Stress-Induced Reversible and Mild-to-Moderate Irreversible Thallium Defects
Are They Equally Accurate for Predicting Recovery of Regional Left Ventricular Function After Revascularization?

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Background—In patients with coronary artery disease, stress-redistribution-reinjection thallium scintigraphy provides important information regarding myocardial ischemia and viability. Although both reversible and mild-to-moderate irreversible thallium defects retain metabolically active, viable myocardium, we hypothesized that stress-induced reversible thallium defects may better differentiate reversible from irreversible regional left ventricular dysfunction after revascularization.

Methods and Results—Twenty-four patients with chronic coronary artery disease underwent prerevascularization and postrevascularization exercise-redistribution-reinjection thallium single photon emission CT, gated MRI, and radionuclide angiography. After revascularization, mean left ventricular ejection fraction increased from $30 \pm 9\%$ to $37 \pm 13\%$ at rest ($P<0.001$). Before revascularization, abnormal contraction at rest was observed in 56 of 110 reversible and 20 of 37 mild-to-moderate irreversible thallium defects (51% and 54%, respectively). After revascularization, regional contraction improved in 44 of 56 reversible compared with 6 of 20 mild-to-moderate irreversible thallium defects (79% and 30%, respectively; $P<0.001$). The final thallium content (maximum tracer uptake on redistribution-reinjection images) was significantly higher in regions with reversible defects that improved than in those that did not improve after revascularization (86$\pm$16% versus 66$\pm$9%, $P<0.001$). In contrast, final thallium content was similar in regions with mild-to-moderate irreversible defects that improved and in those that did not improve after revascularization (69$\pm$9% versus 65$\pm$10%, $P=NS$). Furthermore, when asynergic regions were grouped according to the final thallium content, at 60% threshold value, functional recovery was observed in 83% of regions with reversible defects compared with 33% of regions with mild-to-moderate irreversible defects ($P<0.001$).

Conclusions—These findings suggest that although both reversible and mild-to-moderate irreversible thallium defects after stress retain viable myocardium, the identification of reversible thallium defect on stress in an asynergic region more accurately predicts recovery of function after revascularization. Even at a similar mass of viable myocardial tissue (as reflected by the final thallium content), the presence of inducible ischemia is associated with an increased likelihood of functional recovery. (Circulation. 1998;98:501-508.)

Key Words: coronary disease ■ scintigraphy ■ myocardium ■ ischemia ■ revascularization

Paradigms concerning the relationship between myocardial perfusion and contraction have changed over the past 2 decades. Substantial data now exist to indicate that impaired left ventricular function at rest in patients with coronary artery disease is not necessarily an irreversible process. Among patients with preoperative left ventricular dysfunction, it has been estimated that nearly one third may exhibit improvement in global left ventricular function after revascularization. This is the same patient population, however, that experiences high perioperative morbidity and mortality, which explains the reluctance of cardiac surgeons to operate on them. Because enhanced left ventricular function after revascularization is associated with improved survival, the clinically important task is to distinguish patients with functionally recoverable myocardium from those who have predominantly scarred, nonrecoverable myocardium. Regional left ventricular dysfunction arising from a transient period of myocardial ischemia (repetitive stunning) and/or a prolonged period of myocardial hypoperfusion at rest (hibernation) may be reversible, whereas regional dysfunction arising from transmural myocardial infarction or mixed scarred and viable myocardium may be irreversible after revascularization. The distinction between reversible and irreversible asynergic regions may be made by demon-
strating stress-induced ischemia (reversible thallium defect) in regions that are asynergic on the basis of repetitive stunning and/or hibernation and scar or lack of ischemia (irreversible thallium defect) in regions that are asynergic as a result of transmural infarction or mixed scarred and viable myocardium. Such a distinction prospectively has important clinical implications, especially in patients who are being considered for interventional therapy.

