Redistribution of Thallium at Rest in Patients with Stable and Unstable Angina and the Effect of Coronary Artery Bypass Surgery

Bruce C. Berger, M.D., Denny D. Watson, Ph.D., Lawrence R. Burwell, M.D., Ivan K. Crosby, M.D., Harry A. Wellons, M.D., Charles D. Teates, M.D., and George A. Beller, M.D.

SUMMARY To determine the significance of redistribution (RD) of thallium-201 ($^{201}$TI) at rest in patients with coronary artery disease, 14 patients with unstable angina (UA) and 15 patients with stable angina (SA) referred for angiography underwent serial myocardial $^{201}$TI imaging over 3 hours. No patients were imaged during pain. Anterior and left anterior oblique images were divided into six segments for analysis. The extent of coronary artery disease and the $^{201}$TI perfusion pattern were similar for UA and SA patients. In the 29 patients, 91 of 174 segments had decreased $^{201}$TI uptake on the 10–20-minute images. At least one initial defect was present in 26 of 29 patients, but only 14 of 29 had ECG evidence of infarction. On delayed 3-hour images, 69 of 91 segments with diminished initial uptake showed RD, while 22 defects persisted. Angiography demonstrated that 66 of 69 segments with RD had significant (>70%) corresponding coronary artery stenoses. Wall motion analyses of 63 segments with RD revealed that 52 were normal or hypokinetic and 11 were akinetic or dyskinetic. Of 13 persistent defects, six were normal or hypokinetic and seven akinetic or dyskinetic ($p>0.02$). In 22 patients who underwent coronary bypass surgery, 37 of 48 segments (77%) with decreased initial $^{201}$TI uptake and subsequent RD preoperatively reverted toward normal initial uptake postoperatively. In addition, 13 of 18 persistent defects preoperatively showed improved $^{201}$TI uptake postoperatively.

Thus, resting $^{201}$TI defects may not represent myocardial scar. Patients with UA or SA may show RD of $^{201}$TI at rest. Myocardial revascularization is usually associated with improvement in early $^{201}$TI uptake in segments with initial defects and RD preoperatively.

PERFUSION DEFECTS on the resting thallium-201 ($^{201}$TI) scans 20 minutes after intravenous injection of the radionuclide in the absence of clinical or electrocardiographic evidence of acute ischemia are thought to represent areas of myocardial scar.1 Localized regions of diminished myocardial $^{201}$TI uptake also occur in the presence of exercise-induced ischemia,2, 3 during an episode of variant angina pectoris,4 and with acute myocardial infarction.5 Results of a recent study6 suggest that patients with unstable angina pectoris who are imaged in a pain-free period may have defects on resting scans that do not represent myocardial infarction. Other studies have shown that serial myocardial imaging after a single dose of $^{201}$TI administered during exercise can differentiate between transient regional underperfusion or ischemia, which demonstrates redistribution of $^{201}$TI over time, and regions of irreversibly injured myocardium, which did not show redistribution.2

Because myocardial uptake of $^{201}$TI is proportional to regional blood flow,7 serial imaging at rest in the presence of severe coronary artery disease might be useful in differentiating underperfused but viable myocardium from infarction or scar. Regions of viable myocardium perfused by vessels with high-grade stenoses might be expected to show diminished early $^{201}$TI uptake with subsequent redistribution. Areas of myocardial fibrosis would have persistently diminished $^{201}$TI uptake. The goals of this study were to determine 1) the significance of resting $^{201}$TI defects with and without redistribution in patients with stable and unstable angina pectoris, and 2) the effect of coronary artery bypass surgery on resting regional perfusion by comparing preoperative and postoperative $^{201}$TI scintigrams.

Methods

Patient Selection

Fifteen consecutive patients referred to the University of Virginia Medical Center for cardiac catheterization for the evaluation of stable angina pectoris refractory to medical management underwent myocardial $^{201}$TI imaging at rest. An additional 15 consecutive patients with unstable angina pectoris referred for catheterization were also imaged in the resting state. Informed consent was obtained from each patient. Unstable angina was defined as a recent (usually less than 7 days) progression of frequency and severity of typical angina,
episodes of rest pain refractory to medical therapy. Patients with unstable angina were stabilized in the Coronary Care Unit and myocardial infarction was excluded. All patients were free of pain for at least 12 hours before imaging. All patients had a 12-lead ECG before imaging. One patient with unstable angina and a recent acute myocardial infarction had normal coronary arteries at catheterization and was excluded from the study. No patients had associated valvular, congenital or cardiomyopathic heart disease.

