

CASE REPORT

Open Access



F-18 FDG PET/CT scan in recurrent prosthetic valve endocarditis without detectable abnormality on echo: a case report

Nurnadiah A. Denil^{1*} , Reana D. Arunasalem¹ and Siti Zarina Amir Hassan¹

Abstract

Background Infective endocarditis poses many clinical and diagnostic challenge. The diagnosis of infective endocarditis is made by high index of clinical suspicion based on the American Heart Association modified Duke's criteria, and the main imaging modality of choice is echocardiography.

Case presentation Here, we reported a case of recurrent infective endocarditis revealed by FDG PET/CT study despite completion of antibiotics and negative on echocardiography. A 38-year-old female with history of double-valve replacement for aortic stenosis presented with 1-week history of chest pain, dyspnea and intermittent fever. She was treated with 5 weeks of antibiotic with IV Cephalexin for prosthetic valve endocarditis. The repeated blood culture after IV antibiotic was negative for infection. She represented again with episodes of palpitation. Post-treatment blood investigation showed normal leukocyte level with increasing CRP and Troponin T level. The repeated blood culture and transesophageal echo was negative. The F-18 FDG PET/CT showed a mild hypermetabolic focus at the inferior basal myocardial wall adjacent to the prosthetic valve, however not involving the paraaortic region which is likely secondary to ongoing inflamed myocardium. As the fear of another relapse of endocarditis, oral suppression antibiotic therapy was continued for another 6 months.

Conclusions This case report illustrates a patient with a prosthetic valve replacement detected by F-18 FDG PET/CT, which one could have overlooked an endocarditis if one had relied on transesophageal echo (TEE) alone. F-18 FDG PET/CT is a promising adjunctive tool in the diagnostic workup of patients with suspected IE, particularly prosthetic device endocarditis where the TEE sensitivity is lower. In our patient, the positive F-18 FDG PET/CT governs the subsequent therapeutic consequences which include adjustment of antibiotic and length of treatment, and it prevents unnecessary intervention.

Keywords Infective endocarditis, FDG, PET-CT, Prosthetic valve

Background

Infective endocarditis (IE) is defined by infection of a native or prosthetic heart valves, the endocardial surface or indwelling cardiac device [1]. IE has been an old health

issues, predated from the pre-antibiotic and antibiotic eras, where the condition typically affected the young or middle-aged adults with underlying rheumatic heart disease or congenital heart disease [1]. Over the decade, the incidence is rising worldwide and there is a change in the risk factor profile, patient demographic characteristics and the microbiology. Principal risk factors include prosthetic valve replacement, haemodialysis venous catheters, diabetic mellitus, immunosuppression and intravenous drug use [2]. The higher incidence of IE is also largely contributed by increased number of implantable

*Correspondence:

Nurnadiah A. Denil
nadiahdnil@yahoo.com

¹ Department of Nuclear Medicine, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

cardiac devices and increased number of older patients at high risk for infective endocarditis. The preeminence of *Staphylococcus aureus* as the responsible organism replacing the streptococcal species has further exacerbated the condition altering the antibiotic prophylaxis measures. Despite advances in the surgery and diagnostic methods, 1-year mortality from IE has not changed and still approaches 30% in this twenty-first century [2].

Infective endocarditis poses many clinical and diagnostic challenges. The diagnosis of IE is made by high index of clinical suspicion based on the American Heart Association modified Duke's criteria and the main imaging modality of choice is echocardiography. This case report illustrates a patient with a prosthetic valve replacement detected by ¹⁸F-fluorodeoxyglucose positron emission tomography computed tomography (F-18 FDG PET/CT), which one could have been overlooked an endocarditis if one had relied on transesophageal echo (TEE) alone.

Case presentation

A 38-year-old woman presented with 1-week history of chest pain, dyspnea, and intermittent fever. Ten months earlier, she had undergone a double-valve replacement where the diseased valves were replaced by a prosthetic mitral and aortic valve. The patient reported to have undergone molar tooth extractions 2 weeks prior to presentation for dental carries and was not advised for antibiotic prophylaxis. Upon presentation, her vital signs were within the normal range with low grade fever and there is a 3 over 6 pansystolic murmur in the sternal border, otherwise normal physical examination. The initial blood investigation showed raised leukocytosis $14.0 \times 10^9/l$ (normal 4–10) predominantly neutrophil (80%) and lymphocyte (14%), low haemoglobin level 10.5 g/dl (normal 12.0–16.0). The C-reactive protein level is 47.3 mg/l (normal), and raised myocardial enzymes, creatine kinase-MB level is 83U/l (normal <25) and Troponin T level is 1200 pg/ml (normal <14).

