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Comparison of Dobutamine Echocardiography and Positron Emission Tomography in Patients With Chronic Ischemic Left Ventricular Dysfunction

ROBERT K. M. CHAN, MBBS, FRACP, KENNETH J. LEE, MBBS, FRACP, PAUL CALAFIORE, MBBS, FRACP, SALVATORE U. BERLANGIERI, MBBS, FRACP, W. JOHN McKAY, MBBS, FRACP, ANDREW M. TONKIN, MD, FRACP

Melbourne, Australia

Objectives. **The aim of this study was to correlate dobutamine-induced contractile reserve as detected by echocardiography with findings on positron emission tomography in patients with chronic ischemic left ventricular dysfunction.**

Background. **Contractile reserve induced by low dose dobutamine infusion has been proposed as a marker of myocardial viability.**

Methods. **Sixty patients with stable coronary artery disease and left ventricular dysfunction (mean ejection fraction [±SD] 29 ± 10%) underwent transthoracic echocardiography with dobutamine infusion (up to 10 μg/kg body weight per min) and positron emission tomography with nitrogen-13 ammonia and fluorine-18 (F-18) fluorodeoxyglucose as a perfusion and a metabolic tracer, respectively. Regional wall motion, perfusion and metabolism were analyzed semiquantitatively by using a 16-segment model. Segments with F-18 fluorodeoxyglucose uptake >50% were considered viable on positron emission tomography.**

Results. **After dobutamine infusion, hemodynamic variables changed significantly, and myocardial ischemia was evident in 17 patients. All 60 patients had dysfunctional myocardium considered viable on positron emission tomography (8 ± 4 segments/patient), whereas 52 patients had dysfunctional myocardium with contractile enhancement by dobutamine echocardiography (4 ± 2 segments/patient, p = 0.01). The extent of dysfunctional myocardium with contractile reserve appeared to correlate less closely with the total extent of viable dysfunctional myocardium identified by positron emission tomography than with the number of such segments associated with a pattern of perfusion-metabolism mismatch.**

Conclusions. **In patients with chronic ischemic left ventricular dysfunction, echocardiography can be used to identify enhancement in the contractile function of viable dysfunctional myocardium after infusion of low dose dobutamine. In this study, the presence and extent of such enhancement were relatively less than the values obtained from positron emission tomography.**

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In patients with left ventricular dysfunction associated with coronary artery disease, myocardial viability is an important determinant of management and prognosis. If viable myocytes are present within a myocardial region that is dysfunctional because of severe ischemia at rest, restoration of blood flow to the region by coronary revascularization can potentially reverse the contractile dysfunction. If a significant amount of such ischemic viable dysfunctional myocardium is present, revascularization can lead to an improvement in regional and, possibly, global left ventricular function (1).

Positron emission tomography is currently the most sensitive imaging modality available for identifying myocardial viability (2). It measures regional myocardial metabolism, which reflects the presence and extent of viable tissue. These data are correlated with perfusion data that localize ischemia at rest. Recently, the presence of contractile reserve as demonstrated by improved function after infusion of a low dose of dobutamine has been proposed to be another useful marker of myocardial viability (3–6). With advances in the technology of digital image acquisition, improved regional contractile function can be detected by echocardiography, a potentially simpler, cost-effective and widely available technique. The purpose of this study was to evaluate low dose dobutamine echocardiography in a cohort of patients with chronic ischemic left ventricular dysfunction and to correlate the presence of dobutamine-induced contractile reserve with the findings of positron emission tomography.

Methods

Study patients. The study group comprised 60 consecutive patients in clinically stable condition who had angiographically significant coronary artery disease (defined as the presence of

From the Departments of Cardiology and Nuclear Medicine, Austin and Repatriation Medical Center, Melbourne, Australia. This work was supported by a Postgraduate Medical Research Scholarship from the National Health and Medical Research Council of Australia, Canberra (Dr. Chan).

