Utility of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Cardiac Infections

Abstract

Diagnosis of cardiac infections, which includes infective endocarditis (IE) and cardiac device infections, despite having a high death rate, is still challenging. Frequently used modalities such as echocardiography, computed tomography (CT), and magnetic resonance imaging cannot confirm the presence of an active infection or extracardiac findings. Taking these things to consideration, newer guidelines have suggested the inclusion of ^{18}F fluorodeoxyglucose positron emission tomography/CT (^{18}F FDG PET/CT) in the workup of patients with suspected prosthetic valve IE. In this pictorial essay, we are demonstrating the utility of ^{18}F-FDG PET/CT in varied cases of IE, cardiac implantable electronic devices, and coronary stent infection and how they helped in solving diagnostic dilemmas.

Keywords: *Cardiac implantable electronic device, fluorodeoxyglucose, infection, infective endocarditis, positron emission tomography-computed tomography, stent infection*

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Introduction

Cardiac infections include a group of conditions involving the endocardium, prosthetic valves, or cardiac implantable electronic devices (CIED). Despite their low incidence, these infections are often associated with significant morbidity and mortality, and they frequently necessitate extensive diagnostic testing. Early treatment improves prognosis; therefore, early diagnosis is crucial for good patient management. Unfortunately, clinical symptoms, the most common being fever of unknown origin, are usually ambiguous. The integration of imaging findings and laboratory data is often required for an accurate and prompt diagnosis.

To assess the structure of the heart, wall thickness, wall motion, and cardiac function, echocardiography is usually employed as the first-line imaging modality. Computed tomography (CT) and magnetic resonance imaging (MRI) can be used for better tissue characterization. However, these modalities may not be able to confirm whether there is an active infection or not. Furthermore, the findings may be limited to the cardiac region only. Whole-body ^{18}F-fluorodeoxyglucose positron emission tomography/CT (^{18}F-FDG PET/CT) scans can help determine disease activity and extracardiac involvement. In patients with clinical symptoms and doubtful echocardiographic findings, it may even act as a problem solver.

As neutrophils, monocyte/macrophage cells, and lymphocytes exhibit high levels of glucose transporters (especially GLUT1 and GLUT3) and hexokinase activity, increased FDG uptake is a characteristic of infection and inflammation.[1] Although ^{18}F-FDG PET/CT has been widely used to assess systemic infections, it has never been widely utilized to assess heart infections owing to normal physiological uptake. This very variable and unpredictable nature of physiological cardiac FDG uptake has limited the application of cardiovascular PET/CT imaging when compared to other noncardiovascular indications. The development of various methods for myocardial suppression has been able to circumvent this problem to a larger extent. Myocardial suppression is usually achieved through a combination of fasting and dietary modifications to shift cardiac myocyte metabolism to use free fatty acids as a substrate. This includes a combination of prolonged (12–18 h) fasting, conversion to a high-fat, low-carbohydrate, protein-permitted diet, and intravenous unfractionated heparin (UFH; 50 IU/kg intravenous bolus of UFH approximately 15 min before ^{18}F-FDG administration).[2]

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In this pictorial essay, we are discussing ^{18}F-FDG PET/CT findings in various cases of infective endocarditis (IE), CIEDs, and coronary stent infection and how they helped in solving diagnostic dilemmas.

Infective Endocarditis

After sepsis, pneumonia, and intra-abdominal abscess, IE is regarded as the most prevalent life-threatening infection, leading to increased morbidity and death.[3] The epidemiology of IE has become increasingly complex with today's various healthcare-associated conditions that lead to infection. The mainstay of diagnosis is based on positive blood cultures and imaging findings that need to be interpreted in conjunction with clinical signs. These are considered either minor or major criteria and are integrated into the modified Dukes criteria, finally reported either as rejected, possible, or definite diagnosis of IE.[4] Based on the valves affected, IE can be classified into two major groups: native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE).

Native Valve Endocarditis

^{18}F-FDG PET/CT is found to have a very low sensitivity (36%) and a high specificity (99%) in the diagnosis of NVE.[5] Negative ^{18}F-FDG-PET/CT results in NVE cannot be ruled out because of their low sensitivity. However, the main indication for performing ^{18}F-FDG-PET/CT in a patient with suspected NVE is for the detection of disseminated disease, as distant foci help establish the final diagnosis. If done with appropriate patient preparation, the intracardiac infection may be visualized as an additional finding, which in turn can increase diagnostic confidence.