Chest radiography showed clear lung fields, previous aortic valve and mitral valve replacement with sternotomy wires and no evidence of septic pulmonary infiltration (Fig. 1). Transthoracic echocardiography (TTE) done upon admission showed no evidence of vegetations or abscess. The computed tomography (CT) was done in suspicion of concurrent pulmonary embolism; however, findings were non-diagnostic and showed no surrounding abscess in the aortic and mitral valve replacement to suggest endocarditis. Although the patient did not have any significant clinical signs or remarkable imaging findings to suggest infectious endocarditis, her blood culture grew methicillin-resistant *Staphylococcus epidermidis*. Due to high risk of prosthetic valve endocarditis, a repeated transesophageal echo (TEE) showed vegetations attached

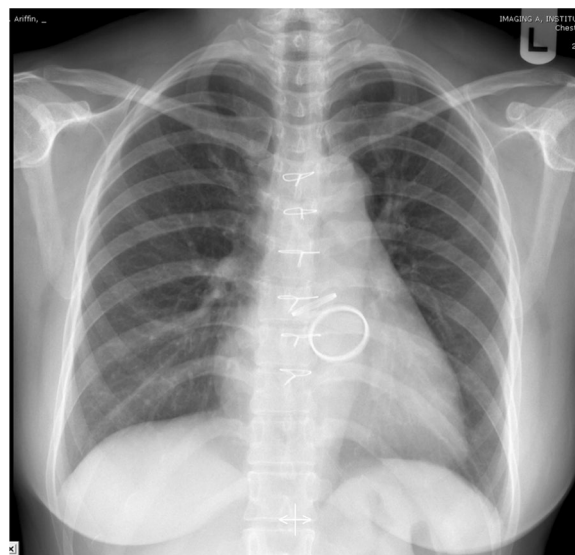


Fig. 1 Chest radiograph showed clear lungs field, previous aortic and mitral valve replacement, and sternotomy wires. No plain radiographic findings of pulmonary inflammation

to the prosthetic aortic valve measuring 1.5×0.6 cm with mild transvalvular leakage seen in which was not present in the initial TTE (Fig. 2). The mitral prosthetic valve is stable and functioning. Overall, hypokinetic basal septal and inferior wall with left ventricular ejection fraction is estimated at 46%. Subsequent CT angiogram further supported the diagnosis which showed prosthetic valve endocarditis with paravalvular abscess.

She was treated with 3 weeks of intravenous (IV) antibiotic, IV Cephalexin for prosthetic valve endocarditis and repeated blood culture after IV antibiotic was negative for infection. Patient was discharged home supplemented with oral antibiotics and warfarin.

Shortly after discharge, patient represented with episodes of palpitation and intermittent fever. She has completed 5 weeks of antibiotics. Post-treatment blood investigation showed normal leukocyte level of $8.3 \times 10^9/l$. The C-reactive protein was otherwise increasing in trend, from 14.4 to 29.1 mg/l and the level of Troponin T was significantly high, 4201 pg/ml.

A repeated TEE was normal, the previously seen paravalvular abscess was no longer detected after completion of antibiotic. The working diagnosis at the time was a recurrent endocarditis with negative blood culture and echocardiography. We, therefore performed a F-18 FDG PET/CT study with cardiac PET infection protocol to look for infective foci.

Patient underwent a cardiac infection preparation protocol where the main recommendation includes high fat, low carbohydrate diet over 12–18 h period

