbiological data, but excluding PET/CT findings. The modified Duke criteria were determined after the follow-up.

^{18}F-FDG-PET/CT

A whole-body or cardiac ^{18}F-FDG-PET/CT scan (Discovery VCT, General Electric Medical Systems, Milwaukee, WI, USA) was performed in all patients. Mean time from hospital admission to PET/CT was 5 days in NVE and 13 in PVE. In order to reduce physiological glucose uptake of the myocardium, patients were on low-carbohydrate diet for 24 hours before the PET-scan and fasted at least 10 hours before the study.[17] Mean injected dose of ^{18}F-FDG was 280 MBq (range 147-371 MBq). An average of 72 minutes (range 52-98 minutes) later a whole-body PET acquisition (3 minutes per bed position) was performed following CT scan for anatomical reference and attenuation correction. One patient had only cardiac PET/CT.

Blood glucose levels were $<10\ \mathrm{mmol{\bullet}L^{-1}}$ prior to injection of the tracer in all patients. PET images were reconstructed with 128×128 matrix size in full 3D mode using maximum-likelihood reconstruction with ordered-subsets expectation maximization algorithm (VUE Point, GE Healthcare).

Visual analysis of the images was performed by an experienced nuclear medicine specialist and results were re-evaluated by the research team for consensus. All image analyses were done blinded with respect to patient's clinical details. A positive finding was defined as an increase in ^{18}F-FDG accumulation in the valve or valve prosthesis area. The presence of visual FDG uptake in attenuation corrected images was confirmed in non-attenuation corrected images when appropriate. In addition to the valves, the images were evaluated for the presence of abnormal ^{18}F-FDG accumulation elsewhere in the body.

^{18}F-FDG uptake was also measured semiquantitatively as maximum standardized uptake value (SUV_{max}) which was obtained by normalizing the tissue concentration of FDG activity and the patient's weight and as target-to-background ratio (TBR). The SUV_{max} was measured in a volume of interest covering the valve or prosthesis area based on co-registered CT images. Mean volume size was 14.6 cm^3 in the aortic and 13.1 cm^3 in the mitral position. The mean background radioactivity in the blood was measured in the ascending aorta excluding the vessel wall (mean radioactivity in a volume of interest of 6.8 cm^3) to calculate TBR.

Statistical Analysis

Values are shown as medians or means with range of values. ^{18}F-FDG uptake in the affected valve and another valve of the same patient were compared using Wilcoxon signed rank test and in the valves of patients with definitive, possible, or rejected PVE by Kruskall-Wallis test. A value of $P < .05$ was considered significant. Statistical analyses were performed using SAS for Windows, version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Clinical characteristics, TEE findings, microbiological findings, and diagnostic classification based on the modified Duke criteria of the patients are presented in Table 1.

Clinical Characteristics in Suspected NVE

Seven patients had suspected NVE. The mean age of these patients was 53 years and 6 were males. Time from the onset of symptoms to PET/CT was on average 48 days (range 5-150 days) and from the onset of antimicrobial treatment 5 days (range 3-7 days). Surgery was performed in 4 cases with definite IE and histological examination confirmed the diagnosis. The patient with the paravalvular abscess died after surgery.

Clinical Characteristics in Suspected PVE

There were 16 patients with suspected PVE. Mean age was 67 years and 14 were males. Time from surgery to PET/CT varied from 4 weeks to 28 years (Table 3). Times from the onset of symptoms and from commencement of antimicrobial treatment to PET/CT were on average 16 days (range 5-62 days) and 13 days (range 0-59 days), respectively. Surgery was performed in 2 cases (Patient #12 and #20 in Table 1). Histology and microbiological tests confirmed the diagnosis in the case with definitive IE whereas, in the other case with possible PVE histology showed no signs of IE. During follow-up, 4 patients (25%) died due to IE, heart failure, chronic obstructive pulmonary disease, or colon cancer.

