Clinical Assessment of Myocardial Viability

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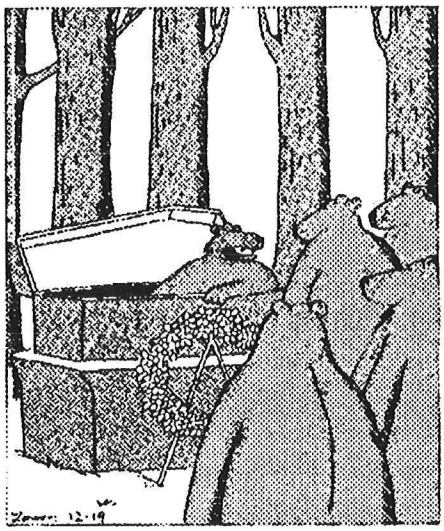

"For crying out loud, I was hibernating,
don't you guys ever take a pulse?"

Internal Medicine Grand Rounds

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Resting left ventricular (LV) dysfunction is a powerful prognostic indicator in patients with coronary artery disease and carries important therapeutic implications. For example, two large randomized trials showed that patients with LV dysfunction and triple vessel disease have improved survival with bypass surgery as compared to medical therapy.[1,2] It is not certain whether this survival benefit applies to patients with severely depressed LV function (ejection fraction <0.35) because the CASS study excluded such patients and the VA Cooperative Study did not include enough of them. Such patients have increased surgical mortality, although in the non-randomized CASS Registry, patients with severely depressed LV function lived longer than medically treated patients.[3] Other studies have reported recovery of LV function after bypass surgery in high risk patients with severely depressed LV function.[3-12] Thus, clinicians are often faced with the difficult dilemma of deciding whether the risks of bypass surgery outweigh its benefits in patients with coronary artery disease and severe LV dysfunction. In order to resolve this dilemma, several clinical methods have been developed to identify "myocardial viability" and thereby predict which patients will exhibit LV functional recovery after revascularization. This review will focus on the definition of myocardial viability, its biology, and current clinical techniques to assess it.

Resting LV Dysfunction

The concept of myocardial viability is based on the fact that resting LV dysfunction may be reversible or irreversible depending on the underlying pathology. Irreversible LV dysfunction is typically due to myocardial necrosis or fibrosis. Obviously, necrotic tissue will not recover function after revascularization. However, there is ample evidence that even severe LV dysfunction may be partially or completely reversible. Figure 1 shows pre- and post-operative ventriculograms from a patient with an occluded LAD and an akinetic anterior wall. After successful bypass surgery the akinetic anterior wall became normal with an improvement in ejection fraction from 0.37 to 0.76. Table 1 lists several reversible causes of resting LV dysfunction. In patients with coronary artery disease, one must consider the possibility that resting LV dysfunction is due to an unrelated, but potentially reversible cause such as hypertension, alcohol, viral myocarditis, etc. Reversible LV dysfunction in the setting of coronary artery disease is commonly due to ischemia, stunning, or hibernation.

Several studies have shown that patients with reversible LV dysfunction in the setting of coronary artery disease have improved survival compared to patients with irreversible LV dysfunction.[2-6,13,14] *Therefore, the rationale for clinical assessment of myocardial viability is to determine which patients are likely to have recovery of LV function after coronary revascularization.*

Fig 1. Rahimtoola's classic patient with hibernation.

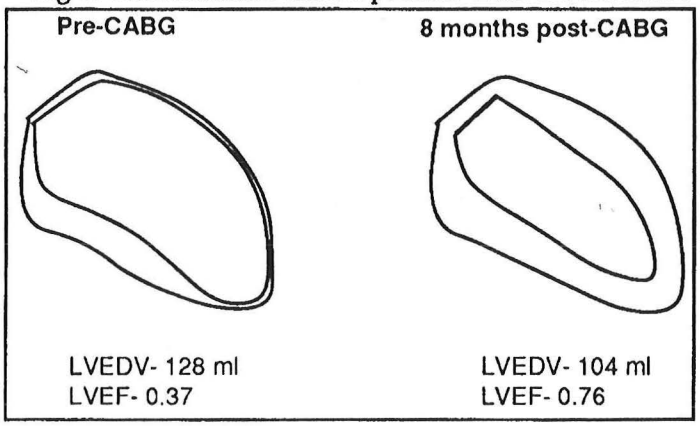


Table 1. Reversible Causes of Resting Wall Motion Abnormalities

Excessive afterload (i.e. hypertensive crisis)
Reduced preload (i.e. volume depletion)
Sepsis
Toxins (alcohol, tricyclics, cocaine, lithium, cobalt)
Viral myocarditis
Post-partum cardiomyopathy
Arrhythmias
Myocardial ischemia
Myocardial stunning
Hibernating myocardium