Twelve patients with stable angina and 13 patients with unstable angina underwent coronary artery bypass grafting. Of the three patients with stable angina not undergoing surgery, one had single-vessel disease, one had severe three-vessel disease with poor left ventricular function and refused surgery, and one died before a scheduled operation. One patient with unstable angina died before operation. All surgical patients had repeat resting 201Tl scans 7–10 days after revascularization. Three patients had aneurysmectomies and are excluded from postoperative evaluation due to altered left ventricular geometry. Hence, 22 patients underwent repeat rest 201Tl imaging after surgery.

**Imaging Procedure**

Patients were injected with 1.5 mCi of 201Tl (New England Nuclear Corp.) at rest and imaging was started 10 minutes after injection in the anterior projection and continued in the 45° left anterior oblique (LAO), 30° LAO and 70° LAO projections. Anterior and one of the three oblique images, usually the 45° LAO projection, were repeated 1 hour and again 2–4 hours after 201Tl administration. All images were recorded for 10 minutes with at least 300,000 counts collected on an Ohio Nuclear 420 Portable Gamma Camera using an all purpose (GAP) medium-resolution collimator and a 25% window centered on the 80-keV X-ray peak. In addition to conventional scintiphotography on transparency film, all thallium studies were stored in a computer (DEC Gamma 11, Digital Equipment Corp. or MDS MUGA-CART, Medtronic Corp.) for standardized image formation and quantitation of relative myocardial thallium uptake. Myocardial images were first formed on the computer video display and photographed using a modified exponential gray scale with no background subtraction. This nonlinear intensity scale facilitated visual perception of small brightness decrements in regions of intense thallium activity and allowed for better delineation of small defects as compared with the regions of uniform linear intensity scale.

Thallium images were quantitatively assessed by first performing a background subtraction procedure using the bilinear interpolation method described by Goris et al. Slightly more complex weighting functions, which differ from the original formula, were used to provide proximity weighting near the edges of the background-defining region and to produce more rapid fall-off of the computed background as it is extrapolated beneath the myocardial rim, particularly near intense background-producing regions such as the liver and stomach. After background subtraction, the images were rephotographed for visual assessment. Images were then smoothed and relative myocardial activity was determined by observing profiles crossing preselected target regions on the myocardium. Time-activity curves were then constructed from peak profile counts from regions in the anterolateral, apical and inferior segments on the anterior projection image and septal, inferoapical and posterolateral segments on the pertinent LAO image. The images and quantitative data from each patient were examined jointly by three of the investigators without knowledge of the catheterization results. Segments that had reduced 201Tl uptake by visual assessment were graded as significant if the activity in the region was reduced by more than 25% relative to the area of most intense uptake. Any change in relative 201Tl activity of 15% or greater on the 2–4-hour delayed image was designated as "redistribution." Otherwise, a defect was judged to be persistent. The defect detection threshold of 25% was arbitrarily chosen based upon analysis of thallium scintigrams in a much larger group of patients who underwent coronary angiography at the University of Virginia Medical Center. This appeared to be the optimum threshold for achieving the highest sensitivity while maintaining a high specificity for detection of significant coronary stenoses. This threshold applies only for the imaging procedures used in the study and may be different for other gamma cameras and computer processing techniques.

For the postoperative studies, improvement in regional 201Tl uptake was defined as a change from the redistribution pattern toward normal initial uptake or a change from a persistent defect to the redistribution or normal initial uptake patterns. Changes in absolute regional thallium counts were not used in the criteria for postoperative improvement, since other technical and physiologic variables might have affected the absolute amount of thallium in the myocardium. Technical factors were held constant for both pre- and postoperative studies. The camera, collimator, collimator distance to the chest wall, camera angle to the patient and window settings were identical for pre- and postoperative studies. The same technician performed both scintigraphic studies and the injection site on the patient's arm was always imaged to ensure that no infiltration of thallium occurred.

There was no significant (r > 0.98) operator variability in reproducing the quantitative data by computer processing. In 25% of the cases evaluated, there were questionably positive segments by visual assessment alone. In these instances, the quantitative criteria described above were applied to resolve the question. The quantitative method was used to provide more definable and reproducible criteria for image interpretation than could have been achieved by subjective assessment alone. The nature of this study precludes a meaningful conclusion, however, about
the sensitivity of the quantitative approach for coronary artery disease detection, because all of these patients had severe coronary artery disease.

