Assessment of myocardial sympathetic innervation with ^{18}F-FDOPA-PET/CT in patients with autonomic dysfunction: Feasibility study in IPD patients

Pamela K. Woodard, MD[a]

[a] Hugh Monroe Wilson Professor of Radiology, Washington University School of Medicine, St. Louis, MO

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In their manuscript, ''Assessment of myocardial sympathetic innervation with ^{18}F-FDOPA-PET/CT in patients with autonomic dysfunction – Feasibility study in IPD patients'', Goyal et al.[1] present data from a feasibility study evaluating the uptake of ^{18}F-FDOPA on myocardial PET/CT scans in patients with Idiopathic Parkinson's Disease (IPD) and autonomic-dysfunction. In this study they assess 28 patients with IPD who have both autonomic-dysfunction by autonomic function tests (AFTs) and striatal dopaminergic-dysfunction and compare them to 22 control subjects. Both IPD patients and control subjects undergo cardiac-PET/CT (40 minutes post IV-injection of 185-259MBq ^{18}F-FDOPA) and brain-PET/CT (60 minutes post-IV injection) acquired in the same imaging session. Results showed that striatal and myocardial ^{18}F-FDOPA-PET/CT uptake ratios (striatal-to-occipital (SOR) and whole myocardium-to-mediastinal (MwMR, respectively) were significantly lower in IPD patients in comparison to controls. MwMR correlated negatively with drop in systolic blood pressure (SBP) during AFTs ($P = 0.002$), and mean MwMR in patients with abnormal-AFTs was significantly lower than in patients with borderline-AFTs ($P = 0.002$). Moreover, nearly half (9/20) of the IPD patients with abnormal-AFTs showed severe functional deterioration, becoming bed-ridden or wheel-chair bound with severe autonomic symptoms, in comparison to IPD patients with borderline-AFTs (2/8) (McNemar test $P = 0.022$) when followed on average for over 2 years, suggesting that cardiac ^{18}F-FDOPA-PET/CT has the potential to play a role in predicting patient decline.

As noted by the authors, IPD is a neurodegenerative disease which can involve nor-adrenergic sympathetic neurons of the myocardium in addition to dopaminergic neurons in the basal ganglia. It is well documented that dysfunction and denervation of myocardial nor-adrenergic sympathetic neurons can occur in IPD and can cause dysautonomia.[2,3]

Moreover, a number of single positron emission computed tomography (SPECT) and PET radiotracers to include ^{123}I-MIBG, ^{11}C-HED, and ^{11}C-Epinephrine, have been used to evaluate cardiac sympathetic dysfunction.[4-7] Thus, that cardiac PET/CT imaging can be used to evaluate cardiac sympathetic dysfunction isn't new.

Moreover, in as early as 1997, David Goldstein and colleagues in the New England Journal of Medicine showed sympathetic cardioneuropathy in dysautonomias using ^{18}F-fluorodopamine (^{18}F-FDA) PET.[8] Fluorodopamine is metabolite of LDOPA of which ^{18}F-FDOPA is an analogue, and studies of ^{18}F-FDOPA metabolism suggest that it too is metabolized by aromatic amino-acid decarboxylase[8,9] into ^{18}F-FDA. So, that ^{18}F-FDOPA, it's precursor, can be used to assess cardiac dysautonomia is also not surprising.

However, these authors show that both cardiac and brain ^{18}F-FDOPA-PET/CT can feasibly be performed in a single imaging session using a single injection of the ^{18}F-FDOPA radiotracer. While the authors saw no significant correlation between cardiac and striatal ^{18}F-FDOPA tracer uptake, and this finding is consistent with

Reprint requests: Pamela K. Woodard, MD, Hugh Monroe Wilson Professor of Radiology, Washington University School of Medicine, St. Louis, MO ; *woodardp@wustl.edu*

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those of others who have shown cardiac and nigro-striatal neuro-degeneration to be independent of each other,[10,11] information about both striatal dysfunction and cardiac dysautonomia is of importance given that both sets of information can contribute to diagnosis, direction of patient care, and prediction of patient outcomes.

This combined examination may be especially useful in early or suspected IPD as cardiac sympathetic-dysfunction can begin prior to the development of classical IPD symptoms. As pointed out by the authors, additional advantages of acquiring both scans in a single session include not only more information, but also the added information with a lower radiation dose to the patient given the single radiotracer, savings in cost and time, and increased patient convenience.

Given that this study was a feasibility study, the study is small in size and limited to patients with advanced IPD. Additional clinical trials with larger numbers of IPD patients across a range of disease development should be performed in order to bring this promising clinical PET methodology for IPD to routine clinical use and appropriate placement in IPD assessment guidelines.

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