Assessment of Myocardial Viability by Dobutamine Echocardiography, Positron Emission Tomography and Thallium-201 SPECT

Correlation With Histopathology in Explanted Hearts

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Objectives. We examined the relationship among viability assessment by dobutamine echocardiography (DE), positron emission tomography (PET) and thallium-201 single-photon emission computed tomography (Tl-SPECT) to the degree of fibrosis.

Background. DE, PET and Tl-SPECT have been shown to be sensitive in identifying viability of asynergic myocardium. However, PET and Tl-SPECT indicated viability in a significant percentage of segments without dobutamine response or functional improvement after revascularization.

Methods. Twelve patients with coronary artery disease and severely reduced left ventricular function (EF 14.5 ± 5.2%) were studied with DE prior to cardiac transplantation: 5 had additional PET and 7 had Tl-SPECT studies. Results of the three techniques were compared to histologic findings of the explanted hearts.

Results. Segments with >75% viable myocytes by histology were determined to be viable in 78%, 89% and 87% by DE, PET and Tl-SPECT; those with 50–75% viable myocytes in 71%, 50% and 87%, respectively. Segments with 25–50% viable myocytes showed response to dobutamine in only 15%, but were viable in 60% by PET and 82% by Tl-SPECT. Segments with <25% viable myocytes responded to dobutamine in 19%; however, PET and Tl-SPECT demonstrated viability in 33% and 38%, respectively. Discrepant segments without dobutamine response but viability by PET and SPECT had significantly more viable myocytes by pathology than did those classified in agreement to be nonviable but had significantly less viable myocytes than those classified in agreement to be viable (p < .001).

Conclusions. These findings suggest that contractile reserve as evidenced by a positive dobutamine response requires at least 50% viable myocytes in a given segment whereas scintigraphic methods also identify segments with less viable myocytes. Thus, the methods may provide complementary information: Nuclear techniques appear to be highly sensitive for the detection of myocardial viability, and negative tests make it highly unlikely that a significant number of viable myocytes are present in a given segment. Conversely, dobutamine echo may be particularly useful for predicting recovery of systolic function after revascularization.

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Assessment of myocardial viability is of critical importance for the management of patients with chronic coronary artery disease and reduced left ventricular function. Asynergic but viable myocardium has been assumed to improve its systolic function after revascularization, whereas nonviable segments do not. Thus, patients with a large portion of dysfunctional but viable myocardium are believed to benefit from revascularization, whereas only transplantation can be offered to those with few remaining viable segments (1–3). In addition, revascularization of viable myocardium may be beneficial by preventing remodeling and electrical instability.

Several techniques such as dobutamine echocardiography (DE) (4–7), positron emission tomography (PET) (8,9) and Tl-201 single-photon emission computed tomography (Tl-SPECT) using a stress-redistribution-reinjection protocol (10) or a rest-redistribution protocol (11,12) have been proposed for the assessment of myocardial viability. Several studies that compared these tests to each other and to wall-motion analysis after bypass surgery have been reported: Sensitivity for detection of viability in asynergic segments was found to be acceptable for all three techniques, although some studies reported DE to be slightly less sensitive (13–19). However, most studies

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show that a high percentage of segments unresponsive to dobutamine or without improvement of wall motion after revascularization are still viable by PET or TI-SPECT (13,17,19,20–25). Furthermore, it has recently been shown that the dobutamine response of dysynergic myocardium is directly related to the degree of thallium uptake (19,23,26).

Thus, we hypothesized that a positive dobutamine response may require a higher percentage of viable myocytes in a given segment than does the demonstration of perfusion and/or metabolism by PET or TI-SPECT. To address this hypothesis, we studied patients prior to heart transplantation with DE, PET and TI-SPECT and compared the results with the histopathologic findings in the explanted hearts.

