Use of Thallium-201 Redistribution Scintigraphy in the Preoperative Differentiation of Reversible and Nonreversible Myocardial Asynergy

ALAN ROZANSKI, M.D., DANIEL S. BERMAN, M.D., RICHARD GRAY, M.D., RONALD LEVY, M.D., MARJORIE RAYMOND, R.N., JAMSHID MADDahi, M.D., NANCY PANTALEO, R.N., M.S., ALAN D. WAXMAN, M.D., H.J.C. SWAN, M.D., PH.D., AND JACK MATLOFF, M.D.

SUMMARY Thallium-201 (201TI) redistribution scintigraphy might differentiate reversibly from nonreversibly asynergic myocardial segments and thus predict the response of these segments to coronary artery bypass grafting (CABG). To test this hypothesis, 25 consecutive patients undergoing CABG, preoperative stress-redistribution 201TI scintigraphy, and both pre- and postoperative resting equilibration radionuclide ventriculography were evaluated. For both types of scintigraphic study, each patient was imaged in the same three views. Because of the effects of CABG on septal motion, this region was considered separately.

Postoperative improvement was noted in 54% of 72 preoperative asynergic segments. Improvement was common not only in hypokinetic but also in akinetic and dyskinetic segments, and occurred in a similar proportion of studies performed early (less than 2 weeks) or late (3–6 months) after CABG. Thallium-201 redistribution scintigraphy was highly predictive of the pattern of postoperative asynergy: The redistribution pattern was normal in 90% of segments with reversible asynergy and abnormal in 76% of segments with nonreversible asynergy. The presence or absence of pathologic Q waves was less sensitive in this differentiation. Septal segments, however, frequently demonstrated abnormal wall motion postoperatively, despite normal 201TI redistribution scintigraphy. Resting left ventricular ejection fraction (LVEF) was generally unchanged postoperatively, but in some patients with multiple areas of reversible asynergy it did improve.

Thus, 201TI redistribution scintigraphy appears to reliably distinguish viable from nonviable asynergic myocardial regions, and predicts the response of these segments to CABG.

MYOCARDIAL ASYNERGY often occurs in coronary artery disease and may be present in patients with and without prior myocardial infarction.1–4 Such segments may show reversal of asynergy after aorto-coronary revascularization.5–10 This observation has led investigators to conclude that such asynergy does not always represent myocardial scar.4, 11, 12

Thallium-201 (201TI) scintigraphy may be useful in evaluating the cellular state of such asynergic myocardium.13–20 After i.v. injection, at rest, or during exercise, the initial distribution of 201TI in the myocardium is principally determined by the relative distribution of coronary blood flow at the time of injection.19, 20 Subsequently, however, this distribution changes, and during this redistribution phase, underperfused but viable myocardial zones manifest delayed accumulation and relatively slow washout of 201TI, resulting in an equalization of radiotracer in ischemic and normal zones.18–20 Scarred myocardial regions, however, fail to show this equalization of 201TI content compared with normal zones during redistribution.19 Consequently, asynergic myocardial segments associated with a normal 201TI redistribution pattern should be viable, and thus capable of mechanical improvement after aortocoronary bypass surgery. Asynergic segments associated with abnormal 201TI redistribution patterns should be nonviable, and thus incapable of reversible asynergy after surgery.

In testing this hypothesis, this study examines the relationship between redistribution 201TI scintigraphy and the response of resting myocardial asynergy to aortocoronary revascularization.

Methods

Patient Population

Twenty-five consecutive patients undergoing coronary artery bypass surgery who also underwent preoperative 201TI stress-redistribution myocardial scintigraphy and both preoperative and postoperative resting equilibrium radionuclide ventriculography were evaluated.

Twenty-two males and three females, mean age 55 years, were studied. Fourteen patients had a history of myocardial infarction. Of these, 11 had Q waves consistent with previous transmural myocardial infarction and three had confirmed nontransmural infarction. Eleven other patients had a history of chronic stable angina pectoris without prior myocardial infarction. Four patients had two-vessel disease and 21 had three-vessel disease. Fifty-six of the 71 diseased...
vessels had at least one 90% occlusion, and 42 vessels were either subtotally or totally occluded.