Definition of Stunned versus Hibernating Myocardium

A wall motion abnormality with a significant amount of viable myocardium is capable of recovery if reperfused after acute ischemia (stunned myocardium), or if revascularized in the setting of chronic ischemia (hibernating myocardium). Hibernating and stunned myocardium, usually viewed as distinct phenomenon, are attributed to differences in the relationship between perfusion and metabolism. Hibernating myocardium is thought to be chronically underperfused; the myocyte somehow downregulates metabolic requirements to the proper level of oxygen consumption without permanent injury.[6,15,16] Stunned myocardium occurs in tissue which was recently ischemic and has undergone restoration of normal perfusion; mechanical function remains depressed during the postischemic period.[16,17] Importantly, stunned myocardium does not recover function until 7-10 days after reperfusion.[18-22] Many studies showing that LV function is not improved by reperfusion are fundamentally flawed because they evaluated LV function too early after thrombolytic therapy to avoid the effects of stunning.

Definition of Stunned Myocardium. Myocardial stunning is a well recognized phenomenon that has been extensively studied in animal models of acute ischemia. The hallmark of stunning is postischemic myocardial dysfunction that persists despite restoration of normal perfusion to ventricular segments that are not irreversibly damaged. As reviewed by Bolli,[17] myocardial stunning is a clinically important phenomenon that occurs in man following reperfusion therapy for acute myocardial infarction. It may also occur after unstable angina, spontaneous or exercise-induced ischemia, PTCA, and cardiac surgery. The clinical diagnosis of myocardial stunning requires demonstration of 1) normal or near-normal perfusion and 2) a reversible contractile abnormality after an acute ischemic event.

Biology of Stunned Myocardium. Although the mechanism of stunning is not completely understood, most investigators agree that two fundamental processes are involved: disruption of intracellular calcium transients and oxygen free radical generation.

Oxygen free radicals are highly reactive oxygen metabolites characterized by the presence of an unpaired electron that forms an open bond. These molecules include the superoxide anion ($\bullet O_2^-$), hydrogen peroxide (H_2O_2) and hydroxyl radical

(•OH).[23] Under normal circumstances, tissue oxygen metabolism produces a small amount of these metabolites. Tissue injury is prevented by intracellular enzymes such as superoxide dismutase, catalase, peroxidase, and glutathione, that scavenge the toxic radicals and prevent their excessive accumulation. However, during ischemia and/or reperfusion there is excessive production of oxygen free radicals, such that the normal defense systems are saturated and unable to prevent oxygen free radical mediated tissue damage. The cascade of oxygen free radical formation as well as their mutual interaction is summarized by the sequence of reactions in Figure 2.

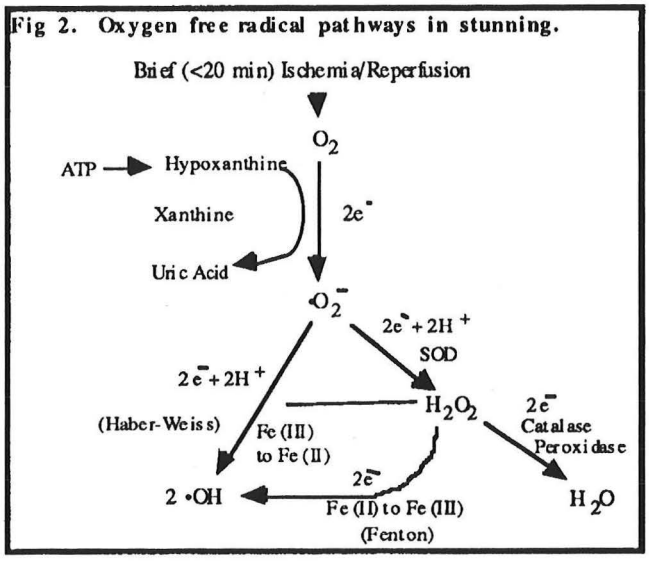


Fig 2. Oxygen free radical pathways in stunning.