Methods

Study population. The study population consisted of 12 patients (all male; mean age 52 ± 9 years) with severe left ventricular dysfunction due to ischemic cardiomyopathy (mean ejection fraction [EF] 45.5 ± 6.2%) who ultimately underwent transplantation. All patients had a history of myocardial infarction (antero 12, inferior 10; none within 3 months of transplantation) and all had severe multivessel disease on coronary angiography. Each patient gave written informed consent to participate in the study.

Echocardiography. Echocardiography was performed in all patients using either a Vingmed 800 (Vingmed Sound, Horten, Norway) with a 3.5-MHz transducer or a HP 1500 (Hewlett-Packard Imaging Systems, Andover, MA). In addition to a standard M-Mode, 2-D and Doppler echocardiographic study, parasternal long axis and short axis views (level of the papillary standard M-Mode, 2-D and Doppler echocardiographic study, Packard Imaging Systems, Andover, MA). In addition to a standard M-Mode, 2-D and Doppler echocardiographic study, parasternal long axis and short axis views (level of the papillary muscle) and apical two- and four-chamber views were recorded at baseline and at each stage of the dobutamine protocol. Five and 10 μg/kg/min were administered for at least 5 min before imaging. The dosage was increased in 5-μg increments each for 3 min. Dobutamine was discontinued before the target dosage of 40 μg/kg/min was reached when one of the following criteria occurred: systolic blood pressure ≥240 mm Hg; diastolic blood pressure ≥120 mm Hg; severe hypotension (systolic blood pressure <90 mm Hg); significant arrhythmias, signs of ischemia (worsening of regional wall motion, angina), or severe patient discomfort.

Digitized cycles of each view were stored for later side-by-side display in a quadscreen format to facilitate the comparison of images at rest and during different rates of dobutamine infusion. Images were also recorded on videotape.

Echocardiograms were read by investigators unaware of the clinical, angiographic and scintigraphic findings in each patient. The standard 16-segment model was used for semiquantitative wall-motion analysis. Wall motion was described as normal, mildly hypokinetic, severely hypokinetic, akinetic or dyskinetic.

Segments were judged to be viable when wall motion was normal or mildly hypokinetic at rest or when wall motion in severely hypokinetic or akinetic segments improved by at least one grade after dobutamine administration.

PET imaging. Positron emission tomography (PET) scanning was performed in a nonselected subgroup of five patients (PET was unavailable in the remaining patients for logistic reasons). The PET imaging was performed using N-13 ammonia and F-18 deoxyglucose (FDG) as tracers of regional myocardial blood flow and glucose utilization. After an overnight fast, patients were positioned in the PET scanner with a Velcro strap fastened across their chest to minimize motion. A 20-min transmission scan was obtained first to correct emission images for photon attenuation. Then, 10–15 mCi of N-13 ammonia were injected as a bolus, and 5 min later a 20-min image was acquired. After physical decay of N-13 (40 min), 10 mCi of FDG were injected, followed 40 min later by a 20-min image acquisition.

A high resolution PET scanner (ECAT 931/8; CTI/Siemens Knoxville, TN) was used to acquire 15 transaxial images with an interplane spacing of 6.5 mm. Images were reconstructed with a Shepp filter (cutoff frequency: 3 cycles/pixel, effective in-plane resolution: 11 mm [full width half maximum] FWHM) and reoriented into short and long axis images. Visual inspection was used to classify myocardial segments according to relative tracer uptake as follows: PET normal (normal uptake of N-13 and F-18 activity), PET matched defect (concordantly reduced uptake of both tracers) and PET mismatch (maintained F-18 activity in segments with reduced N-13 activity). Analysis was performed using the same 16-segment-model as for echocardiography by investigators unaware of the echocardiographic and histopathologic results. Viability was defined by either normal perfusion or by presence of a perfusion-metabolism mismatch.