Cardiac Catheterization

All patients underwent coronary arteriography and left ventriculography using the Judkins or Sones techniques. Ventriculography was performed in the 30° right anterior oblique (RAO) projection, and 22 of 29 patients also had LAO ventriculograms. Cineangiograms were interpreted independently by two of the investigators, and differences of interpretation were resolved by consensus with a third angiographer present. Coronary stenoses were graded as 0–49%, 50–69%, 70–89%, 90–99% and totally obstructed. Coronary stenoses were considered significant if luminal diameter was reduced by 50% or more. Left ventricular wall motion was graded qualitatively as normal, hypokinetic, akinetic or dyskinetic.

Imaging-Angiographic Comparison

Anterior and LAO \(^{201}\)TI images were divided into three segments each, as were the RAO and LAO ventriculograms (fig. 1). Anterior scintigrams were compared with the 30° RAO ventriculogram, and the 45° LAO scintigrams and ventriculograms were compared for correlation of wall motion and \(^{201}\)TI uptake.

Electrocardiographic Data

The presence of Q waves of 0.04 second or greater duration was considered to represent transmural myocardial infarction. Their location was matched with the appropriate myocardial segment on \(^{201}\)TI scans.

Statistical Analysis

The chi-square test or Fisher's exact test was used to determine the significance of differences in rates of occurrence.

Results

Clinical Data

Stable Angina

There were 14 men and one woman, ages 31–68 years (mean 52 years). Thirteen of 15 were receiving propranolol in doses of 40–320 mg/day. All were receiving nitrates in sublingual, oral or topical form, alone or in combination. Two were on maintenance digoxin.

Unstable Angina

There were 12 men and two women, ages 32–74 years (mean 54.3 years). Thirteen of 14 were receiving propranolol in doses of 20–320 mg/day. All were receiving nitrates in sublingual, oral or topical form, alone or combination.

There was no significant difference between the stable and unstable angina groups with respect to age, medication or incidence of prior infarction and ST-T wave abnormalities on the resting ECG.

Angiographic, imaging and electrocardiographic data for the 29 patients in the study are summarized in table 1.

Catheterization Data

There was no significant difference between the stable and unstable angina groups with respect to extent of coronary artery disease or degree of left ventricular asynergy. The stable angina group had 2.6 diseased vessels per patient, and the unstable angina group had 2.3 diseased vessels per patient. The prevalence of asynergy was similar for the two groups.

\(^{201}\)TI Scintigraphic Analysis

Stable Angina

Ninety segments in 15 patients were analyzed. On the initial anterior and LAO images, 44 segments showed normal TI uptake, while 46 segments showed

**FIGURE 1.** Schematic representation of thallium-201 \(^{201}\)TI images and ventriculograms used for analysis of segmental \(^{201}\)TI uptake and left ventricular wall motion. Anterior and 45° left anterior oblique (LAO) \(^{201}\)TI images and 30° right anterior oblique (RAO) and 45° LAO ventriculograms are divided into three segments each.
TABLE 1. Coronary Artery Stenosis, Thallium-201 Uptake Patterns and Electrocardiographic Changes in 29 Patients

<table>
<thead>
<tr>
<th>Coronary disease*</th>
<th>Segmental thallium-201 uptake†</th>
<th>Q waves‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1VD 2VD 3VD</td>
<td>N  RD  PD</td>
</tr>
<tr>
<td>SA</td>
<td>2      2    11</td>
<td>44  35  11</td>
</tr>
<tr>
<td>UA</td>
<td>3      4    7</td>
<td>30  34  11</td>
</tr>
<tr>
<td>Total</td>
<td>5      6    18</td>
<td>83  69  22</td>
</tr>
</tbody>
</table>

*Extent of coronary disease in 29 patients.
†174 segments in 29 patients.
‡Number of patients with or without Q waves.

Abbreviations: N = normal; PD = persistent defect; RD = redistribution; SA = stable angina; UA = unstable angina; VD = vessel disease (> 70% stenosis).

decreased or absent activity. On delayed images, 35 of these 46 initial defects showed partial or total redistribution. The remaining 11 segments had persistently decreased 201TI activity.

