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DISCUSSIONS IN PET IMAGING

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CONTINUING EDUCATION FOR MEDICAL PROFESSIONALS

PET and PET/CT Imaging in Myocardial Infarction

By Marcelo F. Di Carli, M.D., FACC

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Explain the pathophysiology of ischemic right ventricular dysfunction.
- Describe the basic principles of PET and PET/CT imaging protocols for patients with coronary artery disease.
- List indications for PET and PET/CT in patients after myocardial infarction.
- Recognize the basic imaging patterns identified in patients with CAD.

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Left ventricular (LV) function, the extent of coronary artery disease (CAD), and the magnitude of residual ischemia and viability are well-established and powerful predictors of outcome after myocardial infarction.[1] The occurrence of severe LV systolic dysfunction (i.e., LV ejection fraction <35%) post-MI, especially if associated with heart failure, is indicative of very poor survival rate.[1] Despite therapeutic advances, patients with CAD and severe LV dysfunction have a poor prognosis when treated with medical therapy alone.[2] Surgical revascularization appears to afford a long-term survival benefit in selected patients,[3] but identifying those patients with low ejection fraction who would benefit most from revascularization remains controversial, due to the high surgical risk.

In some patients with CAD, LV dysfunction results from myocardial infarction with attendant necrosis and scar formation. Strong and consistent evidence indicates, however, that such myocardial dysfunction may be reversible with revascularization in many patients; this is otherwise referred to as hibernating[4] and/or stunned[5] myocardium. Consequently, the differentiation of ventricular dysfunction caused by fibrosis from that arising from viable but dysfunctional myocardium has important implications for patients with low ejection fraction. Serious heart failure in these patients may be attributed to severe, widespread hibernation (or stunning, or both) rather than to necrosis of a critical mass of myocardium. Failure to identify patients with these potentially reversible causes of heart failure may lead to progressive cellular damage, heart failure, and death.

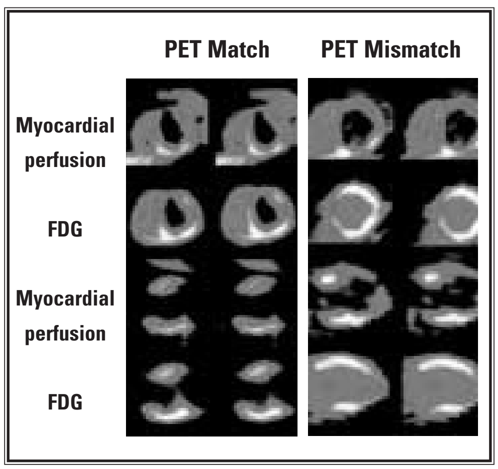

Figure 1. Representative mid-short-axis and vertical long-axis PET images of myocardial blood flow (obtained with N-13 ammonia) and FDG metabolism in patients with prior myocardial infarction. Left: Large and severe perfusion deficit involving anterior, anterolateral, anteroseptal, and apical walls, with a concordant reduction in FDG uptake, consistent with nonviable myocardium (PET match). Right: Similarly large and severe perfusion deficit with relatively preserved FDG uptake, consistent with viable but hibernating myocardium (PET mismatch).

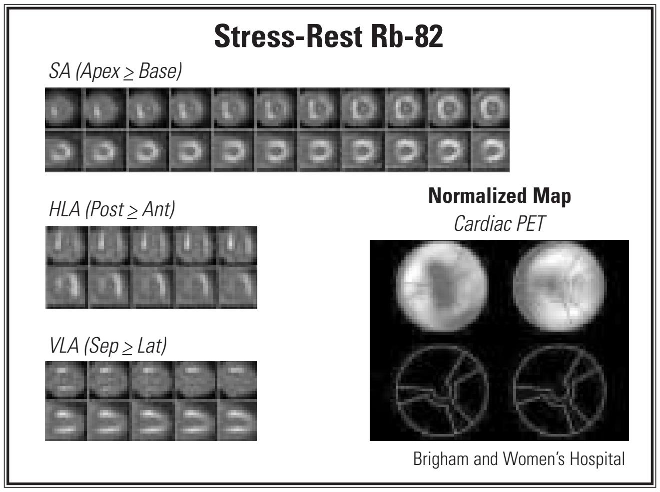

Figure 2. Stress and rest myocardial perfusion PET images obtained with Rb-82 in a patient with prior MI and LV dysfunction. Images demonstrate a large and severe stress perfusion defect involving the mid- and apical anterior, anterolateral, and anteroseptal walls, and the LV apex, showing complete reversibility consistent with extensive and severe ischemia in mid-LAD territory.

