The last 3 decades have witnessed an unprecedented improvement in the outcome of patients with acute coronary syndromes. The widespread use of thrombolytic therapy and percutaneous coronary interventions, in association with increasingly potent anti-thrombotic agents, has contributed to significant reductions in mortality and morbidity in these patients. Although overall survival has improved, a downside of this success has been the greater number of patients with residual left ventricular (LV) dysfunction undergoing progressive LV remodeling and congestive heart failure. This problem is compounded by the rising age of our population and the higher prevalence of comorbidities such as diabetes mellitus that confer an increased risk of coronary artery disease (CAD) and congestive heart failure. Patients with CAD represent by far the most numerous cohort among those with congestive heart failure, and their treatment remains a partial success. Typically, these patients have multivessel disease, increased LV volumes, and variable degrees of regional and/or global systolic dysfunction, although more cases of isolated diastolic dysfunction have been reported recently. In these patients, coronary revascularization may lead to symptomatic and prognostic improvement, and these clinical benefits are accompanied by evidence of reverse LV remodeling. In this context, the concept of myocardial viability was developed and a number of different techniques have been used to demonstrate the presence of viable tissue before coronary revascularization.

The aim of this review article is to summarize our current understanding of the concept of myocardial viability and its clinical implications in patients with CAD and chronic LV dysfunction. Throughout this review, we use the term viability to describe dysfunctional myocardium subtended by diseased coronary arteries with limited or absent scarring that therefore has the potential for functional recovery. Viability is a retrospective definition, but it does not imply evidence of functional recovery after interventions. The term hibernation, which often is used synonymously for tissue viability, is a prospective definition based on evidence of functional recovery after interventions.

Myocardial Stunning and Hibernation
Acute myocardial ischemia rapidly impairs contractile function. This dysfunction can persist for several hours after transient non-lethal ischemia but eventually is followed by full functional recovery. The latter phenomenon is known as myocardial stunning. In patients with CAD, repeated episodes of demand ischemia may lead to cumulative stunning (Figure 1) that could be a substrate in the development of chronic postischemic LV dysfunction. The concept of myocardial hibernation was derived from clinical observations. More than 30 years ago, clinicians and surgeons started to notice that chronic myocardial dysfunction, present before coronary bypass, often improved after revascularization.

In pathophysiological terms, a severe reduction in coronary flow reserve is common in both stunning and hibernation, and recovery of function in hibernating myocardium after coronary revascularization is paralleled by restoration of an adequate coronary flow reserve (Figure 2).

Clinically, in different patients, similar degrees of LV dysfunction may be associated with large differences in the amount of viable myocardium, and even extreme degrees of wall thinning do not necessarily indicate the absence of viability. The timing of coronary revascularization is very important because in some patients CAD progression may occur very rapidly, precluding later interventions.

An algorithm for identifying and treating patients with CAD and chronically dysfunctional but viable myocardium is presented in Figure 3.

Assessment of Viability
At present, we lack controlled prospective randomized studies, but indications exist from retrospective studies that patients who undergo preoperative assessment of viability have better in-hospital and 1-year outcomes when a viability test is added to clinical and angiographic data.

A detailed description of the technical characteristics of each imaging modality has been reviewed comprehensively in previous articles and American Heart Association/American College of Cardiology scientific statements.

Dobutamine stress echocardiography (DSE) is used to assess myocardial contractile reserve. Low-dose dobutamine (5 to 10 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)) can lead to increased contractility in dysfunctional segments that are viable. At higher doses (up to 40 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \) plus atropine to increase heart rate),
wall motion in these viable segments may further improve or diminish, reflecting inducible ischemia. This “biphasic response” is highly predictive of recovery of function after revascularization. They generally show little improvement in wall motion with DSE and do not improve after revascularization. Dobutamine echocardiography evaluates contractile reserve as a predictor of improvement of ventricular function, and like radionuclide techniques, general agreement exists about its predictive accuracy (class I).