TI-SPECT imaging. Thallium-201 single-photon emission computed tomography (TI-SPECT) imaging was performed in a nonselected subgroup of seven patients (TI-SPECT was not available in the remaining patients for logistic reasons). All patients underwent rest-redistribution TI-SPECT imaging according to a standardized clinical protocol. Several minutes after the injection of 2–3 mCi thallium-201, rest imaging was performed. Then, 3 to 4 h later the patient returned for redistribution imaging.

Thallium images were obtained with a single-head large field-of-view SPECT camera equipped with a low energy all-purpose parallel hole collimator (Apex 415, APC-3, Elscint Haifa) using a 25% window centered at 68 keV. Thirty projection images were acquired by continuously rotating the camera through a 180° arc starting from the 55° right anterior oblique (RAO) position. Transaxial images were reconstructed using a fifth-order butterworth filter with a cutoff frequency of 0.3 and were then reoriented into short and long axis images.

Abbreviations and Acronyms

DE = dobutamine echocardiography
EF = ejection fraction
PET = positron emission tomography
TI-SPECT = thallium-201 single-photon emission computed tomography
for image interpretation. The distribution of thallium was visually assessed in 16 segments by experienced observers who were unaware of the echocardiographic and histopathologic results. The following score was used: 0 = normal Tl-uptake, 1 = mildly reduced uptake, 2 = moderately reduced uptake, 3 = severely reduced uptake, 4 = no uptake. Viability was defined as normal, mildly or moderately reduced Tl-uptake (score ≤ 2) as visualized on the redistribution images.

**Histopathology.** At surgery, the native heart was excised according to standard surgical technique. The left ventricle was cut into a basal, mid- and apical third perpendicular to the left ventricle’s long axis. After fixation with formalin for at least 12 h, each of the three slices was cut again to yield six cross sections of the ventricles. Transmural tissue samples, 2–3 mm thick, which included endocardium and epicardium, were cut as large as possible for histologic examination. Samples were taken to match each of the 16 segments according to the segment model used by echocardiography. Trichrome staining was used to facilitate identification of fibrous tissue.

Specimens of each segment were examined for gross and histologic evidence of coagulation necrosis and fibrosis. In cases where there was thinning of the ventricular wall, sections were “normalized” to noninfarcted wall thickness, which along with histologic evaluation was used to classify segments as containing <25%, 25–50%, 50–75%, or >75% viable myocytes. For comparison, the following pathology score was used: 0 = <25% viable myocytes, 1 = 25–50%, 2 = 50–75%, 3 = >75% viable myocytes.

**Statistical analysis.** Statistical analysis was performed on a personal computer (Macintosh, Apple Computer) using a commercial software package (JMP 3.0, SAS Institute). A p value < .05 was considered to indicate statistical significance. Univariate one-way analysis of variance (ANOVA) was utilized to characterize differences between segments classified according to the results of diagnostic methods and pathology. Multivariate ANOVA was used to study effects of differences among patients together with effects of the segmental classification.

**Results**

Patients underwent heart transplantation 2.8 ± 1.9 months after they had been studied. None had myocardial infarction or episodes of unstable angina in the time between tests and surgery. For logistic reasons, PET and TI-SPECT imaging could be performed in subgroups of only five and seven patients of the total cohort.

**Dobutamine echocardiography.** One-hundred-eighty-eight segments could be analyzed by echocardiography. Wall-motion abnormalities at rest were found in 164 segments (87%). Of those, 71 (43%) improved after dobutamine (60 segments by one grade and 11 by two grades). By predefined criteria, echocardiography classified 54% of all segments to be viable. Compared with histology, where 15 segments could not be analyzed, echocardiography classified 78% of segments with more than 75% viable myocytes (pathology score 3), 71% of those with 50% to 75% (score 2), 15% of those with 25% to 50% (score 1), and 19% of those with less than 25% viable myocytes (score 0) to be viable (Table 1, Fig. 1).

