

# Combined Assessment of Microvascular Integrity and Contractile Reserve Improves Differentiation of Stunning and Necrosis After Acute Anterior Wall Myocardial Infarction

Michael L. Main, MD, FACC, Anthony Magalski, MD, FACC, Becky A. Morris, RDCS, Michael M. Coen, MA, David G. Skolnick, MD, FACC, Thomas H. Good, MD, FACC  
*Kansas City, Missouri*

<b>OBJECTIVES</b>	We sought to determine the relative accuracy of myocardial contrast echocardiography (MCE) and low-dose dobutamine echocardiography (LDDE) in predicting recovery of left ventricular (LV) function in patients with a recent anterior wall myocardial infarction (MI).
<b>BACKGROUND</b>	Left ventricular dysfunction after acute MI may be secondary to myocardial stunning or necrosis. Myocardial contrast echocardiography allows real-time echocardiographic perfusion assessment from a venous injection of a fluorocarbon-based contrast agent. Although this technique is promising, it has not been compared with LDDE.
<b>METHODS</b>	Forty-six patients underwent baseline wall motion assessment, MCE, and LDDE two days after admission, as well as follow-up echocardiography after a mean period of 53 days.
<b>RESULTS</b>	Perfusion by MCE predicted recovery of segmental function with a sensitivity of 69%, specificity of 85%, positive predictive value of 74%, negative predictive value of 81%, and overall accuracy of 78%. Contractile reserve by LDDE predicted recovery of segmental function with a sensitivity of 50%, specificity of 88%, positive predictive value of 72%, negative predictive value of 73%, and overall accuracy of 73%. Concordant test results occurred in 74% of segments and further increased the overall accuracy to 85%. The mean wall motion score at follow-up was significantly better in perfused versus nonperfused segments (1.9 vs. 2.6, $p < 0.0001$ ) and in segments with contractile reserve, compared with segments lacking contractile reserve (1.9 vs. 2.5, $p < 0.0001$ ).
<b>CONCLUSIONS</b>	Myocardial contrast echocardiography compares favorably with LDDE in predicting recovery of regional LV dysfunction after acute anterior wall MI. Concordant contractile reserve and myocardial perfusion results further enhance the diagnostic accuracy. (J Am Coll Cardiol 2002;40:1079-84) © 2002 by the American College of Cardiology Foundation

In patients with a recent myocardial infarction (MI), regional left ventricular (LV) dysfunction may occur as a result of necrosis or myocardial stunning ("prolonged, postischemic dysfunction without necrosis") (1). Differentiating between these two conditions is important: necrotic tissue is subject to infarct expansion, which, in turn, promotes LV dilation (2), whereas stunned tissue is viable and eventually regains normal contractile function, provided adequate tissue perfusion is restored.

Low-dose dobutamine echocardiography (LDDE) is the current reference method for assessing myocardial viability after infarction; transient improvement in regional myocardial function with inotropic stimulation predicts recovery of regional myocardial function with a high specificity (3-5). Unfortunately, this technique is somewhat time-consuming, interpretation is difficult, and studies cannot be performed in patients already receiving inotropic support or exhibiting complex ventricular arrhythmias.

Myocardial contrast echocardiography (MCE) has

emerged as a potentially useful means of studying myocardial perfusion in coronary artery disease, including assessment of microvascular integrity after MI (6,7). Recently, we (8) and others (9-11) have demonstrated that "perfusion-contraction mismatch" identified by MCE early after infarction reliably predicts spontaneous recovery of regional LV function in the weeks after MI. Compared with LDDE, MCE is relatively quick and easy to perform and is safe in critically ill patients.

The aim of this study was to compare the accuracy of power pulse inversion MCE with that of LDDE in patients with akinetic myocardial segments after a recent anterior wall MI. In addition, we sought to determine the frequency and incremental diagnostic benefit of concordant test results.

