

## PSYCHOLOGICAL REVIEW

### Hibernating Myocardium

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According to estimates, up to 50% of patients with coronary artery disease and impaired left ventricular function have areas of viable myocardium. This dysfunctional, yet viable myocardial tissue, which can improve functionally after myocardial oxygen supply is reestablished, has been called hibernating myocardium. The possible pathophysiological mechanism that leads to hibernating myocardium is controversial: is the phenomenon due to persistent ischemia or is it the result of repetitive episodes of ischemia and reperfusion, such as myocardial stunning? Regardless of the mechanism, the presence of viable myocardial tissue indicates that structural and biochemical cellular changes occur, and the recovery of left ventricular function after revascularization depends on the severity and extent of these changes. Whether these changes reflect a long-lasting state of cellular dedifferentiation, an adaptive process that is reversible, or eventually lead to cellular degeneration has not been determined. Perhaps early detection of hibernating myocardial tissue via noninvasive imaging techniques used to assess contractile response, integrity of the cellular membrane, myocardial metabolism, and myocardial blood flow and subsequent early coronary revascularization may prevent infarction and deterioration in left ventricular function. Knowledge that reversible changes and areas of viable myocardium can occur in patients with left ventricular dysfunction will assist healthcare providers in the care and management of patients with hibernating myocardium. (*American Journal of Critical Care*. 2001;10:84-93)

According to estimates, up to 50% of patients with coronary artery disease (CAD) and impaired left ventricular function have areas of viable myocardium. This dysfunctional, yet viable myocardial tissue, which can improve functionally after myocardial oxygen supply is reestablished, has been called hibernating myocardium. Detection of hibernating myocardial tissue and subsequent early coronary revascularization may prevent infarction and deterioration in left ventricular function. Revascularization may also improve impaired left ventricular function if hibernating myocardium is present.<sup>1</sup> This article reviews the pathophysiology and clinical aspects of hibernating myocardium resulting in left ventricular dysfunction.

CAD is the leading cause of morbidity and mortality in developed countries.<sup>2</sup> A consequence of CAD is impaired left ventricular function that may be associated with angina, signs and symptoms of heart failure, or both.<sup>2-4</sup> The extent of this dysfunction is one of the most important determinants of a patient's prognosis.<sup>2,3</sup>

In patients with impaired left ventricular function caused by CAD, myocardial dysfunction may be due to infarction with irreversible loss of cardiomyocytes, necrosis, and scar formation; acute myocardial ischemia with associated myocardial stunning; or myocardial hibernation<sup>3,5,6</sup> (see Table 1 for definition of terms). Left ventricular dysfunction further contributes to myocardial ischemia by increasing myocardial oxygen demand and reducing coronary blood flow.<sup>3,11</sup> If ischemia persists, structural changes occur that lead to heart failure.<sup>3</sup>

Apoptosis	Self-destruction of a cell via the activation of a genetically regulated program of intentional suicide <sup>1</sup>
Hibernating myocardium	Chronically impaired, yet viable myocardial tissue that results in left ventricular dysfunction at rest due to persistently hypoperfused myocardium or repetitive stunning <sup>4</sup>
Infarction	Tissue necrosis after the cessation of blood supply
Ischemia	An imbalance between myocardial blood supply and myocardial tissue need <sup>4</sup>
Stunned myocardium	Transient depression of left ventricular function due to a temporary reduction of myocardial blood flow <sup>4</sup>

Myocardial hibernation occurs in some patients who have CAD and impaired left ventricular dysfunction.<sup>12</sup> Hibernating myocardium may reflect viable myocardial tissue that can improve functionally after myocardial oxygen supply is reestablished.<sup>13</sup> Rahimtoola suggests that “hibernating myocardium is a state of persistently impaired myocardial and left ventricular function at rest due to reduced coronary blood flow that can be partially or completely restored to normal either by improving blood flow or by reducing oxygen demand.”<sup>14,15</sup>

Myocardial function downgrades to the extent that blood flow and function are in equilibrium, and as a result, neither myocardial necrosis nor signs or symptoms of ischemia are present.<sup>16</sup> If the balance between myocardial oxygen supply and need is temporarily or permanently altered, signs and symptoms of ischemia or necrosis occur.<sup>17</sup> Hibernating myocardium is described by Hearse<sup>18</sup> as “exquisitely regulated tissue successfully adapting its activity to prevailing circumstances.”