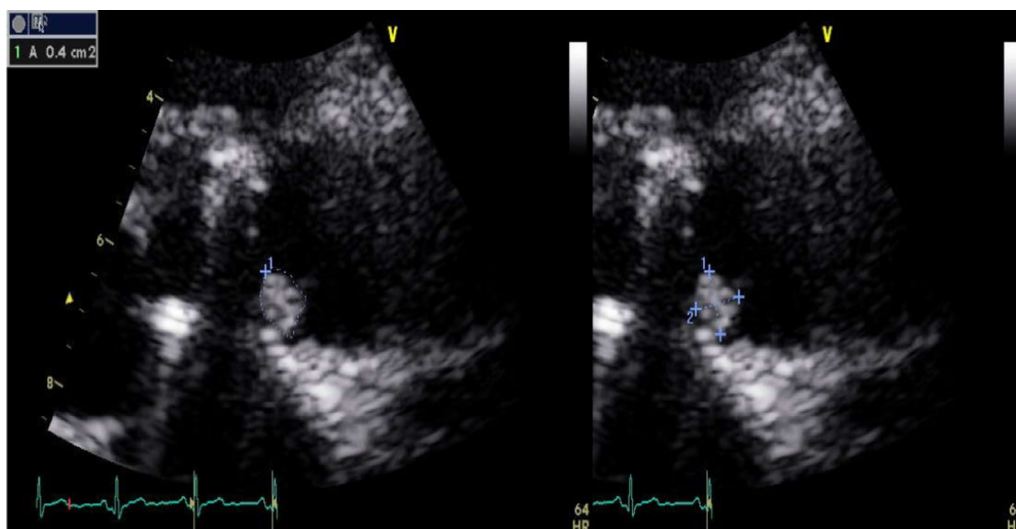


Fig. 2 A repeated transesophageal echo (TEE) showed vegetations attached to the prosthetic aortic valve measuring 1.5×0.6 cm with mild transvalvular leakage in which was not present in the initial TTE assessment. The mitral prosthetic valve is stable and functioning

with intravenous heparin 50 IU/kg 15 min prior to FDG injection.

The scan showed mild FDG hypermetabolism seen at the inferior basal myocardial wall (SUVmax 2.9) adjacent to the prosthetic valve, however not involving the paraaortic region which is likely secondary to ongoing inflamed myocardium (Fig. 3). Additionally, F-18 FDG PET/CT did not show any distant cardioembolic infection. As the fear of another relapse of endocarditis, oral suppression antibiotic therapy was continued for another 6 months.

Discussion

Here, we illustrate an important role of F-18 FDG PET/CT in diagnosing prosthetic valve infective endocarditis. Infective endocarditis (IE) is defined by infection of a native or prosthetic heart valves, the endocardial surface or indwelling cardiac device [1]. With the development of antibiotic, and a decline in rheumatic heart disease and advances in the surgery & diagnostic method, the mortality from IE has not improved over the last 20 years, with 1 year mortality exceeding 30% [1]. IE continued to evolved with a change in the patients' demographics characteristic and microbiology profile. Concurrently, the average patients are older with increasing comorbid, and the Staphylococci superseded the oral Streptococci as the most frequent organism causing infective endocarditis [2]. Furthermore, the incidence of IE is exacerbated by the impact of reduced use of prophylaxis antibiotic alongside with the increase in surgically implanted cardiac devices & prosthetic valves [3].

Reaching a quick and accurate diagnosis in cases of suspected IE is the main challenge. Delayed in diagnosis results in delay in the initiation of therapy which results in complications & worse clinical outcome. The clinical presentation is heterogenous, it could range from low grade febrile illness to acute sepsis with or without heart failure syndrome. Acutely life-threatening complications are major cerebral or coronary embolisation from vegetations, chordal rupture, and valve perforation [1, 2].

The American Heart Association (AHA) recommend use of modified Duke criteria (a constellation of major and minor clinical, microbiological, and anatomical criteria) for the evaluation of patients with suspected IE. Although these criteria remain useful for diagnostic aid, it has variable sensitivity and specificity and less sensitive in patients with prosthetic valve endocarditis and cardiac implantable device infections (CIED) as well as IE affecting the right side of the heart [4]. Both major criteria are less sensitive in PVE and ICED: negative blood cultures are common (>20%) and transthoracic echocardiography (TTE) can miss pacemaker lead involvement and prosthetic valve endocarditis in up to 60% of cases [2].

For many years, echocardiography remains the imaging of choice to evaluate impaired structural condition of the heart including infectious process. It is rapid, straightforward and in many cases diagnostic [5]. Transthoracic echocardiography (TTE) is recommended as initial modality of choice with sensitivity of 50–90% for native valve endocarditis, however lower at 40–70% of PVE. Its limitation includes poor imaging quality due to echoic prosthetic valves and inability to differentiate between infectious and non-infectious mass. In addition,