**Unstable Angina**

Eighty-four segments in 14 patients were analyzed. On initial images, 39 were normal and 45 showed decreased or absent 201TI activity. Thirty-four of these 45 initial defects had redistribution on delayed images, while 11 defects persisted. Figure 2 shows redistribution in representative sequential myocardial images and corresponding 201TI time-activity curves from a patient in the unstable angina group. Initially, there is diminished 201TI activity in the septum compared with the posterolateral wall. The time-activity curves verify

**Figure 2.** Sequential 45° left anterior oblique (LAO) resting images and the corresponding thallium-201 (201TI) time-activity curves in a patient with unstable angina and significant stenosis of the left anterior descending coronary artery. The ordinate indicates myocardial counts above background and the abscissa indicates time in hours. The arrows delineate the myocardial regions from which relative 201TI activity was measured. At 20 minutes, there is a defect in 201TI activity in the septal segment. By 1 hour the defect has filled in and 201TI counts in both septal and posterolateral segments are nearly identical. At 4 hours, 201TI is washing out of the posterolateral wall more rapidly than from the septum. At this time the posterolateral wall has relatively less 201TI activity than the septum.
the visual impression of an initial, significant defect. Delayed images show that the defect fills in and corresponds to equalization of segmental $^{201}$TI counts by 75 minutes. Figure 3 shows another example of an initial septal defect with redistribution on delayed images and the corresponding $^{201}$TI activity curves. Again, the quantitative data confirm the visual interpretation of a significant initial reduction in septal $^{201}$TI activity on the 20-minute image.

Figures 4 and 5 illustrate abnormal $^{201}$TI uptake in multiple myocardial segments on anterior and LAO images in two patients with multivessel coronary artery disease. In both examples, redistribution of $^{201}$TI occurred in segments with abnormal initial uptake. The time-activity curves of relative myocardial $^{201}$TI activity generated from sequential images display the degree of these abnormalities.

Figure 6 shows a persistent posterolateral defect on sequential images and the corresponding $^{201}$TI activity curves. The abnormal gradient (> 25%) in $^{201}$TI activity between the posterolateral and septal segments persists throughout the imaging sequence. In this example, $^{201}$TI uptake and washout from the septal segment are normal.

There was no significant difference between stable and unstable angina patients with respect to the number of segments with normal $^{201}$TI uptake, redistribution, or persistently diminished $^{201}$TI uptake. There were no significant differences between the stable and unstable angina groups with respect to clinical characteristics, type and dose of antianginal medication, extent of coronary disease and left ventricular asynergy or scintigraphic findings. For all subsequent analyses, the stable and unstable angina groups will be considered together.

$^{201}$TI Activity vs Coronary Stenoses

Table 2 summarizes the correlation between $^{201}$TI uptake patterns and presence of coronary artery stenoses. All patients had at least one diseased vessel and 26 of 29 had at least one initial defect.

Of 174 scan segments analyzed in the 29 patients, 83 had normal early $^{201}$TI uptake, 69 diminished or absent $^{201}$TI activity with subsequent redistribution, and 22 persistent defects. All segments with persistent defects were associated with coronary stenoses > 70%, and 66 of 69 segments (96%) with redistribution had corresponding significant stenoses. Fifty-five of 69 (80%) were perfused by vessels with > 90% stenosis. All three segments with redistribution but without significant coronary stenoses had normal wall motion and were not associated with Q waves. The prevalence of diseased vessels was significantly higher for segments with redistribution ($p < 0.001$) and persistent defects ($p < 0.02$) than for segments with normal $^{201}$TI uptake. However, 61 of 83 segments (73%) with normal $^{201}$TI uptake at rest were perfused by stenotic arteries.

$^{201}$TI Activity vs Wall Motion

The relationship between $^{201}$TI uptake patterns and segmental wall motion assessed ventriculographically is summarized in table 3. Wall motion analysis of segments for which appropriate ventriculograms were available revealed that 69 of 83 segments (83%) with normal initial $^{201}$TI uptake had normal or hypokinetic wall motion. Eight segments with normal initial uptake were akinetic or dyskinetic. Six of these eight involved the apical or inferoapical segments. Fifty-two of 63 segments with redistribution were judged to have normal or hypokinetic wall motion. Eleven segments

---

**Figure 3.** Sequential resting 45° left anterior oblique (LAO) images in a patient with stable angina and a left anterior descending coronary artery stenosis. The ordinate indicates myocardial counts above background and the abscissa indicates time after thallium-201 ($^{201}$TI) administration. An initial defect in anteroseptal $^{201}$TI uptake with subsequent redistribution is observed. Time-activity curves confirm an initial decrease with accumulation of $^{201}$TI activity in the septal segment and normal $^{201}$TI washout from the posterolateral segment. (Arrows delineate the regions from which relative $^{201}$TI activity was measured.)
with redistribution were akinetic or dyskinetic. Eight of these 11 involved the apical or inferoapical segments. Six of 13 segments with persistent defects showed normal or hypokinetic wall motion, while seven were akinetic or dyskinetic.

