

Diagnosis of Vascular Prosthesis Infection: PET or SPECT?

The well-established gold standard for imaging infection is scintigraphy with radiolabeled autologous white blood cells (WBCs). Indeed, 2 years ago, in a metaanalysis of all papers published in the previous 20 years on imaging techniques for the diagnosis of infection (1–4), the importance of WBC scanning in this field clearly emerged, with few exceptions. In particular, for the diagnosis of vascular graft infection, although scintigraphy with WBCs was found to be most accurate, the authors concluded that the new hybrid modalities SPECT/CT and PET/CT would have highly enhanced the use of WBCs and

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¹⁸F-FDG, respectively, allowing precise localization of abnormal uptake in the vascular graft. Thus, the possibility of exact anatomic localization of pathologic uptake seems as important as the choice of radiopharmaceutical. However, 2 other important factors remain to be validated when a technique is proposed for in vivo diagnosis of infection: standardization of image acquisition times and standardization of image interpretation criteria, including quantitative and semiquantitative measurements.

During the last few years, ¹⁸F-FDG PET has been widely used for the

diagnosis or follow-up of many inflammatory diseases. Because ¹⁸F-FDG is not specific for infection but is taken up by inflammatory cells with high glucose metabolism (5), many investigators have suggested the use of ¹⁸F-FDG PET for detecting infection and, in particular, for evaluating suspected vascular graft infections (6–16). For example, in a patient with infection after orthopedic surgery, ¹⁸F-FDG PET also revealed an aortic valve infection (17). Unfortunately, because many of the studies on this topic have been case reports or have included few patients, it is not yet possible to accurately assess the value of ¹⁸F-FDG PET in the diagnosis of vascular graft infection. Similarly, it is difficult to draw any conclusions about the best image acquisition times, interpretation criteria, and methods of quantitative analysis.

Nevertheless, the data accumulated so far allow us to pose a few considerations.

CT—with its excellent spatial resolution, widespread availability, and high sensitivity—has been the first-line imaging method for assessing graft infection. In infections that are of low grade or in the early stages, the sensitivity of CT decreases because of morphologic changes preventing inflammation from being distinguished from noninflammatory changes, such as those after surgery or due to scarring or therapy (14,18). Today, scintigraphy with autologous WBCs labeled with ¹¹¹In-oxine or ^{99m}Tc-hexamethylpropylene amine oxime is the technique of choice for identifying graft infection, because of high sensitivity and specificity (97.7% and 88.6%, respectively, for ^{99m}Tc-WBCs). Labeled WBCs accumulate at and thus identify sites of infection through diapedesis, chemo-

taxis, and vascular permeability. Moreover, the labeling procedures, acquisition modalities, and interpretation methods are well established, guaranteeing that similar results will be obtained in different departments and countries (1,19). The 2 major drawbacks of this method are the need to manipulate blood and the lengthiness of the examination. Of course, ¹⁸F-FDG PET strongly competes with WBC scintigraphy. Indeed, after intracellular phosphorylation, ¹⁸F-FDG is trapped within neutrophils in relation to the respiratory burst; thus, the detection of inflammatory sites is independent of the homing and timing of leukocyte migration. For this reason, ¹⁸F-FDG PET results may be available within 1 h of ¹⁸F-FDG administration as opposed to 24 h in the case of labeled-WBC studies (20). However, the best choice of acquisition time for ¹⁸F-FDG PET studies still needs further investigation and standardization, and in the case of vascular graft infection, a recent study with ^{99m}Tc-hexamethylpropylene amine oxime-WBC proposed acquisitions only within 2 h after the injection of the labeled leukocytes (21). For PET studies, some authors have suggested that images be acquired early (30 min after injection) and others have also suggested dual imaging (acquiring the first image within 1 h and the second image at about 2 h) to differentiate between inflammation and tumors or infection. Abnormal uptake of ¹⁸F-FDG is often found in vasculitis, giant-cell arteritis, Takayasu's arteritis, venous thrombosis, retroperitoneal fibrosis, and aseptic inflammation (14,20). In addition, asymptomatic and elderly patients may present with increased ¹⁸F-FDG uptake in the lamina muscularis of large vessels or in atherosclerotic plaques