Thallium scintigraphy has occupied a unique place in cardiac diagnostic imaging for both detecting coronary artery narrowing and distinguishing viable from scarred myocardium.\textsuperscript{21,22} Although both reversible and mild-to-moderate irreversible thallium defects retain metabolically active, viable myocardium by PET,\textsuperscript{23–25} the mere presence of viable myocardium may not necessarily translate into recovery of function in asynergic regions after revascularization. In this study, we hypothesized that myocardial revascularization is more likely to result in functional improvement of asynergic regions with reversible stress-induced thallium defects rather than mild-to-moderate irreversible thallium defects.

**Methods**

**Patient Selection**

Patients with coronary artery disease and left ventricular dysfunction who were candidates for revascularization were prospectively enrolled in our protocol. Twenty-four patients (23 men, 1 woman) with angiographically proven coronary artery disease, ranging in age from 42 to 76 years (mean, 57±10 years) underwent prerevascularization and postrevascularization stress-redistribution-reinjection thallium single photon emission CT (SPECT), gated cardiac MRI, and radionuclide angiography.

Before revascularization, all cardiac medications were discontinued in 16 of 24 patients for at least 48 hours before imaging. In the remaining 8 patients, all imaging studies were performed while the patients were receiving the same cardiac medications for each study. After revascularization, 18 patients were studied after discontinuation of all cardiac medications, and 6 patients were studied while receiving the same medical regimen for each study. Cardiac medications included either 1 or a combination of nitrates, calcium channel blockers, ACE inhibitors, and digitals. Prerevascularization MRI, thallium, and radionuclide angiography were performed within a mean of ±1 month. An average of 8 months elapsed between the revascularization procedure and the postrevascularization MRI and radionuclide angiography. No patient had unstable angina, myocardial infarction, or congestive heart failure during the follow-up period.

Fifteen patients underwent coronary artery bypass graft surgery and 9 patients underwent percutaneous transluminal coronary angioplasty. All 3 major coronary arteries were revascularized in 12 patients, 2 vessels in 2 patients, and 1 vessel in 10 patients. The adequacy of revascularization was based on review of the operative reports documenting the successful placement of bypass grafts, and for patients who underwent angioplasty, by immediate postangioplasty angiographic documentation of successfully dilated vessels. Informed written consent for the study protocol was obtained from each patient, and the Institutional Review Board on human research approved the study protocol.

**Thallium SPECT Imaging**

All patients underwent exercise thallium SPECT as previously described,\textsuperscript{26} except for 1 patient who underwent pharmacological stress testing. Patients exercised on a treadmill according to a symptom-limited, standardized, multistage exercise protocol with continuous monitoring of heart rate and rhythm, blood pressure, and symptoms. Nine of the 24 patients (38%) achieved >85% of predicted maximal heart rate during exercise. In the remaining 14 patients, the exercise was terminated because of cardiac symptoms. At peak exercise, 2 to 3 mCi of thallium was injected intravenously, and the patients continued to exercise for an additional 45 to 60 seconds. Approximately 10 to 15 minutes after termination of stress, thallium imaging was begun. Seven patients were imaged with a single-headed SPECT camera (Apex 415, Elscint), and the remaining 17 patients were imaged with a 3-headed camera (Triad, Trioton). SPECT in plane and z-axis resolution was ~15.5 mm, with a line source used in an elliptical chest phantom (with lungs). Pixel size was ~4.7 mm for the single-headed and 3.66 mm for the 3-headed camera. Redistribution images were obtained at rest ~3 to 4 hours after stress. Immediately thereafter, all patients received a second injection of 1 mCi of $^{201}$TI, and SPECT imaging was performed ~10 to 15 minutes after the second administered dose (reinjection imaging). Thallium images were reconstructed as a series of whole-body transaxial tomograms for direct comparison with the corresponding MRI images as described below. Transaxial images view the heart at an oblique angle. To minimize the effects of slicing through the myocardium tangentially, we studied midventricular transaxial slices.