Case 1

A 21-year-old male presented with intermittent fever for 4 weeks and chest pain for 2 weeks. Echocardiography revealed an abscess in the region of the aortic valve. ^{18}F-FDG PET/CT was done in this patient after adequate patient preparation, which revealed increased FDG uptake in the region of the aortic valve with multiple splenic infarcts [Figure 1]. A diagnosis of IE involving the aortic valve was made. The patient was started on intravenous antibiotics and symptoms subsided on follow-up.

Prosthetic Valve Endocarditis

In a recent meta-analysis,[6] ^{18}F-FDG PET/CT was found to have a pooled sensitivity and specificity of 86% and 84%, respectively, for the diagnosis of PVE. As they can provide evidence for both intracardiac infection and disseminated diseases, they have been added as a major criterion in the diagnosis of PVE by the 2015 ESC Guidelines for the management of IE.[7] Prosthetic valve-related artifacts can reduce the diagnostic accuracy in echocardiography, and these are best visualized in 18F-FDG. Nonattenuation-corrected PET images should be used for interpretation to avoid attenuation artifacts.

Case 2

A 31-year-old male, a known case of rheumatic heart disease, post mitral valve, and tricuspid valve replacement 2 years ago, presented with fever and chest pain for 3 weeks. Noncontrast CT of the chest showed no abnormalities, and echocardiography showed no vegetation. An ^{18}F-FDG PET/CT was performed, which showed increased FDG uptake anterior to the prosthetic mitral valve with multiple splenic emboli [Figure 2]. A diagnosis of PVE was made and the patient was started on intravenous antibiotics, to which the patient showed a good response clinically.

Case 3

A 24-year-old male, a known case of aortic valve repair, presented with fever for 6 weeks and chest pain for 2 weeks. Echocardiography was inconclusive. A ^{18}F = FDG PET/CT was done, which showed increased FDG uptake in the prosthetic aortic valve region [Figure 3]. A diagnosis of

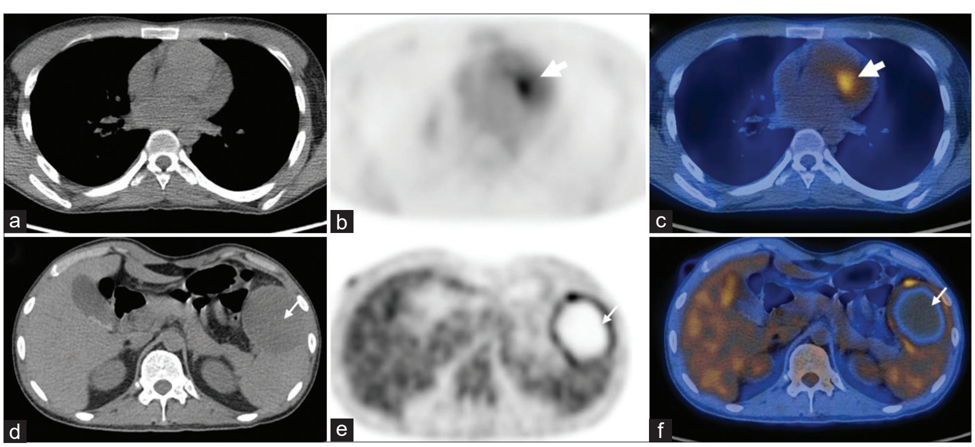

Figure 1: Top row: Axial Noncontrast CT (a) ^{18}F-FDG PET (b) and fused PET/CT (c) images showing increased FDG uptake in the region of the aortic valve (bold white arrows). Bottom row: Axial noncontrast CT (d) ^{18}F-FDG PET (e) and fused PET/CT (f) images demonstrating a hypodense lesion with no significant FDG uptake in the spleen (white arrows), indicating splenic infarction. ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/ computed tomography

PVE was made and the patient was started on intravenous antibiotics. A repeat ^{18}F-FDG PET/CT was done after 5 months, which showed resolution of previously seen uptake in the region of the prosthetic aortic valve [Figure 3]. This case illustrates the utility of ^{18}F-FDG PET/CT in the assessment of response to antibiotic therapy in PVE.