Patients with CAD and severe left ventricular dysfunction or heart failure have a poor prognosis when treated with medical therapy alone.<sup>5</sup> Mortality rates may be as high as 60% at 1 year after diagnosis.<sup>1</sup> In patients with moderate heart failure, optimal medical therapy may improve survival to no better than 70% at 2 years after diagnosis.<sup>1</sup>

Compared with medical management, coronary artery bypass grafting (CABG) markedly improves long-term survival and functional status in patients with CAD and severe left ventricular dysfunction.<sup>19</sup> However, the prevalence of perioperative mortality and morbidity is higher after CABG in patients with severe left ventricular dysfunction,<sup>20</sup> particularly patients with left ventricular ejection fraction (LVEF) less than 0.35.<sup>1</sup>

Revascularization in these patients remains controversial because of the high surgical risk.<sup>5</sup> Some uncontrolled studies, however, indicate that CABG has a promising role in patients with heart failure and substantial hibernating myocardium.<sup>4</sup> The concept of revascularization for heart failure to improve LVEF, a strong prognostic indicator in these patients, has been given new consideration.<sup>4</sup>

## Pathophysiology

A “flow-function” relation exists between myocardial blood flow and systolic function.<sup>21,22</sup> As myocardial blood flow decreases, a corresponding decrease in contractile function occurs.<sup>21-23</sup> This relation is known as “perfusion-contraction matching.”<sup>21,22</sup> Chronic underperfusion accompanied by a limited coronary flow reserve results in a reduction of oxygen delivery.<sup>24</sup> Although dysfunctional, the heart maintains its viability by adapting to this sustained reduction of resting myocardial blood flow, and a state of sustained low-flow perfusion-contraction matching develops, with balanced reductions in myocardial function and oxygen consumption.<sup>21,22,24</sup>

This physiological process that leads to hibernating myocardium is thought to be the result of a gradual down-regulation of myocardial metabolism, and therefore contractile function, in response to the reduction in resting myocardial blood flow caused by coronary artery stenosis.<sup>25</sup> This down-regulation of myocardial metabolism is an attempt by the cardiomyocytes to reduce oxygen consumption,<sup>12</sup> thus creating a match between oxygen supply

and demand.<sup>13</sup>

This theory has been challenged by studies<sup>25-28</sup> that indicate that resting myocardial blood flow in hibernating myocardial tissue may not differ from that in normally contracting myocardium. Animal studies<sup>21,22,25-29</sup> led to the hypothesis that myocardial stunning results from repeated episodes of ischemia rather than from persistent underperfusion or decreased resting myocardial blood flow. Stunned myocardium is defined as a fully reversible condition characterized by postischemic myocardial dysfunction with relatively normal resting myocardial blood flow in patients with CAD.<sup>2,6</sup>

When coronary blood flow is reduced over a short period and reperfusion occurs in less than 10 minutes, myocardial dysfunction is reversible and cardiac performance is completely restored.<sup>6,22</sup> In myocardial stunning, reperfusion does not occur for up to 20 minutes, causing prolonged, although reversible, myocardial dysfunction.<sup>6,22</sup> Tissue necrosis does not necessarily occur, but alterations in myocardial ultrastructure are present.<sup>6,22</sup>

Vanoverschelde et al<sup>22</sup> describes the stunned myocardium, in terms of the flow-function relation, as a state of perfusion-contraction mismatch, resulting in an imbalance between oxygen supply and demand.<sup>2,6,29</sup> Myocardial function is decreased despite normal oxygen consumption at rest. The difference between hibernation and stunning most likely is solely one of degree: in hibernation, resting myocardial blood flow is low, whereas in stunning, resting myocardial blood flow is normal, but maximal blood flow is reduced.<sup>21</sup>