## METHODS

**Study design.** We prospectively studied patients with a confirmed recent anterior wall MI (12). Inclusion criteria included: 1) biochemical evidence of recent myocardial necrosis; 2) wall motion abnormalities, as shown by echocardiography, within the distribution of the left anterior descending coronary artery (LAD); and 3) antegrade flow within the LAD by angiography before the study. Patients

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#### Abbreviations and Acronyms

IRA	= infarct-related artery
LAD	= left anterior descending coronary artery
LDDE	= low-dose dobutamine echocardiography
LV	= left ventricular
MCE	= myocardial contrast echocardiography
MI	= myocardial infarction
TIMI	= Thrombolysis In Myocardial Infarction trials

with a previous anterior wall MI were excluded. The Institutional Review Board of St. Luke's Hospital approved the study, and patients gave written, informed consent before participation.

Patients underwent LDDE and MCE a mean of two days (range 0 to 6) after hospital admission. All patients also underwent coronary angiography before the study. Patients returned a mean of 53 days after the baseline examinations for follow-up echocardiography to assess their recovery of function.

**Patient group.** Fifty-two patients underwent LDDE and MCE after admission with an acute anterior MI. Four patients died before follow-up, and two patients did not return. The remaining 46 patients (29 men and 17 women; mean age  $60 \pm 15$  years) comprised the study group.

Coronary angiography identified single-vessel disease in 27 patients, two-vessel disease in 12 patients, and three-vessel disease in 7 patients. Only two patients had undergone previous coronary artery bypass graft surgery, and in both cases, the infarct-related artery (IRA) was the saphenous vein graft to the LAD. Thrombolytic therapy was administered to 9 patients, whereas 43 patients underwent a percutaneous coronary intervention. All patients had enzymatic evidence of recent myocardial necrosis (mean peak creatine kinase, MB fraction of 241 IU/l).

Thrombolysis In Myocardial Infarction (TIMI) trial flow grade 3 was present in the IRA before MCE in 43 patients. In the remaining three patients, two had TIMI flow grade 2 and one had TIMI flow grade 1. With the exception of one patient who presented with subacute stent thrombosis approximately one week after hospital discharge, there were no known significant adverse clinical events between viability assessment and follow-up echocardiography.

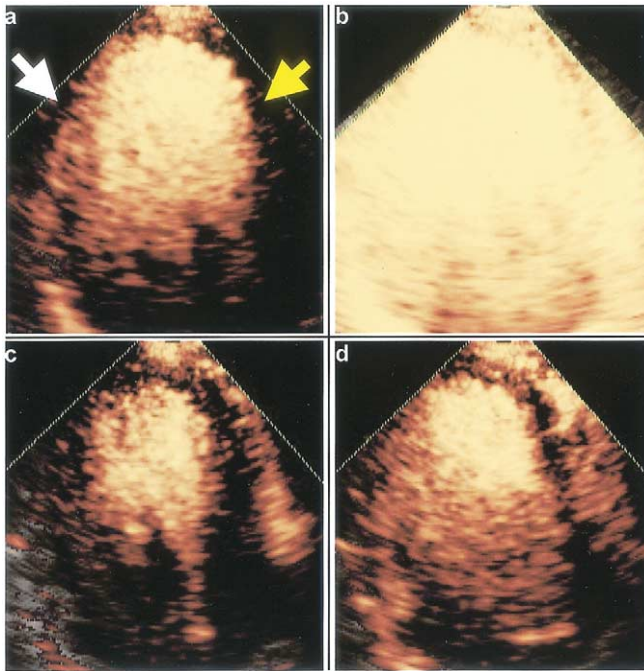
**Echocardiography.** Imaging was performed using an ATL HDI 5000 echocardiography machine (ATL Ultrasound, Bothell, Washington). Baseline imaging was performed at bedside with the patient in the left lateral decubitus position. If an intra-aortic balloon pump or arterial sheath was in place, imaging was performed with the patient supine. Apical four-chamber, apical two-chamber, apical long-axis, and parasternal short-axis views were digitally acquired in all patients. Tissue harmonic imaging was used to enhance endocardial resolution.