**Thallium Data Analysis**

To objectively compare relative regional thallium uptake, 5 myocardial regions of interest representing the posterolateral, anterolateral, anteropapical, anteroseptal, and posteroseptal myocardium were drawn on each visually selected thallium stress tomogram and on each corresponding thallium redistribution and reinjection tomogram as previously described.\textsuperscript{27} Each region was then assigned to one of the three vascular territories as follows: the anteropapical, anteroseptal, and posteroseptal regions, representing the left anterior descending coronary artery territory; the anterolateral and posterolateral regions of the upper tomograms, representing the left circumflex artery territory; and the posterolateral region of the lower tomograms, representing the right coronary artery territory. The SPECT and MRI slices had different slice thicknesses and different interslice separations (slice separation, 6.88 mm for thallium SPECT and 10 mm for MRI). Therefore, we performed a weighted resumming of the SPECT images to match the MRI slice thickness. An average of ~3 midventricular MRI slices per patient were divided into 5 regions of interest that visually matched the regions drawn on the thallium SPECT images. Because each region encompassed a relatively large amount of myocardial tissue, it is unlikely that minor differences in visual matching between the 5 regions would alter the results appreciably.

**Regional Myocardial Thallium Uptake**

The myocardial region on the stress-redistribution-reinjection thallium images that corresponded to the region with the highest thallium uptake on the thallium exercise image series was used as the reference region for calculating relative thallium uptake. Thallium uptake in all other myocardial regions was expressed as a percentage of the activity in this reference region. The presence of a thallium defect on the stress images was defined as thallium activity <85% of the normal reference region. A defect was considered reversible if thallium activity increased by ≥10% on the subsequent redistribution or reinjection images and the final defect activity was ≥50%.\textsuperscript{24} A defect was considered completely reversible if the increase in thallium activity from stress to redistribution or reinjection images resulted in final thallium activity ≥85%. Irreversible thallium defects were also subgrouped on the basis of severity of reduction in tracer activity: mild-to-moderate (50% to 84% of peak activity) and severe (<50% of peak) defects. On repeat stress thallium studies after revascularization, myocardial perfusion was considered normal if regional thallium activity was ≥85% on the stress images. Myocardial perfusion was considered improved after revascularization if the thallium activity on stress images increased from before to after revascularization by ≥10%.

**Magnetic Resonance Imaging**

ECG-gated MRI was performed with a 0.5-T magnet (Picker) in 9 patients and 1.5-T magnet (Sigma, GE) in 15 patients as previously described.\textsuperscript{21} Each MRI slice was 10 mm thick.
Qualitative MRI Analysis
To assess regional systolic wall thickening, corresponding transaxial end-diastolic and end-systolic MRI images were analyzed visually. The stress-redistribution-reinjection thallium slice that best matched the corresponding MRI slice was selected visually. Systolic wall thickening was assessed qualitatively as normal or asynergic (hypokinetic or akinetic) by two observers, blinded to the thallium data, with the movie display of superimposed MRI end-diastolic and end-systolic images before and after revascularization. The MRI wall thickening data on the first 8 patients were read as either normal or abnormal. In the subsequent 16 patients, in addition to binary visual readings, abnormal regions were further classified as hypokinetic, severely hypokinetic, or akinetic. Differences were resolved by consensus. To avoid the problem of postoperative paradoxical septal motion, wall thickening was used for the classification of wall motion. Myocardial regions with impaired systolic wall thickening before revascularization were studied again after revascularization and classified as regions with reversible or irreversible left ventricular dysfunction.

Quantitative MRI Analysis
Quantitative end-diastolic, end-systolic, and systolic wall thickening measurements were also assessed before and after revascularization from corresponding anatomically matched MRI slices. This quantitative method was then applied to the regions judged to be normal or asynergic on the basis of qualitative analysis. At the center of each region of interest, opposing points on the epicardial and endocardial borders were identified manually, so that a line between the two points was approximately perpendicular to the two surfaces. The length of the line joining these two points was calculated and considered to represent regional wall thickness. The intraobserver variability was assessed by determining thickness values at each of the 5 sectors on each of 8 MRI images (4 at end diastole and 4 at end systole) and then repeating the sequence of thickness measurements 5 times (a total of 200 thickness measurements). We found that for end diastole, the SD ranged from an average of 1.1 to 1.7 mm, and averaged over all sectors and all subjects, it was 1.5 mm. At end systole, it ranged from an average of 0.9 to 1.4 mm, and averaged over all subjects and all sectors, it was 1.2 mm.