Chronic myocardial stunning occurs when ischemic episodes are frequent and repetitive and recur at short intervals.<sup>6,29</sup> Myocardial function remains persistently depressed, resulting in chronic left ventricular dysfunction.<sup>6</sup> A complete definition of hibernating myocardium must include chronic myocardial stunning as a component, because recent studies<sup>2,29</sup> suggest that the 2 conditions may coexist or share a common mechanism.

The exact cellular mechanisms and biochemical changes that accompany hibernating myocardium remain elusive.<sup>13</sup> They may be protective responses of the cardiomyocytes to effectively reduce oxygen demand in the setting of reduced oxygen activity.<sup>12,13</sup> Examination of tissue samples obtained at the time of CABG revealed both intracellular and extracellular structural changes in the dysfunctional, but viable myocardium.<sup>7,15,21,22,24,30-32</sup>

The intracellular changes are characterized by a depletion of contractile proteins (sarcomeres); degradation of structured sarcoplasmic reticulum; accumulation of glycogen; the presence of numerous, abnormally shaped mitochondria; and nuclei with altered chromatin distribution.<sup>2,4,7,15,22,24,30</sup> These cellular changes are suggestive of cellular dedifferentiation or embryonic regression, an adaptation to altered blood flow.<sup>2,7,15,21,22,24</sup> However, whether this dedifferentiation is a long-lasting viable state that is reversible or eventually leads to cellular degeneration and apoptosis, or programmed cell death, remains controversial.<sup>2,7,15,21,22,24</sup>

Some studies<sup>15,24,30-32</sup> revealed extracellular alterations that included an increase in the extracellular space and the development of fibrosis. Elsassar et al<sup>30</sup> suggest that the fibrosis is probably due to loss of cardiomyocytes and can be regarded as "replacement or reparative" fibrosis. These investigators<sup>30</sup> and others<sup>31,32</sup> conclude that hibernating myocardium is not a completely adaptive response to underperfusion. The adaptive mechanisms become insufficient, cardiac structure and function deteriorate, and cellular degeneration accompanied by cardiomyocyte loss with fibrosis leads to eventual cell death.<sup>30-32</sup> The combination and degree of cellular degeneration with fibrosis in hibernating myocardium may determine the degree and speed of recovery after revascularization.<sup>30-32</sup>

## Clinical Manifestations

Hibernating myocardium should be suspected in patients with CAD and left ventricular dysfunction.<sup>2</sup> Clinical states in which hibernating myocardium has been detected include stable and unstable angina, acute myocardial infarction, and severe left ventricular dysfunction or heart failure.<sup>2,3,9</sup> The clinical manifestations may reflect these states and include manifestations of decreased myocardial contractility and decreased cardiac output.<sup>2,5,33,34</sup>

Signs and symptoms of left ventricular dysfunction result from pulmonary vascular congestion and inadequate

perfusion of the systemic circulation.<sup>33,34</sup> Depending on the severity of the left ventricular dysfunction, patients may experience dyspnea, orthopnea, productive cough with frothy sputum, fatigue, poor exercise tolerance, decreased urine output, edema, or chest pain.<sup>2,33,34</sup> Physical examination may reveal cyanosis, rales, cool extremities, hypotension or hypertension, tachycardia, an S3 gallop, or increased jugular venous distention.<sup>33,34</sup> Monitoring via a pulmonary artery catheter may reveal decreased cardiac index and increased ventricular filling pressures.<sup>33,34</sup>

