Transient Defects of Resting Thallium Scans in Patients with Coronary Artery Disease

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SUMMARY Defects on resting thallium-201 ($^{201}$TI) scans in patients who do not have evidence of acute myocardial ischemia have been thought to represent myocardial scar. Our study of 20 patients with stable but severe coronary artery disease (CAD), including nine with ECG evidence of myocardial scar, was undertaken to reexamine the significance of such defects. Imaging was performed in two views, beginning within 10 minutes after TI administration and repeated over a 2-4-hour period. Images in each of the two projections were divided into three zones, for a total of 120 zones in 20 patients. An initial defect was present in 43 zones in 15 patients, while five patients demonstrated totally normal studies. On later scans 18 defects persisted while 25 filled in. Twelve of 18 persistent defects were associated with ECG evidence of infarction, compared with only six of 25 transient defects ($p < 0.01$). Correlation with angiographic left ventricular wall motion was possible for 12 of 18 persistent defects and 18 of 25 transient defects. Six of 12 persistent defects, compared with only one of 18 transient defects, were associated with akinesia/dyskinesia ($p < 0.01$). In addition, 17 of 18 transient defects were associated with either normal left ventricular wall motion (12 defects) or hypokinesia (five defects). Finally, 23 of 25 transient defects, compared with only 41 of 77 normal zones, were associated with severe CAD ($p < 0.001$).

Thus, in resting patients with stable CAD: 1) serial imaging reveals that many initial defects fill in over time; 2) initial resting defects on TI scans may not indicate myocardial scar; and 3) transient defects are usually associated with severe CAD, but normal or only mildly abnormal left ventricular wall motion.

DEFECTS ON THALLIUM-201 ($^{201}$TI) myocardial scans may be the result of regional ischemia, infarction or scar. A previous study from our laboratory suggests that serial imaging can distinguish defects due to transient ischemia, which fill in over time, from those due to infarction or scar, which persist. When $^{201}$TI is administered at rest, defects observed in patients who do not have symptoms or electrocardiographic evidence of acute myocardial ischemia have been thought to represent myocardial scar. Defects could also occur at rest in such patients if regional blood flow were reduced to noninfarcted myocardium. Previous investigators have demonstrated zones of chronically decreased myocardial blood flow in patients with severe coronary artery disease. Therefore, defects on early resting scans may be the result of a chronic reduction in regional blood flow due to severe coronary artery stenosis rather than acute myocardial ischemia or previous scar. If serial imaging can differentiate ischemia or underperfused areas from scar, we would anticipate that defects due to underperfusion would fill in, while those due to scar would persist. To assess the significance of defects on resting thallium images, a group of patients with severe coronary artery disease were studied with serial images obtained early (5-10 minutes) and late (2-4 hours) after the injection of $^{201}$TI.

Methods

Twenty patients with angiographically documented severe coronary artery disease (> 75% luminal narrowing of at least one coronary artery) without evidence of acute myocardial ischemia were selected for the study. Patients with coexistent valvular, myopathic, and/or congenital heart disease were excluded. The nature of the study was explained to each patient and informed consent was obtained.

Study Protocol

A resting 12-lead ECG was obtained at the time of the study in each patient. One and one-half millicuries of $^{201}$TI (thallous chloride) (New England Nuclear, Billerica, Massachusetts) was given I.V. with the patient in the supine position, and sequential imaging in the anterior and 50° left anterior oblique (LAO) projections began 5-10 minutes later. Repeat images were obtained 30-45 minutes and 2-4 hours after the initial views. No patient was fasting before study. Images were recorded for a preset time of 5 minutes each with an Ohio Nuclear Series 420 mobile scintillation camera which was interfaced with an MDS PAD computer system (Medical Data Systems, Ann Arbor, Michigan) and equipped with a medium resolution parallel hole collimator. All images were recorded at the 80-kev mercury x-ray peak with a 25% window. A minimum of 200K counts was obtained in each image.

