Accurate diagnosis of prosthetic heart valve infection has major implications on patient management and outcome. If the presence of prosthetic or periprosthetic valve endocarditis is misclassified, it can lead to delayed antibiotic or surgical intervention, which may adversely affect patient outcomes, and that is not inconsequential. Prosthetic valve endocarditis constitutes up to 30% of all cases of infective endocarditis in developed countries, and the frequency is greatest during the initial 6 months after valve surgery. The in-hospital mortality among patients with prosthetic valve endocarditis can be as high as 47%, particularly for *Staphylococcus aureus* endocarditis.

Although the diagnosis of infectious endocarditis is usually initiated by clinical suspicion, increased inflammatory biomarkers, and positive blood cultures, accurate localization of infection at the prosthetic valve site is accomplished by imaging, primarily with transesophageal echocardiography. However, in nearly 10% to 20% of instances, blood cultures or transesophageal echocardiographic results are inconclusive, thus leading to a high proportion of unconfirmed cases of suspected prosthetic valve endocarditis. Delay in initiating antibiotic treatment can lead to untoward structural damage beyond the prosthesis itself, which may cause acute heart failure as well as systemic complications, such as embolism and cerebral hemorrhage. Unlike the native valve, prosthetic valve endocarditis commonly extends beyond the valve ring into the annulus and periannular and myocardial tissue, causing dehiscence of the prosthesis with significant hemodynamic and conduction disturbances. On histological examination, infected mechanical valves exhibit neutrophil-rich inflammatory infiltrates with neovascularization and possible microorganisms. The latter makes labeling white blood cells or applying radiotracers that are incorporating inflammatory cells desirable imaging options that may lead to improved sensitivity for detecting prosthetic valve endocarditis than the more conventional anatomy-based approaches, such as echocardiography and computed tomography.

Indium-111-labeled or ⁹⁹ᵐTc-labeled autologous white blood cells are used clinically for the evaluation of infectious processes that include painful prosthetic joints. However, the sensitivity of white blood cell imaging for detecting infection can vary depending on factors such as viability of white blood cells after in vitro labeling and migration rate of the cells to the infection site. The latter becomes a particular limitation among patients who are on antibiotic therapy, in whom cell chemotaxis is decreased. Beyond the sensitivity issues, the labeling process of white blood cells is time consuming, labor intensive, and costly. There is the potential risk for pathogen contamination during the in vitro labeling of the cells and patient misadministration. After labeled white blood cells are injected, image acquisition is delayed by 24 h or longer, and the planar images tend to be count poor, with low spatial resolution. Other efforts for infection imaging with ⁶⁷Ga citrate and ¹¹¹In-labeled platelets have not produced high sensitivity or anatomic localization to be clinically meaningful.

Unlike the in vitro labeling process of white blood cells, ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) is based on in vivo FDG targeting of the preexisting inflammatory cells at the infectious site. With the stimulation of cytokines, inflammatory cells (macrophages, neutrophils, and lymphocytes) overexpress the glucose transporter 1 and accumulate FDG in high concentration. Thus, imaging the inflammatory cells at the site of the infection with FDG may have a higher sensitivity than labeled
white blood cells, particularly for patients who are on antibiotic therapy or in the setting of chronic infections. Beyond improved sensitivity, other advantages of FDG PET/CT include high spatial and target-to-background contrast resolution tomographic images, the relatively simple and non-labor-intensive procedure of injecting FDG and acquiring images within 1.5 to 2 h, and lower radiation dose.

There are a number of publications supporting the role of FDG PET/CT for detecting vascular prosthesis, implantable pacemaker and defibrillator infections, and more recently prosthetic valve endocarditis, including the iPIX case series by Tanis et al. (1) in this issue of iJACC. In a contemporary cohort of patients with presumed prosthetic valve endocarditis, Saby et al. (2) reported the sensitivity and specificity of FDG PET/CT to be 73% and 80%, respectively. However, when the results of PET/CT were combined with other clinical, microbiological, and echocardiographic parameters, the sensitivity of the modified Duke criteria dramatically increased to 97%.

Nonetheless, it is important to point out that these preliminary data do not advocate FDG PET/CT as a “first-line” or “confirmatory” imaging study for detecting prosthetic valve endocarditis. Rather, it should be reserved for patients with clinical suspicion of endocarditis and inconclusive or negative results on initial transesophageal echocardiography. Although cardiac CT alone may also be helpful in some situations, it is also purely anatomic, and changes that may be present in acute prosthetic valve endocarditis could also be the consequence of surgery or an earlier infection.

Identifying inflammatory cells early at the site of the prosthetic valve infection (by FDG PET) before the development of morphologic damages from the infectious process (detectable by echocardiography or CT) is a laudable goal to pursue. Although the latter makes intuitive sense, it would be important to determine the false-positive rate of FDG PET/CT, such as uptake seen at the aortic root graft when imaged early after valve replacement surgery. In patients undergoing FDG PET/CT for cancer evaluation, false-positive FDG uptake can occur in sites of infection as well as a variety of noninfectious inflammatory diseases. Thus, until a well-designed prospective study demonstrates that the early detection of inflammatory cells by hybrid FDG PET/CT alters therapeutic intervention and improves patient outcome, the technique should be used judiciously, only in patients with suspected prosthetic valve endocarditis and inconclusive or negative results on initial transesophageal echocardiography.

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