The extent and severity of reversible left ventricular dysfunction may be limited to a part of the left ventricle or may involve global impairment of the ventricle.<sup>2</sup> An echocardiogram can provide 2-dimensional data on ventricular function and ejection fraction.<sup>33</sup> The hibernating area may have various degrees of dysfunctional wall motion, such as hypokinesia (decreased movement), dyskinesia (impaired movement), or akinesia (no movement).<sup>2,6</sup> The ejection fraction is decreased depending on the severity of left ventricular dysfunction. Coronary angiography can also reveal regional wall motion abnormalities and a low ejection fraction.<sup>33</sup>

An electrocardiogram may or may not show changes.<sup>13</sup> Transient ST elevation with persistent inversion of the T wave may occur, or the ST segments may be normal.<sup>13,33</sup> The most common dysrhythmias include ventricular tachycardia, ventricular fibrillation, premature ventricular beats, accelerated idioventricular rhythm, and sinus bradycardia.<sup>33</sup>

## Diagnosis

The presence of hibernating myocardium, a mismatch between regional contractile function and regional viability, can be determined by noninvasive imaging techniques.<sup>2,21,35-37</sup> The 3 techniques useful for predicting whether an abnormality in wall motion will improve after revascularization are dobutamine echocardiography, thallium imaging with rest redistribution or reinjection, and positron emission tomography (PET).<sup>21</sup> These methods probe different mechanisms associated with cellular viability.<sup>36</sup> Table 2 is a summary of the accuracy of the diagnostic tests.

Test	Sensitivity, %*	Specificity, %*	Predictive value, %†	
			Positive	Negative
Dobutamine echocardiography	84	81	83	81
Thallium imaging			69	90
Rest/redistribution	86	47	ND	ND
Reinjection	90	54	ND	ND
Positron emission tomography	88	73	82	83

\*Data from Wijns et al<sup>2</sup> and Rahimtoola.<sup>36</sup>  
†Data from Rahimtoola.<sup>36</sup>  
ND indicates no data available.

### Dobutamine Echocardiography

Echocardiography performed during the infusion of increasing doses of dobutamine is an inexpensive, widely used, and accurate method for detecting hibernating myocardium and predicting regional and global recovery of function after revascularization.<sup>2,12,36</sup> The response of hibernating myocardium to stimulation of  $\beta$ -adrenoceptors by dobutamine can be used to determine the presence of inotropic contractile reserve.<sup>36</sup> Hibernating myocardium contracts in response to a low dose of dobutamine (5-10  $\mu\text{g}/\text{kg}$  per minute), a response that represents the recruitment of contractile reserve, but the function of the hibernating tissue may deteriorate after the infusion of a high dose of dobutamine (up to 40  $\mu\text{g}/\text{kg}$  per minute) because the flow reserve (ie, the ability of myocardial blood flow to increase in response to increased oxygen requirements) is reduced and cannot meet the increased metabolic demand, resulting in ischemia with further reduction in contraction.<sup>2,12,38</sup> This “biphasic” response (ie, improvement at low dose and deterioration at high doses) is needed for the optimal assessment of myocardial hibernation and accurate prediction of recoverability of contractile function.<sup>12,22,38</sup>

The sensitivity and specificity of dobutamine echocardiography in predicting the reversibility of myocardial dysfunction are 84% and 81%, respectively.<sup>2,9,22</sup> Evidence indicates that for patients with severely dysfunctional

myocardium, compared with PET or thallium imaging, dobutamine echocardiography has a lower negative predictive value (higher false-negative rate) and that the real amount of tissue viability is underestimated.<sup>27,35,36</sup> Therefore, hibernating myocardium in patients with heart failure might not be detected when dobutamine echocardiography is used, and such patients would be denied the potential benefits of revascularization.<sup>8,36</sup>

### Thallium Imaging

The use of nuclear imaging techniques to detect hibernating myocardium relies on the demonstration of membrane integrity.<sup>2,36</sup> Thallium 201 (201Tl) is a radioisotope, analogous to potassium in its volume of distribution, that is widely available and can be detected by single-photon emission computed tomography.<sup>2,21,39</sup> The distribution, redistribution, and retention of 201Tl by myocardial cells is an active process that is a function of cell viability, cell membrane activity, and blood flow.<sup>13,36,40</sup>