Gated Equilibrium Radionuclide Angiography
Gated equilibrium radionuclide angiography was performed at rest in all 24 patients with a conventional Anger camera, with the patients in the supine position. Red blood cells were labeled in vivo with 25 mCi of 99mTc pertechnetate. Time-activity curves were generated, from which the left ventricular ejection fraction was computed as previously described.27 The reproducibility limit of this technique is 4%26; therefore, we defined as change in ejection fraction any change that was ≥4% ejection fraction units.

Statistical Analysis
Data are presented as mean±SD. In this analysis, each myocardial region was considered an independent piece of information. For comparison of differences, a 2-tailed Student’s t test for paired and unpaired samples was applied. The χ2 test was applied to determine the significance of range of occurrence. A value of P<0.05 was accepted as the minimal level of significance.

Results
Clinical, Hemodynamic, and Left Ventricular Ejection Fraction Changes Before to After Revascularization
Before revascularization, 20 of the 24 patients (83%) studied had angina. With regard to symptoms of heart failure, 19 patients were in NYHA functional class I or II and 5 in functional class III or IV. In all 24 subjects, left ventricular ejection fraction ranged from 17% to 46% (mean, 30±9%) at rest.

After revascularization, 22 of the 24 patients had no symptoms of angina, and there was a significant increase in the mean left ventricular ejection fraction at rest from 30±9% before to 37±13% after revascularization (P<0.001), with 14 of 24 patients (58%) manifesting substantial improvement (≥4%) in resting ejection fraction after revascularization. Mean rate-pressure product on treadmill exercise increased from 20.1±6.3 mm Hg · bpm−1·10−3 before to 25.3±5.9 mm Hg · bpm−1·10−3 after revascularization (P<0.005). Similarly, mean METs achieved during treadmill exercise increased from 6.3±2.9 before to 8.7±3.2 after revascularization (P<0.001).

Reversible and Mild-to-Moderate Irreversible Thallium Defects
Two hundred twenty-one regions (a mean of 9 regions per patient) were revascularized. During thallium stress studies, perfusion defects developed in 164 regions, of which 110 were reversible on redistribution-reinjection studies and 37 were mild-to-moderate irreversible by quantitative analysis (67% and 23%, respectively).

Relation to Regional Wall Thickness and Thickening in Asynergic Regions
Before revascularization, abnormal systolic wall thickening at rest was observed in 56 of 110 reversible and 20 of 37 mild-to-moderate irreversible thallium defects (51% and 54%, respectively). Quantitative analysis of regional wall thickness and systolic wall thickening was feasible in 45 of 56 asynergic regions with reversible thallium defects and 19 of 20 asynergic regions with mild-to-moderate irreversible thallium defects (80% and 95%). Twelve regions had to be excluded from quantitative MRI analysis because of poor endocardial border delineation and/or blood motion artifacts. Prerevascularization end-diastolic thickness was similar in asynergic regions with reversible and mild-to-moderate irreversible thallium defects (6.2±2.2 versus 6.0±2.0 mm, P=NS). However, end-systolic wall thickness (7.8±2.5 mm) and systolic wall thickening (1.6±1.9 mm) were significantly higher in asynergic regions with reversible when compared with end-systolic wall thickness (6.1±1.7 mm, P<0.01) and systolic wall thickening (0.08±1.3 mm, P<0.005) in asynergic regions with mild-to-moderate irreversible thallium defects.

