Emergence of ^{18}F-FDG positron emission tomography in the detection and characterization of cardiac implantable device infections

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There is rapid increase of patients with cardiac implantable electronic devices (CIED) such as such as pacemakers, defibrillators, prosthetic valves, and left ventricular assist devices that improves quality of life and longevity in these individuals.[1,2] The downside, however, is an increasing rate of CIED infections accounting for a relative increase in morbidity and also mortality.[2,3] The identification and characterization of CIED infections may pose a challenge due to atypical clinical manifestation and frequent inconclusive findings on echocardiography.[4] Clinical diagnosis of CIED infection relies on systemic signs of inflammation, local signs of infection of the CIED pocket-lead (edema, erythema, skin erosion, purulent fluid, etc.), bacterial cultures of blood and extracted devices, and detection of vegetation's on lead tips on echocardiography. The commonly used clinical Duke-Li classification, however, yields a low sensitivity for the detection of CIED infections. In addition, the Duke-Li criteria may not be suitable to identify early infection of CIED for a timely and effective intervention.[5,6] Of course, when there are unequivocal clinical signs of pocket infection, and/or vegetation's with systemic symptoms, then the diagnosis is definitive and extraction of the CIED commonly ensues. Conversely, in case of equivocal clinical and echocardiographic findings in patients with suspicion for CIED infection, there is an emerging and promising role of ^{18}F-fluorodeoxyglucose (FDG)-PET imaging despite limited data available.[7,8]

In this issue of the Journal of Nuclear Cardiology, Salomaki et al.[9] add further important information on the evolving and promising role of ^{18}F-FDG-PET imaging in the diagnosis of CIED infection. The study consisted of 30 patients with suspected CIED infection who underwent ^{18}F-FDG-PET/CT. Notably, the authors also investigated ten patients with asymptomatic CIED, who underwent cancer related ^{18}F-FDG-PET/CT, as control group for study purpose. The final diagnosis of CIED infection was based on available clinical and bacteriological data. On visual analysis of ^{18}F-FDG-PET/CT images in suspected CIED infection $\leq$ 8 weeks of implantation (group 1), ^{18}F-FDG-PET/CT images were positive in all nine patients, but only four had confirmed CIED infection. In more detail, six patients presented abnormal ^{18}F-FDG uptake both in the pocket area and in leads, two patients only in the pocket area and one patient in the leads. The exact reason for apparent false-positive findings remains uncertain but may be related, at least in part, to post-interventional sterile inflammatory process owing to endogenous repair mechanisms in the pocket area or to mild foreign body reaction in the area of the lead implantation. The authors' state that abnormal findings of ^{18}F-FDG uptake to signify CIED infection on attenuation corrected images were confirmed on non-attenuation corrected images.[10,11] This should have excluded false-positive

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findings due to erroneously elevated owing to an attenuation over-correction based on the CT captured metal density. Group 2 included ^{18}F-FDG-PET/CT images in patients with suspected CIED infection > 8 weeks of implantation. In this group 2, ^{18}F-FDG-PET/CT was positive in all eight cases with a definitive CIED infection, while no uptake was detected in patients without CIED infection. These observations may outline that the false-positive findings on ^{18}F-FDG-PET/CT in patients with suspected CIED infection within an eight weeks period to likely be related to a sterile inflammatory process rather than bacterial infection. Of further interest, the authors also examined twelve patients without local signs of CIED infection, but fever of unknown origin (FUO) (N = 6) or bacteremia with typical endocardial pathogen or recurrent bacteremia with no identified focus (N = 6) (group 3). As it was observed, four patients had abnormal ^{18}F-FDG uptake in CIED leads, whereas only one of these had definitive CIED infection. These three apparent false-positive ^{18}F-FDG uptake findings were paralleled by the presence of pericarditis, antibiotic therapy, and unknown source, respectively. In this group of patients with FUO, it may be intriguing to speculate that systemic inflammation may have led to a mild local reactive and sterile inflammatory process that favors some ^{18}F-FDG uptake at the site of the pocket and lead implantation difficult to discern from true bacterial infection. As regards the quantification of ^{18}F-FDG uptake with SUVmax and TBR in groups 2 and 3, these parameters were significantly higher the pocket area in patients with a definitive CIED infection than patients without CIED infection (SUVmax: 4.8 ± 2.4 vs 2.0 ± 0.4 and TBR: 2.0 ± 1.1 vs 0.9 ± 0.3) or patients in the control group (SUV max: 2.0 ± 0.8 and TBR: 0.9 ± 0.4). Further, SUV max value of leads was higher in patients with CIED infection compared to control group with borderline statistical significance (SUVmax 4.6 ± 2.9 vs 2.4 ± 0.5) and no significant difference in TBR value was observed. When applying the cut-off value of TBR ≥ 1.8 (for both the pocket area or leads), it yielded a sensitivity of 90%, specificity of 73%, positive predictive value of 75%, and negative predictive value of 89% for the detection of definitive CIED infection. Overall, it appears that quantification of the SUV max and TBR for groups 2 and 3 may be helpful for the identification of CIED infection in the pocket area, while this may not be the case for the cardiac leads. The exact cause of this discordant observation remains uncertain but may be related to differences between both groups in leukocyte infiltration, populations, and disease activity affecting both pocket and leads, respectively.[12] The promising results of the diagnostic accuracy of ^{18}F-FDG and PET in the identification of CIED infection in this population remains uncertain due to low numbers and differences in inflammatory disease entities, that warrants further larger-scale clinical investigations. In aggregate, ^{18}F-FDG and PET shows a high sensitivity and moderate specificity for the identification of definitive CIED infection in groups 2 and 3. Conversely, the diagnostic accuracy for the detection of definite CIED infection in group 1 is limited owing to ongoing inflammatory repair mechanism in the pocket region and foreign body reaction around the implanted leads. Given these limitations, findings of increases in ^{18}F-FDG in CIED in this group necessitates appropriate interpretation in the clinical context in order to avoid unnecessary and potential harmful CIED removal.[13]

Overall, the results of Salomaki et al. in the current issue[9] raise the awareness of the emerging role of ^{18}F-FDG and PET in the identification and characterization of CIED infections that may contribute to an optimal clinical decision-making process and thus patient care. Conversely, these observations also provide critical information for the physicians to be cautious with the interpretation of ^{18}F-FDG PET, in particular in patients with recent implantation or other intervention of CIED, given the observed low specificity in such cases. Although that the role of ^{18}F-FDG PET in the detection of CIED infections is expanding, a balanced read out taking all confounding factors into account and expertise are of paramount importance to fully exploit its potential as the current and other investigations suggests.[9,14,15]

Disclosure

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