^{18}F-FDG-PET/CT Findings in Suspected NVE

Of the seven patients with NVE, visual analysis of ^{18}F-FDG-PET/CT images showed increased tracer uptake in the aortic valve region in only one patient who also had a paravalvular abscess (Table 2; Figure 1). In the remaining six cases with NVE, the visual analysis was negative even in the presence of large vegetations on TEE (Figure 1). Median SUV_{max} of the affected valves was 2.7 (range 2.4-8.3) and TBR 1.3 (range 1.0-2.9) that were comparable with the non-affected valves (2.5 (range 1.4-3.5) and 1.2 (range 1.0-1.9), $P = .813$ and $P = .813$, respectively). Thus, PET/CT was positive only in 1 of the 6 definite cases of NVE, indicating that the sensitivity for the detection of infection in the native valves is low.

^{18}F-FDG-PET/CT Findings in Suspected PVE

In definite PVE, visual analysis of PET/CT images showed ^{18}F-FDG uptake of the prosthetic valve area in all 6 cases. The SUV_{max} of 4 was identified as a cut-off point differentiating visually PET positive and negative cases. In all patients with definite PVE, SUV_{max} of the affected valve was higher than 4 and TBR higher than 1.8. Median SUV_{max} and TBR of the affected valve were significantly higher compared with the SUV_{max} and TBR of the native valve of these patients (5.8 (range 4.1-9.0) and 2.3 (range 1.9-3.8) vs 2.5 (range 1.9-3.4), and 1.1 (range 1.0-1.2), $P = .031$ and .031).

In possible PVE, ^{18}F-FDG uptake of the prosthetic valve area was visually detected in 3 of 5 patients. SUV_{max} was higher than 4 in all of these 3 cases. In the group of possible PVE, median SUV_{max} and TBR of the prosthetic valves were 5.2 (range 3.4-8.4) and 2.0 (range 1.5-3.0), and 3.0 (range 2.8-3.3) and 1.3 (range 1.0-1.7) in the native valves of the same patients. In the 3 patients with possible PVE and positive ^{18}F-FDG finding, positive blood culture and clinical data, including positive response to antimicrobial therapy, supported the diagnosis of PVE despite negative TEE findings. In addition one of these patients (Patient #14 in Table 3) had biological aortic and mitral prostheses, but ^{18}F-FDG uptake only at the aortic valve prosthesis area (Figure 2). In 2 patients with possible PVE and negative ^{18}F-FDG finding of the prosthetic valve, an alternative diagnostic finding was detected in PET/CT: pneumonia in one and colon tumor and metastasis in the other.

Median SUV_{max} and TBR of the prosthetic valve of the rejected group were 4.8 (range 2.9-7.8) and 2.2 (range 1.3-3.3), and 2.5 (range 2.1-3.3) and 1.2 (range 0.9-1.6) in the native valves. Four patients in this group

