EDITORIAL

Metabolic imaging and contractile reserve for assessment of myocardial viability: Friends or foes?

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Each year in the United States, more than 500,000 patients undergo coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty. Although these treatments can improve symptoms and disability in almost every patient, it is in the subgroup of patients with severe depression of left ventricular function that they probably confer the greatest advantages and prolong survival.[1-5] Innovations in operative techniques, myocardial protection, and postoperative care have undoubtedly contributed in important ways to these outstanding results. Yet not every patient with coronary artery disease benefits from surgical revascularization because CABG continues to entail significant immediate risks, particularly when global left ventricular function is severely depressed.[5,6] Careful selection of individual patients with left ventricular dysfunction for coronary revascularization is therefore mandatory. Although risk stratification in these patients has typically included a combination of clinical, hemodynamic, and angiographic parameters, several recent studies have indicated that assessment of residual myocardial viability, that is the potential for functional recovery after CABG or percutaneous transluminal coronary angioplasty, could also provide useful prognostic information, with an effect additive to that of the usual clinical assessment.[7-13]

Several modalities, including thallium 201 imaging,[14-20] positron emission tomography,[21-24] and, more recently, low-dose dobutamine echocardiography,[18-20,25-28] have been proposed to predict the reversibility of left ventricular dysfunction in patients with ischemic heart disease. Although these modalities share the same final purpose, that is, to predict which segment is likely to resume contractile function after revascularization, the mechanisms by which they identify viable myocardium is quite different. Thallium imaging and positron emission tomography rely mainly on the ability of the plasma membrane of cardiac myocytes to actively take up cations or glucose, whereas dobutamine echocardiography specifically assesses the contractile reserve of the dysfunctional myocardium. Thus although each of these tests probably reflects the presence of viable myocytes within a dysfunctional segment, they address different intracellular processes and may therefore provide different information with regard to the potential return of contractile performance after revascularization.[18]

Hitherto, studies addressing the contribution of thallium imaging, positron emission tomography, and low-dose dobutamine echocardiography to the detection and treatment of residual viable myocardium have mainly concentrated on their respective ability to predict the return of regional contractile function after revascularization. As recently reviewed by Bax et al,[29] the results of these studies suggest that the scintigraphic approaches are more sensitive than dobutamine echocardiography, which in turn exhibits a higher specificity and positive predictive accuracy than its scintigraphic counterparts. Notwithstanding the potential interest of the metaanalysis of Bax et al,[29] the results should nonetheless be interpreted with caution. Indeed, it included only a limited number of direct head-to-head comparisons between 2 or more of the available modalities. One cannot therefore exclude the possibility that some unaccounted for factors, including differences in patient selection, in the mode and efficacy of revascularization, in the criteria to define viable myocardium, or in the duration of follow-up, contributed to its results. As a consequence, if we want to understand better the potential differences in the diagnostic accuracy of the various imaging modalities, why these differences exist, and how they impact on our ability to identify viable myocardium, we need to concentrate solely on those studies that directly compared 2 or more of these modalities, either in the same patients or the same segments.

So far, most of these comparative studies have concentrated on the comparison between thallium single

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photon emission computed tomography (SPECT) and dobutamine echocardiography.[30-35] Their results have consistently shown that the number of dysfunctional segments exhibiting thallium redistribution or a preserved thallium uptake significantly exceeded that of segments with residual inotropic reserve. More recently, investigators have also compared metabolic imaging (using fluorodioxyglucose) and dobutamine echo.[36-40] In this issue of the Journal, Cornel et al[41] provide the results of their comparison between these 2 approaches in 40 patients with left ventricular ischemic dysfunction. Quite interestingly, their results are almost identical to those of the comparisons between thallium SPECT and dobutamine echo, that is, that the number of akinetic segments with preserved FDG uptake by SPECT significantly exceeds that of segments with recruitable contractile reserve, whereas the degree of agreement between SPECT and echocardiography is considerably better in segments lacking evidence of metabolic viability. To a large extent also, their observations concur with those of previous investigators who compared FDG-positron emission tomography imaging and dobutamine echocardiography, with the exception perhaps that the degree of agreement between the 2 methods in segments with metabolic viability is clearly higher in the study of Cornel et al than in the previous reports (20% vs 40% to 50%).[36-40]