After acquisition of baseline images, LDDE was performed to assess contractile reserve. Dobutamine was in-

fused intravenously in serial 3-min stages at 5, 10, and 20  $\mu\text{g}/\text{kg}$  per min. Images were again digitally acquired at the conclusion of each dobutamine stage and displayed in a standard quad-screen format for subsequent review. Beta-blockers were administered on the day of the study, as clinically prescribed.

Next, MCE was performed as previously described (8), using power pulse inversion imaging. Specific instrumentation settings included the following: a mechanical index of 0.16, low dynamic range, and maximal line density. These settings allowed a frame rate  $>15$  Hz during perfusion imaging. Optison (Tyco/Mallinkrodt, St. Louis, Missouri) was slowly injected as a bolus (0.3–0.5 ml of contrast at  $\sim 1$  cc/s) through a preexisting intravenous catheter, using a saline flush. Optison is a commercially available "second-generation" fluorocarbon-based echocardiographic contrast agent (7). After venous injection, these microbubbles traverse the pulmonary circulation, acting as red blood cell tracers within the systemic circulation, including the myocardial microvasculature (13). The injection was terminated once the contrast agent appeared in the right ventricular cavity. Separate injections were performed for each of the three apical views. A physician performed all contrast injections, with slight adjustments in contrast quantity and bolus rate, depending on the adequacy of an initial test injection in the apical four-chamber view. We injected the minimal amount of contrast agent necessary to achieve myocardial opacification outside the infarct zone, while avoiding attenuation and blooming artifacts. Manually triggered, transient, high mechanical index imaging ("flash imaging") was employed at peak contrast intensity to destroy microbubbles within the myocardium, to exclude artifact, and to observe myocardial replenishment (14) (Fig. 1). For frame rates  $>15$  Hz, five sequential "flash" frames were used.

**Echocardiographic analysis.** An experienced echocardiographer (Dr. Magalski) who had no knowledge of the clinical and angiographic data scored all echocardiographic images. For each patient, LDDE (including baseline imaging), MCE, and follow-up echocardiography were assessed at separate sittings to avoid bias. Digital LDDE and follow-up echocardiographic images were reviewed in a quad-screen format using commercially available software (ProSolv, Indianapolis, Indiana) and workstation components, whereas MCE images were recorded and reviewed on videotape. Wall motion scoring for LDDE and follow-up echocardiography were performed using the standard 16-segment model of the American Society of Echocardiography (15). Segments were scored as normal, hypokinetic, or akinetic. Akinetic segments at baseline within the distribution of the LAD, including the anterior, anteroseptal, septal, and apical walls, were included in the subsequent analysis. The MCE images were also scored using the standard 16-segment model, with a similar semi-quantitative scoring scheme based on visual analysis, as normally perfused, "patchy" perfusion, or perfusion defect.



**Figure 1.** These myocardial contrast echocardiography (MCE) images were obtained in a 52-year-old man, two days after he presented with an anterior myocardial infarction. (a) Apical long-axis perfusion image revealing a normally perfused posterior wall (white arrow) and an anteroseptal and apical transmural perfusion defect (yellow arrow). In these power pulse inversion MCE images, the left ventricular (LV) cavity appears yellow, whereas the perfused myocardium appears orange. (b) “Flash” imaging with a high mechanical index (see text for details). (c) The image immediately after “flash” or destruction frames. Note a lack of contrast effect throughout the myocardium, with residual LV cavity opacification. (d) Several cardiac cycles later after microbubble replenishment, perfusion is again noted in the posterior wall, with a perfusion defect in the left anterior descending coronary artery distribution. As predicted by MCE, follow-up echocardiography nearly two months later revealed continued akinesia throughout the infarct zone.

