Journal of the American College of Cardiology Vol. 47, No. 5, 2006

ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2005.11.038

EDITORIAL COMMENT

Hibernating Myocardium

Another Piece of the Puzzle Falls Into Place*

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Revascularization of hibernating myocardium (HM) (1–5) improves or normalizes left ventricular (LV) ejection fraction (EF) and the patient's New York Heart Association functional class (6). Allman et al. (7) have analyzed data from 24 studies involving 3,088 patients who had LVEF of 0.32 ± 0.08 and follow-up at 25 ± 10 months. Patients who had revascularization when compared to "medical therapy" showed that (7): 1) in those with HM, mortality was lower (3.2% vs. 16.0 %, $p < 0.0001$), and 2) the lower the LVEF, the greater was the reduction in mortality. In addition, the composite of subsequent myocardial infarction (MI), heart failure, and unstable angina was also lower (6.0% vs. 12.2%, $p < 0.001$) (8). These benefits were not seen in patients without HM but who nonetheless had been revascularized (7,8).

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In this issue of the *Journal*, Ambrosio et al. (9) have presented the findings of a carefully performed study which shows that in patients with either non–Q-wave MI or no previous MI but with LV wall motion abnormality and HM, there is remodeling of the LV; that is, LV end-diastolic volume (EDV) and end–systolic volume (ESV) are increased and the LV is more spherical. Thus, they have documented that the mere presence of LV systolic dysfunction with HM can lead to LV *remodeling*. They have also documented that: 1) revascularization in those with HM results in *reverse remodeling*; that is, there is a reduction of the increased LVEDV and LVESV, the LV is less spherical, and LVEF increases (for all changes $p < 0.00l$); 2) this reverse remodeling was not seen in patients who did not have HM but nonetheless had been revascularized; and 3) the extent of the reverse remodeling was related to the number of viable segments identified by "low-dose" dobutamine echocardiography and the LV spericity index at baseline (for both changes, $p < 0.001$).

The study by Ambrosio et al. (9) was well done: 1) the inclusion criteria were appropriate; 2) patients who had acute coronary syndrome in the preceding three months were excluded; 3) left ventricular dysfunction was reconfirmed three weeks later, just before revascularization; 4) off-line analysis of the echocardiograms was performed by two investigators without knowledge of clinical and angiographic data, and disagreements in interpretation were resolved by consensus; 5) reproducibility of the LV volume measurements was very good, the mean ± SD difference for LVEDV was −0.57 ± 12 ml ($r = 0.96$); 6) the intra- and interobserver agreement of stress-echocardiographic readings in their laboratory had previously been documented to be >90%; 7) the follow-up study was performed 7.6 ± 3.3 months after revascularization; and 8) hibernating myocardium was diagnosed by the response of the LV to "low dose" dobutamine.

Similar reverse remodeling was also seen in an ongoing, long-term prospective study (G. La Canna, personal communication, 2005). Patients with HM who before revascularization had shown improvement of LVEF with low-dose dobutamine had, by the time of hospital discharge after coronary artery bypass graft surgery, reductions in LVEDV (from 194 ± 46 ml to 179 ± 41 ml; $p < 0.007$) and in LVESV (from 141 ± 40 ml to 102 ± 40 ml, $p = 0.0001$), and increases of LVEF (from 0.29 ± 0.10 to 0.43 ± 0.13, $p < 0.0001$) (10). In retrospect, remodeling and reverse remodeling should have been obvious from the beginning (Fig. 1) (1).

The early remodeling documented in the study by Ambrosio et al. (9) provides one aspect of the early phase of HM and provides an opportunity to develop a probable course of progression and regression of LV remodeling (Fig. 2). The early stage of HM, when patients only have wall motion abnormalities and remodeling either has not occurred or is only minimal (Figs. 2B and 2C) may reverse to normal (Fig. 2A), and thus may also be the "golden time" for revascularization of HM. With time, LV remodeling progressively increases and the amount of benefit of reverse remodeling may decline (Figs. 2C to 2D). In the end stage of the disorder (Fig. 2E), the benefit of revascularization needs to be studied. If the patients only have single-vessel disease, revascularization for HM will also need to be performed even if LV remodeling has occurred (Figs. 1, 2C and 2D).

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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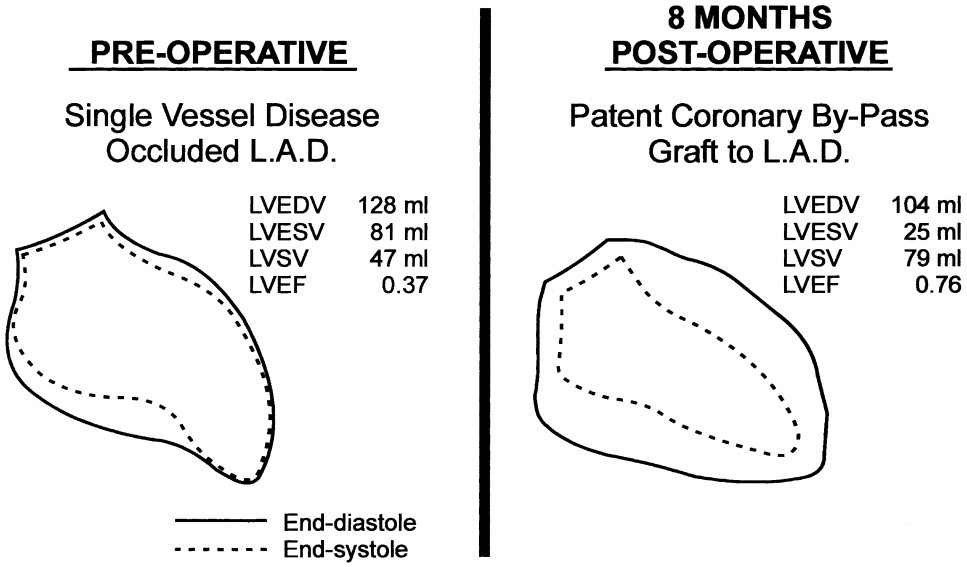

Figure 1. Preoperative and postoperative left ventricular function in a patient with hibernating myocardium. Adapted from Rahimtoola (1). LAD = left anterior descending coronary artery; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVSV = left ventricular stroke volume.