Myocardial contrast echocardiography uses acoustically active gas-filled microbubbles as contrast agent that have a diameter smaller than red blood cells (<7 μm) and remain confined within the intravascular space. Myocardial contrast echocardiography produces myocardial opacification and facilitates the identification of LV borders compared with conventional echocardiography. Tissue capillary blood flow determines myocardial perfusion and is the product of capillary blood volume and myocardial blood velocity, both of which can be assessed by myocardial contrast echocardiography. Once the contrast agent has reached a steady-state concentration in the bloodstream, during continuous intravenous infusion, a burst of high-intensity ultrasound is used to destroy the microbubbles within the myocardium. Subsequent microbubble replenishment is observed over the next 10 to 15 cardiac cycles and reflects myocardial blood velocity. Segments are classified as viable if homogeneous contrast intensity is present, whereas the absence of contrast enhancement reflects nonviable myocardium in which necrosis of myocardial cells has resulted in obstruction and collapse of the microcirculation. Myocardial contrast echocardiography has a high sensitivity for predicting functional recovery after revascularization but low specificity compared with DSE. The optimal strategy appears to be a combination of perfusion assessed by myocardial contrast echocardiography and contractile reserve by DSE. The strengths of echocardiography-based techniques include safety, portability, low cost, and widespread availability of equipment. The main limitation is that the technique is highly operator dependent with high interobserver and intercenter variability. Furthermore, spatial resolution is relatively low and diagnostic accuracy is reduced in patients with poor acoustic window or significant LV impairment.

Single-photon emission computed tomography (SPECT) is a widely available modality with well-established clinical and prognostic validation. The tracers currently used include the potassium analog thallium-201 (201Tl) and technetium-99m (99mTc) –labeled compounds. Myocardial uptake of 201Tl is dependent on regional flow and sarcolemmal membrane integrity. Several protocols can be used with 201Tl that require injection of a tracer either after stress or at rest with subsequent late imaging following the
redistribution of the tracer. The initial acquisition soon after 201Tl injection primarily reflects delivery of the tracer through blood flow. The images acquired 4 to 24 hours after tracer injection are a marker of sarcolemmal integrity, which in turn reflects tissue viability.37,38

99mTc-sestamibi and 99mTc-tetrofosmin are the 2 most commonly used 99mTc-labeled tracers. Both are lipophilic molecules, and their intracellular retention requires intact mitochondrial function with preserved membrane potential. Similar to 201Tl, uptake of these agents provides information on both myocardial perfusion and viability.39 However, compared with 201Tl, the 99mTc-labeled tracers undergo much less redistribution with time. They emit higher-energy photons than 201Tl, which are ideal for SPECT and are subjected to a reduced amount of soft-tissue attenuation. These features result in higher-quality images and fewer artifacts compared with 201Tl. Relative to 201Tl protocols, less radiation exposure is present as a result of the shorter half-life of 99mTc. The use of gated SPECT provides information on regional and global LV function and viability simultaneously.40

SPECT has higher sensitivity and lower specificity than techniques based on the assessment of residual contractile recovery, although specificity improves with gated SPECT.41 The main limitations of this technique include exposure to significant amounts of ionizing radiation, rather low spatial resolution, and attenuation artifacts. The combined use of SPECT and multislice computed tomography may improve diagnostic performance of SPECT by removing attenuation artifacts.

**Positron Emission Tomography**

Early studies demonstrated that myocardial ischemia and infarction could be distinguished by analysis of positron emission tomography (PET) images of the perfusion tracer 13N-labeled ammonia (13NH3) and the glucose analog 18F-fluorodeoxyglucose (FDG) acquired after an oral glucose load.42 Regions that showed a concordant reduction in both myocardial blood flow and FDG uptake (“flow-metabolism match”) were considered to be irreversibly injured, whereas regions in which FDG uptake was relatively preserved or increased despite having a perfusion defect (“flow-metabolism mismatch”) were considered ischemic but still viable.43 However, this approach has inherent limitations, particularly related to FDG and the way in which it is currently used.