Contractile reserve by LDDE was defined as transient improvement of at least one grade (akineti c to either hypokinetic or normal). Segmental recovery of function was defined as improvement of at least one grade from baseline to follow-up echocardiography (akineti c to either hypokinetic or normal). Sensitivity, specificity, positive and negative predictive values, and overall accuracy were calculated for recovery of function for both techniques and for concordant test results. Overall accuracy, or “rate of correct classification,” was defined as the sum of true-positive and true-negative test results divided by the total sample number. Concordant test results were defined as all segments for which MCE and LDDE showed agreement for the prediction of segmental recovery of function (perfusion and contractile reserve or perfusion defect and lack of contractile reserve). Wall motion scores were analyzed with repeated measures analysis of variance, with the fixed effects of group (perfusion vs. no perfusion) and time (baseline vs. follow-up), a group  $\times$  time interaction, and an intrasubject correlation structure. A  $p$  value  $<0.05$  was deemed statistically significant.

## RESULTS

All 16 myocardial segments were adequately visualized by LDDE and follow-up echocardiography in all patients, and a total of 329 akinetic segments were identified within the distribution of the IRA ( $7.3 \pm 0.7$  segments/patient). Three percent ( $n = 10$ ) of segments were not adequately visualized during MCE. Thus, 319 akinetic myocardial segments were available for complete analysis. On follow-up imaging, 61% ( $n = 195$ ) of segments were akinetic; 12% ( $n = 39$ ) were hypokinetic; and 27% ( $n = 85$ ) were normal.

Myocardial contrast echocardiography revealed normal perfusion in 28% ( $n = 90$ ) of akinetic segments, “patchy” perfusion in 8% ( $n = 26$ ), and a perfusion defect in 63% ( $n = 203$ ). The combined end point of either normal or patchy perfusion predicted segmental recovery of function with a sensitivity of 69%, specificity of 85%, positive predictive value of 74%, negative predictive value of 81%, and overall accuracy of 78%. In addition, the mean wall motion score index at follow-up was significantly better in perfused segments, compared with segments with a perfusion defect (Fig. 2).

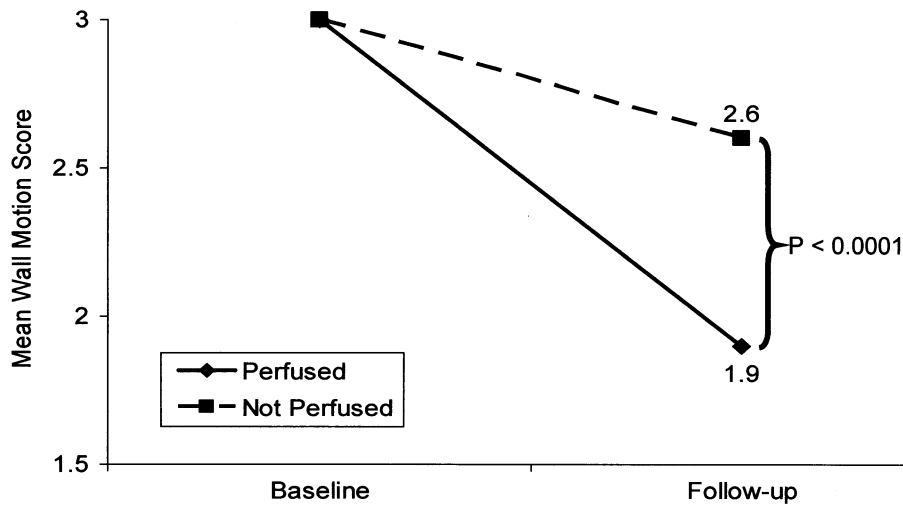
Low-dose dobutamine echocardiography revealed contractile reserve in 27% ( $n = 87$ ) of segments. Contractile reserve predicted recovery of function with a sensitivity of 50%, specificity of 88%, positive predictive value of 72%, negative predictive value of 73%, and overall accuracy of 73%. In addition, the mean wall motion score index at follow-up was significantly better in segments with contractile reserve, compared with segments lacking contractile reserve (Fig. 3).