After revascularization, visual analysis of the MRI data showed improvement in systolic wall thickening in 44 of the 56 regions with reversible thallium defects compared with only 6 of the 20 regions with mild-to-moderate irreversible thallium defects (79% and 30%, respectively; P<0.001, Figure 1). Of the above-mentioned 44 regions with reversible defects that were assessed visually by MRI, quantitative MRI analysis was feasible in 36. Of the 14 regions with mild-to-moderate irreversible thallium defects that did not exhibit visually improved wall thickening after revascularization, quantitative MRI analysis was feasible in 13. These 13 regions had significantly lower postrevascularization end-diastolic and end-systolic wall thickness (6.4±2.2 and 6.6±2.3 mm, respectively) than the above-mentioned 36 regions with reversible defects whose function improved (8.5±2.1 and 10.0±3.1 mm, respectively, P<0.005). Simi-
larly, postrevascularization systolic wall thickening was significantly lower in the 13 regions with mild-to-moderate irreversible thallium defects (0.2 ± 1.4 mm) than in the 36 regions with reversible thallium defects (1.5 ± 3.2 mm, \(P < 0.001\)). Patient examples with reversible and mild-to-moderate irreversible thallium defects and their functional outcome after revascularization are shown in Figures 2 and 3.

**Relation to Severity of Systolic Wall Thickening Abnormality**

In addition to binary readings, visual assessment of the severity of systolic wall thickening abnormality (hypokinetic, severely hypokinetic, or akinetic) was made in 16 patients. From a total of 76 abnormal regions (that were also classified according to the degree of wall motion abnormality), 44 showed reversible defects, 15 mild-to-moderate irreversible, 7 severe irreversible thallium defects, and 10 normal stress thallium uptake. Among the 44 regions with reversible defects, 28 were hypokinetic, 4 severely hypokinetic, and 12 akinetic. Among the 15 regions with mild-to-moderate irreversible defects, 6 were hypokinetic, 3 severely hypokinetic, and 6 akinetic (\(P = \text{NS}\)). Thus, there was no significant difference in the severity of systolic wall thickening abnormality among regions with reversible and mild-to-moderate irreversible thallium defects.

**Prerevascularization and Postrevascularization Thallium Patterns and Functional Outcome After Revascularization**

Among the 24 patients studied, a total of 221 regions were revascularized and 97 regions were not. Of the 221 revascularized regions, systolic wall thickening was normal in 121 regions (55%) before revascularization and abnormal in 100 (45%). After revascularization, systolic wall thickening improved in 60 asynergic regions (60%) and remained unchanged in 40 (40%). Mean regional thallium uptake on the stress (69 ± 17%), redistribution (80 ± 16%), and reinjection (83 ± 17%) images was significantly higher in asynergic regions that improved than in those that did not improve after revascularization (50 ± 19%, 55 ± 18%, and 55 ± 18%, respectively, \(P < 0.001\)). Of the 100 asynergic regions, 11 had normal thallium uptake, 56 reversible defects, and 33 irreversible defects; 20 mild-to-moderate and 13 severe. Of the 11 asynergic regions with normal stress thallium, 10 (91%) demonstrated improved systolic wall thickening after revascularization. A flow diagram of prerevascularization systolic wall thickening regardless of final thallium content (top) and at same final thallium content of 60% threshold value (bottom). Pie charts comparing proportion of asynergic myocardial regions that improved after revascularization in reversible (left) and mild-to-moderate irreversible (right) thallium defects.

**Figure 1.** Improved postrevascularization systolic wall thickening is shown in a patient with prerevascularization mild-to-moderate irreversible thallium defect. Matched transaxial tomograms are displayed for thallium stress, redistribution, and reinjection (left), with corresponding end-diastolic and end-systolic MRI tomograms before and after revascularization (right). Mild-to-moderate septal thallium abnormality is seen during stress (arrows) that persists on redistribution and reinjection images (irreversible defect). Corresponding MRI tomograms demonstrate abnormal systolic wall thickening in septal region before revascularization, which remains abnormal after revascularization.