The uptake of 201Tl into cells is rapid, and the early pattern of distribution is proportional to blood flow; the late pattern of distribution indicates tissue with an intact intracellular-to-extracellular potassium gradient, a finding strongly predictive of cell viability.<sup>13,21</sup> In normal myocardium, uptake is initially high but decreases rapidly within hours.<sup>2</sup> In hibernating myocardium, the uptake is initially low but then increases, a phenomenon related to redistribution of the radioisotope.<sup>2</sup>

Thallium 201 can be administered during use of exercise- or rest-imaging protocols.<sup>2,13,40</sup> Exercise- or stress-imaging protocols require the intravenous administration of thallium at peak exercise levels.<sup>12</sup> Images are obtained within 5 minutes to assess for initial distribution of the thallium.<sup>12</sup> Areas of decreased uptake reflect ischemia or old infarction.<sup>10</sup> Within a few hours, thallium will redistribute into ischemic, viable tissue, but not infarcted tissue.<sup>10</sup> Imaging is done again 3 to 4 hours after administration of the thallium to assess for redistribution, which may suggest the presence of viable myocardium.<sup>10,12</sup> Scarred or infarcted tissue appears as a “fixed 201Tl defect,” and neither the initial distribution nor the redistribution images indicate uptake of thallium.<sup>10,41</sup> However, fixed defects have shown improvement after revascularization.<sup>41</sup> Therefore, with conventional stress-imaging protocols, the extent of viable myocardium may be underestimated.<sup>39,41</sup>

Use of rest-imaging protocols that involve rest-redistribution or reinjection of 201Tl has improved the accuracy of the detection of viable myocardium.<sup>12,13,40,41</sup> Some investigators<sup>12,13,40,41</sup> recommend a protocol in which images are obtained 24 hours after the initial 201Tl injection to detect reversibility in the fixed defect. In another effective protocol used to assess for viability, a second dose of 201Tl is injected when the patient is at rest after a 4-hour period of redistribution following stress imaging, and delayed redistribution images are obtained 24 hours after the initial dose.<sup>12,13,40,41</sup> Some investigators<sup>13</sup> recommend injecting thallium solely when the patient is at rest, without any exercise, and obtaining images immediately and again at 4 hours to assess for redistribution. In some studies,<sup>12,13,41,42</sup> 50% of the fixed defects detected with the conventional stress-imaging protocol had improved 201Tl uptake when the rest-redistribution and reinjection protocols were used. The sensitivity and specificity of thallium imaging for detecting viable myocardium are approximately 86% and 47%, respectively, for rest-redistribution protocols and 90% and 54%, respectively, for reinjection protocols.<sup>2,9</sup>

### Positron Emission Tomography

PET is often considered the gold standard for the detection of viable myocardium.<sup>13,43</sup> PET with [18F]fluorodeoxyglucose (FDG) is used to evaluate metabolic activity in underperfused and dysfunctional myocardial tissue.<sup>2,13,21,40,43</sup> FDG is used to trace a key metabolic reaction step in myocardial glucose metabolism.<sup>1,13,21,40</sup> Under normal conditions, the myocardium metabolizes free fatty acids, which are its main source of energy.<sup>1</sup> However, in hibernating myocardial tissue, the myocardium relies on glucose metabolism as its main energy source.<sup>1,13</sup> The uptake of FDG is a marker of glucose utilization in hypoperfused areas.<sup>1,13,21,40</sup> FDG may be concentrated in hibernating myocardium because of the rich glycogen content of this tissue.<sup>21</sup>