Table 1. Background information of all patients

No.	Age gender	Duke	Blood culture	Transesophageal echocardiography	Antibiotic treatment before PET/CT (days)	Comorbidities	CRP $mg \cdot L^{-1}$/ PCT $\mu g \cdot L^{-1}$ on PET/CT day
1	58M	Definite	*Staphylococcus aureus*	Abscess cavity from aortic valve to left atrium, vegetation on aortic valve, vegetation on mitral valve	4	Hypercholesterolemia	125/1.91
2	23F	Definite	*Staphylococcus aureus*	Vegetation on tricuspid valve[a]	6	Hepatitis C, IVDU	118/0.18
3	62M	Definite	*Streptococcus gordonii*	Vegetation on mitral valve	3	HA	10/0.17
4	58M	Definite	*Abiotrophia defectiva*	Vegetation on mitral valve and pronounced regurgitation	7	Osteogenesis imperfecta, CRF	95/0.12
5	62M	Definite	*Streptococcus anginosus*	Vegetation on aortic valve and moderate regurgitation	5	HA, regurgitation of aortic valve	11/0.15
6	39M	Definite	*Staphylococcus aureus*	Vegetation on aortic valve and pronounced regurgitation	4	Atopic eczema	51/4.13
7	66M	Possible	Negative	Vegetation on aortic valve	6	RA, CAD, post CABG, HA	13/0.07
Patients with prosthetic valve							
8	79M	Definite	*Streptococcus dysgalactiae, Klebsiella pneumoniae*	Fistula/abscess cavity around aortic valve prosthesis	28	HA, CRF	44/0.11
9	69M	Definite	*Enterococcus faecalis*	Vegetation on aortic valve prosthesis	6	AF, generalized atherosclerosis, RA	123/NA
10	70M	Definite	*Enterococcus faecalis*	Vegetation on mitral valve prosthesis	8	CAD, post CABG, cardiomyopathy HA, DM, AF, CRF	120/0.64
11	58M	Definite	*Staphylococcus aureus*	No sign of endocarditis	59	HA, AF, DM	124/0.12
12	41M	Definite	*Staphylococcus aureus*	Paraprosthetic regurgitation and abscess cavity around aortic valve prosthesis	3	Atopic eczema	160/NA
13	83M	Definite	*Staphylococcus warnerii*	No sign of endocarditis	5	HA, CAD, PRH	38/0.89
14	67F	Possible	*Staphylococcus epidermidis*	No sign of endocarditis	6	AF, CAD, CRF	143/NA
15	76M	Possible	*Streptococcus mitis*	No sign of endocarditis	10	COPD, AF, RA	67/0.34
16	64M	Possible	*Streptococcus sanguinis*	No sign of endocarditis	18	Gout, mitral valve regurgitation	13/0.06
17	83M	Possible	*Staphylococcus aureus*	No sign of endocarditis	12	CAD, AF, AAA, COPD, asbestosis, gout, CRF	52/0.18

Table 1. continued

No.	Age gender	Duke	Blood culture	Transesophageal echocardiography	Antibiotic treatment before PET/CT (days)	Comorbidities	CRP $mg \cdot L^{-1}$/ PCT $\mu g \cdot L^{-1}$ on PET/CT day
18	57M	Possible	*Staphylococcus lugdunensis*	No sign of endocarditis, swollen root of ascending aorta	9	HA, asthma, 1967 operated aortic coarctation	10/NA
19	69M	Rejected	Negative	Vegetation on mitral valve prosthesis, finding was controlled 3 times within the first month and it stayed the same	9	HA, AF, heart failure, CRF	12/NA
20	63N	Rejected	Negative	Aneurysm, suspected abscess in sinus Valsalva, in the area of right coronary cusp, dilated ascending aorta	22	HA, primary biliary cirrhosis, diverticulosis	49/NA
21	79M	Rejected	Negative	No sign of endocarditis	10	HA, AF, prostate carcinoma operated 1999	12/0.06
22	53F	Rejected	Negative	No sign of endocarditis	0	HA	272/0.18
23	68M	Rejected	Negative	No sign of endocarditis	5	-	123/0.12

HA, Hypertension; *COPD*, chronic obstructive pulmonary disease; *DM*, diabetes mellitus; *IVDU*, intra-venous drug usage; *RA*, rheumatoid Arthritis; *AF*, atrial Fibrillation; *AAA*, abdominal aortic aneurysm; *CAD* coronary artery disease; *CABG*, coronary artery bypass grafting, *CRF*, chronic renal failure; *PRH*, polymyalgia rheumatic; *NA*, not available
[a]Transthoracic echocardiography

Table 2. Results of (^{18}F-FDG) positron emission tomography/computed tomography in patients with native valve endocarditis

No.	Duke criteria	Affected valve	Visual assessment of valves by ^{18}F-FDG-PET/CT	SUV_{max} affected valve	SUV_{max} negative valve	TBR affected valve	TBR negative valve	Other findings of ^{18}F-FDG-PET/CT
1	Definitive	Aortic valve Mitral valve	Aortic valve positive Mitral valve negative	8.3	2.9	2.86	1.00	
2	Definitive	Tricuspid valve	Negative	[a]	1.4 AV	[a]	1.27 AV	Embolic infectious foci of lungs
					1.5 MV		1.36 MV	Synovitis of left shoulder and right knee
3	Definitive	Mitral valve	Negative	2.5	2.4	1.09	1.04	
4	Definitive	Mitral valve	Negative	2.4	2.8	1.04	1.22	Embolic infarction of spleen and kidney, embolic infectious focus in the left foot
5	Definitive	Aortic valve	Negative	2.7	2.1	1.35	1.05	Embolic infectious foci in the muscles of the right lower extremity
6	Definitive	Aortic valve	Negative	2.8	3.5	1.55	1.94	Embolic infectious focus in the left foot
7	Possible	Aortic valve	Negative	2.6	2.6	1.24	1.24	