**Figure 3.** Persistent postrevascularization regional asynergy is shown in a patient with prerevascularization mild-to-moderate irreversible thallium defect. Matched transaxial tomograms are displayed for thallium stress, redistribution, and reinjection (left), with corresponding end-diastolic and end-systolic MRI tomograms before and after revascularization (right). Mild-to-moderate septal thallium abnormality is seen during stress (arrows) that persists on redistribution and reinjection images (irreversible defect). Corresponding MRI tomograms demonstrate abnormal systolic wall thickening in septal region before revascularization, which remains abnormal after revascularization.
Systolic wall thickening and thallium patterns and postrevascularization functional outcome is shown in Figure 4. Systolic wall thickening analysis was feasible in 95 of 97 nonrevascularized regions. Of these 95 regions, systolic wall thickening was normal in 65 regions (68%) before revascularization and abnormal in 30 (32%). After revascularization, systolic wall thickening remained normal in all 65 regions and abnormal in 15 of 30 asynergic regions. Of the 15 regions that demonstrated improvement in regional function after revascularization, 13 (87%) were perfused by collateral vessels supplied by a stenosed artery that was amenable to revascularization.

Severity of Defects and Degree of Thallium Reversibility in Relation to Functional Recovery

Of the 56 asynergic regions with reversible thallium defects, 39 had mild-to-moderate and 17 had severe reduction in thallium activity on the stress images. Systolic wall thickening improved in 35 of 39 regions with mild-to-moderate compared with 9 of 17 regions with severe reversible thallium defects (90% and 53%, respectively; $P<0.007$). When regions with mild-to-moderate and severe reversible thallium defects were further analyzed according to the degree of reversibility (partial or complete), 24 of 39 regions with mild-to-moderate defects had complete reversibility compared with only 2 of 17 regions with severe defects (62% and 12%; $P<0.002$). When the data were analyzed according to the degree of reversibility alone, regardless of the severity of reduction of thallium activity, 30 of 56 asynergic regions (54%) showed partially and 26 regions (46%) showed completely reversible thallium defects. After revascularization, systolic wall thickening improved in 19 of 30 regions with partially reversible compared with 25 of 26 regions with completely reversible thallium defects (63% and 96%; $P<0.008$).

Final Thallium Content in Reversible and Mild-to-Moderate Irreversible Defects

The final thallium content on delayed images (maximum thallium uptake on either redistribution or reinjection images) in regions with reversible and mild-to-moderate irreversible thallium defects was assessed. The thallium uptake on delayed images was significantly higher in abnormal regions with reversible defects ($82\pm17\%$) than in regions with mild-to-moderate irreversible defects ($66\pm9\%$, $P<0.001$). Furthermore, the thallium uptake on delayed images was significantly higher in regions with reversible defects that improved than in those that did not improve after revascularization ($86\pm16\%$ versus $66\pm9\%$, $P<0.001$). In contrast, the thallium uptake in delayed images was similar in regions with mild-to-moderate irreversible defects that improved and in those that did not improve after revascularization ($69\pm9\%$ versus $65\pm10\%$, $P=NS$).

We then grouped the myocardial regions according to the final thallium content on delayed images and compared the proportion of regions that demonstrated functional recovery among reversible and those with mild-to-moderate irreversible thallium defects. A total of 63 asynergic regions were identified with a thallium uptake on delayed images of $\geq60\%$: 48 with reversible and 15 with mild-to-moderate irreversible defects. Functional recovery was observed in 40 of 48 regions with reversible thallium defects compared with 5 of 15 regions with mild-to-moderate irreversible defects (83% and 33%, respectively; $P<0.001$, Figure 1). Similar results were obtained when the thallium uptake was set at $\geq70\%$. A total of 50 asynergic regions were identified with a thallium uptake in delayed images of $\geq70\%$: 43 with reversible and 7 with mild-to-moderate irreversible defects. Functional recovery was observed in 38 of 43 regions with reversible thallium defects compared with 3 of 7 regions with mild-to-moderate irreversible defects (88% and 43%; $P<0.02$).