For assessment of resting myocardial blood flow, ammonia labeled with radioactive nitrogen (<sup>13</sup>N) is administered.<sup>1,12</sup> Regions with high FDG uptake (increased metabolic activity) and low myocardial blood flow (decreased [<sup>13</sup>N]ammonia blood flow) indicate a mismatch representative of ischemic, stunned, or hibernating myocardium.<sup>1,12,13,40</sup> This mismatch between FDG uptake and myocardial blood flow indicates viable tissue that has preferentially shifted toward glucose metabolism rather than fatty acid metabolism.<sup>13,40</sup> A mismatch between FDG uptake and myocardial blood flow indicates viable myocardium, whereas a match presumably indicates scar

tissue.<sup>2,13,40</sup> The extent of the mismatch pattern has both positive and negative predictive accuracies greater than 80% for detection of functional improvement after myocardial revascularization.<sup>1,9,10,12,40</sup> The sensitivity and specificity for PET are 88% and 73%, respectively.<sup>2,9</sup>

PET provides excellent information and is a reliable approach for detecting viable myocardium.<sup>13,40</sup> Unfortunately, PET is not available for clinical use in all hospitals, and the high cost of this technique may prohibit its use in every patient.<sup>12,13,44</sup>

Dobutamine echocardiography is recommended as the first screening test for the detection of viable myocardium.<sup>36</sup> However, because of the high false-negative rate of this technique, thallium imaging or PET should be used in patients in whom the results of dobutamine echocardiography are normal.<sup>36</sup> Ultimately, the screening technique chosen should depend on the medical facility's experience and case mix.<sup>12</sup>

## Treatment

The role of medical therapy in the treatment of hibernating myocardium is not clear.<sup>9,17</sup> However, use of pharmaceutical agents may improve left ventricular function in hibernation.<sup>17</sup> Administration of angiotensin-converting enzyme inhibitors and  $\beta$ -blockers, specifically carvedilol, can decrease mortality and improve signs and symptoms of heart failure.<sup>2,17,45-47</sup> The effects of carvedilol on hibernation in heart failure are under investigation.<sup>37</sup>

The ultimate test of myocardial viability is the recovery of contraction after revascularization.<sup>48</sup> Surgical revascularization can improve long-term survival in patients with CAD and evidence of dysfunctional but viable myocardium.<sup>2,5,49</sup> The most striking benefit of surgical revascularization is the improvement in ejection fraction, which is sometimes dramatic and occurs most often in patients with severe left ventricular dysfunction.<sup>2,49</sup> Mechanical revascularization by means of percutaneous transluminal coronary angioplasty can improve ventricular function in patients with dysfunctional but viable myocardium.<sup>6,25</sup> However, the restenosis rate in these patients may be more than 40%.<sup>25</sup> Restenosis may prevent functional improvement in viable tissue after an initially successful revascularization.<sup>25</sup> Regardless, the indications for this procedure are widening as improvements are made in the technique and expertise.<sup>50</sup>

The prevalence and degree of functional recovery after coronary revascularization depend on a number of factors, including the severity of global left ventricular dysfunction preoperatively, the technique used for myocardial protection during surgery, the presence or absence of perioperative myocardial infarction, and the adequacy of revascularization.<sup>2</sup> The decision to use revascularization in patients with heart failure and left ventricular dysfunction should be based on an extensive evaluation of the amount of myocardium at risk and the applicability of revascularization.<sup>13</sup> The assessment for surgical or mechanical revascularization should include determining the presence of available target vessels for bypass or angioplasty, the extent of viable myocardium in the distribution of these vessels, and the experience and success of the surgical or angioplasty team with revascularization in patients with severe left ventricular dysfunction.<sup>13</sup> Risk factors for death after CABG, which include age, sex, comorbid conditions, prior surgery, and valvular disease, should be considered.<sup>13</sup> The need for hemodynamic support during angioplasty should be evaluated.<sup>13</sup> In patients with severe heart failure, preoperative evaluation for possible need for a ventricular assist device and subsequent cardiac transplantation after revascularization should also be considered.<sup>13</sup>