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Address for correspondence: Dr. Andrew Tonkin, Department of Cardiology, Austin and Repatriation Medical Center, Austin Campus, Heidelberg, Victoria 3084, Australia.

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at least one lumen diameter stenosis ≥75% in a major epicardial coronary artery) with impaired left ventricular systolic function and were being considered for revascularization. Patients with acute ischemic events including myocardial infarction and hospital admission for unstable angina within 4 weeks of the study were specifically excluded. Left ventricular systolic function was determined with radionuclide ventriculography. All patients underwent positron emission tomography and low dose dobutamine echocardiography to assess myocardial viability. The study was approved by the Human Research Ethics Committee of our institution; informed consent was obtained from all patients before the investigations.

Dobutamine infusion. Dobutamine was infused intravenously in a solution of 5% dextrose through a peripheral arm vein, commencing at a dose of 5 μg/kg body weight per min. After 3 min, the infusion rate was increased to 10 μg/kg per min and continued for 3 additional min. The infusion was terminated at the end of this stage in 30 patients; it was continued in the other 30 patients, who underwent a maximal dose dobutamine stress test. The findings during the higher dose stages (primarily for the detection of ischemia) were not analyzed in this study, which only examined the responses up to the end of infusion of 10 μg/kg per min. Throughout the infusion, a three-lead electrocardiogram (ECG) was continuously monitored. Upper arm blood pressure was measured at the end of each dose interval.

Predetermined end points of the study included systemic hypertension (defined as systolic blood pressure ≥220 mm Hg or diastolic blood pressure ≥120 mm Hg, or both), hypotension (defined as a systolic reading ≤80 mm Hg or a decrease in systolic blood pressure ≥30 mm Hg from baseline, or both), development of angina or ischemic ECG changes (defined as flat or downsloping ST segment depression ≥2 mm from baseline) and significant cardiac arrhythmia.

Echocardiographic imaging and analysis. Before the start of dobutamine infusion, a complete baseline two-dimensional transthoracic echocardiographic and Doppler assessment was performed with the use of a commercially available scanner (XP128/10c, Acuson) interfaced with a digital image acquisition computer (Cineview, Tomtec Imaging Systems) that was programmed to capture eight frames of ECG-gated echocardiographic images of the systolic phase at 60-msec intervals. Images in the parasternal long- and short-axis and apical four- and two-chamber views were acquired before the start of dobutamine infusion and at the end of the 5- and 10-μg/kg per min stages.

After acquisition, echocardiographic images were reviewed by using the image acquisition computer, which displayed images in a quad-screen, cine-loop playback format. Identical left ventricular segments at rest and during administration of 5 and 10 μg/kg per min of dobutamine were analyzed for regional wall motion with use of a standard 16 segment model (7) by two experienced observers who had no knowledge of the positron emission tomographic findings or clinical details. Differences in interpretation were resolved by consensus. By visual assessment of endocardial motion and wall thickening, wall motion in each segment was classified as normal, hypokinetic, akinetic or dyskinetic, each carrying a wall motion score of 1, 2, 3 or 4, respectively. The left ventricular wall motion score index was calculated as the ratio between the sum of all available segmental wall motion scores and the number of segments visualized.

Regional wall motion during the rest echocardiographic study was analyzed, and left ventricular segments were broadly categorized as normal or dysfunctional. The latter category included segments that were hypokinetic, akinetic or dyskinetic. Dobutamine-induced contractile reserve in a dysfunctional segment at rest was defined as an improvement in the wall motion score of that segment during either stage of the dobutamine infusion by one or more grades in comparison with the baseline score. Deterioration in regional wall motion was defined as worsening in wall motion score by one or more grades in comparison with the previous stage. A biphasic response to dobutamine was defined as improvement in wall motion at low doses followed by worsening at higher doses. Interobserver and intraobserver agreement on wall motion score was 92% and 94%, respectively.