AV, Aortic valve; *MV*, mitral valve; SUV_{max}, maximal standardized uptake value; *TBR*, target-to-background ratio (SUV_{max} of valve/SUV of blood background)
[a]No uptake around tricuspid valve region

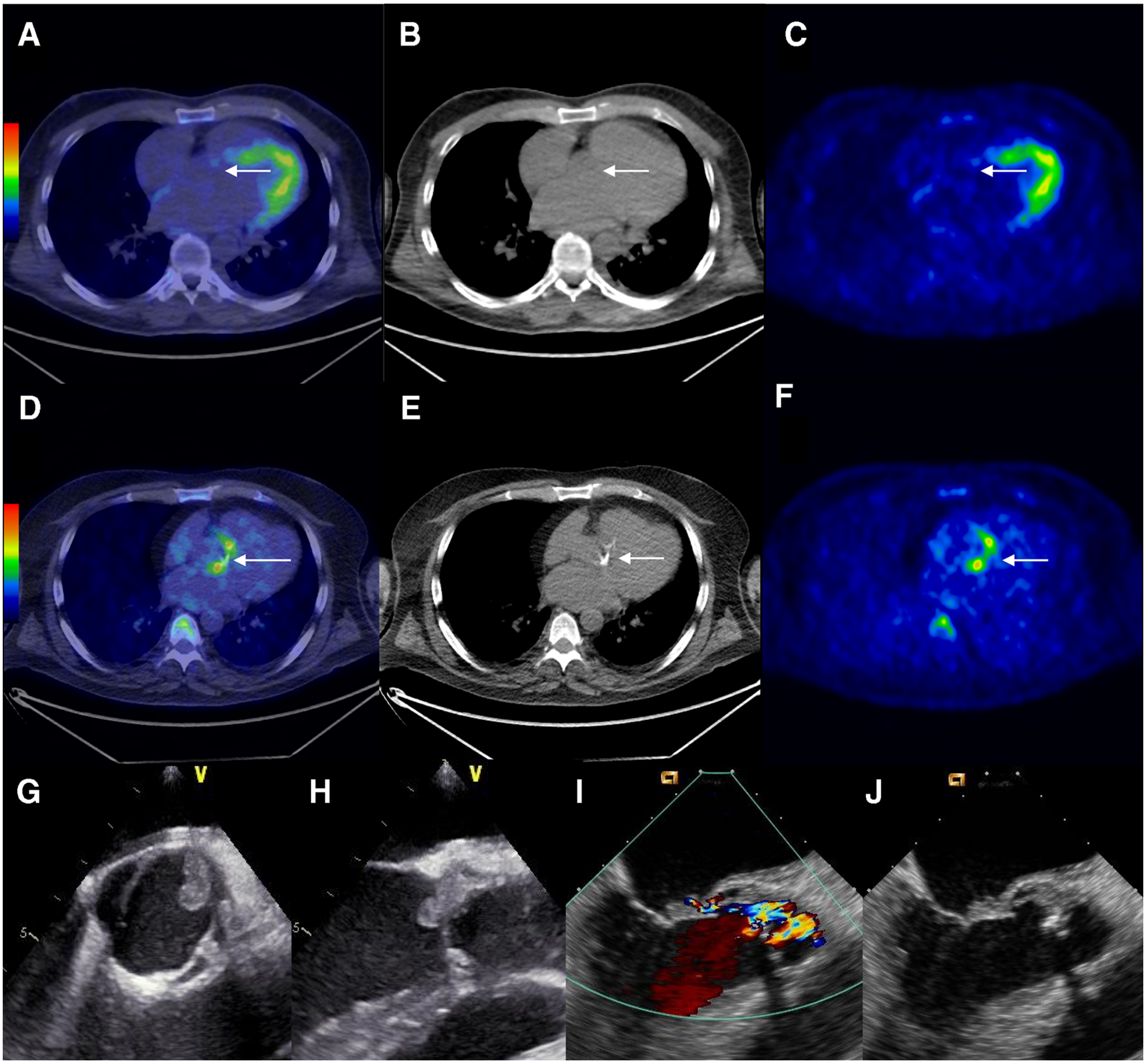

Figure 1. Examples of ^{18}F-FDG-PET/CT (panels **A**-**C** and **D**-**F**) and transesophageal echocardiography (TEE, panels **G**, **H** and **I**, **J**) images of two patients with native valve endocarditis (NVE). The upper row shows no ^{18}F-FDG uptake at the site of aortic valve (arrows in panels **A**-**C**) despite large vegetation on TEE (panels **G**, **H**). Note some physiological ^{18}F-FDG uptake in the myocardium. The lower row shows increased ^{18}F-FDG uptake at the site of aortic valve (arrow in panels **D**-**F**) in a patient with a paravalvular abscess on TEE (panels **I**, **J**).

had prolonged fever of unknown cause after recent (4-14 weeks) valve surgery. They all received anti-inflammatory treatment for suspected post-pericardiotomy syndrome and had an uncomplicated clinical course. In 3 of these 4 patients, PET/CT did not show valvular ^{18}F-FDG uptake. One of these PET/CT negative patients (Patient #19 Table 1) had suspected vegetation on TEE, but that was most likely a remnant of the native valve as there was no progression during 1 year follow-up. However, one patient (Patient #23 Table 3) showed ^{18}F-FDG uptake of the aortic valve prosthesis, which was later classified false positive. In addition, the rejected group included one patient with positive valvular ^{18}F-FDG uptake (Patient #20 Table 3) and echocardiographic suspicion of IE. This patient was operated due to aneurysm of sinus valsalva, the microbiological tests obtained from the valve were negative and histology showed a foreign body reaction around the valve instead of endocarditis.

When comparing the SUV_{max} and TBR values of the prosthetic valves in patients with definitive, possible