Dobutamine echocardiography distinguished best between segments with more and with less than 50% viable myocytes. Sensitivity and specificity for detection of segments with more than 50% viable cells was 76% and 82%, respectively. For the detection of segments with more than 25% viable myocytes it was 66% and 81%, respectively (Table 2). Segments that improved by two grades more frequently had a percentage of viable myocytes >75% than did those improving by one grade (87% vs. 74%) but this difference did not reach statistical significance.

Dobutamine echocardiographic results as compared with histology did not significantly differ for the patient subgroups with additional PET or additional SPECT and the total patient cohort.

**PET imaging.** Of 80 segments that could be analyzed by PET, 37 (46%) presented with normal perfusion and normal FDG uptake, 13 (16%) demonstrated a perfusion/metabolism mismatch and 30 (38%) showed neither perfusion nor metabolism. Thus, 50 segments (63%) were classified to be viable. Viability was detected in 89%, 50%, 60%, and 33% of the segments found to have >75% (pathology score 3), 50–75% (score 2), 25–50% (score 1) and <25% viable myocytes (score 0). Compared with histology, where 15 segments could not be analyzed, echocardiography classified 78% of segments with more than 75% viable myocytes (pathology score 3), 71% of those with 50% to 75% (score 2), 15% of those with 25% to 50% (score 1), and 19% of those with less than 25% viable myocytes (score 0) to be viable (Table 1, Fig. 1).

Dobutamine echocardiographic results as compared with histology did not significantly differ for the patient subgroups with additional PET or additional SPECT and the total patient cohort.

**Figure 1.** Viable and nonviable segments as assessed by dobutamine echocardiography (DE), PET and TI-SPECT for the four histologically classified groups. The total number of segments available for each method and the number of segments for each histological group are indicated. Black sectors represent the percentage of segments classified to be nonviable.

<table>
<thead>
<tr>
<th>Viable Myocytes</th>
<th>Viable Segments (%)</th>
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</thead>
<tbody>
<tr>
<td>DE (173)</td>
<td></td>
</tr>
<tr>
<td>&lt;25%</td>
<td>48</td>
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<tr>
<td>25–50%</td>
<td>20</td>
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<tr>
<td>50–75%</td>
<td>24</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>81</td>
</tr>
<tr>
<td>PET (65)</td>
<td></td>
</tr>
<tr>
<td>&lt;25%</td>
<td>21</td>
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<tr>
<td>25–50%</td>
<td>10</td>
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<tr>
<td>50–75%</td>
<td>8</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>26</td>
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<tr>
<td>SPECT (112)</td>
<td></td>
</tr>
<tr>
<td>&lt;25%</td>
<td>28</td>
</tr>
<tr>
<td>25–50%</td>
<td>12</td>
</tr>
<tr>
<td>50–75%</td>
<td>27</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>45</td>
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</tbody>
</table>
Table 2. Sensitivity and Specificity of Dobutamine Echocardiography, PET and Tl-SPECT for the Detection of Segments With >50% and >25% Viable Myocytes

<table>
<thead>
<tr>
<th></th>
<th>DE</th>
<th>PET</th>
<th>Tl-SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>76</td>
<td>79</td>
<td>87</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>82</td>
<td>58</td>
<td>49</td>
</tr>
</tbody>
</table>

Comparison among DE, PET and Tl-SPECT imaging. Agreement between echocardiography and PET was found in 54 of 78 segments (69%); between echocardiography and Tl-SPECT it was observed in 80 of 110 segments (73%). Disagreement was rarely found when echocardiography classified segments to be viable. Of these, 80% and 93% were also classified to be viable by PET and Tl-SPECT, respectively. However, 44% and 53% of segments without dobutamine response were still found to be viable by PET and Tl-SPECT (Fig. 2). Discreant segments without dobutamine response yet viable by PET or Tl-SPECT presented with a greater percentage of viable myocytes in histology than did those classified in accordance by both methods to be nonviable (mean pathology score 1.33 and 1.73 vs. 0.47 and 0.68, p < .05 for PET and Tl-SPECT, respectively) but also presented with significantly less viable myocytes than did segments classified in agreement to be viable (pathology score 2.50 and 2.36 for PET and Tl-SPECT, respectively; p < .05 for both). Thus, a negative dobutamine response but positive nuclear test defined a specific group of segments with an intermediate percentage of viable myocytes (Fig. 3). Multivar-
iate ANOVA revealed significant effects of the segmental classification by diagnostic methods (TI-SPECT: $p < 0.001$; $F = 25.3$; PET: $p < 0.001$; $F = 25.4$) and of patients (TI-SPECT: $p < 0.001$; $F = 5.4$; PET: $p < 0.01$; $F = 4.8$).