Positron emission tomography. Radiopharmaceuticals were prepared in-house by cyclotron (IBA, 10/5) and radiochemistry facilities. Nitrogen-13 (N-13) ammonia and fluorine-18 (F-18) fluorodeoxyglucose were utilized as a perfusion and metabolic tracer, respectively. Emission data were acquired by a whole body positron emission tomographic scanner (ECAT 951, Siemens) that allowed simultaneous imaging of 31 transaxial slices with a 10.8-cm field of view. All patients were studied in the postprandial rest state and received 50 gm of oral glucose loading before imaging. Capillary blood glucose levels were monitored by a glucometer (Accutrend, Boehringer Mannheim) before and during image acquisition; if the levels were elevated, intravenous insulin was administered according to a sliding scale.

A transmission scan of the thorax was first acquired to define the position of the heart and to allow subsequent attenuation correction of the emission data. At the completion of the transmission scan, the patient was administered ~1,000 MBq of N-13 ammonia intravenously, after which data were acquired for 20 min. Then ~350 MBq of F-18 fluorodeoxyglucose was administered intravenously and after a 40-min uptake period, data were acquired for 30 min. Care was taken to ensure that patient position was constant within the scanner for the full duration of the study. On completion of tomographic data acquisition, the images were reconstructed and correction was made for variable soft tissue attenuation. F-18 fluorodeoxyglucose metabolic images were normalized to the corresponding perfusion images, using the region with the maximal N-13 ammonia uptake as the reference region.

The positron emission tomographic images were interpreted by two experienced observers who had no knowledge of the echocardiographic findings or clinical details. In cases of disagreement, the studies were reviewed and a consensus was reached. The left ventricle was divided using the 16-segment model (7), and N-13 ammonia and F-18 fluorodeoxyglucose

Table 1. Semiquantitative Grading of Relative Uptake of Nitrogen-13 Ammonia and Fluorine-18 Fluorodeoxyglucose on Positron Emission Tomography

Grade	Positron Emission Tomographic Tracer Uptake
1	100% ≥ Uptake > 70%
2	70% ≥ Uptake > 50%
3	50% ≥ Uptake > 30%
4	30% ≥ Uptake ≥ 0%

uptake were graded with use of the Bronson color map. This map color coded left ventricular myocardial segments according to their degree of tracer uptake relative to the region with the maximal uptake, with semiquantitative division into 10 percentiles. The N-13 ammonia and F-18 fluorodeoxyglucose uptake in each segment were then scored by using the system illustrated in Table 1. Interobserver and intraobserver agreement in tracer uptake grades was 90% and 92%, respectively.

Nitrogen-13 ammonia and F-18 fluorodeoxyglucose uptake in echocardiographically dysfunctional left ventricular segments was studied in each patient. Segments with F-18 fluorodeoxyglucose uptake >50% (grade 1 or 2) were defined as *viable* on positron emission tomography. If a pattern of perfusion-metabolism mismatch (N-13 ammonia uptake grade greater than that of F-18 fluorodeoxyglucose by ≥1) was also present, the dysfunctional segment was labeled as *viable with mismatch*, indicating well preserved glucose metabolism in the presence of relative hypoperfusion. Segments with F-18 fluorodeoxyglucose uptake ≤50% (grade 3 or 4) were categorized as *nonviable*.

Statistical analysis. Values are expressed as mean value ± 1 SD, when appropriate. Repeated measures analysis of variance and the Scheffé F-test were used to compare hemodynamic variables and echocardiographic wall motion score indexes at different stages of the dobutamine infusion. The Student *t* test was used to test differences between mean values of findings of positron emission tomography and dobutamine echocardiography, and also findings of different subgroups within each imaging modality. Chi-square analysis and the Fisher exact test were used to compare categoric positron emission tomographic and echocardiographic data. Statistical significance was indicated by p values < 0.05.