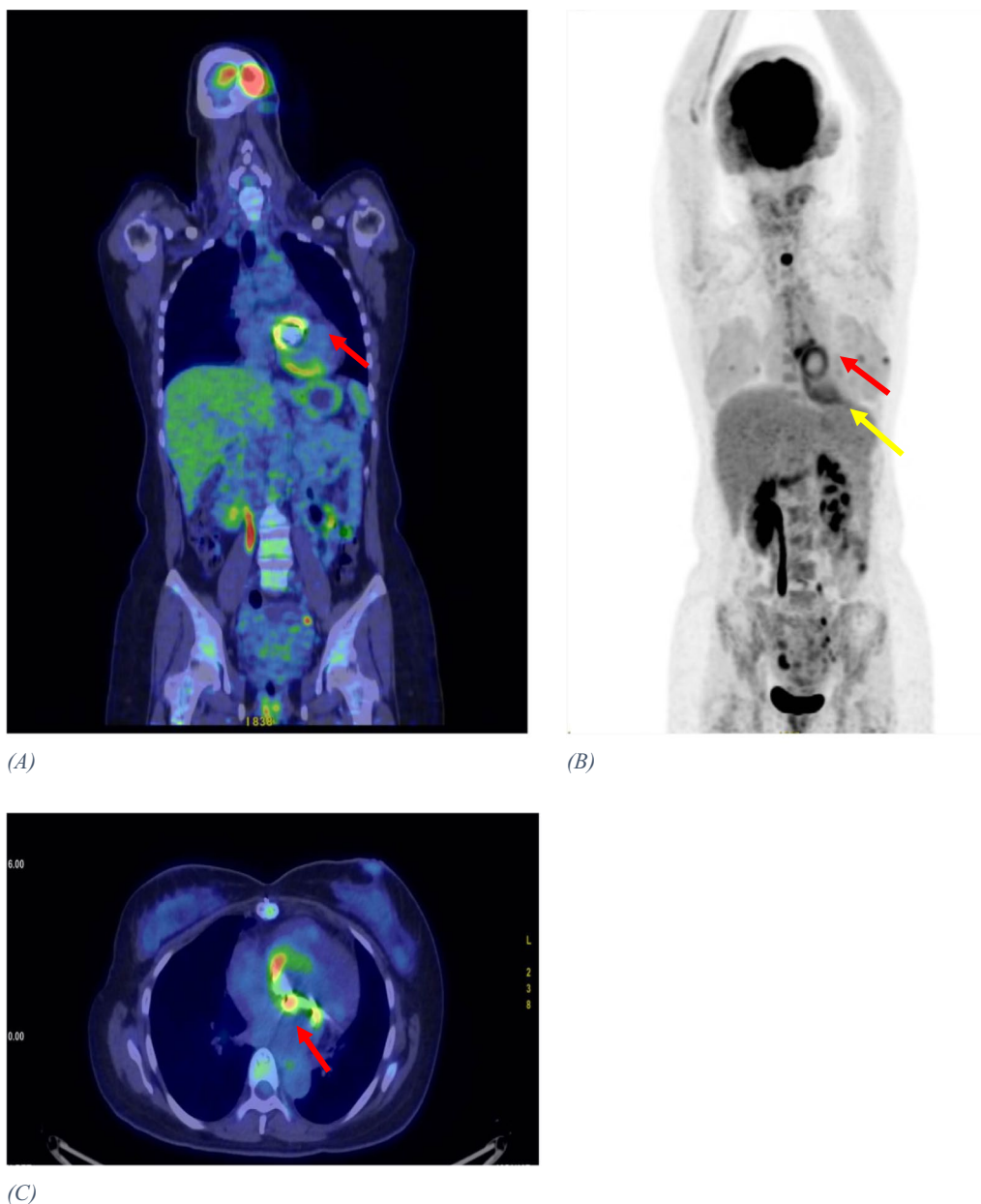


Fig. 3 Fusion computed tomography F-18 fluorodeoxyglucose positron emission tomography images (**A, C**) and maximum intensity projection images (**B**). Coronal (**A, B**) and axial (**C**) reconstruction shows hypermetabolic focal uptake around the inferior basal myocardial wall (SUVmax 2.9) (yellow arrow) and around the aortic prosthetic valve (red arrow)

transesophageal echocardiography (TEE) must be performed when TTE is non-diagnostic or negative with high index of suspicion for IE or when quality of TTE is suboptimal [5]. TEE is more superior to TTE with sensitivity of 90% to 100% and specificity of 90% to detect vegetations and complications such as perforations, abscess in native valve endocarditis [5]. In prosthetic valve endocarditis, the sensitivity is slightly lower at 86% [5]. False positives has been reported with TEE, where

the abnormalities detected can be difficult to differentiate between a small vegetations secondary to post-operative fibrin strands or infected vegetations [5].