Concordant test results (perfusion defect and lack of contractile reserve or perfusion and contractile reserve) were identified in 74% of segments (Fig. 4). Concordant results further enhanced the overall diagnostic accuracy, with a sensitivity of 67%, specificity of 93%, positive predictive value of 81%, negative predictive value of 86%, and overall accuracy of 85%.

Fifteen (33%) of the 46 perfusion studies were reviewed for intraobserver and interobserver variability for perfusion or no perfusion within akinetic segments. Intraobserver and interobserver variabilities were 22% and 26%, respectively.

## DISCUSSION

Residual LV function after acute MI is a primary determinant of long-term survival (16), and patients with a significantly reduced ejection fraction are subject to increased post-MI complications. Thus, differentiation between stunned and necrotic myocardium early after infarction may aid in risk stratification, identifying patients at increased risk of congestive heart failure, ventricular tachycardia, and death. In this study, we have shown that MCE compares favorably with LDDE in detecting stunned myocardium and predicting spontaneous recovery of LV function. In addition, concordant MCE and LDDE test results occurred



**Figure 2.** Comparison of mean wall motion scores at follow-up in initially akinetic segments, stratified by the myocardial contrast echocardiography result. Perfused segments demonstrated a significantly lower (better) wall motion score index at follow-up ( $p < 0.0001$ ). **Solid line** = perfused segments; **dashed line** = segments with a perfusion defect.

in the majority of myocardial segments, further enhancing the overall diagnostic accuracy.

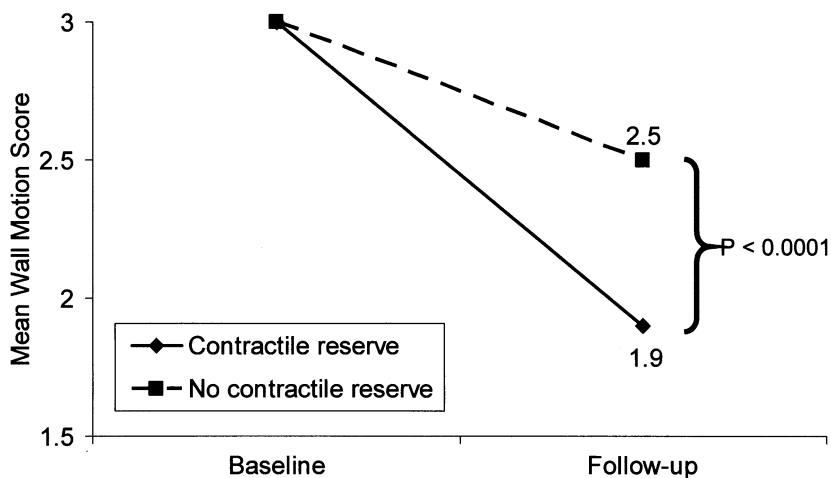
**Comparison with previous studies.** Ito et al. (17) first used MCE to define “no-reflow” after mechanical or pharmacologic revascularization in patients with an acute anterior wall MI. When using an intracoronary injection of contrast agent, there was a lack of contrast effect in the infarct zone (despite anterograde flow in the LAD by angiography) in 23% of patients. This predicted a lack of functional recovery and increased postinfarction complications (18). Recently, we (8) and others (9–11) have extended these findings, using intravenously injected contrast agents to identify “perfusion-contraction mismatch” early after MI.