Results

The clinical characteristics of the 60 patients are shown in Table 2. They underwent dobutamine echocardiography and positron emission tomography within a mean interval of 5 ± 7 days of the other investigation; both studies were performed on the same day in 24 patients. Radionuclide ventriculography was performed at a mean interval of 10 ± 10 days from dobutamine echocardiography. All patients with a history of hypertension had satisfactory blood pressure control by medications before entering the study. Glucose control was adequate in diabetic patients during positron emission tomography.

Table 2. Baseline Characteristics of the 60 Study Patients

Age (yr)	62 ± 11
Male	49 (82%)
LVEF on radionuclide ventriculography	29 ± 10%
Multivessel coronary artery disease	52 (87%)
Previous myocardial infarction	47 (78%)
Abnormal Q waves on ECG	34 (57%)
Angina class (Canadian Cardiovascular Society)	
I or II	39 (65%)
III or IV	21 (35%)
Heart failure functional class (New York Heart Association)	
I or II	19 (32%)
III or IV	41 (68%)
Hypertension	24 (40%)
Diabetes mellitus	10 (16%)
Insulin dependent	2 (3%)

Data are presented as mean value ± SD or number (%) of patients. ECG = electrocardiogram; LVEF = left ventricular ejection fraction.

Hemodynamic responses and tolerance of dobutamine infusion. Hemodynamic variables including heart rate, systolic blood pressure and systolic pressure–heart rate double product at baseline before administration of dobutamine and during the two stages of the infusion are shown in Table 3. At the end of the infusion of low dose dobutamine (10 μg/kg per min), both the mean heart rate and rate-pressure double product were significantly higher than at baseline.

The protocol for infusion of dobutamine was well tolerated and successfully completed in all patients. No patients manifested any predetermined end point or other significant side effect resulting in premature termination of their study. In particular, there were no serious complications related to dobutamine infusion, including unstable angina, myocardial infarction or death.

Regional wall motion at rest and during dobutamine infusion. During rest echocardiography, a complete regional wall motion assessment of all left ventricular segments could be performed in 54 patients. In six patients, part of the left ventricle (1 to 10 segments) could not be adequately assessed because of suboptimal images. Wall motion analysis revealed 11 ± 3 dysfunctional segments/patient. Of the 654 dysfunc-

Table 3. Hemodynamic Variables and Wall Motion Score Index at Baseline and During Dobutamine Infusion

		Dobutamine Infusion	
	Baseline	5 μg/kg per min	10 μg/kg per min
Heart rate (beats/min)	77 ± 14	76 ± 15	83 ± 15*†
Systolic blood pressure (mm Hg)	121 ± 20	126 ± 21*	125 ± 21
Heart rate–systolic blood pressure product (beats/min × mm Hg × 10^2)	85.8 ± 36.6	88.2 ± 37.6	94.5 ± 39.2*†
Wall motion score index	2.1 ± 0.4	1.9 ± 0.4*	1.9 ± 0.4*

*p < 0.05 versus baseline. †p < 0.05 versus 5 μg/kg per min. Data are presented as mean value ± SD.

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tional segments identified, 256 were hypokinetic, 379 appeared akinetic and 19 had dyskinetic wall motion.

After infusion of 5 μg/kg per min of dobutamine, 52 patients (87%) showed an improvement in contractile function of two to nine segments within dysfunctional myocardium. When the infusion rate was increased to 10 μg/kg per min, 22 of these 52 patients had inotropic responses in other dysfunctional regions that had not responded at the lower dose. However, in 13 patients, some of the previously observed contractile improvement disappeared, presumably because of ischemia (biphasic response). At the end of the infusion, eight patients had shown no inotropic enhancement, and four of these showed some deterioration in wall motion. The mean wall motion score indexes of the patient cohort after the 5- and 10-μg/kg per min stages of dobutamine infusion were both significantly lower than the baseline score index. Dobutamine-induced contractile reserve was present in 47% of segments with rest hypokinesia in contrast to 23% of akinetic or dyskinetic segments ($p = 0.0001$).