Table 3. Results of (^{18}F-FDG) positron emission tomography/computed tomography in patients with suspected prosthetic valve endocarditis

No.	Duke criteria	Type and location of prosthetic valve	Time from operation	Visual assessment of valves by ^{18}F-FDG-PET/CT	SUV_{max} prosthetic valve	SUV_{max} native valve (mitral or aortic)	TBR prosthetic valve	TBR native valve (mitral or aortic)	Other findings of ^{18}F-FDG-PET/CT	Diagnosis according to ^{18}F-FDG-PET/CT
8	Definite	Mechanical AV	28 years	AV positive	5.8	2.6	2.32	1.04		Endocarditis
9	Definite	Mechanical AV	26 years	AV positive	4.1	2.4	1.86	1.09	Spondylodiscitis C VI/VII	Endocarditis, spondylodiscitis
10	Definite	Mechanical MV	10 years	MV positive	5.7	3.4	2.04	1.21		Endocarditis
11	Definite	Mechanical AV	20 years	AV positive	7.2	1.9	3.6	0.95	Peripheral emboli in lower limbs	Endocarditis
12	Definite	Mechanical AV	18 months	AV positive	5.4	2.3	2.35	1.00		Endocarditis
13	Definite	Biological AV	18 weeks	AV positive	9.0	2.6	3.75	1.08	Spondylodiscitis L I/II, uptake in iliac bone and femur	Endocarditis, spondylodiscitis
14	Possible	Biological AV Biological MV	11 weeks	AV positive MV negative	8.4 AV 3.6 MV		3.0 AV 1.29 MV			Endocarditis
15	Possible	Biological AV	6 years	Negative	3.6	3.3	1.89	1.74	Pneumonia	Pneumonia
16	Possible	Mechanical AV	2 years	AV positive	5.4	2.8	2.08	1.08	Spondylodiscitis Th V/VI	Endocarditis, spondylodiscitis
17	Possible	Mechanical MV	16 years	Negative	3.4	2.9	1.48	1.26	Colon tumor and pulmonary metastasis	Colon tumor and metastasis
18	Possible	Mechanical AV	14 months	AV positive	5.2	3.0	1.73	0.96		Endocarditis
19	Rejected	Mechanical MV	4 weeks	Negative	3.0	2.7	1.25	1.13		No diagnosis
20	Rejected	Mechanical AV	16 months	AV positive	7.8	2.2	3.25	0.92	Uptake in descending colon	Endocarditis, colon tumor
21	Rejected	Mitral valve plastia, support-ring	14 weeks	Negative	3.0	3.3	1.43	1.57		No diagnosis