Cardiac Implantable Electronic Devices

The term CIED includes pacemakers, cardiac resynchronization therapy (CRT) devices, and implantable cardioverter-defibrillators. Complete removal of the device is recommended for successful treatment of definite CIED infection. Antibiotic therapy alone may increase 30-day mortality several fold (not including superficial incision infection requiring only antibiotics). Isolated pocket infections are treated with antibiotics for 14 days before new implantation, whereas systemic infections require 4–6 weeks of antibiotic therapy.[8] The ^{18}F-FDG PET/CT performs markedly better for pocket infections than for lead infections: for pocket infections, pooled sensitivity and specificity were 93% and 98%, respectively, whereas for lead infections, it had poor sensitivity (65%) and good specificity (88%).[9]

Case 4

A 54-year-old male with sick sinus syndrome, who underwent dual chamber rate modulated dual-chamber, rate-modulated (DDDR) pacing 10 years back, presented now with active pus discharge form the pocket. ^{18}F-FDG PET/CT was done to look for the extent of the disease. Increased FDG uptake was noted around the pacemaker in the pocket [Figure 4] while the leads showed no uptake, suggestive of isolated pocket infection.

Case 5

A 37-year-old male, known case of congenital heart block, post-DDDR pacing 15 years ago, and lead replacement 5 years ago, presented with fever for 3 weeks. Pacemaker infection was suspected and ^{18}F-FDG PET/CT was performed, which revealed increased FDG uptake in the device pocket

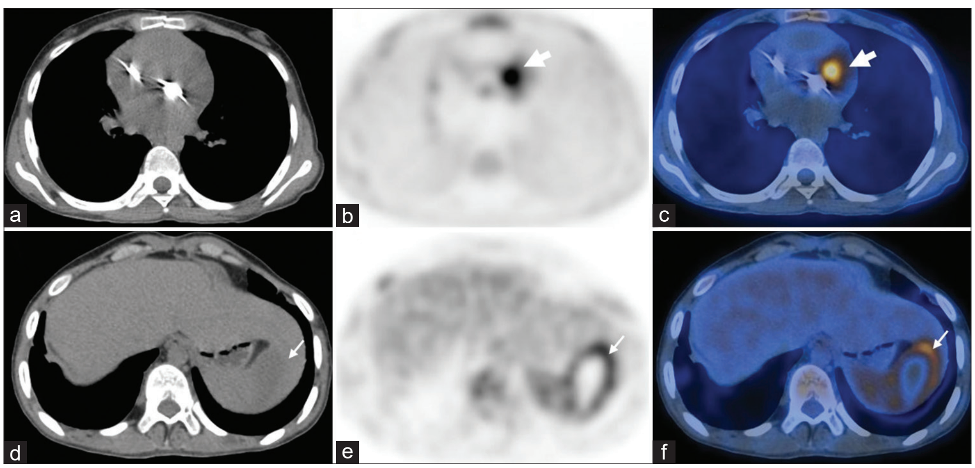

Figure 2: Top row: Axial noncontrast CT (a) ^{18}F-FDG PET (b) and fused PET/CT (c) images showing increased FDG uptake anterior to the prosthetic mitral valve (bold white arrows). Bottom row: Axial noncontrast CT (d) ^{18}F-FDG PET (e) and fused PET/CT (f) images demonstrating a hypodense lesion with no significant FDG uptake in the spleen (white arrows), indicating a splenic infarct. ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/computed tomography