Segments with normal $^{201}$TI uptake or redistribution were similar with respect to prevalence of regional wall motion abnormalities. Segments with normal $^{201}$TI uptake were more likely to have normal or hypokinetic wall motion than segments corresponding to persistent defects ($p < 0.001$). Segments with redistribution were also more likely to be associated with normal or hypokinetic wall motion than persistent defects ($p < 0.02$).

**Postoperative Evaluation**

Twelve patients with stable angina and 10 patients with unstable angina underwent coronary artery bypass grafting without aneurysmectomy. All had repeat myocardial imaging 7–10 days after surgery. Two patients with stable angina had perioperative infarctions manifested by new Q waves and new persistent defects on scan. One patient with unstable angina

![Image of myocardial images showing redistribution of $^{201}$TI at rest](Figure 4)

**Figure 4.** Sequential resting anteroposterior (AP) and 45° left anterior oblique (LAO) images in a patient with unstable angina and three-vessel coronary artery disease. A) Sequential AP images demonstrate decreased initial thallium-201 ($^{201}$TI) uptake in inferior and anterolateral segments (arrows) with subsequent redistribution on delayed images. Time-activity curves confirm this visual impression and show that $^{201}$TI activity is significantly more reduced in the inferior than in the anterolateral segment. By 2 hours, activity between the two regions has equalized. B) Sequential 45° LAO images and corresponding time-activity curves in the same patient show decreased initial $^{201}$TI uptake in anteroseptal and posterolateral segments (arrows) with subsequent redistribution. Delayed $^{201}$TI uptake in both regions results in equalization of counts. These scintigraphic findings indicate three-vessel coronary artery disease.
developed new Q waves without a new persistent scan defect and one had a new persistent defect without Q waves. The 22 patients had 132 segments available for analysis. Figure 7 summarizes changes in segmental $^{201}$TI uptake in the entire group after coronary artery bypass surgery.

**Normal Preoperative $^{201}$TI Uptake**

Sixty-four of 66 segments with normal preoperative $^{201}$TI uptake remained normal postoperatively. Two became persistent defects, one with new Q waves and one without.

**Segments with Preoperative Redistribution**

Table 4 summarizes the changes in $^{201}$TI uptake in postoperative images in the 22 patients who underwent coronary artery bypass surgery. These scintigraphic changes are correlated with preoperative ventriculographic and electrocardiographic findings.

Of 48 segments with redistribution preoperatively, 37 reverted toward normal initial uptake, 10 continued to show redistribution, and one became a persistent defect. Segments with improved $^{201}$TI uptake were less likely to be associated with Q waves than unimproved segments ($p < 0.05$), but there were no
TABLE 3. Correlation of Segmental Thallium-201 Activity with Segmental Wall Motion

<table>
<thead>
<tr>
<th>Thallium-201 pattern</th>
<th>Segments (n)</th>
<th>Normal or hypokinetic (n (%)</th>
<th>Akinetic or dyskinetic (n (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal*</td>
<td>77</td>
<td>69 (90%)</td>
<td>8 (10%)</td>
</tr>
<tr>
<td>Redistribution†</td>
<td>63</td>
<td>52 (83%)</td>
<td>11 (17%)</td>
</tr>
<tr>
<td>Persistent defect</td>
<td>13</td>
<td>6 (46%)</td>
<td>7 (54%)</td>
</tr>
</tbody>
</table>

* p < 0.001 vs persistent defect.
† p < 0.02 vs persistent defect.

TABLE 4. Correlation of Changes in Postoperative Thallium-201 Uptake with Preoperative Segmental Wall Motion and Q waves

<table>
<thead>
<tr>
<th>Thallium-201</th>
<th>No LAO</th>
<th>Q waves†</th>
</tr>
</thead>
<tbody>
<tr>
<td>RD improved</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>RD no change</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>PD improved</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>PD no change</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

† N or H vs A or D; RD improved vs RD no change = NS; PD improved vs PD no change = NS.
Q waves: RD improved vs RD no change = p < 0.05; PD improved vs PD no change = p < 0.02.
Abbreviations: A = akinetic; D = dyskinetic; H = hypokinetic; N = normal; PD = persistent defect; RD = redistribution; v-gram = ventriculogram.