**Discussion**

**Assessment of myocardial viability.** Several noninvasive approaches have been developed for the identification of myocardial viability in regions with contractile dysfunction due to coronary artery disease. The three most frequently proposed methods are based on the identification of very different physiologic markers: PET imaging assesses myocardial metabolic activity, typically using F-18 fluorodeoxyglucose as a marker of glucose utilization and N-13 ammonia for assessment of perfusion; TI-SPECT assesses myocardial perfusion and membrane integrity; and dobutamine echocardiography (DE) assesses myocardial contractile reserve.

Early studies using nuclear methods reported high sensitivity as well as specificity for the detection of asynergic myocardial segments that improved after revascularization (8–12). More recent studies that compared nuclear methods with DE and with regional wall motion after revascularization confirmed the high sensitivity and high negative predictive accuracy of PET and TI-SPECT imaging and in general found dobutamine to be slightly less sensitive (13–19). However, a considerable percentage of segments found to be viable by TI-SPECT imaging did not show contractile reserve by echocardiography and did not improve after revascularization, indicating a limited specificity and positive predictive accuracy of this method (13,17,19,21–23). In these studies, DE was found to be significantly more specific for predicting recovery after revascularization. Only a few studies have compared PET and DE. Although PET has been reported to be more specific and to yield higher positive predictive accuracy than TI-SPECT by some authors (13), similarly to TI imaging segments without dobutamine response have also been found to be viable by PET in a high percentage (20,24). Concordance between echocardiography and nuclear studies was typically only found in approximately 60–70%. While most of the segments that responded to dobutamine were usually found to be viable by nuclear methods, discrepancies were mainly observed in segments without contractile reserve: approximately 50% to 80% of segments without dobutamine response have been reported to be viable by PET and TI imaging (17,19,22,24).

The present study is, to our knowledge, the first to compare all three noninvasive methods with a complete segment by segment histologic examination of explanted hearts. The results demonstrate that in asynergic segments elicitation of contractile response by dobutamine stimulation requires at least 50% of the myocytes to be viable. Approximately 80% of such segments responded to dobutamine, as observed by echocardiography; only few (approximately 15–20%) of segments with less than 50% viable myocytes improved wall motion with dobutamine. Conversely, nuclear methods, using standard criteria, identified viability in a relatively high percentage of segments with even less than 25% of viable myocytes (approximately 30% to 40%). Combining DE with either PET or TI-SPECT allowed for stratification of asynergic segments into three subsets (Fig. 3): 1) Segments found to be viable by both DE and either of the scintigraphic techniques had the highest percentage of viable myocytes on histopathologic examination; 2) segments found to be nonviable by both DE and a scintigraphic technique had the lowest percentage of viable myocytes; 3) segments that were viable by scintigraphy and had no contractile response with dobutamine had a percentage of viable cells intermediate to subsets 1 and 2. Thus, discrepancies among these methods appear to be primarily caused by the fact that dobutamine-induced improvement of mechanical function depends on a greater percentage of viable myocytes than that required for demonstration of perfusion, cell integrity or metabolism by TI-SPECT and PET. These results may explain why dobutamine has been reported to be more specific for predicting functional recovery, while nuclear methods can detect smaller amounts of viable myocytes in asynergic myocardial regions. More importantly, these results indicate that the combined use of echocardiography and nuclear methods may enhance our understanding about the degree of viability in a given segment and may offer information above and beyond simplistic classification as either viable or nonviable.