The integrity of the myocardial contractile apparatus has also been extensively studied, using inotropic stress, in dyssynergic myocardial segments early after MI. Several

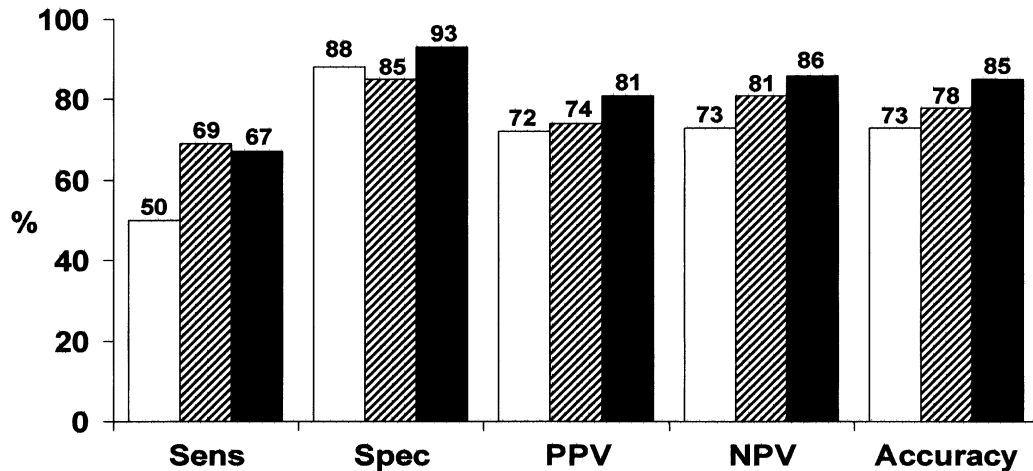
studies in the early 1990s concluded that contractile reserve elicited during low-dose dobutamine infusion accurately predicts recovery of segmental myocardial function with particularly good specificity (3–5).

Since then, several investigations have compared the ability of LDDE and MCE to predict recovery of LV function early after MI, but all used intracoronary contrast agents, and MCE and LDDE were not simultaneously performed (19–21). The use of intravenous contrast agents and simultaneous contractile reserve and perfusion assessment are unique to the present study.

**Recommendations for clinical use.** Based on our results, both LDDE and MCE appear clinically useful for assessing myocardial viability early after infarction. For each measure of diagnostic utility, intravenous MCE performed at least as well as LDDE—the reference standard technique. At our institution, the majority of patients with an acute MI are



**Figure 3.** Comparison of mean wall motion scores at follow-up in initially akinetic segments, stratified by the low-dose dobutamine echocardiography result. Segments with contractile reserve demonstrated a significantly lower (better) wall motion score index at follow-up ( $p < 0.0001$ ). **Solid line** = contractile reserve; **dashed line** = lack of contractile reserve.



**Figure 4.** Diagnostic accuracy of low-dose dobutamine echocardiography (LDDE), myocardial contrast echocardiography (MCE), and concordant test results. For each measure of diagnostic utility, MCE performed at least as well as LDDE, with the former having a higher sensitivity. Concordant test results occurred in 74% of segments and, when present, further enhanced the overall accuracy. **White bars** = LDDE; **lined bars** = MCE; **black bars** = concordant test results. NPV = negative predictive value; PPV = positive predictive value.

treated with an urgent, primary percutaneous coronary intervention. Those patients initially treated with thrombolytic therapy at other hospitals undergo early coronary angiography, and their coronary anatomy is always known at the time of viability assessment. As such, we are not routinely interested in using dobutamine echocardiography to exclude residual LAD stenosis or to evaluate ischemia in the circumflex or right coronary artery distribution; MCE alone may be sufficient. At institutions where a primary coronary intervention or early angiography after thrombolytic therapy is not routinely performed, LDDE may be the preferred diagnostic technique to exclude inducible ischemia, in addition to viability assessment.

Compared with LDDE, MCE has several distinct advantages. Although both sonographers and echocardiographers require additional training to avoid potential obstacles in the performance and interpretation of MCE examinations (such as blooming and attenuation artifacts), in our experience, this technique is now easily learned and applied, and studies are usually feasible, even in patients with difficult two-dimensional images. In addition, studies are quickly and safely performed at bedside, even in critically ill patients already requiring inotropic support or exhibiting complex ventricular ectopy.