There are several potential levels of action to interfere with these three species of oxygen metabolites: inhibition of xanthine oxidase (by allopurinol), dismutation of the superoxide anion (by SOD), reduction of hydrogen peroxide (by CAT), chelation of iron (by desferrioxamine), and direct scavenging of the highly toxic hydroxyl radical by dimethylthiourea or N-2-mercaptopropionyl glycine (MPG).[24] Each of these compounds has been used in different models of myocardial stunning to suggest that oxygen free radicals are involved in the pathogenesis of stunned myocardium in acute, open-chest animal models.[25] More recently, the attenuation of postischemic dysfunction following the administration of SOD plus CAT in the conscious, chronic dog model[26] has strengthened the hypothesis by eliminating the potential generation of oxygen metabolites associated with acute surgical preparations. The strongest evidence in support of the oxygen free radical hypothesis comes from the elegant, recent work from Bolli, et al. Using spin trap alpha-phenyl N-tert-butyl nitrone (PBN) and electron paramagnetic resonance spectroscopy, they provided the first direct demonstration of oxygen free radical adducts in the ischemic-reperfused vascular bed.[27,28] Moreover, the magnitude of oxygen free radical production correlated well with the severity of the preceding ischemia and the burst of radical production could be abolished by the previous administration of oxygen free radical scavengers (SOD plus CAT).[29] These observations were initially made in the open-chest dog model and have been recently extended to the more physiologic conscious, chronic dog model.[30]

A number of lines of evidence point to abnormal calcium homeostasis in myocardial stunning. Intracellular calcium concentration increases within 10-20 minutes after ischemia in isolated hearts.[31,32] Ryanodine, an inhibitor of cellular calcium overload, inhibits myocardial stunning.[33] Likewise, acidosis, which inhibits cellular uptake of calcium as well as intracellular calcium binding, also attenuates stunning.[34] Krause, et al[35] showed that the sarcoplasmic reticulum loses its ability to actively transport calcium during stunning in the canine model. Finally, nifedipine may protect against stunning independently of its effects on hemodynamics.[36]

Definition of Hibernating Myocardium. The term hibernating myocardium was first used by Rahimtoola[6] to describe LV dysfunction in the setting of chronic myocardial ischemia with recovery of function after coronary revascularization. This concept is based on the observation that patients with coronary artery disease and chronic LV dysfunction may have marked improvement in wall motion after coronary revascularization. Inherent in the definition of hibernating myocardium is the assumption that the LV is chronically underperfused, such that the heart downregulates contractile function to accomodate reduced oxygen supply without metabolic evidence of ischemia or irreversible cell damage.[6,15-17] Accordingly, the clinical diagnosis of myocardial hibernation would require demonstration of 1) abnormal perfusion and 2) a reversible LV contractile abnormality associated with chronic ischemic heart disease.

Biology of Hibernating Myocardium. Unfortunately, our understanding of myocardial hibernation is limited by a lack of experimental models of this condition and by the fact that clinical studies have not measured myocardial perfusion and function simultaneously.[17] Importantly, abnormal perfusion with reversible myocardial dysfunction is common to both myocardial hibernation and transient myocardial ischemia. As noted previously, myocardial stunning may occur after transient ischemia. Thus, hibernating myocardium may not be chronically underperfused, but instead could represent the cumulative effects of repeated episodes of transient ischemia with intermittent stunning. In experimental models of stunned myocardium, repeated brief episodes of ischemia cause prolonged contractile dysfunction compared to single ischemic events.[37] It is well recognized that clinically silent episodes of ischemia occur frequently throughout the day in patients with severe coronary artery disease.[38] Under such a scenario, transient ischemia, which may be clinically silent, could occur frequently enough to prevent the recovery of contractile function in the stunned myocardial segments.

There is some evidence to support the concept that myocardial hibernation is actually a chronic or intermittent form of myocardial stunning. Tillisch et al,[39] showed normal perfusion by PET in a subset of patients with chronic stable angina in whom regional wall motion abnormalities were reversed by coronary bypass surgery. Recently, Vanoverschelde et al,[40] measured regional myocardial blood flow by PET in 26 patients with regional contractile abnormalities due to chronically occluded coronary arteries without prior infarction. Resting myocardial blood flow in the abnormal segments was not significantly different from adjacent normal segments. However, the ability of coronary flow to increase during maximal vasodilatation (coronary flow reserve ratio) was impaired in the abnormal segments, suggesting that intermittent increases in oxygen demand would cause myocardial ischemia. Finally, the concept of contractile reserve argues against chronic underperfusion of hibernating myocardium. Contractile reserve refers to the ability of a wall motion abnormality to improve with inotropic stimulation.[41-44] Patients with stunned myocardium after acute myocardial infarction clearly have contractile reserve in response to dobutamine.[45-48] We and others have shown that dobutamine also elicits contractile reserve in patients with chronic coronary artery

disease and hibernating myocardium.[49-52] If hibernating myocardium were in fact chronically underperfused with metabolic downregulation, one might predict that the increase in oxygen demand associated with dobutamine would provoke ischemic wall motion abnormalities rather than contractile reserve.[53]

