Role of PET Imaging in Management of Implantable Electronic Device Infection*

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Cardiovascular implantable electronic device (CIED) infections typically manifest in 2 distinct presentations—local generator pocket infection or systemic infection associated with bloodstream infection (BSI) with or without cardiovascular implantable electronic device-related infective endocarditis (CIED-IE) (1). While diagnosis of CIED pocket infection can generally be established based on presence of inflammatory changes at the generator site, diagnosis of CIED lead infection or CIED-IE (without concomitant pocket infection) can be challenging. CIED lead infection or CIED-IE can originate from the device itself or due to hematogenous seeding of device leads from a distant source of BSI (2). Currently, transesophageal echocardiogram (TEE) is considered the test of choice for diagnosis of device lead infection or CIED-IE (3,4). However, a number of clinical questions regarding the role of imaging in CIED infection remain. Should cardiac imaging be obtained in every patient with a CIED who develops a BSI? What is optimal management for a CIED recipient who develops BSI with no identified source of BSI and a negative TEE evaluation? How does one differentiate between superficial cellulitis at device pocket site versus true generator infection? Moreover, although TEE can identify local cardiac complications of lead infection, such as myocardial abscess or valvular endocarditis, choice of imaging modality for diagnosis of systemic embolization, and patient selection criteria for such imaging, remain unclear.

Several recent investigations (5-8) have evaluated the role of 18-fluorodeoxyglucose (FDG) positron-emission tomography (PET)/computed tomography (CT) scanning to address the aforementioned clinical questions. In one investigation, Sarrazin et al. (5) evaluated whether FDG PET/CT could be used to accurately diagnose or exclude CIED infection. Among 42 cases of suspected CIED infection, 32 had findings consistent with device infection on PET/CT whereas 10 had negative scans for device infection. Positive PET/CT results had an excellent correlation with clinical findings, microbiologic data, and echocardiographic evidence of device infection. Patients with negative PET/CT were managed with antimicrobial therapy alone, without device extraction, and none had relapsed over 1 year of follow-up. Based on these observations, the authors suggested that PET/CT can be helpful in guiding appropriate therapy by differentiating cases of device infection from uninfected cases.

In another study, Ahmed et al. (6) assessed the role of FDG PET/CT in the early diagnosis of CIED pocket infection. Eighty-six patients were evaluated with FDG PET/CT in this prospective observational study and findings were correlated with clinical presentation, management, and outcome of cases independent of FDG PET/CT findings. Analysis of FDG activity in the generator pocket area by a receiver operative characteristic curve analysis demonstrated a high diagnostic accuracy (area under the curve = 0.98) for the early identification of patients with confirmed generator pocket infection. Based on these findings, the authors suggested that FDG PET/CT can be helpful in making management decisions by differentiating patients who need device extraction from those who have no infection or where infection is

*Editorials published in JACC: Cardiovascular Imaging reflect the views of the authors and do not necessarily represent the views of JACC: Cardiovascular Imaging or the American College of Cardiology.

From the Divisions of Infectious Diseases and Cardiovascular Diseases, Mayo Clinic College of Medicine, Rochester, Minnesota. Dr. Sohail has received funds from TYRX Inc. and Medtronic for prior research unrelated to this study administered according to a sponsored research agreement (SRA) between Mayo Clinic and study sponsor that prospectively defined the scope of the research effort and corresponding budget; and he has received honoraria/consulting fees from Medtronic and Spectranetics. Dr. Baddour has received royalty payments (authorship) from UpToDate, Inc.; and Editor-in-Chief payments from Massachusetts Medical Society (Journal Watch Infectious Diseases).
superficial and can be managed with antimicrobial therapy alone.

The current study by Amraoui et al. (9) in this issue of iJACC is unique because they evaluated the role of FDG PET/CT scanning to identify septic emboli to distant sites in patients with CIED lead endocarditis. In this prospective study, FDG PET/CT was performed in 35 patients who presented with CIED lead infection. Septic emboli were identified in 10 (29%) patients. Of them, 2 patients had septic pulmonary emboli, 1 had an infected vascular prosthesis and 7 patients had occult spondylodiscitis. The findings in the latter group are what make this investigation unique. Amraoui et al. (9) report that 4 of them were asymptomatic while the other 3 had back pain with a negative CT scan. Although magnetic resonance imaging (MRI) is considered the test of choice for diagnosis of discitis or vertebral osteomyelitis, MRI was not suitable in these patients due to non-MRI-compatible CIEDs. Parenteral antimicrobial therapy was extended to 10 to 14 weeks in patients with PET/CT evidence of spondylodiscitis.