The uptake of FDG by the myocardium and scan quality depend on many factors such as dietary state, cardiac workload, sympathetic drive, and the presence and severity of ischemia.44 Many patients with heart failure are insulin resistant, and the amount of endogenous insulin released after oral glucose loading will not induce maximal stimulation of myocardial glucose/FDG uptake.45 To minimize these problems and to avoid the need of a simultaneous 13NH, scan, which requires a cyclotron on site, an alternative protocol, the main feature of which is the use of the hyperinsulinemic euglycemic clamp, has been developed.46 During the clamp, plasma free fatty acid levels are dramatically reduced, and metabolism in insulin-sensitive tissues switches to glucose use (Figure 4).47,48 FDG is injected during the steady-state phase of the clamp, resulting in high and rapid myocardial FDG uptake and low tracer concentration in the blood pool, leading to improved image quality even in patients with insulin resistance. The scan acquisition time is reduced to 15 to 20 minutes, starting 20 to 30 minutes after FDG injection. This approach has been tested in a European multicenter study.49

PET-FDG data also can be analyzed using a quantitative approach that, however, requires longer dynamic acquisitions. A threshold value for the metabolic rate of glucose of $\geq 0.25 \mu\text{mol} \cdot \text{g}^{-1} \cdot \text{min}^{-1}$ allowed the best prediction of improvement in functional class of at least 1 grade after revascularization.50

The main strengths of PET compared with SPECT are its superior spatial resolution and attenuation correction. PET is generally regarded as the gold standard for viability assess-
ment. Reduced availability of PET scanners and the need for a cyclotron on site have been the main limitations to wider clinical applications. Recently, however, the number of scanners available has increased to \( \approx 1200 \) in the United States and 400 in Europe. In the United States, the annual procedure volume for cardiology was estimated to be 154,000, of which \( \approx 68,000 \) were viability and \( \approx 86,000 \) were rubidium-82 perfusion scans (information from scanner manufacturers).

Stress/redistribution/reinjection or rest/redistribution with \(^{201}\)TI, resting sestamibi SPECT, and perfusion \(^{13}\)NH/FDG PET is classified as class I level of evidence B for the prediction of the improvement in regional and global LV function. The ability to predict improvement in heart failure symptoms after revascularization is less well established and is classified as IIa level of evidence B for PET.\(^{19}\)

### Cardiovascular Magnetic Resonance

Cine imaging with gradient echo sequences provides information on global LV function, regional wall motion, and thickening. It has been used in conjunction with dobutamine stress similarly to DSE.\(^{51,52}\) An important advance has been the application of gadolinium-chelated contrast agents to detect perfusion defects, microvascular obstruction, and areas of scarred tissue/fibrosis.\(^{53-58}\) Gadolinium-chelated contrast agents have paramagnetic properties that yield a bright signal in areas where they accumulate, are metabolically inert, and are safe to administer via a peripheral line as a single bolus with a negligible risk of nephrotoxicity, except in patients with end-stage renal failure. Gadolinium-chelated contrast agents do not penetrate myocytes with intact membranes. However, they diffuse and accumulate within the extracellular space when its volume of distribution is increased (eg, replacement fibrosis) or into myocytes with ruptured cell membrane (eg, acute infarction). Depending on the dose, 10 to 15 minutes after injection, a “late” steady-state phase is reached when gadolinium-chelated contrast agents have washed out of normal myocardium but remain in scarred or acutely infarcted tissue. The latter are characterized by a

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**Figure 4.** Euglycemic, hyperinsulinemic clamp and FDG-PET scanning. A, Plasma insulin concentration; B, exogenous glucose infusion rate; C, plasma glucose; D, free fatty acid (FFA) concentrations. Adapted from Ferrannini et al.\(^{47}\) Used with permission from the publisher. Copyright © 2002, the American Physiological Society. Bottom, Corresponding apical views of in vivo short-axis images (left, both rows: right to left = apex to base) and ex vivo digital photograph of the six 1-cm-thick short-axis slices of the same patient’s heart (explanted during the transplantation procedure) after TTC staining (right, both rows: right to left = apex to base). On the heart specimen (right), remote nonischemic myocardium is stained in red; infarcted nonviable tissue remains unstained. Note the patchy nature and mosaic pattern of infarction in the patient’s heart specimen and the good agreement between FDG uptake and scar distribution. LAD indicates left anterior descending artery; RV, right ventricle. Adapted from Chareonthaitawee et al.\(^{48}\) Used with permission from the publisher. Copyright © 2002, Springer Verlag.
bright, hyperenhanced signal on specialized T1-weighted inversion recovery scans, whereas the signal from normal myocardium has been “nulled” and appears black.56 This has led to the aphorism that “bright is dead.”