Cardiac computed tomography (CT) scanning is equivalent to TEE but can be used as an adjunct imaging modality in cases where the anatomy is not clearly delineated to assess paravalvular anatomy & complications (e.g. paravalvular abscess and mycotic aneurysms) [1]. An interesting findings is that the initial TTE and CT cardiac

could not detect any signs of endocarditis which was later revealed with TEE and cardiac CT angiography. Additional CT angiography allows for exclusion of significant coronary disease [1].

Single-photon emission computed tomography (SPECT) utilises the radiolabelled leukocyte. The technique relies on accumulation of neutrophils in the region of IE and it is most sensitive in the acute phase of infection. Study done by have shown that SPECT was more specific (100% vs 71%) but less sensitive (64% vs 93%) compared to 18F-FDG PET/CT in 39 patients with suspected prosthetic valve endocarditis [6]. Earlier studies have shown that this technique has low sensitivity of 40% in native valve IE [6]. The disadvantage is the technique requires blood handling in preparation of radiopharmaceuticals, with risk of impurities and compared to 18F-FDG PET/CT, the scan requires longer acquisition and lower spatial resolution [6].

In this case, the TEE could not detect the presence of post-treatment relapsed endocarditis, while 18F-fluorodeoxyglucose positron emission tomography computed tomography (18F-FDG PET/CT) revealed endocardial inflammation. Combining CT imaging with metabolic imaging by 18F-FDG PET promise for improved assessment of 'possible' IE according to the modified Duke criteria. This imaging modality highlights the regions of increased glucose metabolism or active inflammation [2].

Based on current evidence, FDG PET/CT should be considered for detection of disseminated disease in suspected endocarditis. In recent years, there are growing data that have been published on FDG PET/CT in native and prosthetic valve endocarditis. F-18 FDG PET/CT technique has contributed significant value in diagnosing prosthetic valve infection & CIED endocarditis [7]. For prosthetic valve endocarditis, F-18 FDG PET/CT is highly recommended due to its high sensitivity and specificity of 86% and 84% [8]. By incorporating the findings of 18-F FDG PET with the modified Duke's criteria, the sensitivity of modified Duke's criteria has increased from 52 to 91%. A recent large study that included 330 patients with both native valve and prosthetic valve endocarditis has found that 76% of prosthetic valve endocarditis cases who were initially classified as possible IE according to modified Duke criteria were reclassified to definite IE based on FDG PET/CT imaging. In this study, the advantage of 18-F FDG PET/CT includes detection of distant emboli or extracardiac infectious foci in 47/129 (28%) of patients [7].

The key aspect in performing a F-18 FDG PET/CT in suspected infective endocarditis is to suppress the physiological cardiomyocyte uptake of F-18 FDG, in such that the tracer uptake is limited to active inflammatory cells in the myocardium [9]. Special dietary requirement for

the patients are at least 24 h of low carbohydrate & fat diet and fasting period of at least 12 h prior to administration of FDG [8]. The guideline recommended giving IV unfractionated heparin 10 IU/kg 30 min prior to radiotracer administration which will increase the plasma levels of free fatty acids and increase utilisation of fatty acids by the myocardium [9]. Coexisting comorbid such as diabetic mellitus and confounding factors such as insulin administration, glucose containing IV medications and peritoneal dialysis may contribute to the difficulty in suppressing myocardial glucose uptake and will affect the quality of image [9].

FDG PET/CT images should be interpreted with caution. Issues that need to be considered when interpreting images for suspected prosthetic valve endocarditis includes the risk of false positive. Both FDG uptake and intensity, as well as heterogeneity should be confirmed with non-attenuation-corrected images. Metallic streak artefact on CT from the prosthetic valve can generate artefactual activity on FDG PET/CT attenuation-corrected images; however, this artefact can be verified by comparison with non-attenuation-corrected PET images or use of metal artefact reduction techniques [3].

One of the limitations of FDG PET/CT is the static image. Breathing, cardiac and motion artefacts needs to be taken into account when interpreting images. Small intracardiac lesion may be missed due to cardiac motion artefact. Other optional strategy includes combination of FDG PET and ECG-gated CT angiography to increase the sensitivity and determine the extent of infection [8]. The ECG-gated CT angiography (CTA) eliminates motion artefacts thereby increasing sensitivity to detect abscess and vegetation especially during the diastolic phase [8].

