Prospective Evaluation of Viable Myocardium by Quantitative Dipyridamole-Thallium-201 Scintigraphy and Radionuclide Ventriculography*

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Improvement of myocardial function is a major goal of coronary revascularization. Considerable interest remains in the preoperative identification of viable myocardium. We examined 26 consecutive patients with left ventricular dysfunction undergoing coronary artery bypass grafting. Serial dipyridamole-thallium imaging and radionuclide ventriculography was performed preoperatively and postoperatively. The relationship between preoperative and postoperative thallium perfusion and segmental wall motion was analyzed. The mean preoperative ejection fraction was 32 ± 9 (21 to 51%) and increased to 41 ± 12 (17 to 67%) postoperatively (p>0.01). Seventy-seven percent of patients improved their global ejection fraction postoperatively by >5%. Thallium perfusion improved postoperatively in 84% of reversible defects vs 63% of partially reversible defects and 35% of fixed defects. Segments with either reversible or partially reversible thallium defects showed an improved postoperative wall motion in 71% and 65%, respectively. Postoperative wall motion improved in 43% of fixed defects. Overall, 67% of hypokinetic segments showed improved postoperative wall motion while only 29% of akinetic or dyskinetic segments improved postoperatively. Preoperative thallium redistribution coupled with preserved wall motion was predictive of improvement in wall motion postoperatively and indirectly indicates myocardial viability. However, 43% of fixed defects also showed improved postoperative wall motion. A significant improvement in global ejection fraction was found and could be predicted by a linear regression analysis utilizing clinical and thallium parameters. (Chest 1995; 107:335-40)

LAO = left anterior oblique

Key words: dipyridamole; revascularization; thallium imaging; radionuclide ventriculography

Coronary revascularization by either surgical or percutaneous techniques is being performed with increasing frequency. In patients with coronary disease, left ventricular function is the most important prognostic indicator of survival and a major determinant of outcome in those undergoing revascularization. Improved left ventricular function is a major goal of revascularization with the assumption that this will result in improved morbidity and mortality. Thus, considerable interest exists in the preoperative identification of viable ("stunned" or "hibernating") myocardium. The role of coronary revascularization in an individual patient can be better delineated if noninvasive techniques can reliably detect dysfunctional, but still viable myocardium. Thallium-201 stress imaging has been shown to be a valuable technique for assessing myocardial viability. Reversible myocardial perfusion defects reliably correlate with improved regional wall motion following revascularization. However, myocardial segments with fixed defects during thallium stress imaging may also show improved ventricular function with revascularization, suggesting the presence of viable myocardium.1-4 Approximately 40% of fixed thallium defects during exercise imaging demonstrate redistribution with either reinjection of thallium or delayed imaging.1,2 Positron emission tomography can also accurately predict myocardial viability in segments with fixed perfusion defects3 but is not readily available.

Pharmacologic stress testing with dipyridamole-thallium imaging offers a safe and effective alternative to exercise studies in evaluating coronary artery disease.5,6 As dipyridamole produces more potent vasodilation of the coronary arteries than maximal exercise, pharmacologic stress testing may be preferred in patients with severe left ventricular dysfunction who are unable to perform adequate exercise. Dipyridamole stress may produce less severe myocardial ischemia than exercise and thus facilitate redistribution and enhance the detection of viable myocardium in high-risk patients with poor exercise tolerance. Furthermore, the need for resting reinjection of thallium after dipyridamole may be less im-

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portant due to a large splanchnic reservoir of thallium that may functionally “reinject” thallium at rest.

The aim of our study was to assess the utility of preoperative quantitative dipyridamole-thallium imaging in detecting viable myocardium in patients with depressed left ventricular function undergoing coronary revascularization. Serial dipyridamole-thallium imaging and radionuclide ventriculography were performed before and after revascularization. The relationship between preoperative perfusion defects and improved myocardial perfusion and left ventricular regional and global systolic function postoperatively was analyzed.