Data Display and Analysis

Myocardial images were displayed on a cathode ray...
tube with a 128 × 128 matrix, matched for contrast and peak intensity, and photographed on Polaroid film. Images were interpreted independently by two experienced observers without knowledge of the cardiac catheterization results. For this purpose, the images were divided into three zones for each view (fig. 1). Thallium activity in each one was graded qualitatively on a scale of 0–2 as follows: 0 = absent; 1 = reduced; and 2 = normal. Half-grades were also used to denote activity that was either severely reduced but not totally absent (i.e., grade 0.5) or activity which although decreased was almost normal (i.e., grade 1.5). If ²⁰¹Tl activity in any zone was reduced or absent, but subsequently displayed an increase of one grade or more on later views, these zones were considered to show redistribution. Three examples of redistribution are illustrated in figure 2.

Zones with reduced or absent activity which showed no increase in grade of activity over time were considered persistent defects (fig. 3). Differences of opinion with regard to grade of ²⁰¹Tl activity were resolved by consensus.

Coronary and Left Ventricular Angiography

Cardiac catheterization with coronary and left ventricular (LV) angiography was performed using either Sones or Judkins technique. Left ventriculograms were obtained in all patients in a 30° right anterior oblique (RAO) projection and in 11 patients in the 60° LAO projection. The LV and coronary angiograms were reviewed independently by two experienced observers without knowledge of the imaging data and scored according to the following system: Each major coronary artery was examined and the presence or absence of a lesion noted. Lesions were scored on a scale of 0–4 as follows: 0 = < 50% diameter narrowing; 1 = ≥ 50% and < 75% narrowing; 2 = ≥ 75% and < 90% narrowing; 3 = ≥ 90% and ≤ 99% narrowing; and 4 = complete occlusion. When more than one lesion was noted in a single artery, it was assigned the score of the most severe lesion. The left ventriculogram in the RAO view was divided into anterior, apical and inferior thirds. Wall motion was qualitatively scored as normal (N), hypokinetic (H), akinetic (A), or dyskinetic (D). When 60° LAO angiograms were available, they were subdivided into septal, apical-inferior and posterior thirds and scored as described above. As with the nuclear images, differences of opinion were resolved by consensus.

Electrocardiographic — Angiographic — Imaging Correlation

Electrocardiographic, angiographic and imaging data were correlated as follows: ECGs obtained at the
time of imaging were analyzed for presence and location of previous myocardial infarction (MI) according to the criteria of Lipman et al. The zones of myocardium supplied by each of the three major coronary arteries were matched to the appropriate zone on the 201TI image and left ventriculogram. While the anterior scan zones (anterolateral, apical and inferior) do not strictly correspond to the same zones on the 30° RAO LV angiogram (fig. 1), especially in the inferior zone which on scan is probably composed of both septum and inferior wall, this was done since RAO 201TI scans are frequently technically inadequate. Likewise, on the 50° LAO scan the septal, apical-inferior, and posterior zones were assumed to correspond to these same areas on the 60° LAO LV angiogram (fig. 1).

Statistical Methods

The significance of differences in the distributions of discontinuous parameters was assessed using Fisher’s exact test for 2 × 2 tables and chi-square test for larger tables. All data are expressed as mean ± SEM.

Results

Patient Population

Twenty patients with severe but stable coronary artery disease were studied (eight females, 12 males, mean age 54 years, range 32–69 years). At the time of the study, 13 patients were taking regular doses of nitrates and 16 were taking propranolol in doses from 40–320 mg/day. Electrocardiographic, angiographic and scan data are summarized in table 1. Electrocardiographic evidence of transmural MI was present in eight patients. In the remaining 12 patients, seven had nonspecific ST-T changes on the ECG; one had fixed, diffuse, deep T-wave inversions consistent with subendocardial infarction; one had left anterior hemiblock with incomplete right bundle branch block; and three had normal tracings.