**Comparison with previous studies.** The present study examined patients with very severely reduced left ventricular function who ultimately underwent heart transplantation. This patient population may represent an extreme end of the spectrum compared to patients who undergo testing for myocardial viability in everyday clinical practice. However, several reasons make it likely that the concepts confirmed by the present study can indeed be expected to explain the results found in other patient populations.

First, the relations between nuclear methods and echocardiography found in the present study are very similar to what we (23–25) and others (17,19,20,22) have reported for patients who were evaluated for revascularization. In accordance with the present study, discrepancies were most frequently observed in segments not viable by echo but viable by PET or TI-SPECT (17,19,20,22–25). Previous results were also similar regardless whether stress-redistribution-reinjection or rest-redistribution protocols were used for TI studies (17–19,22,25).

Second, previous studies have demonstrated that the relation between nuclear methods and echocardiography are similar for patient groups with severe or moderate left ventricular dysfunction (17,19,22,25), although better agreement between the methods has been reported for hypokinetic as compared to akinetic segments (19).

Third, sensitivity and specificity for the detection of segments with more than 50% viable cells in the present study for all three methods are within the range of what has previously been reported for the prediction of functional recovery of segments after revascularization (6,7,17,19,21,24). Thus, the concept, that generally at least roughly 50% of a segment’s myocytes have to be viable to allow functional recovery after
vascularization but that less than 50% viable cells are sufficient to result in positive nuclear tests may prove to be valid in a clinical setting, as well.

Information on histopathologic correlations has so far been scarce. In 1976 Bodenheimer et al. (27), using transmyocardial needle biopsies in patients undergoing coronary bypass surgery after nitroglycerin ventriculography, reported that segments with less than 10% muscle loss responded to nitroglycerin, while unimproved zones demonstrated significant fibrosis. In a more recent study, Depre et al. (28) reported 24 ± 13% fibrosis (range 0–50%) in biopsies of myocardial regions with postoperative wall-motion improvement after revascularization, while segments without improvement had 49 ± 20% fibrosis. However, these results were based on a total of only eight needle biopsies from regions without postoperative improvement, and included only a single biopsy with more than 60% fibrosis. The small size of the specimen obtainable by in vivo needle biopsies and their potentially limited representation of very heterogenous tissue may prove to be additional limitations.

Other explanations for the disagreement between echocardiography and nuclear methods. Other explanations for the discordance between echocardiography and nuclear studies and for the lower specificity of nuclear methods to predict functional recovery after revascularization have recently been proposed (26).

First, there is always a potential for anatomic misalignment between nuclear studies and the echocardiogram. Because the standard for functional recovery in most studies is the echocardiographic determination of improved wall motion, this fact has been suspected to favor echocardiography in previous studies. However, the results of the present study, which compared all three methods with histology, make it rather unlikely that this fact has significantly distorted previous results. Although anatomic misalignment between the respective imaging methods themselves and between imaging methods and pathology remains a problem and may explain some of the scatter for all three methods in the present study, it does not appear to explain the basic differences between the obtained results.

Second, the generally applied criteria to define viability by TH imaging may be suboptimal. Several studies, including the present one, have demonstrated that the magnitude of regional thallium uptake is related to the likelihood that administration of dobutamine will elicit a contractile response. Segments with a higher level of thallium activity have a greater likelihood of responding to dobutamine stimulation (19,21,26). Thus, better agreement between echocardiography and TH, as well as higher specificity of TH for the prediction of recovery after revascularization, may be achievable by using quantitative criteria and higher threshold levels of thallium activity (30).

