Role of Revascularization to Improve Left Ventricular Function

Harsh C. Patel, MD, Stephen G. Ellis, MD*

KEYWORDS

• Revascularization • LV function • Viability • Ischemic cardiomyopathy
• Percutaneous coronary intervention • Coronary artery bypass grafting

KEY POINTS

- Coronary revascularization to improve left ventricular (LV) function and improve mortality in patients with ischemic cardiomyopathy remains controversial, especially in the absence of angina or ischemia.
- A large body of observational evidence suggests that patients with dysfunctional but viable myocardium may experience improvement in mortality and LV function after revascularization.
- Results of randomized trials conducted in the last decade dispute the value of viability testing or coronary revascularization in improving outcomes of patients with ischemic cardiomyopathy.
- Clinical equipoise persists regarding the role of coronary revascularization in certain patients.
- Surgical revascularization has been preferred over percutaneous revascularization in patients with LV dysfunction based on observational data, but high-quality randomized comparative effectiveness data are lacking.

INTRODUCTION

Mortality from coronary artery disease (CAD) has decreased in developed countries over the past several decades.[1] As a result, however, the prevalence of ischemic cardiomyopathy is increasing and presently it is the most common cause of heart failure in developed countries. In the large ADHERE registry of patients hospitalized for heart failure in the United States, almost 60% had a history of CAD.[2] Despite improvement in medical therapy and increased utilization of implantable cardioverter defibrillators and cardiac resynchronization therapies, mortality from ischemic cardiomyopathy remains high.

Left ventricular (LV) function has generally been considered to be one of the strongest prognostic factors in patients with CAD.[3] The role of coronary revascularization to improve LV function and reduce mortality has been investigated in several studies over the past few decades. Most of these studies, which have largely been retrospective and nonrandomized and containing small sample sizes, have demonstrated a benefit from revascularization, especially in those patients with a significant amount of viable myocardium. More recently, however, 3 prospective randomized studies, the Surgical Treatment for Ischemic Heart Disease (STICH) trial,[4] the Heart Failure Revascularization (HEART) trial,[5] and the PET And Recovery following Revascularization (PARR-2) trial,[6] have contested the value of revascularization or viability testing in patients with ischemic cardiomyopathy. Unfortunately, all of these studies had several

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Department of Cardiovascular Medicine, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA
* Corresponding author. Cleveland Clinic Main Campus, 9500 Euclid Avenue, Desk J2-3, Cleveland, OH 44195.
E-mail address: elliss@ccf.org

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major limitations, thus tempering their impact on clinical practice. Furthermore, most of these studies focused primarily on surgical revascularization, making it even more difficult to draw conclusions regarding the role of percutaneous revascularization.

The objectives of this article are to provide a brief overview of the concepts of myocardial hibernation and stunning, compare the various methods of viability testing, and review the current literature including analysis of the recent trials on the role of coronary revascularization in ischemic cardiomyopathy. Recent guideline recommendations from various societies are reviewed and factors affecting the choice of surgical versus percutaneous revascularization are discussed.

THEORETIC BASIS OF FUNCTIONAL IMPROVEMENT WITH REVASCULARIZATION IN ISCHEMIC CARDIOMYOPATHY

The proposed mechanism by which LV function improves following revascularization in ischemic cardiomyopathy is the revitalization of previously dysfunctional but still viable myocardial tissue. The concept of stunning was originally described more than 30 years ago[7] to explain the observation that myocardium that is transiently ischemic displays contractile dysfunction, which ultimately recovers early after restoration of normal resting blood flow. Studies with serial assessment of ventricular function showed that approximately two-thirds of stunned segments display early recovery of contractility by 3 months and only 10% show delayed recovery at 14 months after revascularization.[8] Although stunned myocardium has normal resting blood flow with blunted coronary flow reserve, hibernating myocardium has severely reduced resting blood flow, yet remains viable by adaptively reducing contractility and cellular activity to decrease basal metabolic demand. In contrast to stunned myocardium, hibernating myocardium generally shows delayed recovery after revascularization, with approximately two-thirds of hibernating segments recovering after 14 months in one study.[8] This time dependence of recovery has important implications because early evaluation after revascularization may underestimate the degree of true functional recovery.[9]

According to the current paradigm, stunning and hibernation exist along a continuum of chronic myocardial dysfunction. Repeated episodes of transient ischemia over time lead to progression from stunned to hibernating myocardium and ultimately to necrosis and scar. Several animal and human studies with histologic evaluation have shown that these processes often coexist in the same myocardial segments with hibernating myocytes showing more severe ultrastructural changes than stunned myocytes.[9,10] Clinically, the distinction between stunned and hibernating myocardium may be more difficult to discern and less relevant because they both constitute viable myocardium. Studies have shown that up to 60% of patients with ischemic LV dysfunction may have viable myocardium that may recover with revascularization.[11,12] However, not all viable myocardium recovers after revascularization and the probability of recovery and reverse remodeling is affected by several factors including the timeliness,[13,14] completeness,[15] and long-term patency of revascularization. Prolonged myocardial hibernation may progress to necrosis, limiting functional recovery after revascularization. Extent of viability is also important and several studies have shown that at least 25% to 30% of dysfunctional myocardium needs to be viable for improvement in LV ejection fraction (EF) after revascularization.[16,17] However, extensively remodeled ventricles with severe dilation may not recover after revascularization even in the presence of viability.[18]

ASSESSMENT OF MYOCARDIAL VIABILITY AND ISCHEMIA

The role of viability testing has been at the center of the discussion regarding the value of revascularization in patients with ischemic LV dysfunction. Many studies, including the recent randomized trials (STICH[4] and HEART[5]), have not distinguished between patients evaluated using different viability testing methods. However, there are important fundamental differences between the tests that must be emphasized. The various imaging modalities can be broadly divided into those that assess cellular integrity (such as single-photon emission computed tomography or SPECT, PET, and late gadolinium enhancement cardiac magnetic resonance or CMR) and those that assess contractile reserve (such as dobutamine echo or dobutamine CMR).

Among the tests of cellular integrity, SPECT is by far the most commonly used because of the ready availability of the nuclear isotopes thallium-201 and technetium-99m. However, SPECT has the lowest spatial resolution (10–14 mm) of any test of cellular integrity, which can affect diagnostic accuracy.[19,20] Furthermore, technetium-99m agents sestamibi and tetrofosmin do not undergo significant redistribution following initial myocyte uptake, which is proportional to myocardial blood flow. Thallium-201, by contrast, is a