ASSESSMENT OF ISCHEMIA AND VIABILITY

From a clinical perspective, evaluation of each of the three predictors of outcome after myocardial infarction—LV function, magnitude of residual myocardial ischemia, and viability—is important to optimize management decisions such as medical therapy versus revascularization. Several approaches to assessment of residual ischemia and viability use PET and hybrid PET/multidetector CT imaging.

The selection of the approach (rest perfusion + FDG metabolism, or rest-stress perfusion + FDG metabolism) should be tailored to the clinical question to be addressed in an individual patient. Rest myocardial perfusion and FDG imaging may be appropriate for a patient in whom the question is the extent of viability of one or more dysfunctional myocardial territories, particularly when a perfusion defect is present at rest (Figure 1). Rest-stress perfusion imaging with or without subsequent FDG imaging may be more appropriate in a patient for whom information about both stress-induced ischemia and viability is required (Figure 2). The rest-stress myocardial perfusion protocols are particularly well suited for patients with relatively preserved myocardial blood flow at rest, in whom LV dysfunction may be caused by stunning rather than hibernation.

Whatever the approach, regional myocardial perfusion with nitrogen-13 ammonia, rubidium-82, or oxygen-15 water is performed first (rest alone, or combined rest and stress imaging). This is followed by the delineation of regional glucose uptake with FDG, providing an index of myocardial metabolism and, thus, cell viability.

Three distinct perfusion-metabolism patterns can be observed in dysfunctional myocardium (Figure 1):

- normal blood flow associated with normal FDG uptake;
- reduced blood flow associated with preserved or enhanced FDG uptake (so-called perfusion-metabolism mismatch, reflecting hibernating myocardium); and
- proportional reduction in blood flow and FDG uptake (so-called perfusion-metabolism match, reflecting scar).

DELINEATION OF CORONARY ARTERY STENOSES

In addition to the functional assessments (myocardial perfusion and metabolism) obtained with PET, hybrid PET/MDCT technology also allows delineation of the extent and severity of underlying coronary artery stenoses. Breath-hold cardiac CT with retrospective ECG gating can provide detailed information regarding angiographic stenoses of the entire coronary artery tree. Excellent image quality can be obtained with the appropriate use of beta blockers prior to CT scanning (Figure 3). The anatomic information can be especially useful in patients with heart failure in whom the diagnosis of CAD is not yet established. Because not all coronary stenoses are flow-limiting, however, the functional PET data complements the anatomic information by providing instant readings about the clinical significance of such stenoses.

Image fusion of the functional PET data with the coronary CT information can also help identify which of those stenoses are clinically significant. Furthermore, the functional PET data are very useful for sorting out the presence of flow-limiting stenoses within areas of heavy calcification or prior stenting, which produce "blooming" artifacts on CT images (Figure 4).

ASSESSMENT OF LV FUNCTION

A myocardial infarction, especially one that is large and transmural, can produce alterations in both the infarcted and noninfarcted regions that result in changes in LV architecture known as LV remodeling. In addition to the early thinning and elongation that occurs in the infarcted myocardium, secondary changes occur in the noninfarcted zone, characterized by a time-dependent associated increase in the end-diastolic length of viable myocytes that contribute to the overall process of LV enlargement.[6] Although this acute increase in cavity size tends to maintain pump function, the process usually leads to progressive ventricular dilation, heart failure, and decreased survival.[7]

Increased LV volumes and cavity size are also predictors of poor out-

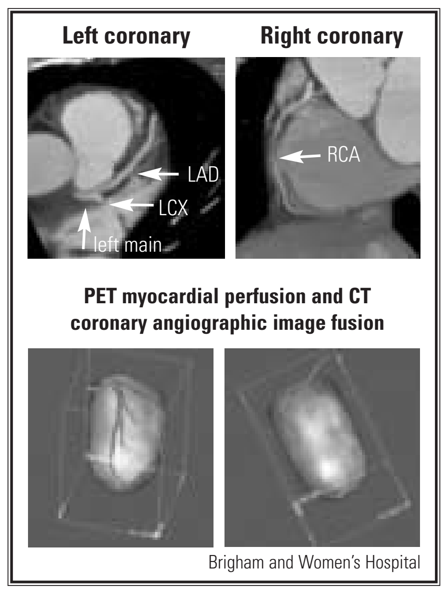

Figure 3. Top: Cross-sectional CT images of left and right coronary arteries following administration of IV contrast, obtained with eight-slice PET/MDCT scanner (GE Medical Systems). Bottom: Fusion of functional myocardial perfusion PET data (3D polar map) and CT coronary angiographic information.