Third, it has been speculated that the follow-up interval in previous studies was too short and that contractile function may return later than 1 to 3 months after revascularization in some segments, particularly when cellular dedifferentiation at the ultrastructural level has occurred (31,32). However, how myocytes that are cell dedifferentiated would appear on PET or TI-SPECT studies, or how they would contract on DE studies, is unknown. Although we cannot exclude that cellular dedifferentiation may play a role for the observed discordance between echocardiography and nuclear studies and for the previously observed limited specificity of nuclear methods, the present findings support the concept that the varying mixture of scar and viable myocytes in a given segment is the main mechanism. Even so-called transmural myocardial infarctions rarely destroy all of the myocytes in a region of myocardium. Virtually always some myocytes are spared, mostly in the subepicardial region. Their number may be large enough to allow identification by PET and Tl-SPECT, but may not suffice to generate effective contraction, so that the affected segment may not be judged viable by DE.

Study limitations. There are several limitations to the present study. First, the problems of patient selection and of anatomic misalignment between the different methods have been discussed above.

The patient population consists only of males and is small. However, the number of transplantations performed in most institutions is limited, and whether and when an individual patient will actually undergo transplantation can be difficult to foresee. In addition, the availability of whole explanted hearts is limited by the harvesting of valves for homografts.

As the exact time of transplantation could not be foreseen, there was a time interval between the performance of the noninvasive tests and the time hearts were explanted and became available for histologic examination. Although in none of the patients myocardial infarction or episodes of unstable angina were documented during the time between imaging studies and transplantation, changes in viability status could conceivably have occurred in some segments. However, as the noninvasive tests were always performed within a few days of each other their results should have been affected similarly. Furthermore, diffuse hypoperfusion may appear normal by PET and Tl-SPECT imaging and may have led to erroneous results.

Also, the limited number of patients who underwent nuclear testing precluded a complete statistical analysis that would include not only the effects of patients and segmental classification but would also investigate statistical interaction between these grouping variables. A general linear model that would account for these effects could not be calculated as the number of available data points was insufficient. Although multivariate ANOVA demonstrated patient effects, we nevertheless believe the findings based on the segmental analysis to be important, as these reflect the influence of the specific state of the myocardium and blood supply on nuclear and echocardiographic findings in a given segment.

Additionally, this study does not provide direct information about the relationship between histology and recovery of myocardial function after revascularization. The only way to obtain complete histologic examination, however, is to study explanted hearts. The alternative approach of performing intraoperative needle biopsies provides only a very limited
number of very small tissue samples that may not be representative of other segments or even of other regions within the sampled segment.

Finally, the results of this study only apply to regional assessment and cannot be extrapolated to conclusions on recovery of global left ventricular function after revascularization.

**Clinical implications.** Results of the present study suggest that identification of myocardial viability and of contractile response may not necessarily be one and the same. It appears that a given segment has to contain at least approximately 50% viable myocytes to allow demonstration of contractile reserve, as evidenced by a positive dobutamine response. Comparison of the results presented here with previously reported clinical data make it likely that a similar percentage of viable myocytes may be required to allow functional recovery after revascularization and that functional recovery may be more accurately predicted by methods directly evaluating contractile reserve, such as DE.

However, scintigraphic methods that assess perfusion and/or metabolism appear also to identify segments with less than 50% or even less than 25% viable myocytes. Although revascularization of these segments may not contribute to a significant improvement of left ventricular systolic function, it may well provide clinical benefits by attenuating ventricular dilatation and remodeling, by reducing the risk of ventricular arrhythmias and by reducing the risk of subsequent fatal ischemic events.

Dobutamine echocardiography (DE) and scintigraphic methods, therefore, may well provide complementary information in the assessment of myocardial viability. Current nuclear techniques appear to be highly sensitive for the detection of myocardial viability in asynergic myocardium, and negative tests make it highly unlikely that a significant number of viable myocytes are present in a given segment. Conversely, DE appears to be particularly useful for identifying segments with a greater number of viable myocytes and may, thus, have particular value for predicting recovery of systolic function after revascularization.

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