METHODS

Study Patients

The study group consisted of 26 consecutive eligible patients who underwent diagnostic cardiac catheterization and were referred for elective coronary artery bypass grafting at the New England Deaconess Hospital. Patients were considered eligible for study if they were stable clinically and had multivessel coronary artery disease with depressed left ventricular function at catheterization. After informed consent had been obtained, each patient underwent dipyridamole-thallium scanning and radionuclide ventriculography prior to surgery. Postoperatively, these studies were again obtained regardless of symptoms after a period of at least 2 weeks.

All patients met the following inclusion criteria: (1) multivessel coronary disease (≥50% stenoses) suitable for surgical revascularization; (2) ejection fraction <45% by contrast ventriculography; (3) no history of alcohol abuse; (4) no significant valvular disease; (5) absence of contraindications to dipyridamole-thallium scanning; and (6) ability to give informed consent. Exclusion criteria included the following: (1) unstable angina requiring intravenous nitroglycerin or urgent revascularization; (2) ≥50% left main stenosis; and (3) refusal to give informed consent.

Myocardial Perfusion Scintigraphy

Dipyridamole-thallium scanning was performed using a standardized protocol (1 to 6 days). Dipyridamole-thallium scanning was performed after catheterization and thus did not bias patient referral for revascularization. Images were collected, beginning 5 min after thallium injection, in the 45° left anterior oblique (LAO), 60° left lateral, and anterior projections using a portable gamma camera. Delayed images were taken at 3 h. Analogue and digitized planar images with quantification of myocardial thallium distribution on initial and delayed images were constructed using a computer (NIC 2000) and commercially available software based on a study by Wackers et al.7 In the analysis of thallium-201 distribution profiles, a defect on the postdipyridamole profile was defined as at least five adjacent segments (50° angle) below the lower limit of normal thallium-201 distribution. The three projections were divided into a total of ten segments as previously described.8 Each segment was classified as showing normal uptake or showing a fixed defect, partially reversible defect, or fully reversible defect. A defect was considered partially reversible if there was ≥25% but ≤75% reduction of the size of the stress defect on resting imaging. All scans were reviewed in a blinded fashion by three experienced reviewers and authors. Postoperatively, the dipyridamole-thallium scans were repeated at an average of 18 days (15 to 36 days) to allow improvement of “stunned” or “hibernating” myocardium. Improved postoperative perfusion was defined as either normalization of thallium uptake or ≥50% reduction in the size of the stress defect.

Radionuclide ventriculography was performed at the same preoperative and postoperative time intervals. Twenty millicuries of in vitro labeled autologous technetium-99m (99mTc) red blood cells was injected intravenously and multigated equilibrium blood pool scintigraphy was performed in the anterior, LAO 45°, and LAO 60° projections. On average, 10 million counts were obtained per view with a minimum of 15 frames per view using a 20% energy window centered on the 140-keV photopeak of 99mTc. A mobile scintillation camera equipped with a slant hole collimator, an R-wave gating device, and a dedicated minicomputer was used. Left ventricular ejection fraction was calculated by standard techniques. Segmental wall motion was analyzed independently by three independent observers in a blinded fashion. The three views were divided into a total of ten segments to match the thallium perfusion scores. Each segment was scored with a five-point grading system: 3=normal; 2=mild hypokinesia; 1=severe hypokinesia; 0=akinesia; and −1=dyskinesia. A regional wall motion score was obtained by summation of all ten segment scores from −1 to 3. Improved segmental wall motion postoperatively was defined as a ≥1 grade improvement in any segment. Because of the well-recognized effects of bypass surgery on interventricular septal motion, this region was analyzed separately.

Coronary Angiography

Diagnostic coronary angiography was performed in multiple oblique projections and left ventricular cineventriculography was performed in the 90° right anterior oblique projection. Maximal luminal diameter narrowing was estimated visually by three independent, blinded observers and differences of interpretation were resolved by consensus. Stenoses of 50% or greater obstruction were considered significant. No patient had 2° or greater mitral or aortic regurgitation or evidence of valvular stenosis at catheterization.