Table 3 continued

No.	Duke criteria	Type and location of prosthetic valve	Time from operation	Visual assessment of valves by ^{18}F-FDG-PET/CT	SUV_{max} prosthetic valve	SUV_{max} native valve (mitral or aortic)	TBR prosthetic valve	TBR native valve (mitral or aortic)	Other findings of ^{18}F-FDG-PET/CT	Diagnosis according to ^{18}F-FDG-PET/CT
22	Rejected	Mechanical AV	11 weeks	Negative	2.9	2.1	1.71	1.24	Uptake in pericardium	Post-pericardiotomy syndrome
23	Rejected	Mechanical AV	6 weeks	AV positive	7.1	2.4	3.09	1.04		Endocarditis

AV, Aortic valve; *MV*, mitral valve; *SUV_{max}*, maximal standardized uptake value; TBR, target-to-background ratio (SUV_{max} of valve/SUV of blood background)

or rejected PVE, no significant difference was found between the groups ($P = 0.301$ and 0.264).

In summary, visual ^{18}F-FDG uptake and $SUV_{max} > 4.0$ was detected in all 6 patients with definite PVE (sensitivity 100%, 95% CI 54.1-100.0%). However, specificity of ^{18}F-FDG-PET/CT was only 60% (95% CI 14.7-94.7%). By using the cut-off value of SUV_{max} of 4.0 as a criterion for definite PVE, 3 of the 5 cases with possible PVE and 2 of the 5 cases of rejected PVE would be defined as definite PVE.

Embolic Foci

Embolic and/or metastatic infectious foci were detected in 7 of 12 (58%) patients with definitive IE (4 NVE and 3 PVE). All of the NVE patients had peripheral infectious emboli in the limbs. Besides that, 1 had pulmonary infection foci and 1 had embolic infarction of spleen and kidney. The patient with splenic and kidney infarction had also an embolic finding in retina, which was not detected by PET/CT. PET/CT showed spondylodiscitis in 2 definite and 1 possible PVE patient. In 1 definite PVE patient, PET/CT showed peripheral infectious emboli in lower limbs. Pulmonary infection as well as splenic and kidney infarctions were confirmed by CT findings and spondylodiscitis by magnetic resonance imaging.

Other Findings

In addition to the case with apparent malignant colon tumor and metastasis detected in 1 case, PET/CT showed high ^{18}F-FDG uptake in the colon in another case (Patient #20 in Table 3) in whom colitis ulcerosa was later diagnosed. Pericardial uptake of ^{18}F-FDG confirmed the diagnosis of postpericardiotomy syndrome in 1 case. In addition, Paget's disease was later confirmed in 1 patient with high uptake of ^{18}F-FDG in iliac bone and femur.

DISCUSSION

The main findings of the present study are that the sensitivity of ^{18}F-FDG-PET/CT for detecting valvular infection in NVE was low in the absence of paravalvular involvement. In contrast, ^{18}F-FDG uptake in the valve region was a consistent finding in definite PVE. These results in this small patient cohort suggest that ^{18}F-FDG-PET/CT is a sensitive method for detecting paravalvular infection in IE.