All 13 patients with no history of previous myocardial infarction showed wall motion improvement during infusion of dobutamine, as did 39 of the 47 patients with previous infarction (p = NS). In the latter, there were no significant differences in inotropic responsiveness to dobutamine in patients with or without abnormal Q waves on ECG (29 of 34 vs. 10 of 13, p = NS).

Positron emission tomographic findings and correlation with dobutamine-induced contractile reserve. In 10 study patients, part of the left ventricle (one to two segments) was not included within the field of view of the positron emission tomographic scanner because of gross cardiomegaly. By using predefined viability criteria on positron emission tomography, viable dysfunctional myocardium, ranging from 1 to 16 segments, was identified in all study patients. Viable dysfunctional segments with perfusion-metabolism mismatch were present in 40 patients (range 1 to 9 segments; mean [±SD] 2 ± 2/patient).

On comparison of the two imaging modalities examined in this study, there were significantly more patients with viable dysfunctional myocardium identified on positron emission tomography (60 of 60) than patients with dysfunctional myocardium that demonstrated contractile reserve on dobutamine echocardiography (52 of 60, p = 0.01). The mean number of dysfunctional segments/patient considered viable on positron emission tomography (8 ± 4) was also significantly higher than the mean number of segments with dobutamine-induced contractile enhancement (4 ± 2, p = 0.001). The relative extent of myocardial viability on positron emission tomography and dobutamine echocardiography is presented in Figure 1. The amount of dysfunctional myocardium with contractile reserve appeared to compare best with that of viable dysfunctional myocardium associated with a pattern of perfusion-metabolism mismatch on positron emission tomography.

The mean number of viable dysfunctional segments/patient on positron emission tomography was similar in patients with Canadian Cardiovascular Society class I or II angina symptoms (9 ± 3) and those with class III or IV symptoms (8 ± 4, p = NS). The mean number of dysfunctional segments with contractile reserve in these two categories of patients was 4 ± 3 and 3 ± 2/patient, respectively (p = NS).

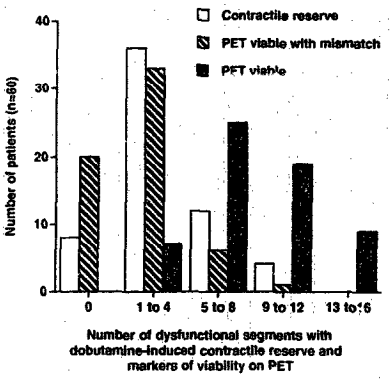

Figure 1. Bar graph grouping the study patients according to the number of segments of dysfunctional myocardium showing 1) contractile reserve on dobutamine echocardiography, 2) viability on positron emission tomography (PET), and 3) viability on positron emission tomography with perfusion-metabolism mismatch.

Discussion

In patients with left ventricular dysfunction secondary to coronary artery disease, positron emission tomography has detected the presence of stunned myocardium (8) and predicted improvement in regional left ventricular function after revascularization in patients with hibernating myocardium (9,10). The presence of hibernating tissue has been shown (11,12) to be associated with improved survival and amelioration of heart failure symptoms after adequate revascularization. Although the true reference standard for verifying the presence of viable dysfunctional myocardium comes from histologic examination (13) or documentation of improved regional wall motion after revascularization (1), positron emission tomography is currently the best available modality for prospectively identifying such viability before revascularization. However, positron emission tomographic facilities are not widely available for general use because of their high operating costs.

Dobutamine stress echocardiography has been demonstrated to be a useful and safe imaging modality for the diagnosis and localization of functionally significant coronary artery disease (14–18). Recently, echocardiography during relatively low dose dobutamine infusion has been used to detect both stunned myocardium after myocardial infarction (19,20) and hibernating myocardium in patients with chronic ischemic left ventricular dysfunction (3–6,21). In these contexts, dobutamine has been shown to enhance contractility in dysfunctional but viable myocardium, hence unmasking its contractile reserve.