Angiographic Data

These results are shown in detail in table 1. Seventeen of 20 patients had at least one major coronary artery with a grade 3 or 4 (i.e., > 90% diameter reduction) lesion. Eight patients had entirely normal 30° RAO ventriculograms, while the other 12 had abnormalities ranging from hypokinesis involving a single segment to frank dyskinesia involving multiple segments.

Imaging Data

These results are shown in detail in table 1. Twenty patients each had six scan zones available for analysis. There was an initial defect on scan in 43 of 120 zones in 15 of the patients. However, 25 (57%) of these defects in 13 patients filled in either completely (22) or

![Figure 2](image_url)  
**Figure 2.** (top) Thallium-201 (201TI) images in the anterior projection from patient 7 illustrate an initial defect in the inferior wall which disappears within 4 hours after 201TI administration. (middle) 201TI images in the anterior projection from patient 1 illustrate an initial anterior wall defect which disappears by 45 minutes after thallium administration. (bottom) 201TI images in the anterior projection from patient 15 illustrate an initial defect in the inferior wall which disappears within 3 hours after 201TI administration.

![Figure 3](image_url)  
**Figure 3.** Thallium-201 images in the 50° left anterior oblique projection (LAO) from patient 12 illustrate an initial defect in the septum which is unchanged throughout the imaging period.
Table 1. Angiographic, Radionuclide and Electrocardiographic Data

<table>
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<th>Pt no.</th>
<th>Coronary angiographic results = stenosis</th>
<th>Left ventriculography</th>
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Grade of stenosis: 0 = 50%; 1 = 50-74%; 2 = 75-89%; 3 = 90-99%; 4 = total occlusion.
Abbreviations: N = normal; H = hypokinetic; A = akinetic; D = dyskinetic; Td = transient defect; Pd = persistent defect.

in part (three) on subsequent images. Twenty-two of 25 of these defects demonstrated complete fill-in, as agreed upon by two observers. Seventy-five percent of these defects filled in within the first 30-45 minutes after 201TI injection; 25% filled in late (i.e., 2-4 hours after injection). The remaining 18 defects (43%) in nine patients persisted throughout the imaging period.Tranient defects did not appear more frequently in any particular scan segment. In contrast, persistent defects occurred more frequently in the apex of the left ventricle than in any other zone.

Correlations between the scan results and the ECG and angiographic data are presented below.

Transient Defects — Electrocardiographic and Angiographic Correlations

Twenty-three of 25 (92%) transient defects were found in the distribution of coronary arteries with ≥ 75% reduction in luminal diameter. The majority of these zones were supplied by coronary arteries with grade 3 (i.e., ≥ 90% but ≤ 99% stenosis) lesions (15 of 25 patients, 60%; p < 0.005). We compared segmental LV wall motion with a corresponding scan zone in 10 patients with a total of 18 zones. The remaining seven zones were present in the LAO projection in patients who had no LAO ventriculograms. Normal regional wall motion was present in 12 of 18 transient defect zones on scan. Hypokinesia was present in five of 18 transient defect zones, while akinesia occurred only once in association with a transient defect. Only six of 25 transient defects were seen in a region corresponding to a transmural infarction on ECG. Three of these zones demonstrated normal wall motion on the LV angiogram, and one had akinesia.

Persistent Defects — Electrocardiographic and Angiographic Correlations

Fifteen of 18 persistent defects were seen in the distribution of coronary arteries with ≥ 75% reduction in luminal diameter. Grade 4 coronary lesions (i.e., total occlusion) were encountered more frequently in association with persistent defects than any other single lesion (11 of 18, 61%; p < 0.005). An LV angiogram was available for comparison in 12 of the 18 zones. Six of 12 scan zones with persistent defects were associated with akinesia or dyskinesia, while the remaining six were associated with normal LV wall motion. Of the six persistent defects associated with normal LV wall motion, five (in patients 4, 11, 14 and 15) were found in regions with corresponding ECG evidence of MI. Electrocardiographic evidence of previous infarction was also seen in five of six persistent defect zones with akinesia or dyskinesia. Patient 13 had a clearcut area of dyskinesia at the apex of the left ventricle in association with a persistent defect on scan in this area even though his ECG revealed only nonspecific ST-T abnormalities. Only two persistent defects were seen in zones without associated evidence of either severe (i.e., ≥ grade 2) coronary artery disease, electrocardiographic evidence of infarction, or severe (i.e., akinesia or dyskinesia) LV wall motion abnormality. One defect was located in the basal septum on the 50° LAO scan (patient 5); the other was located in the posterior zone, also in the 50° LAO view (patient 14).