come in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting (CABG). A preoperative LV end-diastolic dimension ≥70 mm as assessed by echocardiography has been shown to be a marker of poor outcome after revascularization.[8] Similar findings have been reported using LV volumes as assessed by contrast left ventriculography.[9] Patients with LV systolic volume index >100 mL/m^2 failed to improve regional and global LV function after CABG, resulting in lower survival and a higher probability of postoperative heart failure. Combined, these data highlight the importance of having measures of LV function and remodeling when evaluating patients after myocardial infarction.

ASSESSMENT OF ISCHEMIA AND VIABILITY

• *Predicting functional recovery*. Experience with the combined perfusion-FDG approach using PET or the PET-SPECT hybrid technique (SPECT perfusion with FDG-PET imaging) has been extensively documented in 17 studies that included 462 patients.[10] Using the patterns described above, the average positive predictive accuracy for calculating improved regional function after revascularization is 76% (range, 52% to 100%), whereas the average negative predictive accuracy is 82% (range, 67% to 100%). Moreover, previous studies have demonstrated that the gain in global LV ejection factor (LVEF) and symptoms after revascularization is generally related to the magnitude of viable dysfunctional myocardium as determined by the PET mismatch pattern, assessed preoperatively.[11]

• *Detecting CAD*. Myocardial perfusion imaging with PET in patients with chest pain has been demonstrated to have a diagnostic accuracy of >90% for the detection of CAD.[12] This increased accuracy of PET imaging compared with SPECT is the result of better attenuation correction for obese patients with PET, resulting in increased specificity, higher spatial resolution, improved contrast between normal and abnormal segments, and the ability to quantitate myocardial blood flow and calculate coronary flow reserve, thereby increasing sensitivity for the detection of CAD. The sensitivity of Rb-82 PET for detection of CAD ranges from 79% to 97%, with specificity reported between 85% and 100%, compared with coronary angiography.

• *Predicting prognosis.* The demonstration of viable myocardium in patients after myocardial infarction appears to identify those with particularly poor prognosis when treated with medical therapy alone. The available data suggest that these patients have improved survival with revascularization therapy. Previous studies demonstrated that patients with CAD and severe LV dysfunction (ejection fraction <35%) who also have evidence of viable myocardium as assessed by the perfusion-metabolism PET mismatch have a consistently lower event-free survival when treated with medical therapy alone.[13] However, one-year event-free survival in patients with PET mismatch was improved significantly by early referral to CABG.

In contrast, one-year event-free survival in patients without viable myocardium was similar with either medical therapy or revascularization. These findings have been confirmed by virtually all subsequent studies using noninvasive imaging with either nuclear testing or echocardiography.[14] Allman and colleagues recently reported a meta-analysis of 24 studies that documented long-term patient outcomes after viability imaging by SPECT, PET, or dobutamine echocardiography in 3088 patients (2228 men, 860 women) with a mean ejection fraction 32±8% and follow-up for 25±10 months.[14] The results demonstrated that in patients with evidence of viable myocardium, a strong association was present between revascularization and improved outcomes, particularly in patients with severe LV dysfunction. There was no apparent benefit for revascularization over medical therapy in the absence of demonstrated viability, and there was a trend toward higher death and nonfatal-event rates with revascularization. This finding implies that despite an increasing risk of revascularization with worsening LV dysfunction, noninvasive imaging evidence of preserved viability may provide information on clinical benefit to balance against that risk, informing clinical decision making.

