Confounders in FDG-PET/CT Imaging of Suspected Prosthetic Valve Endocarditis

Asbjørn Mathias Scholtens, MD,a Laurens E. Swart, MD,b Hein Jan Verberne, MD, PhD,c Wilco Tanis, MD, PhD,d Marnix G.E.H. Lam, MD, PhD,e Ricardo P.J. Budde, MD, PhDb

RECENTLY, 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY WITH LOW-DOSE COMPUTED tomography for attenuation correction and anatomical correlation (18F-FDG-PET/CT) has seen increasing use to help diagnose prosthetic heart valve (PHV) endocarditis. Based on the available evidence, 18F-FDG-PET/CT has even been incorporated in the latest European Society of Cardiology Endocarditis Guidelines (1). As this is still a novel indication for 18F-FDG-PET/CT, the boundaries between normal and abnormal findings are relatively undefined. We present a number of variations (Figures 1 to 6) that could lead to misdiagnosis and need to be taken into account when reading 18F-FDG-PET/CT in patients suspected for PHV endocarditis. Awareness of these variants specifically in the context of suspected PHV endocarditis and cardiovascular infection in a broader sense is pivotal, as this may prevent false-positive or false-negative 18F-FDG-PET/CT readings.

FIGURE 1 The Importance of Adequate Suppression of Myocardial 18F-FDG Uptake

Maximum intensity projection positron emission tomography (PET) images in sagittal and coronal views of 2 scans (interval 35 days) in the same patient with endocarditis of a St. Jude mechanical prosthetic heart valve (St. Jude Medical, St. Paul, Minnesota) implanted 1 year earlier, with and without additional preparatory measures (A). The intense physiological uptake in the myocardium after the standard 6-h fast makes it difficult to delineate uptake caused by the infection (lower panels), whereas after the preparatory protocol, the myocardial metabolism has switched to free fatty acids and only the infectious process surrounding the prosthetic heart valve ring and ascending aorta shows uptake of 18F-fluorodeoxyglucose (18F-FDG), easily delineated from other structures (upper panels). In some cases, unsuccessful suppression can be very focal in the basal anteroseptum (B), directly adjacent or close to prosthetic valves and seem suspect for infection. (C) Our preparatory protocol, combining a low-carbohydrate diet, prolonged fasting and heparin pre-administration to maximize myocardial suppression (2). CT = computed tomography; IU = international units.
FIGURE 2 18F-FDG-PET/CT in PHV Endocarditis: How Much Is Too Much?

PET/CT images of the valvular plane in 3 different patients with a mechanical prosthetic heart valve (PHV) (A to C) and a patient with a Carpentier-Edwards bioprosthesis (Edwards Lifesciences, Irvine, California), with maximum standard uptake values (SUV\textsubscript{max}) and target-to-background ratios (TBR) (SUV\textsubscript{max} PHV divided by SUV\textsubscript{mean} aortic blood pool). (A) Images show no significant 18F-FDG uptake surrounding the PHV in a patient without endocarditis. (B) Images show intense uptake of 18F-FDG in surgically confirmed infection of the aortic root surrounding the PHV ring. (C) Images show mild to moderate uptake of 18F-FDG surrounding and confined to the PHV ring, in a patient confirmed by follow-up to have no PHV endocarditis. (D) Images show mild, symmetrical 18F-FDG uptake at or near the struts to which the leaflets are fastened (shown in detail in the first CT–maximum intensity projection image), typical of this type of prosthesis. A mild to moderate amount of 18F-FDG uptake around a PHV is a normal variant, possibly due to a mild foreign body reaction or strain on the aortic wall. Abbreviations as in Figure 1.
FIGURE 3 Infection Versus Inflammation

(A) Images show a patient with both aortic and mitral mechanical PHV with intense $^{18}$F-FDG uptake in the entire basal septum extending to both PHV. Minor uptake in the lateral wall is physiological based on incomplete suppression. Antibiotics did not change the clinical presentation, and re-evaluation of biopsy samples led to the diagnosis of sterile granuloma, possibly sarcoidosis. Symptoms diminished under corticosteroid therapy. (B) Images show a patient with suspicion of endocarditis of biological PHV and Bentall prosthesis. There is intense accumulation of $^{18}$F-FDG surrounding the implant (aortic valve and ascending aorta), indicative of widespread inflammation. During implantation, surgical adhesive had been applied to ensure hemostasis. The accumulation of $^{18}$F-FDG is most likely based on sterile inflammation due to the surgical adhesive and not due to infective endocarditis. This was confirmed during unrelated thoracic surgery. These images highlight the inability to reliably differentiate between infection and sterile inflammatory processes. Abbreviations as in Figures 1 and 2.

FIGURE 4 Atrial Variants

In atrial fibrillation, the uncoordinated contraction of the atrial myocardium leads to high energy consumption and a consequent up-regulation of glucose metabolism leading to increased uptake of $^{18}$F-FDG, even though the ventricular myocardial glucose metabolism may be completely suppressed. Such accumulation of $^{18}$F-FDG in the atrial myocardium may be adjacent to PHV and may be hard to differentiate from infectious foci (A). Lipomatous hypertrophy of the interatrial septum is associated with moderately to intensely increased uptake of $^{18}$F-FDG, presented here in a patient without a PHV (B). Especially in patients with PHV in the aortic position, lipomatous hypertrophy of the interatrial septum may be located adjacent to the valve. Typical barbell-shape and fatty density without stranding on CT images are arguments against infection. Abbreviations as in Figures 1 and 2.
FIGURE 5  The Effect of Antibiotic Therapy

Maximum intensity projection and transaxial PET images before (left) and during (right) antibiotic therapy in the same patient. The initial scan shows focal activity at the implanted aortic PHV (arrows). At the end of antibiotic therapy, repeat imaging shows only minimal residual 18F-FDG activity around the PHV, suggesting the infection was treated successfully. However, signs and symptoms of infection returned after cessation of antibiotic therapy, with subsequent surgery showing focal persistence of infection. Although the follow-up scan could therefore be argued to be false negative, it is probably true negative with regard to disease activity, as all clinical and laboratory parameters had also normalized. As this case shows, this does not necessarily imply the complete eradication of pathogens as 18F-FDG-PET/CT imaging visualizes leukocyte activity rather than the presence of pathogens themselves. Abbreviations as in Figures 1 and 2.

FIGURE 6  False Negative 18F-FDG-PET in Valve Vegetation

18F-FDG-PET/CT is not capable of excluding vegetations on PHV, as they are likely to be false negatives. PET shows pathological hyperactivity in the aortic wall, but not in the vegetation (arrows) visible on CT angiography (diastolic phase upper right, systolic phase lower right). Several factors may contribute to low levels of activity in vegetations, from the limited spatial resolution of 18F-FDG-PET/CT to a lesser cellular component in the inflammatory response to vegetations. 18F-FDG-PET/CT should always be combined with echocardiography or CT angiography of the valve to rule out solitary vegetations. Abbreviations as in Figures 1 and 2.

REFERENCES


KEY WORDS computed tomography, endocarditis, fluorodeoxyglucose F18, heart valve prosthesis, positron emission tomography