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Frequency of spondylodiscitis (20% in this study) is higher than what has been observed in our practice and in the published literature (10). A potential explanation for this observed difference is that this particular complication is underdiagnosed because a significant proportion of these patients are asymptomatic and spine imaging is not routinely performed in patients with CIED-IE. However, one would expect these patients to relapse due to a missed diagnosis of spondylodiscitis. Alternatively, it is conceivable that PET/CT is uniquely sensitive in detecting early seeding of the spine and that 4 to 6 weeks of antimicrobial therapy used for CIED-IE is adequate to cure early stages of spondylodiscitis. If this is true, then perhaps PET/CT should be reserved for patients who have back pain as they are more likely to have well-established infection of the spine and would benefit from a longer (≥6 weeks) course of antimicrobial therapy.

There are some important limitations of this investigation by Amraoui et al. (9). They report that blood cultures were positive in 77% of the cases and TEE was positive in 66% for lead endocarditis. It is unclear how the diagnosis of lead endocarditis was confirmed in patients with negative blood cultures and negative TEE. Also, it seems that positive lead tip cultures were used as a major criterion for diagnosis of lead infection. However, the majority of patients underwent lead extraction via percutaneous methods and there is potential for lead tip contamination while being dragged through an infected pocket (11). Another missing piece of information is the location of vegetation in patients with endocarditis. In general, patients with right-sided endocarditis (CIED leads or cardiac valves) tend to have septic embolic to lungs (unless there is right-to-left cardiac shunt), whereas patients with left-sided endocarditis are more likely to have systemic embolization. Therefore, location of vegetation may help to determine what imaging test should be performed in a given patient to evaluate for septic emboli (CT of the chest for right-sided IE vs. whole-body PET/CT for left-sided IE).

Despite these limitations, the investigation by Amraoui et al. (9) is a step forward in defining the role of FDG PET/CT in diagnosis and management of CIED infection and highlights important clinical considerations for patients in whom device infection is complicated by lead or valvular endocarditis. First, all patients with evidence of systemic CIED infection (fever, leukocytosis, positive blood cultures) should be carefully evaluated for the possibility of distant septic emboli. Appropriate imaging, guided by clinical suspicion, should be performed to confirm or exclude hematogenous seeding. FDG PET/CT can be helpful in cases in which a diagnosis of CIED pocket or lead infection is doubtful, and in cases where there is a clinical suspicion of distant septic emboli and standard imaging modalities are either negative (concern for false negative Indium leukocyte scan or CT scan for spine infection) or cannot be performed (non-MRI-compatible CIED). Findings on FDG PET/CT in these cases can be pivotal in guiding management decisions (need for device extraction and defining duration of antimicrobial therapy).

Findings of FDG PET/CT in patients with suspected CIED infection, and associated complications, must be interpreted in clinical context. One should be mindful that prior antimicrobial therapy can result in false negative findings on FDG PET/CT scanning (6). In a prospective observational study, Cautela et al. (7) evaluated the diagnostic yield of FDG PET/CT in 21 patients with suspected CIED infection. Although FDG PET/CT had high sensitivity (86%) and specificity (100%) for diagnosis of device pocket infection, diagnostic yield was low for cases with CIED-IE (sensitivity 31%, specificity 62%). Most false negative findings on FDG PET/CT were attributable to prior antimicrobial therapy. Besides this consideration, institutions must develop standardized and specific protocols for performing and analyzing FDG PET/CT in patients with suspected CIED lead infection or endocarditis. There are data to suggest that delayed (3 h) FDG PET/CT, as compared to standard (1 h) imaging, can increase the diagnostic accuracy of suspected device infection. In a study by Leccisotti et al. (8),
delayed imaging had a higher diagnostic accuracy (70% vs. 51%; \( p = 0.024 \)) of device lead infection. However, there was no significant difference in diagnostic accuracy of delayed versus standard image acquisition for generator or pocket infection.

Currently, we do not believe that there are adequate data to recommend routine use of FDG PET/CT in all patients with CIED lead infection to evaluate for occult distant septic embolization. More data, derived from large validation studies, are needed before definitive recommendations can be made.

**REFERENCES**


**KEY WORDS** FDG PET/CT scanning, lead endocarditis, pacemaker infection, septic emboli, spondylodiscitis