Segments with Persistent Defects Preoperatively

Eighteen segments had persistent defects preoperatively. Unexpectedly, 13 of these showed improved 201Tl uptake after coronary bypass surgery. Twelve segments reverted toward normal 201Tl uptake. One showed the redistribution pattern, and five remained as persistent defects. Twelve of 13 segments that improved did not have Q waves, while four of five unchanged persistent defects did have Q waves (p < 0.02). Figure 9 shows sequential pre- and postoperative 45° LAO images from a patient with stable angina, three-vessel coronary disease and no history or electrocardiographic evidence of prior infarction. The preoperative image sequence shows an apparent persistent defect in the high posterolateral wall. There is delayed 201Tl uptake in all segments on the projection. Postoperatively, improved initial 201Tl uptake is observed in all segments, with normalization of the posterolateral persistent defect. These changes are confirmed by inspection of the pre- and postoperative time-activity curves.

Discussion

The initial myocardial uptake of 201Tl is related to regional myocardial perfusion and the extraction fraction for 201Tl. Defects in uptake of 201Tl in myocardial scintiscans are primarily related to decreased myocardial perfusion and ischemia-induced abnor-
Other studies have shown redistribution of $^{201}$TI into ischemic myocardium after transient coronary occlusion in animals and after exercise stress in man, and that redistribution may begin as early as 5 minutes after reversal of ischemia. In addition, Pohost et al. demonstrated redistribution of $^{201}$TI at rest in dogs in the presence of severe fixed coronary stenoses. Watson et al. postulated that while the initial myocardial $^{201}$TI uptake is proportional to regional perfusion and extraction fraction, “delayed uptake” occurs due to continued exposure to low levels of $^{201}$TI being reintroduced into the blood from other body organs, and may occur without interim changes in the distribution of blood flow.

Some defects seen on initial resting $^{201}$TI images in the absence of clinical or ECG evidence of acute ischemia may be related to decreased resting perfusion and not necessarily to prior myocardial infarction. The patients in this study all had severe coronary artery disease with clinical presentations of severe stable angina, usually refractory to medical therapy or unstable angina. Eighty-three percent of the group had multivessel disease. Sixty-six of 69 segments with initial defects and redistribution at rest in these patients were associated with significant coronary artery stenoses. Of these segments, 80% were perfused by vessels with stenoses $>90%$. In the patients evaluated after coronary artery bypass surgery, 37 of 48 segments with early defects and subsequent preoperative redistribution reverted toward normal early $^{201}$TI uptake after revascularization. This is consistent with reports that coronary bypass surgery results in an increase in regional myocardial blood flow.

Kolibash et al. evaluated regional myocardial perfusion at rest before and after coronary artery bypass surgery in patients with unstable angina using intracoronary and intragraft injections of radio labeled, macroaggregated albumin particles. These investigators found improved perfusion postoperatively in 65% of patients.

Figure 7. Comparison of preoperative (left) and postoperative (right) segmental thallium-201 ($^{201}$TI) uptake. The number of scan segments is shown for each $^{201}$TI uptake pattern. Improvement in initial myocardial $^{201}$TI uptake after coronary bypass surgery is reflected by the number of abnormal preoperative scan segments reverting toward normal initial uptake postoperatively.

Figure 8. Representative sequence of resting thallium-201 ($^{201}$TI) images from a patient with unstable angina and three-vessel coronary artery disease. Initial preoperative images show diminished activity in the anterolateral, apical, inferior, and septal segments. Delayed preoperative images show $^{201}$TI redistribution. The postoperative images showed marked improvement in $^{201}$TI uptake. The initial postoperative images appear similar to the delayed preoperative images.
Figure 9. A) Sequential preoperative (PRE-OP) and postoperative (POST-OP) 45° left anterior oblique (LAO) images and B) the corresponding time-activity curves in a patient with three-vessel disease but no clinical or electrocardiographic evidence of prior myocardial infarction. The initial preoperative study shows decreased thallium-201 (201TI) uptake in anteroseptal and posterolateral segments (arrows). The delayed 2-hour image shows an apparent persistent defect in the high posterolateral region. Postoperatively, initial 201TI uptake is improved in all segments, with normalization of the posterolateral persistent defect. The myocardial time-activity curves show abnormal initial uptake with delayed accumulation of 201TI in both anteroseptal and posterolateral segments preoperatively. The postoperative curves show improved initial uptake and subsequent normal washout of 201TI in both segments.
of abnormal perfusion areas identified preoperatively. Improved wall motion on postoperative ventriculograms corresponded to scan segments showing improved perfusion. In the present study, improvement in $^{201}$TI uptake in a similar series of patients probably reflected enhanced postoperative perfusion or improved membrane transport of the radionuclide or both. Postoperative catheterization was not done, so segmental wall motion after revascularization could not be evaluated.