Flow-Function Relationships in Stunned and Hibernating Myocardium

As noted previously, stunned myocardium occurs when LV dysfunction persists after relief of ischemia. This is illustrated in Figure 3 where a brief episode of ischemia is followed by transient hyperemia and return to normal function. A more severe and prolonged episode of ischemia is followed by a delayed return of LV function to normal (stunning). Measurement of flow and function at any single point in time (arrows) cannot distinguish stunning from ischemia.

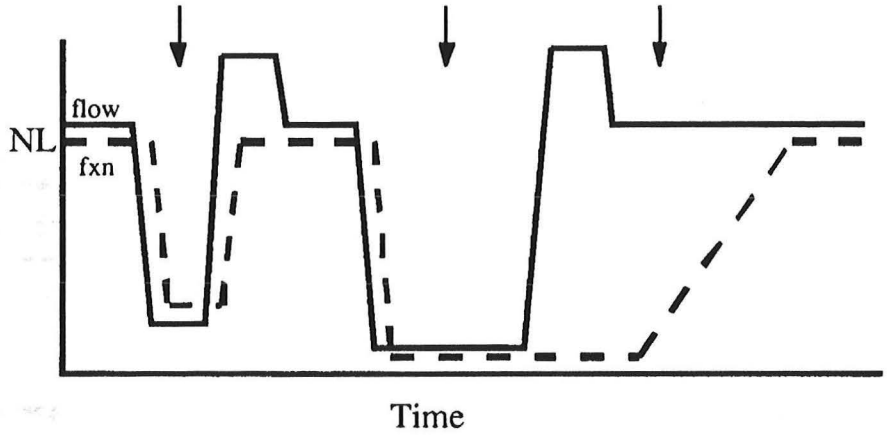


Figure 3. Flow-function relationships in transient ischemia (left) and stunning (right). See text for details. Note that measurement of flow and function at a single point in time (arrows) does not distinguish stunning from transient ischemia.

Hibernating myocardium is classically defined as a reduction in myocardial perfusion that produces contractile dysfunction but maintains myocyte viability so that recovery of LV function occurs when perfusion is restored by revascularization. This hypothesis is illustrated in Figure 4.

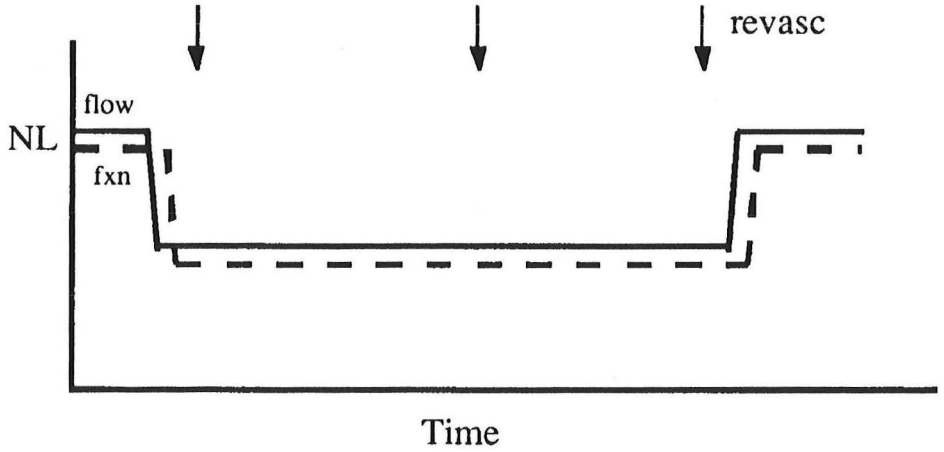


Figure 4. Classic hypothesis for hibernating myocardium. See text.