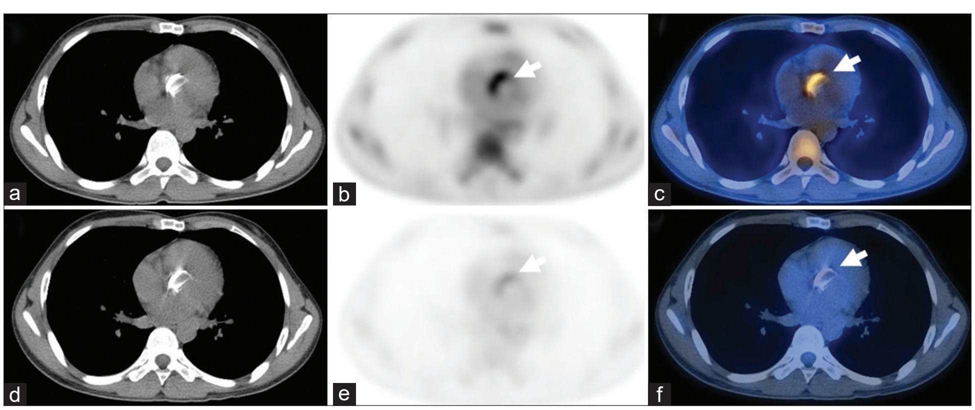

Figure 3: Top row: Baseline ^{18}F-FDG PET/CT scan with axial Non-contrast CT (a) PET (b) and fused PET/CT (c) images showing increased FDG uptake in the region of prosthetic aortic valve (bold white arrows). Bottom row: Follow-up ^{18}F-FDG PET/CT scan with axial noncontrast CT (d), PET (e) and fused PET/CT (f) images showing resolution of previously noted FDG uptake in prosthetic aortic valve region. ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/computed tomography

and also along the intracardiac leads [Figure 5], which was suggestive of both pocket and leads infection.

Coronary Stent Infection

More than 30 years have passed since the invention of coronary artery stents. Less than 30 cases have been reported in the literature since the advent of coronary stents.[10] Although stent infections are uncommon, they are very difficult to treat and potentially fatal.[11] For possible diagnosis of coronary stent infection, at least 3 of the following should be present: placement of a coronary stent within the last 4 weeks; multiple repeat procedures done through the same arterial sheath; the presence of bacteremia, significant fever, or leukocytosis with no other cause; acute coronary syndrome; or positive cardiac imaging.[12] The diagnosis of stent infection cannot be confirmed by a single modality. Early surgical removal of the stent, evacuation of purulent pericardial fluid, excision of epicardial granulomatous tissue, and pericardiectomy with coronary artery bypass surgery are the main surgical interventions.[13]

Case 6

A 64-year-old male, known case of inferior wall myocardial infarction, post right coronary artery (RCA) stenting 1 year back presented with chest pain. Coronary angiogram showed in-stent restenosis in RCA, for which restenting was done 2 months back. At present, the patient presented with high-grade fever. Contrast-enhanced computed tomography showed soft-tissue thickening with phlegm around the stent, suspicious of stent infection. Following which an ^{18}F-FDG PET/CT was done, which showed increased FDG uptake along the stent [Figure 6], suggesting stent infection. The patient was started on intravenous antibiotics, to which he responded well.

Conclusion

Majority of the cardiac infection usually presents as a fever of unknown origin. Frequently used imaging modalities such as echocardiography, CT, and MRI cannot confirm the presence of an active infection or extracardiac foci. ^{18}F-FDG PET/CT can be used as a correlative imaging modality,

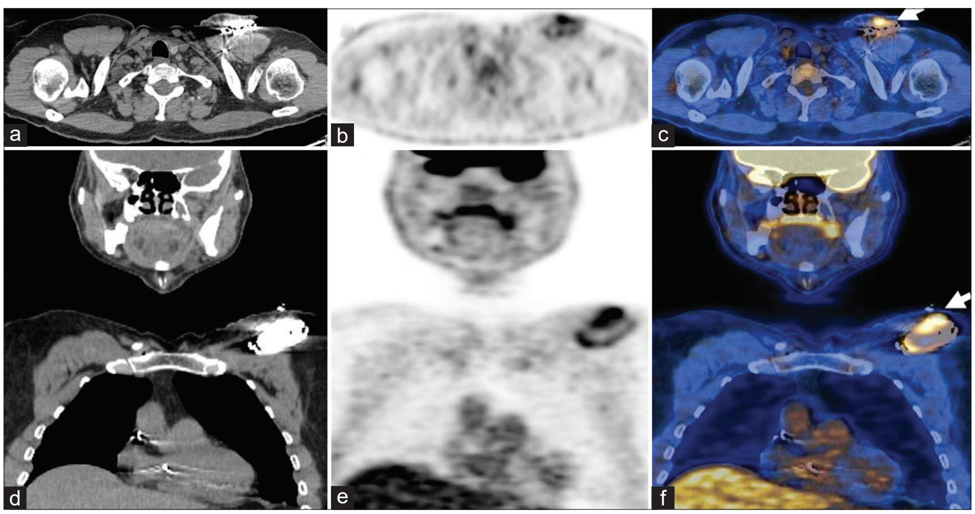

Figure 4: Axial and coronal noncontrast CT (a and d) ^{18}F-FDG PET (b and e) and fused PET/CT (c and f) images showing increased FDG uptake around the pacemaker in the device pocket (white arrow). ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/computed tomography