Altogether, the available comparative studies thus suggest that a spectrum of myocardial dysfunction exists in patients with coronary artery disease: mild degree of myocyte dysfunction being characterized by both a preserved membrane integrity (allowing the transport of both thallium and glucose) and the capacity to respond to an inotropic stimulus, and a more severe form of reversible dysfunction being associated with the inability to respond to inotropic stimuli, in spite of a persistently normal membrane function. On the basis of these studies, one could thus conclude that the higher prevalence of viable segments detected by thallium SPECT or FDG imaging as opposed to dobutamine echocardiography probably reflects the greater capacity of the scintigraphic techniques to identify potentially reversible dysfunction. It should be emphasized, however, that only the serial measurement of mechanical function after revascularization allows determination of the reversibility or irreversibility of injury and that most of the studies examining this aspect have come to the conclusion that the scintigraphic approaches probably overestimate the capacity for contractile recovery of dysfunctional but viable segments whereas dobutamine echocardiography probably underestimates it.[29] One is thus forced to conclude that, with regard to the return of contractile function, none of the currently available modalities provide a definite answer. This is most likely due to the fact that each of these modalities examines a different aspect of myocardial viability and, as a consequence, provides different prognostic information with regard to the recovery of contractile function after revascularization. Over the past 10 years, we have indeed learned that the relationship between the physiological parameters derived from the viability tests and the return of resting contractile function after revascularization is far more complex than we previously anticipated.[42-47] Our current understanding of this relationship can be summarized as follows: (1) the 2 most important factors determining the return of resting contractile function after revascularization are the severity of the underlying tissue fibrosis, which is mostly irreversible, and the severity of the structural abnormalities affecting the cardiomyocytes, the reversibility of which is largely unknown[44-45]; (2) the uptake of FDG during hyperinsulinemic euglycemic glucose clamp[43-45] and that of thallium after reinjection[48] provides a reasonable estimate of the mass of viable cardiomyocytes, regardless of the presence of structural abnormalities; (3) the presence of recruitable contractile reserve seems to depend on the mass of residual myocytes showing little or no myofibrillar loss,[49] and probably also on the presence of sufficient perfusion reserve to permit the increase in contractility.

On the basis of these observations, the following working hypothesis can be proposed. When metabolic imaging and dobutamine echocardiography concur on the presence of residual viable myocardium, the likelihood of tissue fibrosis and myocyte structural alterations is small, and the likelihood of functional recovery after successful revascularization is high.[44,45,49] Moreover, prognostic studies suggest that failure to revascularize patients showing these characteristics is associated with an increased risk of adverse cardiac events, including death.[7-13] When metabolic imaging and dobutamine echocardiography concur on the lack of residual viable myocardium, severe tissue fibrosis is probably present, and revascularization is not likely to bring in any significant functional benefit[44,45,49] or prognostic advantage over medical treatment.[7-13] Finally, when metabolic imaging suggests the presence of viable myocardium but dobutamine echocardiography does not, significant myocyte alterations, exhausted flow reserve, or a combination of these factors are likely present. The recovery of resting contractile function after revascularization is uncertain, and, unfortunately, largely unpredictable. On the basis of this and previous studies, this particular viability pattern probably occurs in about 20% to 45% of "metabolically" viable segments and contributes to both the low specificity of the scintigraphic approaches and the low sensitivity of dobutamine echocardiography. Obviously, additional studies are needed to better define the characteristics of these segments, to predict their capacity for functional recovery after revascularization, and to determine their prognostic significance. These studies should probably include a detailed assessment of the underlying structural alterations affecting the cardiac myocytes, as well as a precise assessment of both the amplitude and time course of recovery after revascularization.

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