A more rational hypothesis describing hibernating myocardium is shown in Figure 5. In this scenario, frequent episodes of ischemia (silent or symptomatic) lead to a chronic form of myocardial stunning wherein post-ischemic LV dysfunction never has time to recover before another ischemic episode causes further stunning. LV functional recovery occurs only after revascularization eliminates the ischemic episodes. Unless flow and function are measured at multiple points in time, one cannot determine whether hibernation is due to chronic underperfusion (Rahimtoola's classic hypothesis)[6] or intermittent stunning (Bolli's hypothesis).[17]

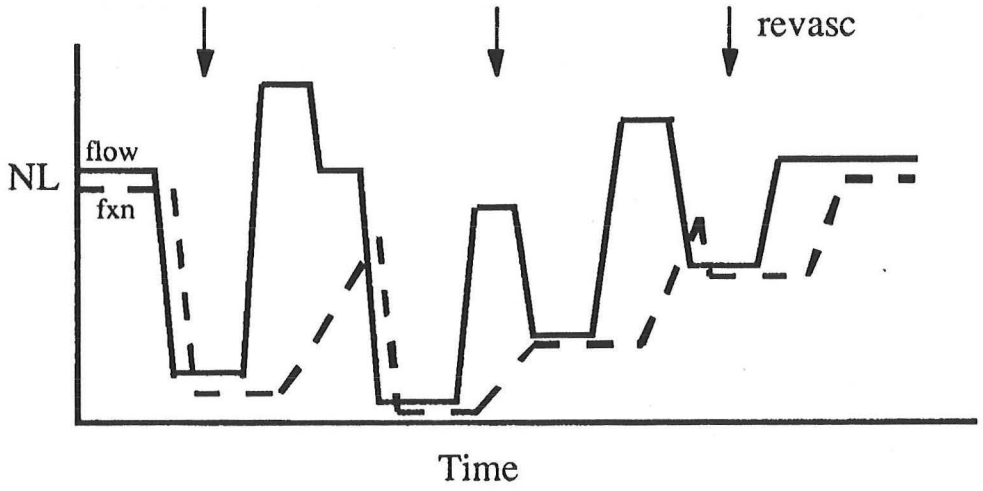


Figure 5 intermittent stunning masquerading as hibernation.

Table 2 compares perfusion, resting contractile function, and reversibility of the contractile dysfunction in infarction, ischemia, stunning, hibernation, and cardiomyopathy. Clearly, the simple assessment of perfusion and resting contractile function do not allow a clear differentiation of these clinical entities. Instead, the identification of reversibility of a wall motion abnormality is needed because it is likely to have the greatest therapeutic and prognostic implications. Accordingly, clinical studies of myocardial viability are of limited value unless they can predict reversibility of LV dysfunction.

Table 2. Perfusion, contraction, and reversibility in clinical syndromes.

	Perfusion	Resting LV Function	Reversible
Infarction	decreased	depressed	no
Ischemia	decreased	depressed	yes
Stunning	normal	depressed	yes
Hibernation	? decreased	depressed	yes
Cardiomyopathy	normal	depressed	sometimes

Myocardial Viability: Perfusion, Metabolism, Contractile Reserve

Clinical methods to assess myocardial viability have focused on detecting perfusion, metabolic activity, or contractile reserve in the region of resting wall motion abnormality. The demonstration of intact perfusion to an area of abnormal wall motion implies that it containes viable cells. Perfusion techniques currently

used include thallium-201 scintigraphy, positron emission tomography (PET), and myocardial contrast echocardiography (MCE). Magnetic resonance imaging (MRI) has great potential to identify myocardial perfusion. Metabolic activity can be currently assessed by PET scanning, although MRI and near-infrared spectroscopy may have potential application. Contractile reserve, the ability of a resting wall motion abnormality to exhibit a contractile response to an inotropic stimulus, can be done using ventriculographic imaging techniques such as contrast or radionuclide angiography, echocardiography, or MRI.

Thallium-201 Scintigraphy

Numerous studies have reported the use of perfusion techniques to identify myocardial viability. The most commonly used perfusion technique is radionuclide imaging using either thallium-201 or technicium-sestamibi. The various technical approaches to identifying myocardial viability by radionuclide imaging were recently reviewed in detail by Dilsizian and Bonow.[55] Briefly, thallium-201 is a potassium analog that is actively transported across the cell membrane via the ATP dependent Na^+ - K^+ pump. Thus, thallium uptake requires perfusion and cell membrane integrity. Because the Na^+ - K^+ pump also extrudes thallium from the cell, it recirculates and can be taken up again by viable cells. This phenomenon is known as redistribution. The two most widely used techniques for identifying myocardial viability using thallium are rest-redistribution imaging and late reinjection. Rest-redistribution imaging differs from the widely used exercise thallium in that images are obtained at rest (not after exercise) following injection of the radioisotope. Repeat images are made either early (3-4 hours later) or late (8-24 hours later) during the redistribution phase. A perfusion defect at rest that "fills in" during redistribution is considered viable. Thallium reinjection involves giving a second injection of radioisotope 3-4 hours after the rest images to improve visualization of perfusion in the area of the resting defect. Although numerous papers have been published describing or comparing these radionuclide methods of detecting myocardial viability, only a handful have compared radionuclide perfusion imaging to LV functional recovery after revascularization (Table 3).