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TABLE 1
Summary of Published Studies Using ¹⁸F-FDG in Vascular Graft Infection

Study	Year	No. of patients	Method*	¹⁸ F-FDG dose [†] (MBq)	Acquisition time [‡] (minutes after injection)	Interpretation criteria [§]	True-positive	True-negative	False-positive	False-negative
Stumpe (7)	2000	7	PET	300–400	30–40	Qualitative	2	5	0	0
Krupnick (12)	2003	1	PET	187	50	Qualitative	1	0	0	0
Chacko (8)	2003	3	PET	2.55/kg	60	Qualitative	2	1	0	0
Keidar (11)	2003	1	PET/CT	370	60	Qualitative	1	0	0	0
Städler (14)	2004	1	PET/CT	375	90	Qualitative	1	0	0	0
Fukuchi (15)	2005	33	PET	185	60	Semiquantitative	10	14	8	1
Jaruskova (9)	2006	7	PET/CT	279–717	40–165 (mean, 70)	Qualitative	6	0	1	0
Tsunekawa (16)	2007	1	PET	185	60	Qualitative	1	0	0	0
Tegler (25)	2007	1	PET/CT	—	—	Qualitative	1	0	0	0
Keidar (29)	2007	39	PET/CT	185–370	90	Qualitative based on morphology	14	22	2	1

*Shows morphologic accuracy in detecting site of ¹⁸F-FDG uptake.

[†]¹⁸F-FDG dose is usually related to image acquisition time.

[‡]Early or delayed imaging may lead to different diagnostic accuracy.

[§]Qualitative or quantitative interpretation may also depend on method used.

because of the presence of macrophages (22).

Another important aspect is the time from surgery: In the early phases of healing and, frequently, in the first months after surgery, ¹⁸F-FDG may give false-positive results. Other examinations must then be performed within the following days or weeks to prove a local decrease or increase of ¹⁸F-FDG uptake. Moreover, about 40% of infections in graft prostheses appear within 4 mo after surgery (23). If imaging is required early after surgery, WBC scintigraphy would therefore seem to be more accurate than ¹⁸F-FDG PET (21).

Unfortunately, as far as quantitative measurement of ¹⁸F-FDG uptake is concerned, few papers have been published. Some authors have proposed a progressively increasing 5-point scale based on visual analysis of ¹⁸F-FDG uptake (7,15), but this method appears to be quite observer-dependent. Still, some work should be done in this direction. Certainly, combining CT with ¹⁸F-FDG PET increases its specificity (9,11,14,24,25). If we compare all published data on the use of ¹⁸F-FDG PET in vascular graft infections (Table 1), it emerges that the combined use of PET and CT improves diagnostic accuracy (in particular, reduces the rate of false-positive cases) by allowing

image interpretation based on morphologic criteria. A valid alternative to PET/CT may be SPECT/CT with labeled WBCs. The usefulness of this hybrid method has recently been demonstrated for bone and joint infections (26,27), although the literature currently includes only one case report on vascular prosthesis infection (28).

In light of the cumulated evidence, scintigraphy with radiolabeled WBCs should still be considered the gold standard for imaging vascular graft infection—particularly when improved by the use of a SPECT/CT camera—because of the extensive validation of the radiopharmaceutical, image acquisition modality, and image interpretation criteria (1). PET and PET/CT with ¹⁸F-FDG may well become a valid substitute for WBC scintigraphy, provided that large clinical trials validate the best acquisition times and the most reliable imaging analysis and interpretation criteria. The paper by Keidar et al. (29) in this issue of *The Journal of Nuclear Medicine* represents a well-designed attempt to achieve such standardization, and similar works are encouraged.

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