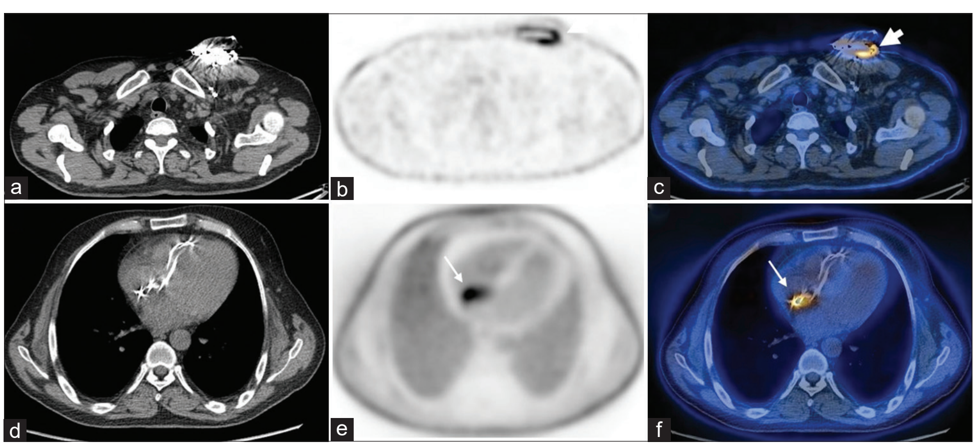

Figure 5: Top row: Axial noncontrast CT (a) ^{18}F-FDG PET (b) and fused PET/CT (c) images showing increased FDG uptake in the pacemaker pocket in the left anterior chest wall (bold white arrows). Bottom row: Axial noncontrast CT (d) PET (e) and fused ^{18}F-FDG PET/CT (f) images showing increased FDG uptake along the intracardiac leads (white arrows). ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/computed tomography

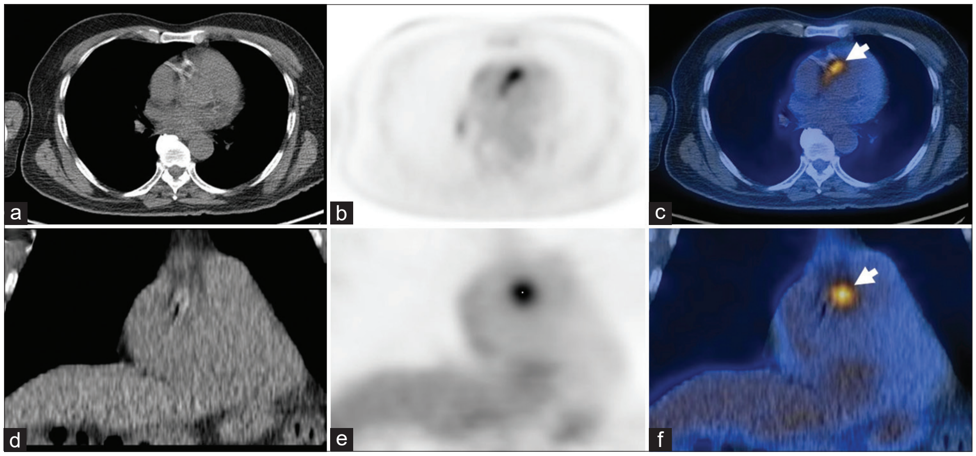

Figure 6: Axial and coronal noncontrast CT (a and d) ^{18}F-FDG PET (b and e) and fused PET/CT (c and f) images showing increased FDG uptake around the stent in RCA (white arrow). ^{18}F-FDG PET/CT: 18F-Fluorodeoxyglucose positron emission tomography/computed tomography. RCA: Right coronary artery

especially in cases, where there is clinical suspicion of infection. ^{18}F-FDG PET/CT has a high sensitivity in diagnosing PVE, though it is limited in the case of NVE. However, the identification of extracardiac foci is valuable in the diagnosis of NVE. ^{18}F-FDG PET/CT is also useful in identifying CIED infection. Another potential utility is its ability to monitor response to therapy to the antibiotic in infection. Thus, along with the first-line imaging modalities, ^{18}F-FDG PET/CT can act as an adjuvant imaging modality, which can be helpful in confirming the diagnosis of cardiac infection and solving diagnostic dilemmas.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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