Exercise Testing

Stress testing was performed on a treadmill using the standard Bruce protocol with 12-lead ECG monitoring. All patients who were being treated with propranolol were asked to withhold this medication for 24–48 hours before testing. Exercise was maximal, only terminated by exhaustion, severe angina, serious ventricular arrhythmia or hypotension.

Thallium-201 Scintigraphy

A dose of 2 mCi of $^{201}$TI was injected intravenously at near-maximal exercise, and exercise was continued for 60–90 seconds. Serial, multiple-view myocardial scintigrams were obtained, beginning approximately 6 minutes (immediate poststress imaging) and 3–6 hours (redistribution imaging) after the injection of $^{201}$TI. For each phase of imaging, 10-minute images were obtained in the anterior, 45° and 70° left anterior oblique (LAO) projections. Imaging was performed using a standard field-of-view Anger camera equipped with 37 photomultiplier tubes, a ⅛-inch-thick NaI crystal, and a high-resolution, parallel-hole collimator. A 25% energy window centered on the 80-keV x-ray peak and another independent 15% window centered on the 167-keV photopeak were used. All scintigrams were recorded on Polaroid film with a triple-lens camera.

The $^{201}$TI images from each patient were examined jointly by three experienced observers without knowledge of the clinical history or the results of radionuclide ventriculography. For both the poststress and 4-hour redistribution scintigrams, the left ventricle was divided into five segments (fig. 1A) and $^{201}$TI activity was visually assessed for each region by a four-point scoring system: 0 = normal; 1 = slightly decreased as compared to the most intense segment, but almost normal; 2 = definitely decreased; and 3 = severely decreased. Differences in scores were mediated by consensus.

Radionuclide Ventriculography

After i.v. injection of 25 mCi of in vitro labeled autologous technetium-99m red blood cells, multiphase equilibrium blood pool scintigraphy was performed in the anterior, 45° and 70° LAO projections (fig. 1B). A mobile scintillation camera equipped with a high-resolution, parallel-hole collimator, an R-wave gating device and a dedicated minicomputer was used.21 For each view, 14 frames were acquired during the first two-thirds of the cardiac cycle. Two hundred thousand counts per frame were collected using a 25% energy window centered on the 140-keV photopeak of technetium-99m. Images were evaluated in a continuous, closed-loop movie format on the computer's video display after image enhancement by space-time smoothing.22

Ejection fraction (EF) measurement was performed by light-pen assignment of end-diastolic (ED), end-systolic (ES), and left paraventricular background regions of interest. EF was calculated using the standard formula, ED counts – ES counts divided by background-corrected ED counts.

Segmental wall motion was analyzed independently by two experienced observers, unaware of the clinical data or the results of the comparative thallium scinti-

![THALLIUM VIEWS](image)

**SCORE CODE FOR REGIONAL UPTAKE:**

0=Normal
1=Slightly Decreased
2=Moderately Decreased
3=Severely Decreased

![WALL MOTION EVALUATION](image)

**SCORE CODE**

3=Nromokinesis
2=Mild Hypokinesis
1=Severe
0=Hypokinesis
-1=Dyskinesis

**FIGURE 1.** (top) Schematic representation of the views used for analysis of segmental thallium-201 uptake. In each view the scintigram is divided into five segments, and the numbered segments are scored. The anteroseptal and apical segments on the 70° left anterior oblique (LAO) view are not scored because the corresponding segments could not be evaluated by blood pool scintigraphy. P = proximal; D = distal. (bottom) Schematic representation of the views used for analysis of left ventricular wall motion by radionuclide ventriculography. In each view, the left ventricle is divided into five segments, corresponding to the segmental division used for thallium-201 analysis. Because of overlap of vascular structures, only the inferior wall is assessed in the 70° LAO view. The score for all motion is listed below. Ant = anterior.
grams. For each scintigraphic view, the left ventricle was divided into five segments (fig. 1B) corresponding to the segmental division used for 201Tl analysis. Each segment was scored with a five-point system: 3 = normal wall motion, 2 = mild hypokinesis, 1 = severe hypokinesis, 0 = akinesis, and −1 = dyskinesis. Because of overlap with the right ventricle and other vascular structures in the 70° LAO view, only the two inferior wall segments were assessed in this projection. Inferior wall left ventricular (LV) segments that were obscured by overlap of the right ventricle in the anterior projection were not analyzed. Because of well-recognized effects of coronary artery bypass surgery on septal motion, this region was analyzed separately.