Analysis on the Basis of Success of Reperfusion

The data were also analyzed on the basis of success of myocardial reperfusion, defined as normal or improved thallium activity on repeat stress thallium studies after revascularization. Successful reperfusion on repeat stress thallium studies was observed in 42 of 60 asynergic regions that demonstrated improved wall thickening compared with only
9 of 40 asynergic regions that did not demonstrate improved wall thickening after revascularization (70% and 23%, respectively; \( P < 0.001 \)). Of the 42 asynergic regions with both improved stress thallium perfusion and regional function after revascularization, 31 exhibited reversible and only 2 had mild-to-moderate irreversible thallium defects on their prerevascularization thallium studies (74% and 5%). In contrast, of the 31 asynergic regions with persistent thallium perfusion and regional contractile abnormalities after revascularization, 12 exhibited mild-to-moderate irreversible and 7 reversible thallium defects on their prerevascularization thallium studies (39% and 23%; \( P < 0.001 \), Figure 5).

**Discussion**

In patients with chronic coronary artery disease and left ventricular dysfunction, the distinction between viable and nonviable myocardium can be difficult when based on regional contraction alone. Assessment of regional perfusion and cell membrane integrity with thallium scintigraphy can shed light on the distinction of reversibility or irreversibility of asynergic regions. In the present study, we demonstrate that a more accurate noninvasive determination of myocardial viability requires the demonstration of myocardial ischemia, because asynergic regions with reversible thallium defects on the prerevascularization thallium studies were more likely to improve after revascularization than asynergic regions with mild-to-moderate irreversible defects (79% versus 30%, respectively; \( P < 0.001 \)).

**Presence of Myocardial Viability Versus Inducibility of Ischemia**

In most cases, the identification of the presence and extent of myocardial ischemia is much more important clinically in terms of patient management and risk stratification than knowledge of myocardial viability. However, in a subset of patients who have already undergone coronary angiography, the relevant clinical question may be whether there is sufficient evidence for myocardial viability in a noncontractile region perfused by a critically stenosed coronary artery. In these patients, it is reasonable to perform rest-redistribution thallium imaging. By planar quantitative analysis, when myocardial viability was defined in a binary manner (\( > 50\% \) or \( < 50\% \)), 57% of severely asynergic regions that were viable by thallium showed improved wall motion after surgery, compared with only 23% of severely asynergic regions that were considered to be nonviable by thallium.\(^{30}\) The relatively low positive predictive value of this and most other studies using rest-redistribution thallium protocol is that in these studies, myocardial viability is defined in a binary manner.\(^{30–34}\) Such classification of asynergic regions as viable or nonviable may be an oversimplification of the rather continuous nature of structural damage in coronary artery disease. In a clinicopathological study by Zimmerman and colleagues\(^{35}\) in which two transmural biopsy specimens were taken from myocardial regions subtended by \( \geq 75\% \) coronary artery stenosis during revascularization, the regional volume fraction of interstitial fibrosis varied in a continuous manner ranging from 14.5 to 59.6 vol%. Although an inverse correlation was observed between regional thallium activity and regional volume fraction of interstitial fibrosis, such good correlation does not necessarily translate to recovery of regional function after revascularization.