Coronary Artery Bypass Surgery

At operation, an attempt was made to revascularize all major and branch vessels with a 50% or greater stenosis. In no case was aneurysctomy performed. On average, 3.2 vessels (range, two to five) were bypassed per patient, with 77% receiving three or more grafts. Sixty-two percent of patients received internal mammary artery grafts.

RESULTS

Clinical Characteristics

Twenty-four male and two female patients with a mean age of 65 years (46 to 78 years) were studied. During the study period, nine patients were excluded due to the development of unstable angina, six patients refused entry into the study, and one patient died prior to revascularization. Eighty-eight percent had a prior documented myocardial infarction. The mean New York Heart Association class of angina was 2.8 preoperatively with a mean heart failure class of 1.9. Postoperatively, the mean values were 0.4 and 0.9, respectively. Ninety-two percent of patients had three-vessel coronary artery disease, and the mean ejection fraction was 34% (19 to 44%) by contrast ventriculography. Preoperatively and postoperatively, there was no significant difference in the
Thallium Scanning

Dipyridamole-Thallium Scanning

Preoperatively, 109 segments (42%) were normal, 63 (24%) showed partial redistribution, 19 (7%) showed total redistribution, and 69 (27%) were fixed. Postoperatively, 156 segments (60%) were normal, 26 (10%) showed partial redistribution, 5 (2%) showed total redistribution, and 73 (28%) were fixed. Eighty-four percent (16/19) of fully reversible perfusion defects showed normalized perfusion postoperatively while partially reversible defects showed improved perfusion in 63% (42/63). Additionally, 35% (24/69) of preoperative fixed defects showed improved thallium uptake postoperatively (Table 1).

Radionuclide Ventriculography

The mean ejection fraction preoperatively was 32 ± 5% (21 to 51%) and increased to 41 ± 12% (17 to 67%) postoperatively (p<0.01). Seventy-seven percent (20/26) of patients improved their global ejection fraction postoperatively by ≥5% (an average increase of 9.7 ± 8%). There were 175 segments with abnormal wall motion preoperatively for an average of 6.7 (range, 4 to 10) segments per patient. Ninety-three (53%) abnormal segments improved postoperatively. The cumulative regional wall motion score was 11.7 preoperatively and improved to 16.6 postoperatively.

Correlation of Preoperative Thallium Imaging and Regional Wall Motion

Ninety-one percent (117/128) of segments with either normal perfusion or complete thallium redistribution had preserved wall motion preoperatively (≥grade 1). In contrast, only 76% (48/63) of segments with partial redistribution and 64% (44/69) of fixed defects had preservation of wall motion preoperatively.

Preoperative wall motion abnormalities improved by at least one grade in 53% of segments after revascularization (Table 1). Seventy-one percent (12/17) of fully reversible segments with abnormal preoperative wall motion showed improved wall motion postoperatively. Similarly, 68% (41/60) of partially reversible segments with abnormal wall motion showed improved postoperative wall motion. An additional 43% (30/69) of segments with fixed thallium defects and abnormal wall motion preoperatively showed improved segmental wall motion postoperatively. Thus, nearly a third (30/93) of all segments showing improved wall motion had fixed thallium defects preoperatively.

Akinetic or dyskinetic segments with fixed thallium defects showed improved postoperative wall motion in only 28% (7/25). In contrast, 52% (23/44) of hypokinetic (grade 1 or 2) segments with fixed defects showed improved postoperative wall motion (Fig 1). No attempt was made to grade the size or severity of fixed thallium defects.

Of the 98 segments showing improved postoperative wall motion, 74 (80%) were hypokinetic preoperatively. Asynergic and dyssynergic segments thus accounted for 20% of all segments showing postoperative improvement. Of all hypokinetic defects, 67% (74/110) improved, while 29% (19/65) of akinetic or dyskinetic segments improved, independent of the perfusion status of these segments.