This technique allows assessment of the transmurality of necrosis, and the minimum amount of myocardium that can be imaged is ≈1 g with a spatial resolution of ≈2 mm.56 The transmural extent of infarction correlates with the likelihood of functional recovery of dysfunctional myocardium after revascularization.54,55,59 These findings are resulting in a paradigm shift. The absence of significant late gadolinium enhancement in thinned (<5 mm) hypokinetic myocardium, previously assumed to represent scarred tissue, often is associated with restoration in wall thickening and function after revascularization.

Main current limitations of this technique are the relative cost, limited availability, comparatively long study times, and the difficulty of performing scans in patients with implanted devices, although new cardiovascular magnetic resonance–compatible materials are being developed. Higher-field (ie, 3-T) clinical scanners may potentially offer better signal-to-noise ratio, reduced scan imaging times, and increased spatial resolution.

**Impact of Revascularization on LV Function and Long-Term Survival**

**Revascularization and Improvement of LV Function**

From the clinical perspective, recovery of global function is more important than regional improvement. Several studies have shown that LV ejection fraction (EF) improved significantly (ie, ≥5%) after revascularization in ≈60% of patients (range, 38%60 to 88%61,15,22,49,60–71). The meta-analysis published by Underwood et al18 demonstrated an increase in LVEF in patients with evidence of hibernating myocardium but no improvement in those without hibernation.

We have examined 20 studies carried out with established techniques to assess viability in patients with LV dysfunction (LVEF ≤45%) caused by CAD that were published between 1998 and 2006. The pooled data are presented in Tables 1

**Table 1. Results of Different Imaging Modalities to Predict Recovery of Global LV Function After Revascularization**

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional nuclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99m Tc-sestamibi 60</td>
<td>19 71 (51–91) 40 (18–62)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT FDG 65,70</td>
<td>94 86 (79–93) 93 (88–98)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>201 Tl rest, reinjection 22,62,63,65</td>
<td>211 84 (79–89) 70 (64–76) 97 (92–100) 93 (86–100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>201 Tl rest redistribution + FDG 64</td>
<td>47 86 (76–96) 92 (84–100) 90 (81–99) 89 (80–98)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>371 84 (80–88) 77 (73–81) 94 (89–98) 91 (85–97)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE 22,49,60,62,63,65,66,72</td>
<td>408 76 (71–80) 81 (77–85) 84 (77–91) 91 (85–96)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE + strain rate 66</td>
<td>55 67 (55–79) 89 (81–97)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic wall thickness 22</td>
<td>43 63 (49–77) 68 (54–82)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>506 74 (70–77) 81 (77–84) 84 (77–91) 91 (85–96)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG 69,70</td>
<td>205 81 (75–86) 65 (59–72)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>205 81 (75–86) 65 (59–72)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive accuracy.

The time course of recovery of viable myocardium can protract up to 14 months.83 This prolonged recovery time can be due, at least in part, to the fact that dysfunctional segments can present different stages of structural abnormality, spanning from normal (stunning) to the characteristic features of
Specificity to predict a majority of studies agree that to yield the best sensitivity and division encompasses the totality of the LV (ie, 100%), the comparisons very difficult. Assuming that the segmental has evolved independently within each technique, has made duce for the segmentation and nomenclature of the LV, which of myocardial viability.89 The lack of a standardized procedure, in direct comparison with99mTc-sestamibi and FDG-PET showed better negative predictive value for segments classified as nonviable 6 months after revascularization. In a comprehensive patient stratification, the presence and extent of myocardial scarring are important predictive factors.83,85,90 In dyskinetic and akinetic segments, the absence of scar or a transmural extension of scar of <25% have been considered predictive of functional recovery, with a positive predictive value of 88% and a negative predictive value of 89%.54

In interpreting these results, we must consider several potential confounding factors. Small-cohort, retrospective studies are limited by patient selection and posttest referral bias, which tend to raise the measured sensitivity and lower the specificity of the diagnostic test.91 Younger symptomatic patients with a higher likelihood of viable myocardium and no extensive comorbidity are more likely to be referred for viability assessment to evaluate feasibility of revascularization.