The findings in these studies raise an important clinical question and a dilemma. Do all of these patients need a diagnostic test for HM? Ideally, yes; but the important *question* is, which non-invasive test(s) should one use (10)? A review has shown the sensitivity, specificity, and predictive accuracies of dobutamine echocardiography; radionuclide studies and positron emission tomography range from 50% to 93% (Table 1) (11). Positron emission tomography is the most sensitive but the least specific. Dobutamine echocardiography provided a good and almost balanced sensitivity and specificity (Table 1). Recently, cardiovascular magnetic resonance (CMR) has brought a lot of excitement to the field (12) because of its sensitivity in detecting and its ability to better determine the extent of infarcted myocardium. A recent review (13) has clarified the strengths and weaknesses of CMR in the diagnosis of myocardial viability; it has also emphasized additional studies of CMR that need to be performed. Two studies using only high-quality, two-dimensional echocardiograms showed that when the LV wall thickness of the affected region of LV systolic dysfunction was ≤5 to 6 mm, the probability of recovery of function was ≤5% (14,15). Baer et al. (16) have docu-

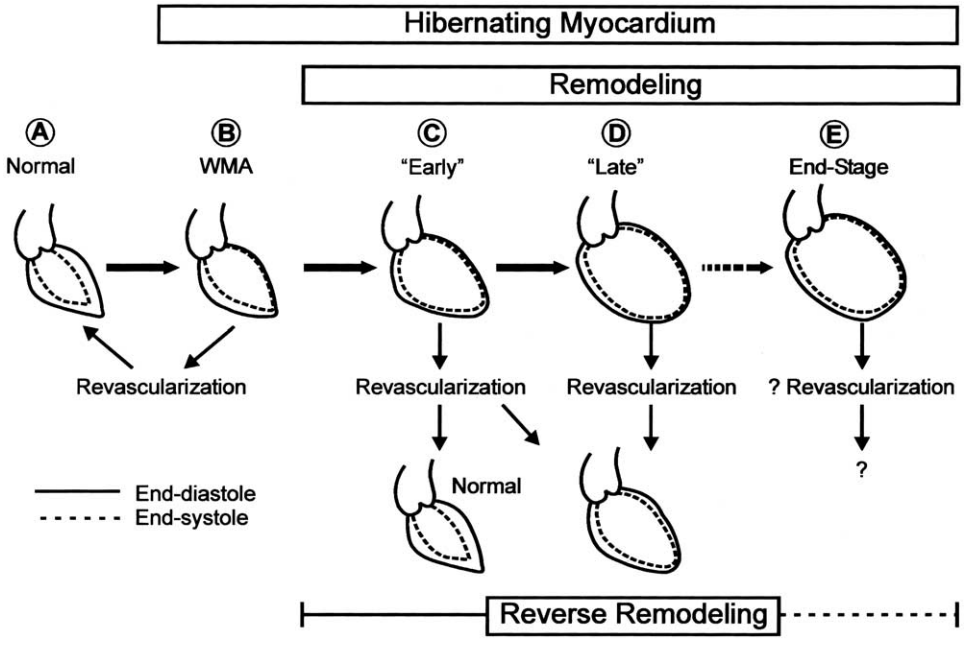

Figure 2. Diagrammatic representation of postulated progressive changes in a patient with hibernating myocardium and no remodeling **(B)**, mild to moderate remodeling **(C and D)**, and end stage **(E)** of the disorder. For details, see text. WMA = wall motion abnormality.

Table 1. Sensitivity, Specificity, and Predictive Accuracies for Improvement of Left Ventricular Function After Revascularization

	Sensitivity (%)	Specificity (%)	Predictive Values of	
			Positive Test (%)	Negative Test (%)
Dobutamine echocardiography*	81	80	77	85
Radionuclide†	81–86	50–66	69–71	77–80
Positron-emission tomography‡	93	58	71	86

*32 studies, 1,090 patients; †53 studies; 1,346 patients; ‡20 studies; 598 patients. Adapted from Bax J et al. (11).

mented that patients with LV wall thickness on CMR of ≥5.5 mm had preserved glucose utilization, whereas those with wall thickness <5.5 mm had reduced glucose utilization. With wall thickness ≥5 to 6 mm, recovery of function was about 50%, and an additive test, dobutamine echocardiogram or radionuclide study, provided equal incremental diagnostic values of about 25% to 30% in predicting improvement of LVEF after revascularization (14,15). Left ventricular wall thickness by echocardiography appears to be the simplest non-invasive test. The role of contrast echocardiography and of Doppler tissue imaging to assess wall thickness and wall motion needs to be explored. Patients who before revascularization showed improvement of wall motion abnormalities with low-dose dobutamine exhibited a greater amount of reverse remodeling after revascularization (9,14,15); thus, low-dose dobutamine echocardiography is clinically useful and can be of incremental clinical value when combined with any of the other test(s), if it is properly done.

The *dilemma* is the lack of perfect, or a 95% accurate, test of HM. Therefore, there continues to be a need for further research and appropriate clinical judgment (17). One such example for the latter can be: In selected patients, if the test(s) for HM are equivocal and revascularization is the best, or possibly the only good, chance of improvement of LV function, revascularization should be seriously considered if it can be performed at low risk with a high probability of success.

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