The magnitude of the improvement in the signs and symptoms of heart failure is directly related to the amount of revascularized viable myocardial tissue present.<sup>2</sup> Patients with hibernating myocardium should undergo revascularization as soon as possible.<sup>15,30-32</sup> The cellular mechanisms and biochemical changes that occur in hibernating myocardium may eventually become insufficient to preserve structural integrity and contractile function.<sup>7,24,31,32</sup> When structural changes are severe or extensive, a situation that may occur in patients who have hibernating myocardium for a long period, functional recovery is usually delayed and is often incomplete after revascularization.<sup>2,12,14,22,24,31,32</sup> A rapid and usually complete recovery of myocardial function occurs with early revascularization.<sup>2,12,14,22,31,32</sup>

## Clinical Implications

Heart failure and left ventricular dysfunction occur in approximately 4.7 million patients in the United States, accounting for 40 000 deaths and \$20 billion in expenditures annually.<sup>51</sup> Up to 50% of patients with CAD and impaired left ventricular function may have areas of hibernating myocardium and could benefit from revascularization.<sup>1,2</sup> More than 10% of patients referred for cardiac transplantation have an element of hibernating myocardium contributing to severe left ventricular dysfunction.<sup>6,12</sup>

These findings have important implications for the investigation and management of patients with viable myocardium.<sup>1</sup> Because of the clinical prevalence of hibernating myocardium and the response to therapeutic intervention, clinicians must recognize and treat this condition.<sup>2</sup> Accurate risk stratification and appropriate referral of patients for coronary revascularization should be strongly considered.<sup>6</sup>

In the era of managed care, primary care providers are managing clinical problems that were previously addressed by specialists.<sup>52</sup> The majority of patients with heart failure and left ventricular dysfunction are followed up by an internist or primary care provider, not necessarily a cardiologist. Consequently, primary medical physicians and advanced practice nurses must keep current with the myriad state-of-the-art diagnostic and therapeutic techniques in the management of heart failure.<sup>52</sup> Knowledge of the reversibility of left ventricular dysfunction will facilitate decision making in the use of these diagnostic techniques.<sup>52</sup> The clinical data they provide will assist physicians and advanced practice nurses in the care and management of the increasing population of patients with hibernating myocardium.<sup>52</sup>

## Conclusion

Myocardial hibernation may result in left ventricular dysfunction in patients with CAD, and severe dysfunction may lead to a decreased LVEF and heart failure.<sup>2,6,12-15,43,51</sup> The exact pathophysiological mechanism of hibernating myocardium is still debatable: is it due to persistent ischemia, or is it the result of repetitive episodes of ischemia and reperfusion, such as stunning?<sup>2,6,12,13,15,25,26,29,30,51</sup> Hibernation and stunning may coexist or share a common mechanism in the same region of myocardial tissue.<sup>2,29,51</sup> Regardless of the mechanism, examination of tissue samples of viable myocardium indicates that structural and biochemical changes occur, and the recovery of left ventricular function after revascularization depends on the severity and extent of these changes.<sup>30-32,51</sup>

Noninvasive techniques can be used to detect viable myocardium and are useful in predicting recovery.<sup>21</sup> These techniques can be grouped into those that are used to assess (1) the integrity of the cellular membrane, (2) myocardial metabolism and myocardial blood flow, and (3) contractile response.<sup>2,13,21,36,40,51</sup>

Detection of viable myocardial tissue and early coronary revascularization of this dysfunctional myocardium may prevent the following: (1) infarction and deterioration in left ventricular function; (2) further cellular and biochemical changes that could ultimately lead to structural alterations and the development of fibrosis and worsening of function; and (3) electrical instability such as ventricular arrhythmias, which may lead to sudden cardiac death.<sup>51</sup> Improvement in left ventricular function, especially when a large area of the myocardium is involved and the improvement is great enough, most likely will lead to improvement in LVEF, quality of life, and longevity.<sup>51</sup> Future studies are recommended to address the cost-effectiveness of current methods of diagnosis and therapy, define the natural history of myocardial hibernation (its prevalence in heart failure), and determine the extent of hibernating myocardium needed to have a beneficial effect on survival, quality of life, and functional improvement.<sup>1,12,51</sup>

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