Technical limitations are also inherent to the revascularization technique. In the case of bypass surgery, these include suboptimal insertion of the distal end of the graft with poor runoff. In the case of percutaneous coronary interventions, incomplete revascularization, restenosis, and late in-stent thrombosis may impair adequate tissue perfusion. Further-

### Table 2. Results of Studies That Evaluated the Improvement in Function on a Segmental Basis

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional nuclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99mTc-sestamibi</td>
<td>30</td>
<td>96 (89–100)</td>
<td>55 (37–73)</td>
<td>87 (75–99)</td>
<td>80 (66–94)</td>
</tr>
<tr>
<td>SPECT FDG67</td>
<td>47</td>
<td>89 (80–98)</td>
<td>86 (76–96)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>201Ti rest, reinjection</td>
<td>104</td>
<td>86 (80–93)</td>
<td>63 (54–73)</td>
<td>69 (60–8)</td>
<td>85 (78–92)</td>
</tr>
<tr>
<td>Total</td>
<td>181</td>
<td>89 (84–93)</td>
<td>68 (61–75)</td>
<td>73 (66–81)</td>
<td>84 (78–90)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE22,66,72,73,77–80</td>
<td>424</td>
<td>76 (72–80)</td>
<td>81 (77–84)</td>
<td>66 (61–71)</td>
<td>89 (86–93)</td>
</tr>
<tr>
<td>DSE SRI66</td>
<td>55</td>
<td>82 (72–92)</td>
<td>80 (69–91)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>End-diastolic wall thickness22</td>
<td>43</td>
<td>94 (87–100)</td>
<td>48 (33–63)</td>
<td>53 (38–68)</td>
<td>93 (85–100)</td>
</tr>
<tr>
<td>Total</td>
<td>522</td>
<td>78 (74–81)</td>
<td>78 (74–81)</td>
<td>64 (59–70)</td>
<td>90 (86–93)</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET-FDG67,70,75,79–81</td>
<td>280</td>
<td>89 (85–93)</td>
<td>57 (51–63)</td>
<td>73 (66–80)</td>
<td>90 (86–95)</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>89 (85–93)</td>
<td>57 (51–63)</td>
<td>73 (66–80)</td>
<td>90 (86–95)</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive accuracy; NPV, negative predictive accuracy; CMR, cardiovascular magnetic resonance; and SRI, strain rate index.

In a comprehensive patient medicine and PET,49,62,63 In a preliminary study in a small group of patients, late-enhancement cardiovascular magnetic resonance in direct comparison with 99mTc-sestamibi and FDG-PET showed better negative predictive value for segments classified as nonviable 6 months after revascularization.67
more, both bypass and percutaneous coronary interventions can lead to new areas of necrosis with scar formation.55,92 Finally, extreme degrees of adverse LV remodeling can hamper the improvement in function independently of the total number of viable segments.93,94

Treatment and Survival Rates
The prognostic value of viability testing and the impact of therapeutic choice on survival have been tested in a meta-analysis of 24 nonrandomized studies carried out between 1992 and 1999 which included 3088 patients with an LVEF <40%. The meta-analysis demonstrated a significant association between revascularization and improved survival rate in patients with LV dysfunction and evidence of myocardial viability independently of the imaging technique used.95,96 This meta-analysis failed to show any benefit of revascularization in the absence of significant viability and reported a higher annual mortality in patients with viable myocardium who were treated medically. An important corollary was the incremental survival benefit after revascularization in those patients with the worst LV function.