Most of the myocardial segments (83%) with an initial defect and subsequent redistribution were associated with normal or hypokinetic wall motion, contraction patterns usually considered to represent viable myocardium.\textsuperscript{16, 17} Also, 86% of segments with an initial $^{201}$TI defect and subsequent redistribution at rest before surgery and conversion to normal early uptake after surgery were not associated with Q waves. These findings suggest indirectly that in patients with severe stable angina or unstable angina, $^{201}$TI imaging may be useful in identifying vascular segments that are hypoperfused or ischemic but still viable, by showing scintigraphic patterns of either normal $^{201}$TI uptake or an initial defect with redistribution. Persistently diminished $^{201}$TI uptake in a particular segment on sequential rest images in the absence of associated Q waves on the ECG may also suggest viability. We anticipated that early defects that did not fill in on late resting $^{201}$TI images would represent prior myocardial infarction or scar. Unexpectedly, however, 13 of 18 persistent defects present before coronary bypass surgery had improved $^{201}$TI uptake after surgery, 12 reverting toward normal uptake and one to the redistribution pattern. Only 8% of improved segments were associated with Q waves, while 80% of segments with unchanged persistent defects had Q waves, which suggests that these areas may not represent myocardial scar but reversible myocardial ischemia. Results of other studies support this concept.\textsuperscript{17, 18} An explanation of some of the persistent defects that evidently did not represent scar may be related to the manner in which they are identified. Figure 9 shows a relative defect in the posterolateral wall that remains evident in the delayed views and is therefore observed and graded as a “persistent” defect. However, although the “defect” is actually accumulating activity in the delayed images, the septal and inferoapical myocardial segments are also accumulating $^{201}$TI at almost the same rate, maintaining a constant ratio with the “defect.” In this case there was no normal myocardial segment with which to compare uptake in the “defect.” Had there been an adjacent myocardial segment with normal $^{201}$TI uptake and washout, the posterolateral segment would have been observed to fill in with activity and thus be classified as an area with redistribution in the delayed images. The postoperative study showed reversion to normal initial uptake and subsequent normal washout in all segments in this projection (fig. 9). Further studies in a greater number of patients who have also undergone postoperative ventriculography will be required to assess the clinical value of this type of scintigraphic information more completely.

There were several segments in which $^{201}$TI activity was not consistent with ventriculographic wall motion. Eight segments with normal $^{201}$TI uptake and 11 with redistribution were associated with akinesia or dyskinesia. This may be explained in part by the necessity of comparing 30° RAO ventriculograms with anterior projection $^{201}$TI images, which results in inappropriate identification of certain segments. Of eight segments with normal early $^{201}$TI uptake and akinesia or dyskinesia, six involved the apical or inferoapical segments of the $^{201}$TI image. Conversely, three of six persistent defects with normal or hypokinetic wall motion involved apical segments. Since apical segments frequently show normal myocardial thinning,\textsuperscript{20} a small apical scar may not be distinguishable from normal variant apical thinning. Another explanation for $^{201}$TI uptake in regions of severe asynergy is the recent evidence that suggests that akinesia and even dyskinesia do not necessarily indicate irreversible myocardial damage. Such regions may contain viable myocardium capable of enhanced contractile function as observed during intervention ventriculography and after coronary bypass surgery, particularly if these segments are not associated with Q waves.\textsuperscript{16, 19}

Although the prevalence of significant coronary artery stenoses was lower in segments with normal $^{201}$TI uptake than in those with redistribution or persistent defects, 73% of segments with normal $^{201}$TI uptake at rest were perfused by significantly stenotic vessels. This indicates that only the most severely stenotic lesions will reduce regional blood flow at rest to the extent that it can be detected by $^{201}$TI imaging.

In patients with unstable angina, Wackers et al. found that positive scintiscans obtained during pain-free periods, preferably within 6 hours of an anginal episode, are diagnostic for acute coronary insufficiency. None of our patients in either group were imaged within 12 hours of chest pain. In the present study, there was no significant difference in the incidence of positive scintigrams between the unstable and stable angina groups with respect to both redistribution and persistent defects. This finding suggests that positive scintigrams reflect the severity of the underlying coronary artery disease and not necessarily the type of anginal syndrome.