Case reports have shown ^{18}F-FDG accumulation in the infected valve in patients with NVE,[18-20] but this has been rare in larger series of patients with NVE.[14-16,21,22] Our study is one of the few series of patients with definite NVE according to the Duke criteria. In line with the studies of Ricciardi et al[21] and Kestler et al[22] our results show that even in the presence of a large

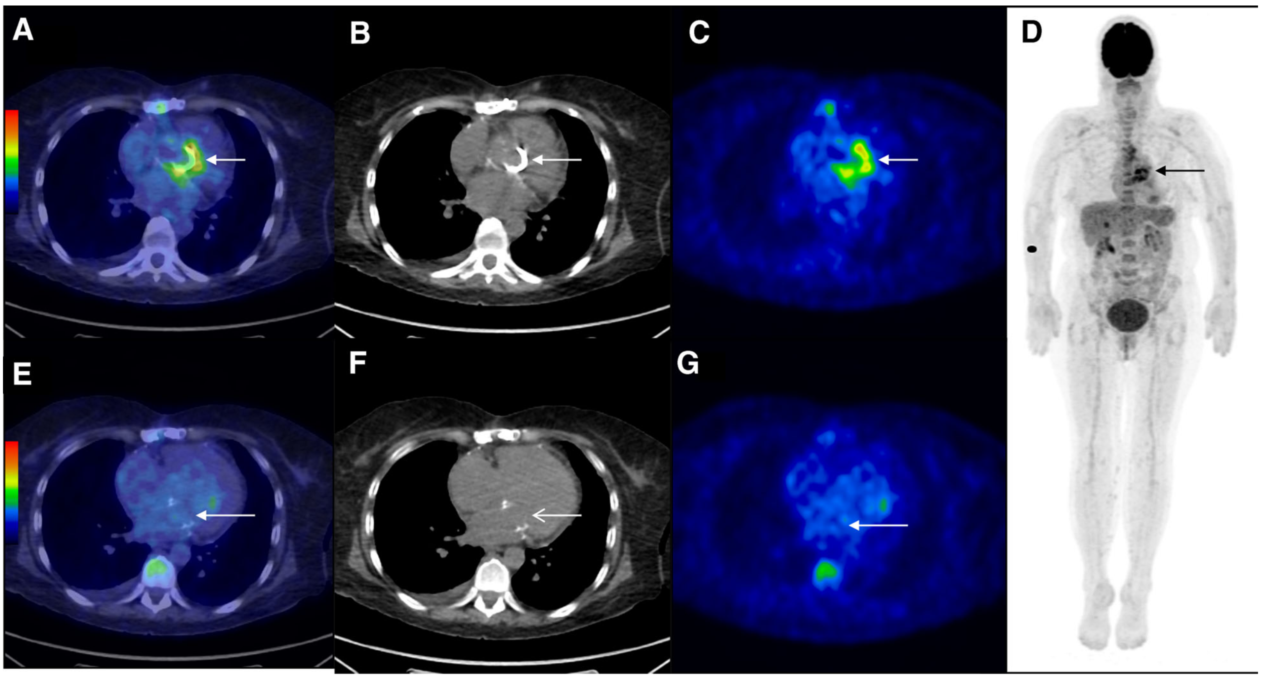

Figure 2. Examples of ^{18}F-FDG-PET/CT images of a patient with prosthetic valve endocarditis (PVE). The *upper row* shows increased ^{18}F-FDG uptake at the site of the aortic valve prosthesis (*arrows* in panels **A**-**C**) and the *lower row* shows no ^{18}F-FDG uptake at the site of mitral valve prosthesis in the same patient (*arrows* in panels **E**-**G**). The whole-body ^{18}F-FDG-PET/CT image shows focal tracer uptake at the site of aortic valve (*arrow* in panel **D**).

vegetation on TEE, ^{18}F-FDG uptake was not detectable in the infected valves. The possible explanation to this is that small size and continuous movement of vegetation may reduce sensitivity of PET. In addition, patients with NVE tend to develop more frequently vegetations than abscesses and vegetations contain less activated inflammatory cells than peri-valvular abscesses. Antimicrobial therapy before ^{18}F-FDG-PET/CT may have also reduced tracer uptake and inflammatory activity in these lesions. Still, as the diagnostic performance of TEE is better in patients with a suspicion of NVE, the need for a new diagnostic method and interest of FDG-PET imaging is less obvious in NVE than in PVE.

