The Role of ^{18}F-FDG PET in Aortic Dissection

Acute aortic dissection is relatively rare (approximately 3 per 100,000 person-years) but has a high mortality: between 10% and 30% at 30 d (1). Early diagnosis and treatment are essential for survival. Peak incidence occurs after the age of 60 y with other risk factors including the male sex and hypertension. A typical clinical presentation is of sudden, sharp, centralized, tearing chest or back pain, but other symptoms (syncope, stroke, myocardial infarction, heart failure) are well recognized. The underlying pathology relates to a tear in the aortic intima, through which blood passes into the media. This process may shear the intima from the media, creating a false lumen that can be localized or

can propagate in both antegrade and retrograde directions. If branching arteries of the aorta arise from the false lumen, their blood flow can be compromised, leading to complications of stroke (carotid arteries) and myocardial infarction (coronary arteries). Additionally, blood can track retrogradely toward the heart and aortic valve, causing cardiac tamponade and aortic valve regurgitation, respectively. The intimal tear is frequently associated with cystic medial degeneration of the aorta and the presence of inflammatory cells (1).

Therapy for aortic dissection depends on the extent of the aortic tear.

If the ascending aorta is involved (Stanford type A), the management is usually surgical repair with aortic reconstruction as necessary. In contrast, if the dissection is confined to the descending aorta (Stanford type B), the treatment strategy is medical with future surveillance by serial aortic imaging. Medical therapy is aimed at lowering blood pressure and therefore aortic wall stress. Multiple agents are usually needed, with β-blockers being universally recommended as first-line agents (2). Surgery is usually indicated only in type B dissection if there is progression of the dissection (aneurysm formation, occlusion of major aortic branches, aortic rupture) or persistent hemorrhage into the retroperitoneal or pleural space (3). Despite this strategy, medical management fails in a sizeable proportion of patients with type B dissection, and early imaging therefore plays a critical role in identifying patients who require surgery. Either CT or MRI is generally used to measure the maximum diameter of the aorta and to exclude complications. CT is preferred in the acute setting because of its short acquisition time in a potentially unstable patient group, whereas after discharge MRI may be more appropriate because of concerns over nephrotoxicity and radiation burden from serial CT studies. Unfortunately, despite close follow-up to detect complications, the death rate among patients with type B dissection remains high—approximately 45% in the 10 y after diagnosis (4). As a result, better imaging methods are still needed for identifying medically treated survivors of type B aortic dissection who are at high risk of complications.

In this issue of *The Journal of Nuclear Medicine,* Kato et al. examine the use of ^{18}F-FDG PET for predicting adverse outcomes in aortic dissection (5). It is believed that proteolytic and

inflammatory processes are at work in the aortic wall in chronic dissection (2), and the authors hypothesized that ^{18}F-FDG uptake by the dissected aorta might be a marker of future adverse outcomes. They prospectively recruited a group of 28 patients with aortic dissection—26 patients with Stanford type B and 2 with type A dissections who were refused surgery because of comorbid disease. Kato et al. also recruited 14 age- and sex-matched controls without known vascular disease. Patients with renal impairment, poorly controlled diabetes, collagen disorders, and traumatic aneurysms were excluded. After CT aortography, PET was performed at both 50 and 100 min after ^{18}F-FDG injection, an average of 13 d after diagnosis. Fused PET/CT images were read for ^{18}F-FDG uptake in 3 areas—at the point of maximal aortic diameter and both proximal and distal to it. Unfavorable patient outcomes were defined as death from cardiovascular causes, progressive aortic dissection or rupture, conversion to surgery, and occurrence of cardiovascular events during the 6-mo follow-up period.

Of the 28 subjects imaged, 8 had unfavorable outcomes and the remaining 20 had a favorable clinical course. Baseline aortic diameter at the dissection site was greater in the unfavorable group, whereas levels of circulating biomarkers such as high-sensitivity C-reactive protein were not different between the 2 groups. Compared with the controls, both groups with dissection had greater ^{18}F-FDG uptake proximal and distal to the dissection. Significantly, ^{18}F-FDG uptake at the point of maximal aortic diameter was higher in those patients destined for unfavorable outcomes than in those in the good prognostic group. Even within the favorable outcome group, lower ^{18}F-FDG uptake was noted

among those who had complete resolution of their dissection than in those whose aortic diameter stayed unchanged. After multiple-regression analysis, ^{18}F-FDG uptake at the maximal area of aortic dissection 50 min after ^{18}F-FDG injection independently predicted adverse outcome with an odds ratio of 7.7 ($P = 0.0171$), although the confidence intervals were wide. The authors established that a cutoff value of 3 for standardized uptake value would yield useful positive and negative predictive values for adverse patient outcomes. ^{18}F-FDG uptake after 100 min did not appear to be as discriminatory as that measured at 50 min, perhaps because the peak ^{18}F-FDG uptake period had passed.

The authors conclude that ^{18}F-FDG PET/CT might have a role in prognosticating patients with type B aortic dissection. Additionally, ^{18}F-FDG uptake might be useful in selecting patients at high risk of near-term complications for early surgery. The study presented by Kato et al. complements one published by Kuehl et al. in 2008 (6). Kuehl et al. also focused on the aorta of 33 patients with aortic syndromes but included subjects with proximal aneurysm as well as dissection. Although high ^{18}F-FDG uptake was noted in the aorta of these patients, the link between ^{18}F-FDG uptake and outcome failed to reach significance, except when PET data were combined with levels of inflammatory biomarkers. This may be because there is believed to be a greater inflammatory signal in dissection than in aneurysm (7).

^{18}F-FDG PET/CT has an established role in oncology, in which it is used to identify metastatic disease and track response to therapy. It has also been suggested that ^{18}F-FDG uptake into atherosclerotic plaque may be a marker of plaque instability (8), and high levels of ^{18}F-FDG in atherosclerotic arteries have been linked to cardiovascular risk factors (9), levels of inflammatory biomarkers (10,11),

and degree of macrophage infiltration of the underlying lesions (12). Arterial ^{18}F-FDG uptake is also finding a role as a surrogate marker of efficacy of novel antiatherosclerosis therapies (13), in which it has proven highly reproducible (14–16). Most importantly, there is accumulating evidence from cohorts of patients with cancer that elevated ^{18}F-FDG levels in the arteries are linked to a future risk of cardiovascular events (17,18).

The paper by Kato adds to several candidate nononcology applications for ^{18}F-FDG PET. Although the study population was small and the follow-up short, the authors are to be congratulated in conducting this demanding imaging study in acutely ill patients. After confirmatory work, future, larger studies might test the strategy of an ^{18}F-FDG PET–guided approach to patient selection for surgery versus current management. Additionally, elevated ^{18}F-FDG uptake soon after diagnosis might help to dictate the frequency of MRI and CT surveillance required on a personalized patient level. Finally, the cell type underlying ^{18}F-FDG uptake in aortic dissection remains unknown. Although it seems likely that, as in atherosclerosis, inflammatory cells are responsible, it will be important to seek autoradiographic confirmation of this from patients who proceed to surgery.

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