Medical therapy was not standardized in the studies analyzed by Allman et al.,95 and the adherence to optimal therapy was not adequately described. In the last decade, the medical treatment of heart failure has continued to improve,97,98 and significant advances have been made in the techniques for coronary revascularization.

To explore potential changes in the outcome of patients with postischemic heart failure with and without viable myocardium that may have occurred from the publication of the results of Allman et al.,95 we pooled the data from 14 nonrandomized studies published between 1998 and 2006 that reported long-term Kaplan-Meier survival curves. Patients were subdivided into 4 groups based on treatment (medical or revascularization by bypass surgery or percutaneous coronary intervention) and the presence or absence of viable myocardium. Of the 14 studies selected, 8 had patients in all 4 groups. The mortality rates were weighted for the number of patients and calculated per year by dividing the mortality by the number of follow-up years to account for different final time points among the studies.

The pooled data are summarized in Table 3.39,99–109

<table>
<thead>
<tr>
<th>Medical therapy viability present</th>
<th>Total Patients, ( n )</th>
<th>Weighted Average Annual Mortality</th>
<th>95% CI</th>
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<tr>
<td>DSE99–105</td>
<td>362</td>
<td>11.23</td>
<td>7.98–14.48</td>
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<tr>
<td>PET106</td>
<td>50</td>
<td>6.25</td>
<td>0.00–12.96</td>
</tr>
<tr>
<td>99mTc-sestamibi105,107</td>
<td>110</td>
<td>11.17</td>
<td>5.29–17.06</td>
</tr>
<tr>
<td>99mTc-sestamibi+PET-FDG108</td>
<td>30</td>
<td>10.33</td>
<td>0.00–21.23</td>
</tr>
<tr>
<td>201Tl rest, reinjection; DSE109</td>
<td>43</td>
<td>9.67</td>
<td>0.83–18.50</td>
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<tr>
<td>Total</td>
<td>595</td>
<td>10.64</td>
<td>8.17–13.12</td>
</tr>
<tr>
<td>Medical therapy viability absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE99,101–105</td>
<td>447</td>
<td>12.05</td>
<td>9.03–15.06</td>
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<td>99mTc-sestamibi107</td>
<td>27</td>
<td>13.85</td>
<td>0.82–26.87</td>
</tr>
<tr>
<td>99mTc-sestamibi+PET-FDG108</td>
<td>26</td>
<td>3.33</td>
<td>0.00–10.23</td>
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<tr>
<td>Total</td>
<td>500</td>
<td>11.69</td>
<td>8.87–14.51</td>
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<td>Revascularization viability present</td>
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<tr>
<td>DSE68,99–105</td>
<td>338</td>
<td>3.09</td>
<td>1.24–4.93</td>
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<td>PET106</td>
<td>43</td>
<td>7.5</td>
<td>0.00–15.37</td>
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<tr>
<td>99mTc-sestamibi105,107</td>
<td>171</td>
<td>3.16</td>
<td>0.54–5.78</td>
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<tr>
<td>99mTc-sestamibi+PET-FDG108</td>
<td>42</td>
<td>0</td>
<td>0.00–0.00</td>
</tr>
<tr>
<td>201Tl rest, reinjection; DSE109</td>
<td>94</td>
<td>1.67</td>
<td>0.00–4.25</td>
</tr>
<tr>
<td>Total</td>
<td>699</td>
<td>3.71</td>
<td>2.31–5.12</td>
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<tr>
<td>Revascularization viability absent</td>
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</tr>
<tr>
<td>DSE68,99,101–105</td>
<td>348</td>
<td>8.78</td>
<td>5.80–11.75</td>
</tr>
<tr>
<td>99mTc-sestamibi107</td>
<td>50</td>
<td>8.77</td>
<td>0.93–16.61</td>
</tr>
<tr>
<td>99mTc-sestamibi+PET-FDG108</td>
<td>25</td>
<td>3.33</td>
<td>0.00–10.37</td>
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<tr>
<td>Total</td>
<td>423</td>
<td>8.45</td>
<td>5.80–11.10</td>
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</tbody>
</table>
Reviewing the most recent literature, we observed that the annual mortality rate in patients treated medically appears to be similar regardless of the presence of viability (Table 3). This is different from what was reported by Allman and coworkers,95 and it could be a reflection of the optimization, by 21st century standards, of patient management.106,108 In a prospective study cohort of 167 patients studied with PET using N-13 ammonia and FDG, Desideri et al117 reported that the risk of cardiac death is not significantly increased if the extent of viability is \( \leq 20\% \) of the LV. The risk of death is increased only when the extent of viable tissue exceeds 20\% of the LV, and together with the presence of left bundle-branch block, it is an independent predictor of mortality.