Normal Scan Zones — Electrocardiographic and Angiographic Correlations

Forty-one of 77 (53%) zones with normal-appearing TI activity were supplied by coronary arteries with
≥ 75% reduction in luminal diameter. Regional LV wall motion was known in 51 of these 77 zones; 39 zones had corresponding normal wall motion, six were hypokinetic and six were akinetic or dyskinetic. Thus, 45 of 51 zones which demonstrated normal uptake of $^{201}$TI demonstrated corresponding normal or hypokinetic wall motion. The six normal scan zones associated with akinesia/dyskinesia were seen in five patients (2, 3, 4, 9 and 20). Three of the six normal zones were associated with akinesia of the apex of the left ventricle. The other normal scan zones, both involving the inferior wall in patient 4, were associated with electrocardiographic evidence of inferior MI.

### Statistical Analysis (table 2)

**Electrocardiographic — Scan Correlations**

Persistent defects were seen in association with ECG evidence of previous transmural MI in 12 of 18 cases (67%), compared with only six of 25 (24%) transient defects ($p < 0.01$). There was also a significant difference in the incidence of electrocardiographic MI between the transient defect scan segments (24%) and the normal segments (5%) ($p < 0.02$).

**Angiographic — Scan Correlations**

Normal LV wall motion or hypokinesia was seen in...
association with 17 of 18 transient defects, compared with only six of 12 persistent defects ($p < 0.01$). Likewise, normal wall motion or hypokinesia was seen in 45 of 51 normal scan zones, compared with six of 12 persistent defects ($p < 0.01$). There was no significant difference between transient defect and normal scan zones with respect to LV wall motion patterns. However, 23 of 25 transient defect zones were perfused by coronary arteries with $\geq 75\%$ reduction in luminal diameter, compared with 41 of 77 normal zones ($p < 0.001$). In addition, the distribution of transient and persistent defects between grades 3 and 4 coronary lesions was also significantly different ($p < 0.001$); four of 19 transient defects were in the distribution of grade 4 lesions, compared with 13 of 16 persistent defects.

Discussion

The initial distribution of $^{201}$TI in the myocardium is related primarily to regional blood flow. If $^{201}$TI is administered to dogs undergoing transient coronary occlusion, to patients during an episode of Prinzmetal’s angina, or during exercise-induced regional ischemia, the distribution of the radionuclide changes over time. The initial distribution is predominately flow-dependent and thus, ischemic and underperfused zones appear as areas of decreased tracer concentration, while the distribution several hours after injection appears to be related primarily to the distribution of viable myocardial cells, and secondarily to flow. Thus, myocardial zones with viable but underperfused cells usually attain a $^{201}$TI concentration equal to that of normally-perfused cells over a period of minutes to hours. In addition, recent work in dogs undergoing partial coronary occlusion demonstrates that redistribution of $^{201}$TI occurs even in the presence of persistently diminished blood flow and does not require restoration of normal flow.

Although resting coronary blood flow is generally thought to be normal in patients with coronary artery disease recent work by Klocke et al. and Cannon et al. has shown by using inert gas washout techniques that some asymptomatic patients with severe coronary artery disease may have decreased regional myocardial blood flow at rest. From these studies it might be anticipated that a reduction in $^{201}$TI concentration to myocardial regions with diminished resting blood flow would occur in some patients with severe coronary stenosis. If enough viable myocytes remained in such regions, defects present on early scans might fill in over time. A recent study by Wackers et al. supports this hypothesis. These investigators observed transient defects on serial $^{201}$TI scans in several patients with severe coronary stenoses who were asymptomatic at the time of $^{201}$TI administration.