Electrocardiographic Data

Q waves were considered pathologic when at least 0.04 second long. Their location was matched with the appropriate myocardial segment on the radionuclide ventriculograms.

Scintigraphic Test Criteria

In the analysis of the 201Tl scintigrams, a stress defect was defined by a segmental score of 2 or more. A normal segmental redistribution pattern was considered present if the corresponding segment showed a score of 0 or 1 on the 3–6-hour image. An abnormal redistribution pattern was defined by a score of 2 or more on the 3–6-hour image. Stress defects not present after redistribution scintigraphy were termed reversible, and persistent defects were termed nonreversible.

For the radionuclide ventriculograms, segmental myocardial asynergy was defined by any resting wall motion abnormality (score of 2 or more). Reversible asynergy was considered present when postoperative segmental wall motion was normal (score of 3) or increased by at least two scores from the preoperative value. By this analysis, a change in wall motion from dyskinesis to akinesis, for example, was not considered improvement. Failure of resting LV wall motion abnormalities to improve postoperatively was considered evidence of nonreversible asynergy.

Coronary Arteriography

Selective cine coronary arteriography was performed in multiple views using the Judkins technique. Significant stenosis was considered present when there was at least 50% diameter narrowing of a major coronary vessel.

Surgical Correlations

At the time of surgery, the left ventricle was examined for the presence and location of myocardial scarring. Myocardial revascularization was considered complete when there was aortocoronary bypass of all significant vascular obstructions. Perioperative infarction was defined by the development of persistent new pathologic Q waves after coronary artery bypass surgery in association with a peak MB-CK of ≥ 40 IU/l.

Statistical Analysis

Agreement between the postoperative wall motion response of asynergic segments and the results of 201Tl redistribution scintigraphy and ECG was measured by Cohen’s kappa statistic (κ).22,24 Kappa ranges in value from −1.0 to 1.0 and can be interpreted as the percentage of agreement between two tests or attributes beyond that which would be expected by chance alone. A value of κ greater than zero reflects greater than chance agreement (κ = 1.0 indicating perfect agreement).

Comparison between preoperative and postoperative LVEF was made by paired t test. A p value ≤ 0.05 was considered significant. Values are expressed as the mean ± SD.

Results

Analysis of Preoperative and Postoperative Wall Motion

Comprehensive wall motion data are shown in table 1. Excluding the septum, there were 250 myocardial segments to be analyzed (five anterior, three 45° LAO, and two 70° LAO segments per patient). Seven segments could not be analyzed because of overlap of other vascular structures. Of the remaining 243 segments, 72 segments demonstrated myocardial asynergy before surgery. Postoperatively, 39 of these asynergic segments (54%) demonstrated wall motion improvement, including 23 hypokinetic, 10 akinetic, and six dyskinetic segments. Thirty-three postoperatively asynergic segments (46%) failed to improve postoperatively, including 23 hypokinetic, five akinetic, and five dyskinetic segments. All but one of the 72 asynergic myocardial segments were subtended by significantly diseased coronary arteries. Sixty-seven of the 71 diseased vessels were revascularized at the time of surgery. Of the four vessels not bypassed, three supplied myocardial segments with normal wall motion. The fourth vessel supplied a posterolateral segment that failed to improve after surgery.

Response of Asynergic Myocardial Segments to Surgery: Prediction by Preoperative 201Tl Redistribution Scintigraphy

Of the 39 asynergic segments with improved wall motion postoperatively, 35 (90%) demonstrated a normal preoperative 201Tl redistribution pattern. In contrast, of the 33 segments with nonreversible asynergy, 25 (76%) had an abnormal 201Tl redistribution pattern preoperatively (table 2).

In all segments, preoperative 201Tl redistribution scintigraphy agreed with the postsurgical wall motion response by a percentage greater than chance alone, and in most segments, the proportion of chance-corrected agreement was more than 75% (table 3).