**Table 1**: Preoperative Thallium Defects

<table>
<thead>
<tr>
<th>Postoperative Improvement</th>
<th>Reversible (n=19)</th>
<th>Partially Reversible (n=63)</th>
<th>Fixed (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thallium uptake, %</td>
<td>84</td>
<td>63</td>
<td>35</td>
</tr>
<tr>
<td>Regional wall motion, %</td>
<td>71</td>
<td>68</td>
<td>43</td>
</tr>
</tbody>
</table>

*Percentage of myocardial segments with improved postoperative thallium uptake and percentage of myocardial segments with improved postoperative segmental wall motion in relationship to preoperative thallium perfusion status. The improvement in postoperative thallium perfusion correlates well with improved segmental wall motion in all three groups.

The number of patients taking digoxin, diuretics, β-blockers, or vasodilators.

One patient suffered a new Q-wave infarction, while three other patients had non-Q-wave events. All four patients with perioperative infarction were included in our analysis. There was one cerebrovascular accident during bypass grafting.

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**Figure 1.** Shown is the percentage of myocardial segments with improved postoperative segmental wall motion in segments with fixed thallium defects preoperatively. If preoperative wall motion is preserved (hypokinetic), wall motion improved postoperatively in 54%. Fixed segments that are akinetic or dyskinetic preoperatively show improved wall motion postoperatively in only 28%.
Multivariate Analysis of Clinical, Thallium, and Radionuclide Variables in Assessing Postoperative Improvement in Global Ejection Fraction

Preoperative angina class, congestive heart failure class, number of fixed thallium segments, wall motion score, diabetes, and ejection fraction were not useful preoperative predictors of improved global left ventricular function with revascularization. By multivariate analysis, only age, number of preoperative segments with thallium reversibility (partial or total), and number of segments with preserved wall motion preoperatively correlated with improved global ejection fraction postoperatively. By regression analysis, an equation to predict the degree of improvement in postoperative global ejection fraction can be generated with reasonable accuracy (R=0.796) (Fig 2): change in ejection fraction=46+3.5 (number of segments with thallium redistribution)—1.6 (number of segments with wall motion score 1 or 2)−0.5 (patient’s age).

DISCUSSION

To our knowledge, this is the first prospective evaluation of preoperative perfusion abnormalities utilizing quantitative dipyridamole-thallium imaging in patients undergoing coronary revascularization with depressed left ventricular function. Improvement in segmental wall motion and global ejection fraction was correlated with preoperative perfusion abnormalities and systolic function. Our study confirms prior observations of a continuum of disease severity as assessed by quantitative thallium scintigraphy and a corresponding continuum of the physiologic response to reperfusion therapy.

The frequency by which abnormal perfusion defects normalized after surgery correlated with the preoperative severity of the perfusion abnormality. Thus, 84% of totally reversible defects showed normal perfusion postoperatively. Partially reversible defects showed improved perfusion in 63% of postoperative segments. Fixed defects showed improved perfusion in 35% of postoperative segments.

Segments with improved perfusion postoperatively frequently showed improved regional wall motion postoperatively, especially if there was preserved preoperative wall motion (grade 1 or 2). Altogether, 71%, 68%, and 43% of reversible, partially reversible, and fixed defects showed improved postoperative wall motion. Eighty percent (74/93) of segments with improved postoperative wall motion were hypokinetic preoperatively. Thus, preoperative thallium redistribution coupled with preserved wall motion was predictive of improvement in wall motion postoperatively and indirectly indicates myocardial viability.

Our findings with dipyridamole-thallium scanning are in concert with earlier reports with exercise thallium imaging.4,9 Reversible defects reliably predicted improved postoperative regional wall motion, while fixed defects underestimated the degree of viable myocardium. Overall, 43% of fixed defects contained viable myocardium (improved wall motion with revascularization), especially if preoperative wall motion was preserved. Fixed defects on dipyridamole-thallium scanning, therefore, are not a contraindication to surgical revascularization.