In conclusion, defects seen on initial 10–20-minute images on resting $^{201}$TI scans do not necessarily represent myocardial scar. Many of these defects will show delayed redistribution if serial imaging is performed over 2–4 hours. Both early and delayed $^{201}$TI images are necessary to differentiate defects showing redistribution of $^{201}$TI from persistent defects. Redistribution of $^{201}$TI at rest is the result of diminished coronary flow and is usually associated with normal or hypokinetic left ventricular wall motion. Patients with both stable and unstable angina may have initial defects with redistribution of $^{201}$TI during pain-free periods. Coronary artery bypass grafting frequently improves $^{201}$TI
uptake in early resting defects observed preoperatively. This may reflect enhancement of nutrient
blood flow, improved 201TI transport secondary to reversal of chronic underperfusion or ischemia.
Defects that appear to persist over a 2-4-hour imaging period may also not represent myocardial scar, par-
ticularly defects not associated with Q waves. These segments may show significantly enhanced early 201TI
uptake after revascularization.

The clinical value of serial 201TI imaging at rest may be in determining the severity of underlying coronary
artery disease in patients with angina pectoris, because rest redistribution is primarily observed in areas per-
fused by the most severely stenotic vessels. Comparison of pre- and postoperative scans might provide
information in a noninvasive manner concerning the efficacy of revascularization in improving regional
myocardial perfusion or reversing resting ischemia.

A practical implication of this study is that initial images obtained soon after 201TI administration at rest
cannot be used alone for comparison with exercise 201TI scintigrams. Defects in similar locations on rest
and exercise scintigrams when obtained at different times are conventionally attributed to infarction or
scar. Defects on initial rest images may reflect underperfused but viable myocardium. Delayed rest im-
ages, obtained 2-3 hours after 201TI injection, are therefore required for comparison with exercise scint-
igrams when evaluating regional myocardial perfusion and viability in patients with coronary artery dis-
ease.

Finally, the application of the computer-derived quantitative imaging techniques described in this
study appears to aid the interpretation of 201TI images significantly. Quantitative data were particularly
useful in confirming diffusely diminished and delayed 201TI uptake in multiple segments in patients with mul-
vessel disease. Quantitative confirmation of delayed uptake in sequential images was essential to establish-
ing the fact that 201TI redistribution had occurred or that an initial defect was persistent.

Acknowledgment

The authors thank Gayle Petroff and Thomas Levy for their technical assistance, Valerie Marshall for secretarial assistance, and Elliott Berger for statistical advice.

References

1. Hamilton GW, Trobaugh GA, Ritchie JL, Williams DL, Weaver WD, Gould KL: Myocardial imaging with in-
2. Pohost GM, Zir LM, Moore RH, McKusick KA, Guiney TE, Beller GA: Differentiation of transiently ischemic from in-
with thallium-201 at rest and during exercise: comparison with coronary arteriography and resting and stress electrocar-
to regional myocardial perfusion. Circulation 51: 641, 1975
10. Maseri A, Parodi O, Severi S, Pesola A: Transient transmural reduction of myocardial blood flow, demonstrated by thallium-201
scintigraphy, as a cause of variant angina. Circulation 54: 280, 1976
11. Schwartz JS, Ponto R, Carlyle P, Forstron L, Cohn JN: Early redistribution of thallium-201 after temporary ischemia. Cir-
culation 57: 332, 1978
680, 1978
16. Helfant RH, Pine R, Meister SG, Feldman MS, Trout RG, Banka VS: Nitroglycerin to unmask reversible asynergy: cor-
17. Bodenheimer MM, Banka VS, Hermann GA, Trout RG, Homayoon P, Helfant RH: Reversible asynergy; histopathologic and
collaterals, and anatomic location. Circulation 50: 714, 1974
19. Horn HR, Teicholz LE, Cohn PF, Hermann MV, Gorlin R: Augmentation of left ventricular contraction pattern in cor-
20. Cook DJ, Bailey I, Strauss HW, Roulea J, Wagner HN, Pitt B: Thallium-201 for myocardial imaging: appearance of the nor-

Downloaded from http://circ.ahajournals.org/ by guest on September 15, 2017
Redistribution of thallium at rest in patients with stable and unstable angina and the
effect of coronary artery bypass surgery.
B C Berger, D D Watson, L R Burwell, I K Crosby, H A Wellons, C D Teates and G A Beller

Circulation. 1979;60:1114-1125
doi: 10.1161/01.CIR.60.5.1114

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/60/5/1114.citation