As the timing of postoperative studies may be im-
TABLE 1. **Clinical Data for the Total Patient Population**

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<th>Case</th>
<th>Cardiac catheterization (RCA &gt; 50% stenosis)</th>
<th>Asynergic segments with improved WM postop</th>
<th>Asynergic segments without improved WM postop</th>
<th>Thallium defects†</th>
<th>Preop LVEF (%)</th>
<th>Postop LVEF (%)</th>
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</table>

*Diseased coronary artery not revascularized at the time of surgery.
†For localization of wall motion and thallium scintigraphic segments 1–10, see figure 1.
Abbreviations: RCA = right coronary artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; WM = wall motion; LVEF = left ventricular ejection fraction; LM = left main.

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TABLE 2. **Comparison of the Thallium-201 Redistribution Pattern with the Postoperative Wall Motion Response in 72 Asynergic Segments**

<table>
<thead>
<tr>
<th>Postoperative wall motion response</th>
<th>Normal</th>
<th>Abnormal</th>
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<tbody>
<tr>
<td>Improved</td>
<td>35</td>
<td>4</td>
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<tr>
<td>Not improved</td>
<td>8</td>
<td>25</td>
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**TABLE 3. Chance-corrected Agreement Between Postoperative Wall Motion Response and Results of Thallium-201 Redistribution Scintigraphy and Electrocardiogram as Measured by the Kappa Statistic**

<table>
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<th>Segment†</th>
<th>κ for 201TI redistribution scintigraphy</th>
<th>κ for ECG</th>
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<td>1</td>
<td>1.00†</td>
<td>0.47*</td>
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<td>10</td>
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</table>

* p < 0.050; † p < 0.001; § Kappa statistic was not computed when for every patient a segment was scored as normal or abnormal.
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Differentiation of Reversible and Nonreversible Asynergy: Comparison of ECG and $^{201}$Tl Redistribution Scintigraphy

Pathologic Q waves were absent in 21 of 35 reversibly asynergic segments (60%), and were present in 19 of 30 (63%) nonreversibly asynergic segments. One patient with left bundle branch block (and seven asynergic segments) was excluded from this analysis.

While the ECG agreed with the postsurgical wall motion response by a percentage greater than chance alone, the percentage of chance-corrected agreement was generally much less than that between $^{201}$Tl redistribution scintigraphy and wall motion response (table 3).

Correlation of Results with the Intraoperative Surgical Findings

Of 43 asynergic zones with a normal $^{201}$Tl redistribution pattern, 41 segments demonstrated no evidence of epicardial scarring. Asynergy was reversible postoperatively in 33 of these 41 segments. Two segments with patchy fibrosis also demonstrated reversible asynergy. In the 29 asynergic segments with an abnormal pattern of $^{201}$Tl redistribution, 12 were found to have epicardial scar tissue while two other segments had evidence of patchy fibrosis. All 14 of these segments failed to show improved wall motion postoperatively. In the 15 remaining segments with no epicardial scar, 11 demonstrated nonreversible asynergy.

Analysis of the Septum

Of the 50 proximal and distal septal segments, 18 segments had normal preoperative wall motion, 25 were hypokinetic, four were akinetic and three were dyskinetic. Postoperatively, 40 segments demonstrated abnormal wall motion, including 20 hypokinetic, 10 akinetic and 10 dyskinetic segments. Twenty-six septal segments showed a reduction in wall motion postoperatively, four segments improved, while 20 segments were unaffected by surgery. The preoperative $^{201}$Tl redistribution pattern was normal in 46 of these 50 segments.

Correlation of Wall Motion and EF Response to Surgery

The mean value of LVEF at rest preoperatively was not significantly different postoperatively (0.53 ± 0.11 vs 0.55 ± 0.12 respectively). In 17 of the 25 patients, the postoperative EF was within 5% of the preoperative value. This figure is within the mean variability of LVEF as measured by equilibrium blood pool scintigraphy. In five patients, the resting EF rose by more than 5% after surgery, including four patients who manifested reversible asynergy in at least three myocardial segments, including at least one area of preoperative akinesis. The remaining three patients had a greater than 5% fall in postoperative EF but demonstrated no worsening of wall motion, except in the septum, and no enzymatic or electrocardiographic evidence of perioperative myocardial infarction.

