Myocardial hibernation: a clinician's perspective

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Patients with myocardial hibernation have reversible left ventricular dysfunction after revascularization. Viability testing can identify those patients whose left ventricular dysfunction is primarily due to hibernation rather than scar. Patients with a substantial amount of hibernating myocardium seem to have a better outcome with revascularization than medical therapy. Patients with poor viability do worse after revascularization than patients with good viability.

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The incidence of heart failure due to systolic dysfunction is increasing, in part, due to the aging of the population and the enhanced survival of patients with chronic ischemic heart disease[1]. Despite advances in medical therapy for the heart failure syndrome, and improvements in surgical and interventional techniques for myocardial revascularization, the prognosis remains poor for patients with ischemic cardiomyopathy, which is characterized by extensive coronary artery disease and diminished left ventricular ejection fraction. Even today, 5-year rates of survival range from only 50-60%, and mortality is greater the lower the left ventricular ejection fraction, the greater the extent of coronary artery disease and the older the patient[2].

Left ventricular systolic dysfunction in patients with ischemic cardiomyopathy results from either scarring, as a consequence of prior myocardial infarction, or myocardial hibernation. The presence of hibernating myocardium suggests that there is sufficient residual blood flow to sustain viability of myocytes and sarcolemmal membrane integrity, but not enough to sustain normal systolic contraction[3]. In the case of hibernating myocardium, by definition, systolic function improves with enhancement of myocardial blood flow as accomplished with coronary revascularization. Many patients will manifest both scarring and hibernation in the same region or in different myocardial zones.

Multicenter randomized studies performed in the 1970s showed that coronary bypass surgery improved survival, mainly in patients with three-vessel disease and impaired left ventricular function[4-6]. However, such patients with severe coronary artery disease and diminished left ventricular performance are at increased risk for early and late perioperative mortality and nonfatal complications. For many years, a hypothesis was proposed, but never confirmed, that ischemic cardiomyopathy patients who had the most favorable outcome were those who had reversible left ventricular dysfunction attributed to myocardial hibernation, whereas patients who succumbed perioperatively were those whose left ventricular dysfunction was primarily due to irreversible myocardial cellular injury. It was further proposed that better selection of such patients for revascularization could be achieved if myocardial viability in dyssynergic segments could be assessed in the preoperative evaluation.

The availability of accurate, noninvasive methods for distinguishing viable myocardium from myocardium that is scarred is of paramount importance for clinical decision-making. Noninvasive imaging techniques that are accurate in distinguishing viable from irreversibly injured myocardium would enable physicians to identify those patients with extensive and severe coronary artery disease and resting left ventricular dysfunction who would benefit most from revascularization strategies[7,8]. Studies in the past decade have suggested that patients who have substantial zones of viable but underperfused myocardium identified by a variety of noninvasive cardiac imaging techniques do have higher

rates of perioperative and late survival, greater improvements in regional and global left ventricular function, a greater reduction in the symptoms of heart failure, and better exercise tolerance after revascularization compared to patients with large areas of myocardial scar[9]. The greater the extent of myocardial viability, the better the outcome. Of great importance is that patients with hibernation as the prominent cause of ischemic cardiomyopathy have a better prognosis for coronary revascularization than after medical therapy[10,11].

The noninvasive techniques that have proven useful in the clinical setting for determination of myocardial viability include positron emission tomographic (PET) imaging of ^{13}N-ammonia as a flow tracer and ^{18}F-fluorodeoxyglucose (FDG) as a tracer to evaluate metabolic integrity. A "mismatch" pattern on PET images showing uptake of FDG in areas of reduced blood flow is indicative of viability. Myocardial perfusion imaging with single-photon emission computed tomography (SPECT) using either ^{201}Tl, ^{99m}Tc-sestamibi or ^{99m}Tc-tetrofosmin is also an excellent technique for viability detection. Quantitative demonstration of > 50% (or > 60%) uptake of these tracers in an area of severe myocardial asynergy is reflective of viability. Low-dose dobutamine echocardiography for determination of inotropic reserve and cine-magnetic resonance imaging (MRI) following the administration of a gadolinium-based contrast agent, are effective nonnuclear techniques for myocardial viability assessment. For the latter, the demonstration of delayed hyperenhancement in dysfunctional myocardial regions is reflective of viability[12]. The accuracy of all of these techniques is comparable but the PET and SPECT approaches have a lower specificity than MRI or dobutamine echocardiography, whereas dobutamine echocardiography has a lower sensitivity for detection of viability than the nuclear techniques. A limitation of all of the techniques except contrast MRI is that a subendocardial scar of only 20 to 30% of the thickness of the left ventricular myocardial wall can prevent improvement in revascularization, even if substantial viability is noninvasively demonstrated in the midwall and epicardial layers. Only MRI has the resolution for distinguishing between subendocardial and epicardial viability.

Viability assessment and clinical decision-making

A number of important conclusions can be derived from the noninvasive viability studies reported in the literature. First, the clinician should realize that many patients, perhaps more than 50%, who have coronary artery disease and diminished left ventricular dysfunction have extensive areas of myocardial hibernation and reversible myocardial dyssynergy. Second, viable but asynergic myocardium can be detected with a high degree of accuracy by a host of alternative noninvasive methods. Data clearly show that patients with extensive zones of viable myocardium have a significantly better outcome after revascularization than do those treated medically[13]. Furthermore, patients with predominantly nonviable myocardium have a rather poor outcome after coronary revascularization compared to those with better viability[7,14].