In contrast, LDDE is relatively time-consuming; usually requires additional personnel to monitor hemodynamics, symptomatic status, and the electrocardiogram; and may induce myocardial ischemia or ventricular tachycardia. Transient improvement in akinetic segments is often subtle, and accurate interpretation requires readers with significant experience in this technique. Also, patients with severe LV dysfunction and heart failure early after MI often require inotropic support with dobutamine or a phosphodiesterase inhibitor, which would confound the LDDE results.

Although a combined assessment of contractile reserve and microvascular integrity enhances the diagnostic accu-

ry, the test results are generally concordant, and performance of both examinations usually provides redundant results. In a busy clinical practice, we believe that MCE is the preferable technique, based on ease of use, safety, and diagnostic accuracy.

Currently, reimbursement for U.S. Food and Drug Administration (FDA)-approved echocardiographic contrast agents is limited to use in enhancing endocardial border delineation in technically difficult studies or salvaging suboptimal Doppler examinations (7). Thus, widespread use of MCE for viability assessment will await further confirmatory studies (22) and FDA approval for use in myocardial perfusion assessment.

**Study limitations.** Our study is limited by a relatively small number of patients. However, the study group was quite homogeneous in that the patients had an acute anterior wall MI with angiographically documented patent IRAs, and the results should be widely applicable. We did not assess the ability of either technique to predict global recovery of function after MI. The use of MCE to predict recovery of overall LV function after a first-time anterior MI is the subject of an ongoing study in our laboratory. Finally, we did not compare these two techniques for infarctions in the circumflex or right coronary artery distribution, and the results may not be comparable in patients with inferior, posterior, or lateral infarctions. The basilar LV segments and lateral wall are often difficult to image with MCE, due to attenuation artifacts, and in these cases, LDDE may be the preferable technique. However, the largest infarcts (in which viability assessment is clinically useful) are usually anterior, and the entire LAD distribution is easily visualized by MCE.

Other modalities are available for the assessment of myocardial viability after infarction, including nuclear scintigraphy, positron emission tomography, and magnetic resonance imaging with contrast media (3,23). We believe that

either LDDE or MCE, or a combination of these two techniques, will be favored based on high diagnostic accuracy, widespread availability, portability, lack of radiation exposure, and relatively low cost.

**Conclusions.** Myocardial contrast echocardiography compared favorably with LDDE for the assessment of myocardial viability in patients with regional LV dysfunction after an acute anterior wall MI. Concordant contractile reserve and myocardial perfusion results were found in the majority of myocardial segments and, when present, further enhanced the diagnostic accuracy.

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**Reprint requests and correspondence:** Dr. Michael L. Main, Cardiovascular Consultants, 4330 Wornall Road, Suite 2000, Kansas City, Missouri 64111. E-mail: mmmain@cc-pc.com.