Relation of $^{201}$Tl Stress-Redistribution Scintigraphy and Segmental Wall Motion Before and After Surgery

In the 243 analyzable segments, 83 manifested stress $^{201}$Tl defects (table 4). Of the 171 segments with normal preoperative wall motion, 26 segments (15%) showed reversible stress-redistribution $^{201}$Tl defects, five (3%) showed nonreversible defects, and 140 had no stress defect. Of the 39 segments with reversible asynergy, 22 (56%) showed reversible $^{201}$Tl defects, four segments had nonreversible $^{201}$Tl defects, and 13 (33%) had normal regional $^{201}$Tl uptake after stress. When analyzed in terms of the degree of asynergy, only nine of 23 (39%) reversibly hypokinetic zones, compared with 13 of 16 (81%) reversibly akinetic or dyskinetic zones, were associated with a reversible $^{201}$Tl defect. Of the 33 segments with nonreversible asynergy, one (3%) showed evidence of reversible $^{201}$Tl defects, 25 (76%) had nonreversible $^{201}$Tl defects, and seven (21%) had normal regional $^{201}$Tl uptake poststress.

Case Illustrations

Comparative blood pool and 4-hour $^{201}$Tl redistribution myocardial scintigrams in three clinical case examples are shown in figures 2–4.

Discussion

LV wall motion abnormalities may improve after aorticcoronary bypass surgery, but the reported incidence has varied widely, from 21–75%. In this study, reversal of LV wall motion abnormalities after myocardial revascularization occurred in 54% of the preoperatively asynergic segments. The frequency of segmental improvement was similar in patients studied 2 weeks postoperatively and those studied 3–6 months after surgery. Postoperative improvement was present not only in hypokinetic segments, but in akinetic and dyskinetic segments as well. This observation, also noted by previous investigators, is complemented by pathologic studies that have shown that severe asynergy may be compatible with the presence of structurally intact myocardium.

Because $^{201}$Tl redistribution scintigraphy reflects the cellular state of the myocardium, it might be ideal for assessing preoperatively the potential reversibility of LV asynergic segments. In this study the preoperative $^{201}$Tl redistribution pattern and the response of asynergic segments to myocardial revascularization were significantly correlated, with 35 (90%) of 39 segments with improved postoperative wall motion exhibiting a normal $^{201}$Tl redistribution pattern, and 25 (76%) of 33 segments with nonreversible asynergy demonstrating an abnormal $^{201}$Tl redistribution pattern.

In 12 segments, $^{201}$Tl redistribution scintigraphy did not correctly predict the postoperative findings. Of these, four segments showed an abnormal $^{201}$Tl redistribution pattern despite improved postoperative wall motion. However, abnormal myocardial segments may demonstrate very slow redistribution, so some of these regions might have shown redistribution over
a longer period of time. In the remaining eight segments, myocardial asynergy failed to reverse postoperatively despite normal regional 201Tl uptake during the redistribution phase. One possible explanation for this subgroup would be perioperative infarction, but this was not evident. Another possible explanation would be graft occlusion (without infarction), but as postoperative coronary arteriography was not performed in these patients, this possibility was not evaluated.

The findings in this study are supported by investigations that have demonstrated a correlation between the pattern of 201Tl redistribution in asynergic segments and the response of such asynergic segments to nitroglycerin or to postextrasystolic potentiation.

Comparison of ECG and 201Tl Redistribution Scintigraphy in the Identification of Reversible and Nonreversible Asynergy

The presence or absence of Q waves may be relatively inaccurate in distinguishing between potentially reversible and nonreversible myocardial asynergy. In this study, preoperative electrocardiography was less useful than 201Tl redistribution scintigraphy in assessing the wall motion response of asynergic segments to surgery. The inaccuracy of equating abnormal Q waves with myocardial scar has also been supported by postmortem studies in which the reported correlations between electrocardiographic and anatomic sites of scar are 70% or less. In addition, clinical studies have noted evidence of 201Tl reversibility in many segments with abnormal Q waves as well as the occasional disappearance of such Q waves after myocardial revascularization.

Surgical Findings

Of 29 segments that showed an abnormal pattern of 201Tl redistribution, only 12 were associated with epicardial scar and two others manifested patchy fibrosis. Fifteen other segments, including 11 with nonreversible asynergy, did not have epicardial scar. These findings are not surprising, because epicardial scarring does not invariably occur in the presence of transmural infarction, and subendocardial necrosis will not lead to the formation of epicardial scar. As expected, with the exception of two zones manifesting patchy fibrosis, myocardial segments associated with normal 201Tl redistribution scintigraphy did not manifest epicardial pathology.