There are many potential advantages of the use of dobutamine echocardiography in assessment of myocardial viability. Echocardiography is a widely available and relatively low cost imaging modality. The use of dobutamine has been shown to be safe in patients with coronary artery disease (22). Viability data obtained during low dose infusion can complement subsequent findings during higher dose stages that provide information on regional and global systolic performance at maximal cardiovascular stress. In patients with significant myocardial dysfunction at rest, echocardiography during dobutamine infusion is also an alternative to exercise testing, which is often limited by poor exercise capacity.

Another strength of the use of inotrope-enhanced contractile reserve as a marker of viability in dysfunctional myocardium is that it directly demonstrates improved contractility and thus provides an indication of potential functional gains after successful revascularization. Other indexes of viability such as metabolic activity, myocardial perfusion and cell membrane integrity may potentially identify patchy areas of viable tissue existing within a predominantly nonviable myocardial region. In a study by Arnese et al. (23), 43% of akinetic segments with no wall motion improvement after administration of dobutamine were judged to be viable on thallium-201 reinjection single-photon emission computed tomography: however, only 18% of these showed recovery of contractile function after revascularization.

In the present study, dysfunctional segments that had relative F-18 fluorodeoxyglucose uptake >50% on positron emission tomography were regarded as viable. With the use of this criterion, clinically relevant viability may have been overestimated and some segments considered viable may not have been capable of improving contractility after revascularization. Although the induction of contractile enhancement by dobutamine has been proposed as a marker of viability, a lack of response does not necessarily imply a complete absence of viable myocardium. Furthermore, the relatively low incidence of contractile reserve induced by dobutamine in dysfunctional segments may be compensated for by the potentially higher specificity of dobutamine in predicting recovery in contractile function after revascularization. The number of dysfunctional segments with contractile reserve as assessed by dobutamine appeared to correlate less closely with the number of all viable dysfunctional segments assessed by positron emission tomography than with the number of such segments associated with a pattern of perfusion-metabolism mismatch (Fig. 1). Such mismatch has been shown (11,12) to be a marker of hibernating myocardium and predictive of favorable outcome after revascularization.

In patients with severe coronary artery disease such as those in this study, administration of dobutamine, even in relatively low doses, can sometimes precipitate myocardial ischemia. As shown in this study, both the heart rate and the heart rate–blood pressure double-product were significantly higher than at baseline at the end of the 10-μg/kg per min dobutamine infusion stage. In total, myocardial ischemia was evident in 17 patients during administration of dobutamine. However, 22 patients had myocardial segments that showed a contractile response only with the dobutamine dose of 10-μg/kg per min. A biphasic response to dobutamine has been reported to be predictive for recovery of contractile function after revascularization. In a study by Afridi et al. (4), although most segments showed functional deterioration at doses >20 μg/kg per min, deterioration was observed in some segments with doses as low as 7.5 μg/kg per min. Thus, when dobutamine infusion is used to assess myocardial viability in such patients, the sensitivity of the method is maximized by performance of repeated wall motion assessment at multiple stages as the infusion rate is slowly increased.

Mechanisms. Previous studies examining the histology of chronic hibernating myocardium obtained from intraoperative biopsy have demonstrated marked cellular changes including cellular swelling, replacement of myofibrillar tissue by glycogen and loss of sarcoplasmic reticulum (13,24–26). These findings suggest the possibility of a regression phenomenon in asynergic but viable myocardial regions in patients with chronic myocardial ischemia. Maes et al (24) found that these "dedifferentiated" regions showed significant recovery of wall motion after revascularization. In the present study, disruption of contractile structure in regions of viable dysfunctional myocardium might have partly explained the relatively limited exten. of dobutamine-induced contractile enhancement in comparison with viability findings on positron emission tomography.