In our study, a significant improvement in global ejection fraction was found postoperatively. Initial studies in patients with preserved systolic function failed to show an improvement in global ejection fraction postoperatively.4,9 Recent studies using both resting thallium-201 scintigraphy and delayed imaging of exercise thallium-201 scintigraphy have shown improved global and regional systolic function after revascularization.10,11 The degree of postoperative improvement in left ventricular dysfunction has been found to correlate with the degree of preoperative dysfunction.10,12 As there were no differences in preoperative and postoperative vasoactive medications, this improvement in ejection fraction is likely due to relief of ischemia and not altered loading conditions.

Other methods have been investigated as predictors of improved regional wall motion after revascularization. Augmentation of segmental wall motion in response to exercise or inotropic stimulation can also

![Figure 2. Linear regression analysis to predict postoperative change in global ejection fraction based on preoperative thallium redistribution, preoperative wall motion score, and patient age. Thallium redistribution (either full or partial), preserved preoperative wall motion, and a younger age predicted an excellent response to surgery.](image-url)
predict improved wall motion in response to revascularization. The accuracy of this method in predicting postoperative improvement in segmental wall motion was significantly greater than analysis of resting Q waves. Furthermore, improved global ejection fraction with isotropic stimulation was correlated with a significant improvement in 5-year survival after revascularization. These findings support the concept that a primary goal of revascularization is to enhance myocardial function in ischemic but viable areas.

Distinguishing viable myocardium from infarction may also be possible with nuclear magnetic resonance imaging. However, cardiac magnetic resonance imaging, like positron emission tomographic scanning, is not currently as accessible to practitioners as is thallium imaging. Exercise echocardiography is also useful in assessing viable myocardium, while the role of both dipyridamole and dobutamine stress echocardiography awaits further elucidation. At present, dipyridamole-thallium imaging to assess perfusion abnormalities in conjunction with radionuclide ventriculography to assess resting wall motion can successfully identify most of ischemic but viable areas that improve with revascularization. However, neither imaging modality alone can accurately predict those patients whose conditions are likely to improve with revascularization.

Methodologic Considerations

As there is no specific time at which redistribution is complete, the distinction between total and partial redistribution is somewhat arbitrary. Thus, we found similar rates of improved postoperative regional wall motion in segments with fully or partially reversible thallium defects. Partial defects showed normalized perfusion postoperatively less frequently in our study compared with prior reports. Delayed imaging or reinjection of thallium at 3 h may have enhanced our detection of viable myocardium.

No attempt was made to grade the severity of fixed thallium perfusion defects. Previous authors have shown that improved detection of viable myocardium can be accomplished by grading the severity of reduced thallium uptake. With reinjection of thallium and improved grading of fixed defects, the sensitivity of dipyridamole-thallium scanning in detecting viable myocardium can likely be markedly improved. Similarly, as delayed improvement in wall motion may be seen up to 6 to 12 months after revascularization, later studies may have shown further improvement in ventricular function.

As septal wall motion is frequently abnormal postoperatively even with normal perfusion, the benefits of revascularization on the interventricular septum cannot be precisely studied. In our study, 20 of 26 septal segments had abnormal preoperative perfusion and only 7 of 26 showed improved segmental wall motion postoperatively. Thus, we likely underestimated the benefits of revascularization to the septum due to the unpredictable effects of surgery on septal motion.

Conclusion

Dipyridamole-thallium scanning is useful in predicting the potential improvement in left ventricular function following revascularization. The presence of persistent thallium defects does not necessarily imply scar or irreversible myocardial damage, especially if there is preserved preoperative regional wall motion. Unfortunately, in the high-risk cardiac surgical candidate in whom detection of viable myocardium is crucial, patients are frequently unable to perform adequate stress testing. Dipyridamole-thallium imaging in conjunction with radionuclide ventriculography appears to be a valuable alternative to stress thallium imaging with similar strengths and limitations. Prospective evaluation is required to confirm if the degree of improvement in ejection fraction can be reliably estimated based on clinical, thallium, and wall motion parameters.

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