Table 3. Thallium-201 imaging in predicting LV functional recovery.

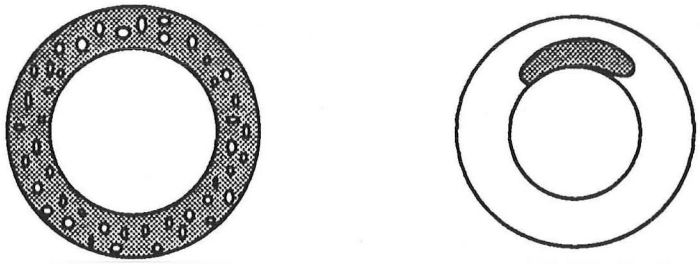
	Pt population	# of pts	# of abn segs	pos pred value	neg pred value
Dilsizian[56]	Chronic CAD	20	23	87%	100%
Ohtani[57]	Chronic CAD	24	61	89%	50%
Ragosta[58]	Chronic CAD	21	176	73%	77%
Udelson[59]	Chronic CAD	18	47	75%	92%
Arnese[60]	Chronic CAD	38	170	33%	94%

Pitfalls of Thallium-201 Scintigraphy

Although thallium imaging has been widely used as a means of detecting viable myocardium, there are some limitations to consider. As seen in Table 3, only a few small studies have actually validated thallium imaging against the clinical goal of LV functional recovery after revascularization. Accordingly, it would be premature to either recommend or deny bypass surgery to a patient on the basis of

thallium imaging alone. There are several reasons why viability in terms of perfusion and cell membrane integrity may not translate into LV functional recovery. First, these studies validated thallium evidence of viability against functional recovery on a segment by segment basis. Improvement in LV function depends on the number and location of viable segments.[61] For example, if all of the anterior and apical segments are viable, LV function is likely to improve after revascularization. Conversely, if only one or two segments in the inferior wall are viable, overall LV function may not improve. Second, islands of viable myocytes can exist in the midst of predominantly fibrotic areas that are incapable of functional recovery (Fig 6).[13,14] Such islands of viability would be expected to take up thallium and thus be considered viable. Finally, subendocardial necrosis involving >20% of the thickness of the LV will preclude normal resting wall motion, despite the fact that the subepicardial layer is comprised of normal myocardium.[62] Thus, it is possible that perfusion imaging is "too sensitive" in detecting viability in segments that cannot recover function after revascularization.

Figure 6. Examples of Viability without Functional Recovery



Dilated Cardiomyopathy with Islands of Viable Myocardium

Subendocardial Infarct

PET Scanning

PET scanning uses radioisotopes to detect both perfusion and metabolic activity. Perfusion can be obtained with ^{13}N-labeled ammonia or ^{15}O-labeled water.[55] One advantage of PET is that perfusion is quantitatively measured in ml/min/g of tissue. Metabolic activity is measured from uptake of ^{18}F-labeled fluorodeoxyglucose (FDG). It is presumed that since normal myocardium preferentially uses fatty acids for high energy phosphate production and ischemic cells shift toward glucose utilization, FDG uptake will be present in hypoperfused regions that are viable. Thus, there is a mismatch between perfusion and FDG uptake in viable myocardium. In contrast, matched perfusion-metabolic defects indicate irreversibly damaged cells that cannot metabolize glucose (or its analog, FDG). Several studies have compared PET imaging to LV functional recovery of LV function (Table 4).

Table 4. PET imaging as a predictor of LV functional recovery.

	Pt population	# of pts	# of abn segs	pos pred value	neg pred value
Tillisch[39]	Chronic CAD	17	67	85%	92%
Pierard[46]	Anterior MI	17	84	55%*	100%*
Tamaki[63]	Chronic CAD	22	46	78%	78%
vom Dahl[64]	Chronic CAD	37	141	48-86%	86%

* analyzed by patient rather than by segment.

