Evolving use of PET viability imaging

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PET ¹⁸FDG viability imaging is frequently used to guide clinical decision-making on the role of revascularization in high-risk patients with heart failure and reduced left ventricular function, coronary artery disease (CAD) and significant comorbidities. Several observational nonrandomized studies have shown that patients with viability will likely benefit from revascularization,^{1–5} with improvement in left ventricular function^{1,5} and survival.¹ The amount of hibernating myocardium can predict the degree of recovery of function and outcome benefit.⁴ However, 4 randomized studies evaluating the value of viability imaging in patients undergoing revascularization have failed to demonstrate outcome differences.^{6–10}

The PET and Recovery Following Revascularization (PARR)-2 trial randomized 430 patients with LVEF ≤ 35% to ¹⁸FDG viability imaging or usual care and showed a nonsignificant trend for 1-year benefit.⁶ Since the imaging recommendations were not adhered to in all the PET patients, a post hoc analysis was carried out in the PET group with management adhering to the PET recommendations and demonstrated significant benefit. Similar benefit was seen with 5-year follow-up in the group with adherence to PET recommendations.⁷ A viability threshold of 7% identified patients who would

benefit with revascularization and was like previous studies.^{4,5} In the Ottawa-5 substudy,¹¹ a significant 1-year benefit was observed in the PET arm, most likely reflecting greater access to PET at an experienced center with well developed expertise in scan interpretation and its accepted use for decision-making.

The Surgical Treatment for Ischemic Heart Failure (STICH) viability substudy evaluated outcomes of 601 patients who had viability imaging with single-photon emission computed tomography (SPECT), dobutamine stress echo, or both.¹² There was no outcome difference in patients with viability randomized to optimized medical therapy with and without surgical revascularization at a median follow-up of 5.1 years. Of note, viability testing was not randomized and did not utilize advanced imaging with PET or cardiovascular magnetic resonance. The other 2 randomized studies^{8,10} were underpowered.

Current guidelines from the American College of Cardiology Foundation/American Heart Association¹³ state that ‘1. Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with de novo HF, who have known CAD and no angina, unless the patient is not eligible for revascularization of any kind. (Level of Evidence: C) and 2. Viability assessment is reasonable in select situations when planning revascularization in HF patients with CAD. (Level of Evidence: B)’. The choice of imaging modality is not recommended and is left to the treating physician. Of note, newly available hybrid PET/magnetic resonance imaging (MRI) systems facilitate co-registered acquisition of metabolic and perfusion PET data as well as anatomic, functional and tissue characterization MRI information and may be particularly useful in these patients.

The physiological and technical aspects of PET ¹⁸FDG viability imaging and scan interpretation have been well described in the PET imaging guidelines co-sponsored by the American Society of Nuclear Cardiology and the Society of Nuclear Medicine and

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Molecular Imaging.¹⁴ In a region of reduced resting perfusion, preserved ¹⁸FDG uptake indicates viability (perfusion-metabolism mismatch or hibernation) and reduced ¹⁸FDG uptake of similar or greater degree is consistent with nonviable tissue or scar (perfusion-metabolism match). Regions with normal perfusion are viable, even with reduced ¹⁸FDG (perfusion-metabolism reverse mismatch), and may represent stunned myocardium. Standardized patient preparation is critical for high quality diagnostic ¹⁸FDG images and needs to favor myocardial metabolism of glucose over fatty acids. An endogenous insulin response is achieved by oral or intravenous glucose loading after a 6 to 12 hour fast and maximizes ¹⁸FDG uptake with less regional heterogeneity. Supplemental insulin may be required to maintain an optimal blood glucose. Obtaining diagnostic images in diabetic patients may be difficult due to cellular insulin resistance or inadequate endogenous insulin and may require the euglycemic-hyperinsulinemic clamp technique (a labor-intensive protocol) or delayed imaging at 2 or 3 hours after tracer injection. The perfusion and metabolic images are reviewed after careful alignment to identify specific perfusion-metabolism patterns that differentiate viable (normal perfusion and metabolism, mismatch, reverse mismatch) from nonviable (matched reduction). The perfusion and ¹⁸FDG images are normalized to the same normal myocardial region which is usually the region on the perfusion image with the greatest activity. This normal region can also be identified or confirmed as normal from stress perfusion images or angiographic data if available. Differences in tracer blood pool activity need to be identified and can be minimized with adjustment of the lower threshold settings. Qualitative or semiquantitative approaches can be used to describe the extent of hibernating myocardium or scar (% of LV) as small (< 10%), moderate (10% to 20%) or large (> 20%).

In this issue of the Journal of Nuclear Cardiology, Wang et al.¹⁵ report the diagnostic accuracy of resting myocardial blood flow (MBF) measured with dynamic ¹³N-ammonia PET for identifying myocardial regions as viable and for predicting echocardiographic improvement of LV ejection fraction ($\geq 8\%$) following coronary artery bypass grafting in 93 patients with CAD. Using 17 segment perfusion/metabolism (¹⁸FDG) polar maps, segments were classified as normal, viable (mismatch or reverse mismatch) or scar (match). Rest MBF differed significantly between the 4 tissue types (normal > reverse mismatch > mismatch > match). Rest MBF $\geq 0.42 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ identified viable segments with a diagnostic accuracy of 87.5% and predicted ejection fraction improvement with a diagnostic accuracy of 77.9%. Similar rest MBF values for predicting viability have been reported in smaller studies.^{16,17} Thus, rest

MBF measured with dynamic perfusion imaging may be useful for assessing viability as an adjunct to conventional static perfusion/metabolism (¹⁸FDG) PET imaging, especially in patients with suboptimal ¹⁸FDG images.

The role of viability imaging in decision-making on the need for revascularization in patients with ischemic heart failure is evolving. Based on early observational studies relating the presence of viability to probable benefit with revascularization, there was much reliance on viability studies for guidance in selection of patients for revascularization. However, enthusiasm for routine use of viability imaging has decreased due to lack of support from randomized trials. Viability imaging still has a role in benefit assessment in selected patients with ischemic heart failure such as those with older age, no angina or ischemia on imaging, large fixed perfusion defects (scar versus hibernating myocardium), moderate or severe left ventricular dysfunction, chronic total coronary occlusion or significant comorbidities (previous coronary bypass surgery, chronic obstructive pulmonary disease, renal impairment).¹⁸ The present direction toward the development of multidisciplinary heart teams with access to current technology may be the best approach for personalized decision-making for these patients.

Disclosures

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