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## REFERENCES

1. Braunwald E, Kloner RA. The stunned myocardium: prolonged, post-ischemic ventricular dysfunction. *Circulation* 1982;66:1146-9.
2. Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction: experimental observations and clinical implications. *Circulation* 1990;81:1161-72.
3. Pierard LA, deLandsheere CM, Berthe C, Rigo P, Kulbertus HE. Identification of viable myocardium by echocardiography during dobutamine infusion in patients with myocardial infarction after thrombolytic therapy: comparison with positron emission tomography. *J Am Coll Cardiol* 1990;15:1021-31.
4. Smart SC, Sawada S, Ryan T, et al. Low dose dobutamine echocardiography detects reversible dysfunction after thrombolytic therapy of acute myocardial infarction. *Circulation* 1993;88:405-15.
5. Watada H, Ito H, Oh H, et al. Dobutamine stress echocardiography predicts reversible dysfunction and quantitates the extent of irreversibly damaged myocardium after reperfusion of anterior myocardial infarction. *J Am Coll Cardiol* 1994;24:624-30.
6. Kaul S. Myocardial contrast echocardiography: 15 years of research and development. *Circulation* 1997;96:3745-60.
7. Main ML, Grayburn PA. Clinical applications of transpulmonary contrast echocardiography. *Am Heart J* 1999;137:144-53.
8. Main ML, Magalski A, Chee NK, Coen MM, Skolnick DG, Good TH. Full-motion pulse inversion power Doppler contrast echocardiography differentiates stunning from necrosis and predicts recovery of left ventricular function after acute myocardial infarction. *J Am Coll Cardiol* 2001;38:1390-4.
9. Swinburn JMA, Lahiri A, Senior R. Intravenous myocardial contrast echocardiography predicts recovery of dyssynergic myocardium early after acute myocardial infarction. *J Am Coll Cardiol* 2001;38:19-25.
10. Lepper W, Hoffmann R, Kamp O, et al. Assessment of myocardial reperfusion by intravenous myocardial contrast echocardiography and coronary flow reserve after primary percutaneous transluminal coronary angiography in patients with acute myocardial infarction. *Circulation* 2000;101:2368-74.
11. Rocchi G, Kasprzak D, Galema TW, de Jong N, Ten Cate F. Usefulness of power Doppler contrast echocardiography to identify reperfusion after acute myocardial infarction. *Am J Cardiol* 2001;87:278-82.
12. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined: a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-69.
13. Skyba DM, Camarano G, Goodman BS, Price RJ, Skalak TC, Kaul S. Hemodynamic characteristics, myocardial kinetics and microvascular rheology of FS-069, a second generation echocardiographic contrast agent capable of producing myocardial opacification from a venous injection. *J Am Coll Cardiol* 1996;28:1292-300.
14. Pelberg RA, Wei K, Kamiyama N, Sklenar J, Bin J, Kaul S. Potential advantage of flash echocardiography for digital subtraction of B-mode images acquired during myocardial contrast echocardiography. *J Am Soc Echocardiogr* 1999;12:85-93.
15. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantification of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358-67.
16. White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 1987;76:44-51.
17. Ito H, Tomooka T, Sakai N, et al. Lack of myocardial perfusion immediately after successful thrombolysis: a predictor of poor recovery of left ventricular function in anterior myocardial infarction. *Circulation* 1992;85:1699-705.
18. Ito H, Maruyama A, Iwakura K, et al. Clinical implications of the 'no reflow' phenomenon: a predictor of complications and left ventricular remodeling in reperfused anterior wall myocardial infarction. *Circulation* 1996;93:223-8.
19. Agati L, Autore C, Testa G, et al. Combined use of dobutamine echocardiography and myocardial contrast echocardiography in predicting regional dysfunction recovery after coronary revascularization in patients with recent myocardial infarction. *Eur Heart J* 1997;18:771-9.
20. Iliceto S, Galiuto L, Marchese A, et al. Analysis of microvascular integrity, contractile reserve, and myocardial viability after acute myocardial infarction by dobutamine echocardiography and myocardial contrast echocardiography. *Am J Cardiol* 1996;77:441-5.
21. Bolognese L, Antoniucci D, Rovai D, et al. Myocardial contrast echocardiography versus dobutamine echocardiography for predicting functional recovery after acute myocardial infarction treated with primary coronary angioplasty. *J Am Coll Cardiol* 1996;28:1677-83.
22. Kaul S. Myocardial contrast echocardiography in acute myocardial infarction: time to test for routine clinical use? *Heart* 1999;81:2-5.
23. Lindner JR, Kaul S. Insights into the assessment of myocardial perfusion offered by the different cardiac imaging modalities. *J Nucl Cardiol* 1995;5:446-60.