Pitfalls of PET Imaging

PET imaging is expensive and not available in most hospitals. Moreover, recent data suggest that FDG uptake is a complex and may be affected by insulin, epinephrine, and a variety of competing substrates.[65,66] Thus, FDG uptake in patients with LV dysfunction may reflect factors other than myocardial viability. In fact, recent studies have shown FDG evidence of viability in regions shown to have extensive fibrosis on transmural biopsy.[67]

Dobutamine stress echocardiography (DSE)

Contractile reserve in patients with depressed LV function has important prognostic implications in patients being considered for bypass surgery.[4,41-44] Prior studies used ventriculography to detect contractile reserve during infusion of epinephrine or nitroglycerin, or after premature ventricular contractions. Such methods are technically cumbersome and have not been widely used. Moreover, ventriculography detects global improvement in LV function during inotropic stimulation, a finding that may reflect hyperkinesis in normal segments even if abnormal segments do not improve. In contrast, DSE directly assesses regional systolic wall thickening in abnormal segments. Cigarroa, et al[49] studied 49 patients with chronic ischemic heart disease and LV dysfunction (mean EF 0.32). Echocardiographic images were obtained at rest and during infusion of dobutamine at 5, 10, 15, and 20 mcg/kg/min. Contractile reserve was defined as improved wall thickening in at least two adjacent segments with resting wall motion abnormalities and an improvement of ≥20% in wall motion score index (i.e. improvement at the 95% confidence level). Figure 7 shows that the presence of contractile reserve predicted post-operative improvement in wall motion score in 25 patients who underwent successful coronary artery bypass surgery.

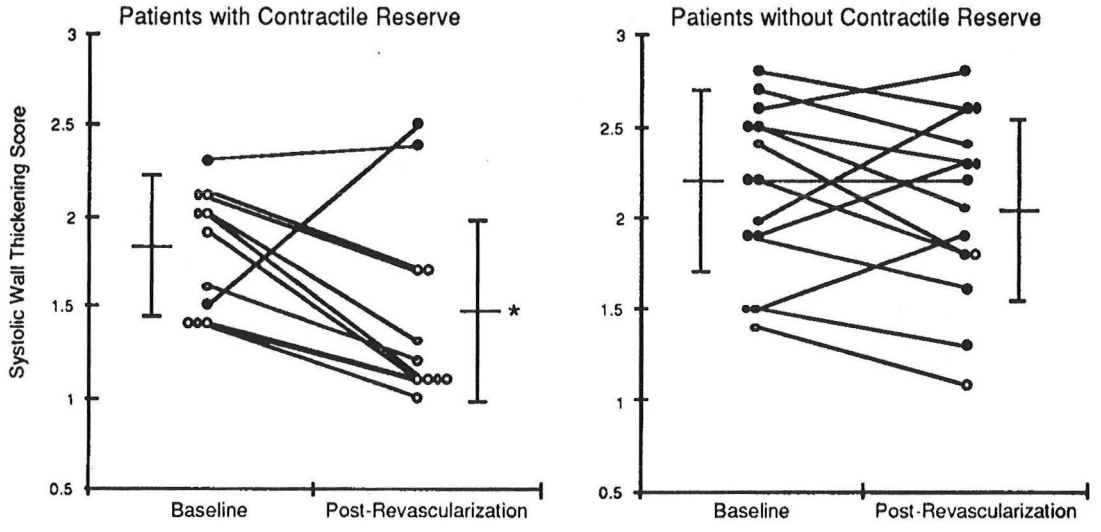


Figure 7. Results of DSE in 25 patients who underwent successful coronary revascularization. Wall motion score index improved after revascularization in patients with contractile reserve (left panel, p=0.003) but not in patients without contractile reserve (right panel).

Several studies have now shown that DSE can identify contractile reserve and predict improvement in regional left ventricular function after coronary revascularization in chronic ischemic heart disease and acute myocardial infarction (Table 5).

Table 5. DSE in predicting LV functional recovery.

	Pt population	# of pts	# of abn segs	Pos pred value	neg pred value
Pierard[46]	Anterior MI	17	84	60%*	100%*
Barilla[45]	Anterior MI	21	NA	77%	NA
Smart[47]	Acute MI	51	NA	90%*	90%*
Salustri[48]	Acute MI	57	189	79%	88%
Cigarroa[49]	Chronic CAD	25	NA	82%*	86%*
LaCanna[50]	Chronic CAD	33	334	90%	77%
Afridi[51]	Chronic CAD	20	114	59-72%	86%
deFilippi[52]	Chronic CAD	23	201	85%	94%
Perrone-Filardi[53]	Chronic CAD	18	79	91%	82%

* data analyzed by patient rather than by segment.