An asynergic region with a mild-to-moderate reduction of thallium activity on rest-redistribution imaging may result from viable tissue (transient ischemia or chronic hypoperfusion) or nontransmural infarction with mixed scarred and viable tissue. If regional asynergy is a consequence of transient ischemia or chronic hypoperfusion, such regions might be expected to exhibit improvement in function after revascularization. Conversely, regions with nontransmural infarction are composed of mixed scarred (often confined to the endocardial layers) and normal (often confined to the epicardial layer) myocardium. Such regions may regain adequate perfusion after revascularization to sustain cellular viability but not contractility. Several experimental studies have examined the influence of subendocardial ischemia on transmural myocardial function.\(^{36–38}\) In an open-chest canine model of partial coronary artery occlusion, the relationship between myocardial contraction and blood flow was examined in the subepicardial and subendocardial walls of the left ventricle.\(^{38}\) During nontransmural ischemia, although there was a close coupling between regional perfusion and function in the subendocardium, there was a striking dissociation between perfusion and function in the subepicardium. Despite the demonstration of preserved subepicardial blood flow, subepicardial function was markedly diminished, similar to that observed in the subendocardial region. These data in animals suggest that the contractile function of the outer left ventricular wall appears to be dependent on the blood flow function of the inner wall, such that severe hypoperfusion or dysfunction confined to the endocardial layers of the myocardium can result in transmural akinesia despite normal epicardial blood flow. Assessment of the magnitude of thallium uptake in this situation may show only a mild-to-moderate defect, because the proportion of scarred myocardium may extend only from one third to one fourth of the transmural thickness of the asynergic region. Unfortunately, current noninvasive imaging techniques lack the resolution to assess differences between endocardial, midwall, and epicardial blood flows. Hence, conditions that affect predominantly subendocardial perfusion, and consequently transmural regional function, cannot be estimated clinically.

The demonstration of stress-induced ischemia could be helpful in differentiating reversible from irreversible regional asynergy. Although mild-to-moderate irreversible thallium defects provide evidence of structural integrity of some myocytes, reversible thallium defects imply the presence of abnormal flow reserve in areas of viable myocardium. The final thallium content (maximum on redistribution-reinjection images) was significantly higher in regions with reversible defects that improved than in those that did not improve after revascularization (\( 86 \pm 16\% \) versus \( 66 \pm 9\% \), \( P < 0.001 \)). In contrast, final thallium content was similar in regions with mild-to-moderate irreversible defects that improved and in those that did not improve after revascularization (\( 69 \pm 9\% \) versus \( 65 \pm 10\% \), \( P = NS \)). Furthermore, when asynergic regions were grouped according to the final thallium content, at 60% threshold value, functional recovery was observed in...
83% of regions with reversible defects compared with 33% of regions with mild-to-moderate irreversible defects \((P<0.001)\). These findings suggest that the regions most likely to improve function after revascularization are those with asynergy arising from repetitive stunning and/or hibernation, which can become transient ischemic (reversible thallium defects), rather than those regions without ischemia (irreversible mild-to-moderate thallium defects). Although the findings in these patients support our conclusion, we acknowledge that the number of patients and myocardial segments submitted to revascularization is not large.

Adequacy of Revascularization and Functional Outcome

Because of the lack of postrevascularization coronary angiography, the success of revascularization cannot be assessed with certainty. However, an important feature of our study is that we examined regional perfusion and function both before and after revascularization. For an asynergic region to improve function after revascularization, it must not only retain viable myocardium but also be adequately revascularized. Thus, the adequacy of myocardial reperfusion may play an important role in the functional outcome of asynergic regions. Although an improvement in thallium uptake from before to after revascularization suggests that a region has been adequately revascularized, the converse may not be true. Lack of improvement in thallium uptake after revascularization may be attributed to either inadequate revascularization or successful revascularization in a region with normal midwall and epicardial blood flow and scarred endocardium. The majority of regions that demonstrated improvement in thallium uptake on postoperative scans had reversible thallium defects, and 97% demonstrated improvement in postoperative function. In contrast, among regions classified before revascularization as having mild-to-moderate irreversible thallium defects, 90% had persistent thallium defects on postoperative scans, and only 22% of regions demonstrated improvement in postoperative function.

Conclusions

These findings suggest that most mild-to-moderate irreversible thallium defects after stress represent an admixture of viable and scarred myocardium that may not improve after revascularization. Conversely, the identification of reversible thallium defect on stress in an asynergic region more accurately predicts recovery of function after revascularization. Even at a similar mass of viable myocardial tissue (as reflected by the final thallium content and supported by histomorphological studies), the presence of inducible ischemia (a reversible defect) is associated with an increased likelihood of functional recovery.

References


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