Semiquantitative PET/CT analysis with standardised uptake value (SUV) can also considered when in doubt after visual assessment with cut off values of SUVratio (bloodpool) > 2.0 for prosthetic valve endocarditis [8].

The detection of infective foci are also limited to the PET/CT resolution in which small infective source can be missed resulting in false negative study. It also remains debatable if the length of antibiotic therapy prior to the scan would affect the sensitivity of F-18 FDG PET-CT to detect infective endocarditis, to differentiate a true positives from a false negative [3].

Nevertheless, in our patients, after completing antibiotic, she was clinically asymptomatic supported by negative blood culture and echocardiography. However, the inflammatory markers were rising.

Considering one of major challenges that remain is the treatment of IE, more studies are still needed, to address the value of F-18 FDG PET/CT for treatment monitoring. In this case, it should be kept in mind that, not only

the F-18 FDG PET/CT can be used to localised other infective foci, it also gives us information that allows us to assess microbial treatment efficacy in our patient.

Conclusions

F-18 FDG PET/CT is a valuable tool in the diagnostic workup of patients with suspected IE, particularly prosthetic device endocarditis where the TEE sensitivity is lower. In our patient, the positive F-18 FDG PET/CT governs the subsequent therapeutic consequences which includes adjustment of antibiotic dose, length of treatment and prevent unnecessary high risk surgical intervention. In the future, F-18 FDG PET/CT with new gating and camera systems may potentially be used as a follow-up tool and reduce the risk of IE relapses, morbidity and mortality.

Abbreviations

AP	Anterior–posterior
CT	Computed tomography
F-18	Fluorine-18
FDG	Fluorodeoxyglucose
IE	Infective endocarditis
max	Maximum
MRI	Magnetic resonance imaging
PET/CT	Positron emission tomography/computed tomography
SUV	Standardised uptake value
TEE	Transesophageal echo
TTE	Transthoracic echocardiography
P	Posterior

Acknowledgements

The authors would like to thank the Director General of Health Malaysia for his permission to publish this article.

Author contributions

All authors contributed to the case report preparation. The idea of case report was conceptualised and written by ND. RD is responsible for report and image collection. SZ approved the manuscript for publication. The main author confirms sole responsibility for the following: case report data and image collection, interpretation of results, and manuscript preparation. All authors have read and approved the manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current research.

Declarations

Ethics approval and consent to participate

The case report has been registered the Medical Research & Ethics Committee, Ministry of Health Malaysia.

Consent for publication

All sources are properly disclosed, and consent was obtained for publication.

Competing interests

The authors declare that they have no competing interests.

Received: 14 November 2023 Accepted: 20 June 2024
Published online: 22 July 2024

References

- Cahill TJ, Prendergast BD et al (2016) Infective endocarditis. *Lancet* 387(10021):882–893
- Cahill TJ, Baddour LM, Habib G et al (2017) Challenges in infective endocarditis. *J Am Coll Cardiol* 69(3):325–344
- Mahmood M, Kendi AT (2017) Role of F-18 FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: a meta-analysis. *J Nucl Cardiol* 26(3):958–970
- Prendergast BD (2004) Diagnostic criteria and problems in infective endocarditis. *Heart* 90(6):611–613
- Habib G, Badano L, Tribouilloy C et al (2009) Guidelines on the prevention, diagnosis and treatment of infective endocarditis. *Europ Heart J* 30:2369–2413
- Rouzet F, Chequer R, Benali K et al (2014) Respective performance of ¹⁸F-FDG PET and radiolabeled leukocyte scintigraphy for the diagnosis of prosthetic valve endocarditis. *J Nucl Med* 55(12):1980–1985
- De Camargo RA, Sommer Bitencourt M, Meneghetti JC et al (2020) The role of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in the diagnosis of left-sided endocarditis: native vs prosthetic valves endocarditis. *Clin Infect Dis* 70(4):583–594. <https://doi.org/10.1093/CID/CIZ267>
- ten Hove D, Slart RHJA, Sinha B (2021) F-18 FDG PET/CT in infective endocarditis: indications and approaches for standardization. *Curr Cardiol Respir* 23(9):130
- Diisizian V, Bacharach SL et al (2016) ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. *J Nucl Cardiol* 23:1187–1226

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.