Effect of Surgery on Septal Motion

Although the 201Tl redistribution pattern was normal in all but four septal segments, after surgery a reduction in septal motion was observed in the majority of septal segments. Others have reported similar effects of coronary artery bypass surgery on septal motion in the absence of perioperative infarction. The cause of this selective reduction in septal motion postoperatively is not known.

Figure 2. Comparative anterior view blood pool and 4-hour thallium-201 (201Tl) redistribution (upper right) scintigrams in a 57-year-old male with apical akinesis before surgery. Pre- and postoperative end-diastolic (ED) and end-systolic (ES) blood pool images and their superimposed edges are shown. Although the poststress 201Tl image (not shown) manifested an apical defect, the 4-hour redistribution pattern was normal. Postoperatively the previously akinetic apex demonstrated normal wall motion. This case is an example of reversible asynergy correctly predicted by a normal pattern of 201Tl redistribution scintigraphy.
Response of LVEF to Surgery

Although the resting postoperative LVEF was not significantly changed in these 25 patients as a group, in five patients, four of whom had extensive and severe reversible asynergy, resting EF rose significantly. This finding suggests that in a subgroup of patients with multiple areas of severely depressed but reversibly asynergic myocardium, LVEF may improve after myocardial revascularization.

Theoretical Considerations

The pathophysiology leading to the development of asynergic yet viable myocardium is poorly understood. Progressive hypoperfusion has been linked to the development of hypocontractile myocardial function in the acute experimental model, but the relationship of resting hypoperfusion to myocardial asynergy in the chronic state has been less well established.

Several resting 201TI studies have suggested the presence of resting regional hypoperfusion in patients with both stable and unstable coronary artery disease without myocardial infarction. Further, various investigators, using inert gas techniques, have documented diminished resting myocardial blood flow in coronary artery disease patients, some of whom have no evidence of prior myocardial infarction. Whether such chronic resting hypoperfusion necessarily implies the presence of chronic resting ischemia remains controversial. Chatterjee and coworkers documented reversal of anterior wall hypokinesis and associated abnormal resting regional lactate metabolism in three patients after myocardial revascularization. Herman et al. also noted regional myocardial lactate production in zones with myocardial asynergy, but the significance of this finding was obscured by the presence of abnormal lactate metabolism in normokinetic zones as well. Although these two studies suggest the presence of chronic resting ischemia, further studies, perhaps with the use of positron imaging techniques, are needed to better define the relationship between resting hypoperfusion and abnormal myocardial metabolism.

If chronic ischemia is the cause of reversible hypocontractile function, then such viable myocardial segments would be highly jeopardized, especially when the degree of resting asynergy is severe. Reversible 201TI defects, a manifestation of exercise-induced ischemia, were more frequent in regions of...
reversible asynergy than in normally contracting
zones (56% vs 15%, respectively), and were most
frequent in those regions manifesting severe, reversible
asynergy (occurring in 39% of reversibly hypokinetic
vs 81% of reversibly akinetic or dyskinetic myocardial
segments).

The finding of normal 201TI scintigrams immedi-
ately after stress in some segments with reversible
asynergy might be considered at variance with the
concept of chronic resting ischemia. In part, this result
may be explained by the fact that myocardial perfu-
sion images reflect only relative rather than absolute
changes in myocardial perfusion.70 Thus, mildly
hyperperfused myocardial segments may not have been
appreciated in the face of more severe perfusion ab-
normalities in other segments. Further, a balanced
reduction in myocardial perfusion could have existed
in patients with three-vessel disease, thereby preclud-
ing appreciation of hypoperfusion in any segment. Re-
cent studies have suggested enhanced detection of
perfusion abnormalities with the use of quantitative
201TI analysis.55-56 Thus, this technique might demonstrate
the presence of perfusion abnormalities in asynergic
regions with visually normal thallium scintigraphy.

The present study clearly suggests that in patients
with chronic ischemic heart disease, hypokontractile
myocardium may remain viable and may improve
after coronary artery bypass surgery and that this
viability may be predicted by preoperative 201TI
redistribution scintigraphy. Nevertheless, the patho-
physiology of reversible asynergy and the long-term
prognostic importance of surgical amelioration of
asynergy remain to be established.

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