Interestingly, ^{18}F-FDG-PET/CT was positive in 1 patient with NVE who also had large para-aortic abscess on TEE that was confirmed during surgery. Early detection of paravalvular complications is often challenging.[13] Based on our finding and some case reports[18,19] further studies seem warranted on the value of ^{18}F-FDG-PET/CT in the detection of paravalvular complications of NVE.

Two recent clinical studies indicate that valvular ^{18}F-FDG uptake is common in PVE and ^{18}F-FDG-PET/CT may even improve sensitivity of detection of PVE as compared with the conventional clinical work-up.[21,23] Our results are in line with those, since ^{18}F-FDG-PET/CT was positive in all cases with definite PVE. We found SUV_{max} of 4.0 or higher in all cases with definitive PVE indicating that it could be used as a cut-off value for objective assessment of scans. However, further studies with larger patient populations are needed to study whether any cut-off point of SUV_{max} can be used in clinical practise. Paravalvular extension is a typical feature of PVE. However, sensitivity of TEE for the detection of paravalvular leak or abscess is limited and therefore, new diagnostic tools are needed. Our results indicate that ^{18}F-FDG-PET/CT has potential for the early detection of paravalvular infection. However, it is important to notice that in previous studies ^{18}F-FDG accumulation has been absent in many patients with definite or possible PVE[14,15,21-23] and therefore, more studies are needed to confirm its diagnostic value in PVE.

Regarding specificity of ^{18}F-FDG-PET/CT, one must bear in mind that distinction between infection and inflammation is not possible. This was highlighted by the two false positive cases in whom ^{18}F-FDG uptake associated with foreign body reaction in 1 patient and with recent valve surgery in another patient. Within the first weeks after surgery, the natural wound healing process may explain the ^{18}F-FDG uptake. This may be of clinical relevance since the risk of PVE is highest in the first 3 months after surgery.[24] Our study included 6 patients who underwent PET/CT 4-18 weeks after valve operation. In 2 of them, a positive ^{18}F-FDG-PET/CT study was associated with possible or definite PVE. In the patient with possible PVE, only 1 of the 2 valve prosthesis was positive supporting the diagnosis of IE. It is of interest that in one patient ^{18}F-FDG uptake was found in the pericardium supporting the diagnosis of postpericardiotomy syndrome (Patient #22).[25] Further studies are warranted to study the accuracy of ^{18}F-FDG-PET/CT in the early postoperative period.

In our study, image quality of ^{18}F-FDG-PET/CT was considered diagnostic in all patients. Diet intervention efficiently reduced physiological uptake of ^{18}F-FDG in the myocardium that is probably essential for good image quality.

In several patients, there were extracardiac findings in the ^{18}F-FDG-PET/CT study that can provide valuable additional diagnostic information. Embolic and/or metastatic infectious foci were detected in 58% of the patients with definite IE. This supports previous studies on PET/CT and IE showing embolic foci in 44-57% of the patients with definite IE.[15,16,22,26]

Limitations

Our study is limited by the small number of the patients. As a result no firm conclusions can be driven based on our results. Also the time interval between admission and PET/CT varied from 1 to 59 days. One of the general limitations of all studies of suspected IE is the lack of a gold standard for IE diagnosis, which could be applied in all patients. The Duke criteria are based on current understanding of the various tests and are subject to revisions according to the new clinical evidence. The cut-off values for SUVmax and TBR in the present study should be tested prospectively in another patient cohort. Furthermore, the optimal imaging and analysis protocols for quantification of valvular FDG uptake remain to be determined in future studies.[27]

NEW KNOWLEDGE GAINED

^{18}F-FDG-PET/CT appears to be a sensitive method for the detection of paravalvular infection associated with PVE. Instead, the sensitivity of PET/CT was limited in NVE.

CONCLUSIONS

^{18}F-FDG-PET/CT appears to detect paravalvular infection in IE and may provide additional information over echocardiography in the evaluation of suspected PVE. However, the sensitivity of ^{18}F-FDG-PET/CT for detecting NVE in the absence of paravalvular involvement is low. More studies with larger patient groups are warranted to study the value of ^{18}F-FDG-PET/CT in the diagnostic workup of PVE.

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Disclosure

The authors have no conflicts of interest to report.

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