Myocardial contrast echocardiography (MCE)

Myocardial contrast echocardiography (MCE) is a relatively new technique that provides the ability to assess perfusion and contractile function simultaneously. MCE has been used extensively in animal and human research over the past 10 years. Briefly, an echocardiographic contrast agent, either sonicated angiographic contrast or commercially prepared albumin-coated microbubbles, is delivered by intracoronary injection at cardiac catheterization. The microbubbles are approximately the size of red blood cells and thus are small enough to pass through the microcirculation without occluding blood flow. These contrast agents are easily visualized echocardiographically as a echodense blush in the myocardium.

The safety of myocardial contrast agents has been well documented and the hemodynamic effects of sonicated angiographic contrast are identical to those seen with non-sonicated contrast in humans and animal models.[68,69] Two recent studies in humans have demonstrated collateral flow to the infarct zone shortly after an acute myocardial infarction by MCE in patients with totally occluded infarct arteries.[70,71] The presence of collaterals by MCE was associated with better regional function than those without collaterals to the infarct zone.[71] Greater than 50% collateralization within an infarct zone predicted improvement in wall motion one month after successful coronary angioplasty of a totally occluded infarct artery.[71] The lack of correlation between collateral flow by MCE and angiography in these studies partly reflects the poor sensitivity of the latter, since angiography can only visualize vessels as small as 100μm. However, some patients demonstrated clear angiographic collaterals despite absence of myocardial perfusion. This may reflect microvascular dysfunction and emphasizes the fact that epicardial coronary patency and tissue perfusion may be dissociated. Accordingly, MCE is now becoming the gold standard for determining collateral circulation and assessing myocardial perfusion after myocardial infarction.

Recent studies suggest that perfusion by MCE is able to predict recovery of LV function after myocardial infarction[72,73] and in patients with chronic ischemic heart disease.[52] Although such studies are promising, MCE is currently limited by the requirement for intracoronary injection of the contrast agent. New contrast agents that are capable of crossing the pulmonary circulation via peripheral venous injection are being developed. One such agent has recently been shown to accurately define myocardial area at risk and infarct size from a peripheral venous injection in the canine model of acute myocardial ischemia.[74]

Magnetic Resonance Imaging

Recent advances in MRI offer great potential for assessing myocardial viability. Due to its excellent spatial resolution, MRI is able to reproducibly detect small changes in wall thickening with dobutamine.[75] Recently, MRI has been shown to accurately measure epicardial coronary flow in the dog.[76] Finally, ^{31}P MRI spectroscopy can detect high energy phosphate concentration in the anterior myocardium as a marker of viability.[77] Thus, the potential exists to assess perfusion, contractile reserve, and metabolic activity in patients with LV dysfunction using MRI imaging. However, since these MRI methods are new, clinical studies to predict LV functional recovery have not yet been done.

Influence of Myocardial Viability on Prognosis

Few studies have addressed the influence of myocardial viability on prognosis. Eitzman, et al[13] reported death (n=6) or nonfatal myocardial infarction (n=3) in 9 of 18 patients with viable myocardium by PET scan who did not undergo revascularization. In contrast, patients with viable myocardium who were revascularized had a good prognosis. Similar results have been reported by DiCarli, et al[78] who showed adverse events in 7 of 17 patients with non-revascularized viable myocardium. More recently, Lee et al[79] studied 129 patients with resting LV dysfunction after myocardial infarction. Nonfatal cardiac ischemic events occurred in 12%/year of the overall group, but in 34%/year of patients with viable myocardium (by PET scan) who were not revascularized. Gioia, et al[80] recently showed that evidence of viability by thallium imaging predicted survival in 85 patients with ischemic cardiomyopathy who underwent revascularization. Patients with viable myocardium who were not revascularized had a 45% mortality (9 of 20) over a mean followup period of 31 months. While the above data are not randomized and suffer from selection bias, they support the concept that the amount of viable myocardium at risk is a important predictor of subsequent cardiac events.[81,82]

Conclusions

Several clinical techniques have been developed to distinguish reversible from irreversible LV dysfunction. These methods have great promise for selection of patients for myocardial revascularization procedures. Nevertheless, much remains to be learned about the biology of myocardial stunning and hibernation in man before these techniques can be fully optimized. In addition, larger prospective studies are needed to determine the accuracy of these techniques in predicting LV functional recovery and survival in patients.

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