Factors influencing predictive value of FDG imaging for evaluating myocardial viability

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Rational management of patients with coronary artery disease (CAD) and poor left ventricular (LV) function relies on proper identification of the subgroup at high risk and those who have the highest potential of benefiting from a particular type of treatment. Before the advent of imaging techniques to determine myocardial viability, many patients with CAD and low ejection fractions (EFs) were relegated to medical therapy. It is now well recognized that patients with CAD and LV dysfunction have a high but variable mortality rate while receiving medical therapy. Many of these patients who have intractable heart failure are considered candidates for cardiac transplantation. Despite favorable survival after cardiac transplantation, because of the shortage of donor hearts, this procedure cannot be performed in many heart failure patients who are potentially eligible. Cardiac transplantation is also an expensive procedure. In many patients with heart failure, LV dysfunction is reversible after myocardial revascularization. The potential for recovery of LV dysfunction after myocardial revascularization represents a practical clinical definition for myocardial viability.

Since its initial clinical application nearly 2 decades ago,[1] myocardial metabolism imaging with fluorine 18 fluorodeoxyglucose (FDG) and positron emission tomography (PET) or single photon emission computed tomography (SPECT) has undergone extensive validation for assessment of myocardial viability. In the earlier studies, recovery of regional LV dysfunction was used as the criterion for determining myocardial viability. Subsequently, recovery of LVEF, improvement in heart failure symptoms, and improvement in survival emerged as more clinically relevant endpoints with which to assess the utility of FDG imaging for evaluating myocardial viability. Interpretive criteria for FDG viability assessment have also evolved. To improve the ability to predict recovery of LV dysfunction, more recent studies have explored the value of additional parameters such as quantitation of the amount of viable myocardium and its relationship to the size of myocardial scar, the degree of LV enlargement, and the presence or absence of contractile reserve. The purpose of this editorial is to review these newer aspects of FDG myocardial viability imaging.

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SIZE OF VIABLE MYOCARDIUM

Several studies have shown that the larger the amount of viable myocardium, the more improvement in LV dysfunction is observed after revascularization. Di Carli et al[2] showed that the total amount of PET mismatch correlated linearly and significantly with percent improvement in functional status after revascularization ($r = 0.87$, $P < .0001$). Patients with large mismatches (≥18%) achieved a significantly higher functional status compared with those with minimal or no PET mismatch (<5%). Similarly, Schoder et al[3] showed a linear correlation between the extent of viable myocardium and LVEF improvement after revascularization.

The optimum threshold for the size of viable myocardium to predict improvement in LV dysfunction has been evaluated by receiver operating characteristic analysis and has varied from study to study. A blood flow–metabolism mismatch of 18% or greater was associated with a sensitivity of 76% and a specificity of 78% for predicting a change in functional status after revascularization.[2] In another study a cutoff value of 31% resulted in the highest sensitivity (86%) and specificity (92%) for predicting improvement in LVEF after revascularization.[4] The difference in threshold values in various studies is related to factors such as the endpoint used for assessment of viability, the severity of baseline LV dysfunction, the size of the scar, and the degree of LV remodeling. In most studies, however, the threshold values ranged from 10% to 20%.[1-3,5-7]

SIZE OF MYOCARDIAL SCAR

In 82 patients with CAD and LVEF of 35% or lower, Beanlands et al[8] evaluated whether the extent of scarred

myocardium influenced the degree of improvement in LV function. The size of myocardial scar was an independent predictor of improvement in LV function after revascularization. Among tertiles of scar scores of I (small, 0%-16%), II (moderate, 16%-27.5%), and III (large, 27.5%-47%), the postoperative changes in LVEF were 9% ± 1.9%, 3.7% ± 1.6%, and 1.3% ± 1.5%, respectively ($P = .003$, I vs III). In another study, 50% FDG uptake was used as the cutoff value for myocardial viability, and it was shown that an extent of scar greater than 40% was unlikely to recover after revascularization.[9]

RELATIONSHIP BETWEEN FDG MYOCARDIAL VIABILITY AND MYOCARDIAL CONTRACTILE RESERVE

The presence of contractile reserve in dysfunctional myocardium, a marker of myocardial viability, has been extensively evaluated by 2-dimensional echocardiographic assessment of regional wall motion during dobutamine infusion. The data from the pooled analysis show that, as compared with FDG PET imaging, dobutamine echocardiography has a higher positive predictive value and a lower negative predictive value for evaluating myocardial viability.[10] These findings imply that FDG PET tends to overestimate functional recovery whereas dobutamine echocardiography tends to underestimate functional recovery. In one study, contractile reserve was noted in slightly less than 50% of myocardial regions with mismatch pattern.[11] Conversely, contractile reserve was present in most segments with preserved perfusion and increased FDG uptake. There is now evidence that segments with viability on FDG PET without contractile reserve have more severe ultrastructural damage when compared with those with contractile reserve.[12,13]

It appears that contractile reserve and radionuclide markers of myocardial viability (myocardial uptake of FDG and thallium 201) are somewhat independent parameters of myocardial viability. As such, recent studies have demonstrated that in a subgroup of patients with LV dysfunction, the combined evaluation of contractile reserve and regional Tl-201 uptake results in improved assessment of myocardial viability as compared with either test alone.[14,15]

INFLUENCE OF LV SIZE

In patients with ischemic cardiomyopathy, a variable amount of ventricular remodeling is present. Ventricular remodeling is a process that results from changes in the infarcted myocardium (infarct expansion) as well as secondary changes in the noninfarcted myocardium (increase in the end-diastolic length of myocytes), both contributing to progressive enlargement of the left ventricle. Louie et al[16] demonstrated that in patients with ischemic cardiomyopathy, preoperative LV diastolic dimension was larger in patients in whom revascularization failed as compared with patients who had successful revascularization (81 ± 4 mm vs 68 ± 3 mm, $P < .05$). In this study a preoperative end-diastolic dimension of 70 mm or greater indicated a poor outcome after revascularization. This finding was confirmed by Yamaguchi et al,[17] who found that in patients with a preoperative LV end-systolic volume index of greater than 100 mL/m_2, LV function did not improve after revascularization and postoperative heart failure was more common.

In this issue of the *Journal of Nuclear Cardiology*, Santana et al[18] present their findings on the independent value of LV functional parameters to predict prognosis in 90 consecutive patients with ischemic cardiomyopathy undergoing myocardial viability assessment. They quantified LVEF, LV end-diastolic volume, LV end-systolic volume, and LV mass from gated FDG PET images. In a risk-adjusted model, LV end-diastolic volume and end-systolic volume added a significant amount in the estimation of events (cardiac death, myocardial infarction, or worsening of heart failure) over the FDG mismatch pattern, thus providing incremental information. In a stratified Cox model, patients with PET mismatch, LVEF lower than 25%, and end-diastolic volume of 260 mL or greater had the lowest survival rate with medical therapy but showed an apparent survival benefit with revascularization without an improvement in heart failure symptoms.

CONCLUSION

Myocardial viability imaging with FDG PET or SPECT has become a powerful method for risk assessment and management of patients with LV dysfunction. Application of computer algorithms to gated FDG images, for objective quantitation of LV function parameters, has made additional prognostic markers available from the same set of images. Routine application of these algorithms along with those designed to quantify the percent of viable and scarred myocardium will further enhance the prognostic utility of myocardial FDG imaging in the evaluation of myocardial viability in patients with ischemic cardiomyopathy.

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