In the present study we also observed that initial defects on resting $^{201}$TI scans were not necessarily associated with zones of previous MI or acute ischemia. Two observations in this study suggest that initial defects which fill in with $^{201}$TI over time usually correspond to regions of myocardium which are probably chronically hypoperfused by severely diseased coronary arteries. First, 17 of 18 transient defect zones were associated with normal regional wall motion or hypokinesia. These wall motion patterns have been shown by others to correlate well with predominately viable myocardium when such areas are biopsied at surgery. Second, 20 of 23 transient defect zones were found in the distribution of severely stenotic (90–99% stenosis) but not occluded coronary arteries. Such lesions would be most likely to cause chronically decreased resting blood flow in these zones.

While the above correlations were statistically significant, there were notable exceptions. Scan segments with normal initial $^{201}$TI activity were associated with akinesia or dyskinesia on the LV angiogram in six cases. However, four of the six normal scan segments associated with akinesia involved the apex of the left ventricle. Since the apex commonly reveals decreased activity on $^{201}$TI scans, it is sometimes difficult to determine if this region is actually normal or abnormal. Although these apical segments were scored as normal, all four demonstrated small defects which we considered in the normal range. The discrepancy between the scan and the angiogram may be related to difficulty in evaluating apical $^{201}$TI activity. Also, the $^{201}$TI images were obtained in the anterior projection, while the comparable LV angiograms were obtained in a 30° RAO projection. This difference in orientation might account for disparity in comparative data.

Normal-appearing scan zones were also seen in association with $\geq 75\%$ compromise of coronary arterial luminal diameter in 41 of 77 such cases. More than half of the normal scan segments were found in the distribution of severe coronary lesions. This is probably related to several factors: 1) resting myocardial blood flow in the presence of severe coronary stenosis may be normal; 2) apparently similar degrees of diameter reduction in the proximal coronary arteries as judged by routine coronary angiography may not have an equal effect on perfusion, since factors other than the degree of stenosis may determine resistance to flow; and 3) the scan demonstrates only relative $^{201}$TI distribution and thus, a segment will appear normal as long as flow to it equals or exceeds that of other myocardial zones even if the absolute value for regional blood flow is reduced.

The observation that certain myocardial zones may demonstrate relatively less $^{201}$TI activity and thus, decreased resting blood flow compared with adjacent zones and yet have normal or only mildly abnormal wall motion, might be explained as follows: Previous investigators have shown in acute animal experiments that regional wall motion does not become grossly abnormal until regional blood flow is decreased by more than 50% of control. There is no information concerning the long-term diminution in flow required in an animal model to produce wall motion abnormalities similar to those in the patients with coronary artery disease, although in view of the adap-
tive mechanisms available to the heart, it is likely that even greater reductions are required. Mueller et al. have shown in dogs that regional defects on \( ^{201} \text{TI} \) scans can be detected when flow is decreased to 60\% of normal or less. Thus, defects could be detected on \( ^{201} \text{TI} \) scans at the same time that regional wall motion is normal or only mildly abnormal.

This study demonstrates that defects may occur on resting TI scans in patients with severe coronary artery disease who do not have evidence of an acute ischemic process or previous MI. It also demonstrates that many of these defects fill in on serial images and that redistribution of \( ^{201} \text{TI} \) usually occurs in zones which have normal or only hypokinetic wall motion. In contrast, initial defects which persist during the course of the imaging period (i.e., 2–4 hours) are usually associated with electrocardiographic evidence of infarction and/or severe regional wall motion abnormalities on LV angiograms. Therefore, when defects appear on initial resting \( ^{201} \text{TI} \) scans, serial images should be obtained to help differentiate viable but underperfused myocardium from zones of myocardial scar.

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