Observational studies in small cohorts of patients have highlighted that a long waiting time between assessment of viability and revascularization affected both the postoperative recovery of function112 and survival by increasing preoperative mortality.113 A comparison of the outcome after early (within 30 days) or late (>30 days) revascularization in 2 parallel groups of patients showed a significant improvement in function and lower mortality in the group with shorter waiting times.114

The impact of the time of revascularization on prognosis has recently been highlighted by Tarakji et al,17 who assessed viability with PET using FDG and rubidium-82 in the largest prospective cohort of 765 consecutive patients. They applied a propensity analysis matching 153 patients who underwent early revascularization within 6 months and 153 who did not. Their conclusion was that early intervention might be associated with decreased mortality from all causes independently of the amount of viable myocardium detected preoperatively. Several issues were not addressed in this study: Only a minority of patients underwent revascularization without evidence of viability; the impact of arrhythmias and implantable cardioverter-defibrillator implantation is uncertain during the progression of the study; and the same applies to medical therapy that was suboptimal by present standards at the beginning of the observation period in 1997.

The impact of the amount of viability on subsequent survival after revascularization remains unclear because contrasting data are reported in a number of other studies that, using the Cox proportional-hazards model, demonstrated a positive prognostic effect on survival.68,99–101,106,107 The presence of scar106 or extensive myocardial remodeling115,116 as independent predictors of survival can add incremental prognostic value to the amount of viable myocardium. These 2 parameters are likely to bear more weight in future studies using late-contrast-enhancement cardiovascular magnetic resonance to assess viability and to add prognostic power to LVEF, which is a baseline predictor of mortality independent of the cause of LV dysfunction.117 It has already been demonstrated that in patients without a history of previous myocardial infarction, late enhancement involving a small amount of myocardium carries a higher risk of adverse cardiac events.118

Long-awaited large, prospective, multicenter, randomized trials testing the prognosis of patients on optimal medical therapy by year 2000 standards plus revascularization against optimal medical therapy alone are ongoing. We hope that they will provide a clearer picture as to whether long-term prognosis is improved by early revascularization in this patient population (Surgical Treatment for Ischemic Heart Failure [STICH]).119 Positron Emission Tomography and Recovery Following Revascularization-2 (PARR-2), the follow-up of PARR-1,90 has recently been completed. This randomized, multicenter trial that enrolled 430 patients seems to show a trend toward better 1-year outcome when PET-FDG–guided therapy is used instead of standard care.

Conclusions

Although different large, randomized trials have demonstrated a significant reduction in mortality for heart failure patients treated medically, symptomatic heart failure continues to have a high mortality rate.120,121 In more than two thirds of cases, heart failure is secondary to CAD.

In the last 3 decades, 2 new causes of LV dysfunction, ie, myocardial stunning and hibernation, have been recognized in addition to tissue necrosis. Both conditions are reversible and imply the presence of viable myocardium. Furthermore, evidence has accrued that they may contribute to LV dysynchrony and heart failure in patients with CAD.

Several powerful imaging techniques can be used clinically to identify viable tissue (and to distinguish it from scar) within dysfunctional LV segments subtended by diseased coronary arteries. This information can be used to stratify patients more effectively and to guide their subsequent treatment. Although we still lack data from ad hoc randomized trials to prove this point unequivocally, a great number of studies in thousands of cases have provided compelling evidence that revascularization of dysfunctional but viable myocardium may lead to reverse LV remodeling and confer prognostic benefits in patients with posts ischemic heart failure.

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Disclosures

None.

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