Tethering of a myocardial segment from adjacent tissue may influence the assessment of contractile response during inotropic stimulation. To limit the impact of tethering, previous investigators (21) required wall motion improvement in two contiguous segments for the diagnosis of contractile reserve. However, this criterion may potentially reduce the sensitivity of detection. In the present study, the effect of tethering was reduced by observing changes in myocardial thickening, which is less susceptible to influences from adjacent segments. Because most study patients had significant left ventricular dysfunction, tethering from adjacent normal or hyperdynamic segments was unlikely to have had a major impact on the overall findings. In contrast, tethering from adjacent nonviable dysfunctional segments might have reduced the degree of, or even abolished, any contractile reserve detectable during dobutamine infusion, hence contributing to the relatively limited inotropic response observed in dysfunctional segments. This possibility was illustrated by the only moderate improvement in the overall wall motion score index between baseline and the end of the infusion of low dose dobutamine.

Limitations of the study. Although the method of wall motion analysis adopted in this study has been shown to be reproducible (27), it uses subjective visual assessment. Because wall motion augmentation during dobutamine infusion can often be subtle and minor on transthoracic echocardiography, this method of detection may be relatively insensitive. Patients in this study were not screened for echogenicity before enrollment. During image acquisition, endocardial definition might have been suboptimal in some segments and underestimation

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of contractile reserve by the reporters could not be excluded. Advances in echocardiography in areas such as Doppler myocardial tissue imaging (28,29) and improvement in endocardial definition using contrast enhancement (30,31) may improve this technique in the future. With transesophageal echocardiography, the presence of dobutamine-induced contractile reserve has been reported to have positive and negative predictive accuracy of 81% and 97%, respectively, in detecting viability on positron emission tomography using F-18 fluorodeoxyglucose alone (3). Magnetic resonance imaging, which is also being investigated for assessment of myocardial viability (32,33), may potentially be applied to detection of contractile reserve (6).

To optimize endocardial definition so that myocardial thickening could be better appreciated, certain minor off-axis modifications were occasionally necessary during echocardiographic image acquisition. In a small proportion of studies, segments acquired at different stages of the dobutamine infusion may not have been imaged from identical views and, hence, may not have been strictly comparable. Furthermore, some segments demonstrated areas of nonhomogeneous wall motion and tracer uptake. Their wall motion scores and tracer uptake grades were reported as the average estimate for the segment.

Interpretation of findings from this study and their application in the clinical setting are limited by the lack of follow-up data on contractile function in patients who underwent revascularization, which is the true reference standard for evaluating viability assessment by noninvasive imaging modalities. The present study suggests that dysfunctional myocardial regions that demonstrate definite contractile enhancement during dobutamine infusion are likely to contain a significant number of viable myocytes that may potentially improve their contractile function after revascularization. However, the absence of an inotropic response does not completely exclude the possible presence of viable myocardium and potential for postrevascularization recovery in contractile function, and other alternative investigations may be necessary.

Conclusions. In the assessment of myocardial viability, contractile reserve can be induced by infusion of a relatively low dose of dobutamine that is safe and well tolerated. Because doses as low as 10 μg/kg per min can result in significant changes in hemodynamic variables, and occasionally myocardial ischemia, repeated wall motion assessment should be performed at multiple stages as the infusion rate is slowly increased to maximize the likelihood of demonstrating contractile improvement after dobutamine. These patients with moderately severe chronic ischemic left ventricular dysfunction, had fewer dysfunctional myocardial segments with dobutamine-induced contractile reserve than dysfunctional myocardial segments defined as viable on positron emission tomography. However, the extent of dysfunctional myocardium with contractile reserve appeared to correlate more closely with that of viable dysfunctional myocardium associated with a pattern of perfusion-metabolism mismatch on positron emission tomography.

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