• *Predicting improvement in symptoms*. Another important challenge in

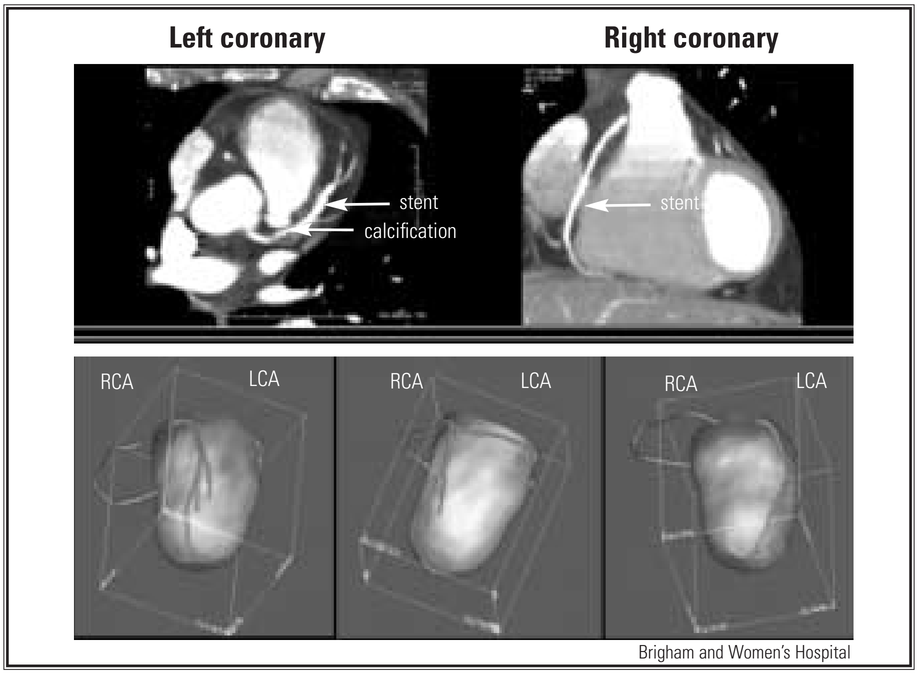

Figure 4. Top: Cross-sectional CT images of left and right coronary arteries following administration of IV contrast, obtained with eight-slice PET/MDCT scanner (GE Medical Systems). Images demonstrate "blooming" artifact caused by metallic stents and coronary calcium, which makes it difficult to determine the presence of flow-limiting stenoses. Bottom: Fusion of functional myocardial perfusion PET data (3D polar map) and CT coronary angiographic information. Functional PET information demonstrates no evidence of stress-induced ischemia.

the management of patients with poor LV function after myocardial infarction is to identify those in whom revascularization can provide a significant alleviation of anginal and especially heart failure symptoms, which is often their primary functional limitation. In one study of 23 patients with LV dysfunction (LVEF 35±14%) and impaired functional capacity (70% in NY Heart Association class II-III), Marwick et al showed that the amount of viable myocardium before revascularization was predictive of a significant improvement in exercise parameters after revascularization.[15] In this study, peak rate-pressure product, maximal heart rate, and exercise capacity increased significantly after revascularization only in patients with multiple viable regions on preoperative PET imaging.

More recently, data from Di Carli et al demonstrated a significant linear correlation between the global extent of a preoperative perfusion-metabolism PET mismatch (reflecting hibernating myocardium) and the percent improvement in functional capacity after CABG in 36 patients with ischemic cardiomyopathy (LVEF 28± 6%).[16] This study found that a perfusion-metabolic PET mismatch involving >18% of the LV by quantitative analysis was associated with a sensitivity of 76% and a specificity of 78% for predicting a significant improvement in heart failure class following CABG.

CONCLUSIONS

The data presented above suggest that assessment of myocardial ischemia and viability post-MI, particularly in patients with severe LV dysfunction, is important to identify those with the highest risk, in whom revascularization can be of clinical benefit. Growing and consistent evidence indicates that patients with relatively large areas of dysfunctional but viable myocardium post-MI, as assessed by PET, have improved function, symptoms, and survival with prompt revascularization, compared with medical therapy alone.

Most important, long-term survival with revascularization in these patients is comparable to that achieved with cardiac transplantation. Several methods are available to the clinician for investigating the presence of tissue viability, and the evidence suggests that the scintigraphic approaches are the most sensitive. These observations imply that noninvasive investigation of the amount of ischemic myocardium should be an important component of the diagnostic evaluation of patients with severe LV dysfunction post-MI. This approach will likely enhance the often difficult process of selecting patients with poor cardiac function in whom revascularization will likely improve both the quality and quantity of life.

ACKNOWLEDGMENT

The author is thankful to Cynthia Johnson for her expert secretarial assistance in the preparation of this manuscript.

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