Radionuclide Imaging of Cardiovascular Infection

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KEYWORDS

• Cardiovascular infection • Pacemaker infection • Infective endocarditis • Radionuclide imaging • [^{18}F] FDG-PET/CT

KEY POINTS

- There is growing evidence to support the role of fludeoxyglucose F 18 ([^{18}F] FDG) PET/computed tomographic (CT) imaging in patients with suspected cardiovascular prosthetic and device infections.
- Diagnosis of cardiac implantable electronic device (CIED)-generator pocket infection (GPI) is challenging because of nonspecific clinical presentations, and [^{18}F] FDG-PET/CT may be most valuable in this group because of its high negative predictive value.
- [^{18}F]-FDG PET/CT could be a problem-solving tool in patients with suspected valve infective endocarditis (IE) (particularly prosthetic valves), with positive blood cultures but negative echocardiogram, and also in the detection of distant septic emboli.
- Evidence is emerging regarding the potential utility of hybrid radionuclide imaging in suspected vascular graft infection.

INTRODUCTION

Cardiovascular infection can be broadly split into 2 main groups: nonvalvular infections, which are usually associated with a CIED or prosthetic material, and valvular infections, which can affect both native and prosthetic valves. Despite this arbitrary classification, both types of infection are associated with significant morbidity and mortality. Furthermore, delays in diagnosing infection in difficult cases may delay appropriate treatment, further complicating the clinical course. The American Heart Association (AHA) has published guidelines for the investigation and management of cardiovascular infections.[1] These guidelines highlight the role of echocardiography and microbiological culture to confirm diagnosis. More recently, PET/CT has been used for infection imaging in patients with both low and high probability of CIED infection, with high sensitivity and specificity. However, the utility of radionuclide imaging to function as a stand-alone noninvasive diagnostic imaging test in patients with suspected endocarditis has been less frequently examined. In this article, the authors summarize the recent advances in radionuclide imaging for the evaluation of patients with suspected cardiovascular infections.

GENERAL PRINCIPLES

The basic principle underlying radionuclide imaging is administration of a tracer that targets the

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function of a particular organ or a particular metabolic process. The tracer is labeled with a radionuclide, and it is the gamma emissions, from the radionuclide as it decays, that are detected by the gamma camera or the PET camera.

Until the mid-1990s, radionuclide imaging provided two-dimensional (2D) functional images of 3-dimensional (3D) structures without the degree of anatomic information afforded by other forms of imaging such as CT and MRI. With the development of hybrid imaging technology, the addition of CT to the gamma camera or PET camera gantry allowed the fusion of functional information with anatomy. This development represented a major breakthrough, allowing accurate 3D localization of tracer distribution.

HISTORICAL PERSPECTIVE

Attempts were made to use radionuclide imaging for detection of endocarditis over 50 years ago; however, these early studies suffered from the limitations of planar (2D) imaging and also the unfavorable imaging characteristics of the then available radionuclide, ^{67}Ga citrate. The radiation dose to the patient was high and imaging continued for 3 or more days after intravenous tracer injection.

The emergence of techniques to radiolabel autologous leukocytes in the 1970s[2,3] constituted a major breakthrough in imaging of infection and inflammation. The radionuclide, either ^{99m}Tc or ^{111}In, bound to a lipophilic chelate, crosses the phospholipid leukocyte cell membrane. Following reinjection of the radiolabeled cells, the leukocyte migration pathway and incorporation of leukocytes into areas of infection or inflammation can be mapped. Both remain in use for leukocyte labeling, and this technique is widely available.

PET/CT offers several advantages over gamma camera imaging including increased sensitivity, increased image resolution, accurate attenuation correction, and accurate quantification, hence autologous leukocyte labeling with a positron-emitting radionuclide presents an attractive alternative to ^{99m}Tc or ^{111}In labeling.[4,5] The short physical half-life of PET tracers is, however, problematic, being insufficient to encompass the time course of labeled leukocyte migration into infection sites.

GENERAL PRINCIPLES OF FLUDEOXYGLUCOSE F 18-PET/COMPUTED TOMOGRAPHIC IMAGING

The positron-emitting radionuclide, [^{18}F] FDG, has been widely used in oncologic imaging for over a decade, and in recent years, it has been proposed for imaging of infection and inflammation.[6–12] The tracer [^{18}F] FDG is taken up by metabolically active cells via glucose transporters, primarily GLUT 1 and also GLUT 4, which is insulin sensitive and present in myocardium and skeletal muscle. Once inside the cell, [^{18}F] FDG is phosphorylated by hexokinase to [^{18}F]-2′-FDG-6-phosphate and remains intracellular without undergoing further metabolism.

Activated neutrophils, monocytes, macrophages, and lymphocytes express high levels of glucose transporters especially GLUT 1 and GLUT 3, hence [^{18}F] FDG uptake by these cells and migration to sites of infection is to be expected. The technique has high sensitivity, but [^{18}F] FDG avidity is also shown by active thrombi, soft atherosclerotic plaques, vasculitis, inflammation, and many primary and secondary malignancies (**Fig. 1**).[6–13] In addition, many tissues, including the myocardium, show high and sometimes heterogeneous physiologic [^{18}F] FDG activity, therefore clinical correlation and consideration of other imaging is required when interpreting [^{18}F] FDG images to avoid significant decrease in specificity.

Dual time point imaging, in which the acquisition is repeated after sufficient delay to allow for reduction in normal physiologic uptake, may be of value in differentiating normal physiologic or inflammatory [^{18}F] FDG activity from pathologic increased accumulation.[14–17] High physiologic myocardial activity may be problematic when using the technique for detection of endocarditis, valve infection, or intracardiac lead infection (LI); however, dietary manipulation has been reported to reduce physiologic uptake.[15,18,19] In the authors' experience, use of a carbohydrate-restricted diet for 24 hours before the standard 4- to 6-hour fast required for [^{18}F] FDG studies (**Box 1**) significantly decreases physiologic myocardial activity and permits adequate visualization of abnormal myocardial activity (see **Fig. 1**; **Figs. 2** and **3**).[20]

There is now a body of published literature detailing the use of [^{18}F] FDG in suspected cardiovascular-related infection, including both case reports and retrospective studies. A summary of radionuclides in current use for imaging of infection and inflammation is provided in **Table 1**. Advantages and disadvantages of the radionuclides are detailed in **Table 2**. [^{18}F] FDG-PET/CT is the authors' preferred option in suspected CIED infection and endocarditis, and accordingly, a more detailed protocol for this radionuclide is presented in **Table 3** and a proposed algorithm is presented in **Fig. 4**.