Based on evidence in the literature, to optimize outcomes in patients with ischemic cardiomyopathy, revascularization strategies might be directed chiefly to patients with coronary artery disease and left ventricular dysfunction who have coronary vessels suited for revascularization and a noninvasive assessment showing presence of viability in perhaps more than 40-50% of the asynergic zones. Patients with good viability are those who would benefit the most from revascularization with enhanced survival, improvement in heart failure symptoms, enhanced exercise capacity and improved quality of life. Patients with ischemic cardiomyopathy with scar as the predominant cause of left ventricular dysfunction could be spared unnecessary coronary revascularization. This would result in a reduction in the cost of care. Figures 1 and 2 show potential decision-making algorithms in patients with coronary artery disease and impaired left ventricular function who are being considered for possible revascularization[15].

It appears that cost savings might also be achieved if SPECT imaging was used to guide clinical decision-making, since a recent study[16] showed no difference in patient management or cardiac event-free survival based on management predicated on FDG PET versus stress/rest ^{99m}Tc-sestamibi imaging. The au-

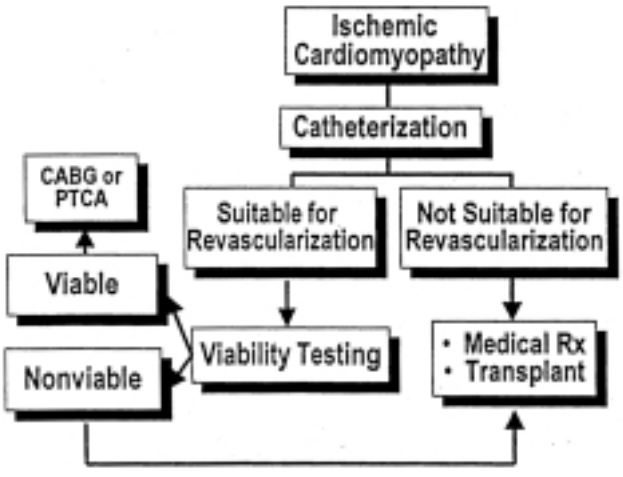

Figure 1. *Approach to decision-making in patients with ischemic cardiomyopathy who have severe coronary artery disease and left ventricular dysfunction. Using this algorithm, all ischemic cardiomyopathy patients have undergone cardiac catheterization. Those with vessels not suited for revascularization are either treated medically or evaluated for cardiac transplantation, whereas those who have vessels suitable for revascularization undergo noninvasive viability studies for detection of hibernating myocardium. Patients with good viability are deemed candidates for revascularization. CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty. From Beller[15], with permission.*

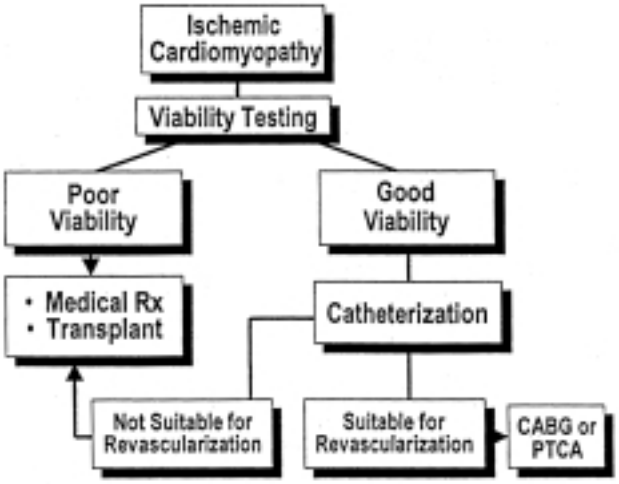

Figure 2. *Alternative decision-making algorithm in patients with ischemic cardiomyopathy who are being evaluated for possible revascularization. With this approach, patients with ischemic cardiomyopathy initially undergo viability testing with cardiac catheterization undertaken in those with viability as the predominant cause of left ventricular dysfunction. Abbreviations as in figure 1. From Beller[15], with permission.*

thors concluded that both techniques can be interchangeably used for management of patients considered for revascularization with suspicion of hibernating myocardium. In the future, contrast-enhanced MRI could prove to be the most accurate noninvasive methodology to be employed in the clinical decision-making algorithms identified in figures 1 and 2. However, no outcome studies have yet been published using this technique.

In summary, clinicians involved in the management of patients with ischemic left ventricular dysfunction, with or without symptomatic manifestations of congestive heart failure, should be aware that noninvasive viability imaging is an important step in the decision-making for therapeutic strategies for such patients. What is still lacking, however, is a large prospective, randomized study to truly determine the worth and cost-effectiveness of such noninvasive testing of viability for guiding therapeutic strategies in patients with ischemic cardiomyopathy. Such a study is soon to be launched in the United States and will be supported by the National Institutes of Health. In this study, patients with coronary artery disease and severely depressed global left ventricular function will be randomized to maximum medical therapy or revascularization. All will have viability studies and event-free survival monitored.

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