Thallium-201 Myocardial Imaging: A Comparison of the Redistribution and Rest Images

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Forty-one patients with chest pain and suspected coronary artery disease underwent thallium-201 myocardial imaging, performed immediately following maximal treadmill exercise, also at "redistribution" 4–5 hr after exercise, and at rest 1 wk later. All had coronary angiography. All images in seven patients without coronary artery disease were normal. Twenty-seven of the 34 (79%) patients with coronary artery disease had new, exercise-induced image defects. The redistribution and rest images were identical in 15/27 (56%) patients (complete redistribution). In 10/27 (37%) patients with exercise-induced defects, some redistribution occurred but defect size on the redistribution image was larger than that on the rest images (incomplete redistribution). In 2/27 (7%) of patients with exercise-induced defects, redistribution was absent. The presence of prior myocardial infarction, regional abnormalities of left-ventricular contraction or the severity of coronary stenoses did not correlate with the presence or absence of redistribution. Overall image quality between the two studies was similar, although image collection times for the redistribution study were prolonged.

We conclude that some redistribution (complete or incomplete) occurs in most patients with exercise-induced image defects. When both fixed and reversible perfusion defects are present, defect size was often larger in the redistribution image and may thus overestimate the extent of prior myocardial infarction.

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Increasing attention has been focused on myocardial imaging for the noninvasive evaluation of the presence and extent of myocardial ischemia and infarction (*1–3*). Currently, thallium-201 is the most commonly used radionuclide for detection of stress-induced myocardial ischemia (*3–6*). In the initial clinical studies with this agent, two tracer injections were used: one during maximal exercise and one at rest. Because of the relatively high residual activity, the rest and exercise studies were usually separated by 1–2 wk. Image defects present only on the exercise study represent stress-induced regional ischemia, whereas defects noted on the resting study usually coincide with previous myocardial infarction (*3–5*). Recently, Pohost et al. (*7*) demonstrated that image defects seen on immediate post-exercise images often reverted to normal, or "redistributed," when imaging was repeated several hours after the initial exercise study. These authors and others (*8–10*) have provided experimental animal data showing that this phenomenon is due to an absolute increase in thallium concentration in the abnormal area coupled with an absolute decrease in thallium concentration in the normal regions (*7,11*). Pohost further suggested that imaging im-

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mediately following exercise and several hours later would provide data comparable to standard rest-exercise imaging.

This study compares the rest images with the redistribution images performed 4–5 hours following an exercise injection in a series of 41 patients.

METHODS

Patient selection and clinical data. We have studied 41 male patients (ages 35–65 yr, mean 51) with stable chest pain syndromes and proven or suspected coronary artery disease. These were the first 41 consecutive patients having coronary angiography who agreed to the three radionuclide studies. All gave informed consent. Coronary angiograms were reviewed by two observers, and the percentage of diameter stenosis of each lesion estimated. Stenoses of more than 50% diameter were categorized as significant coronary artery disease. Biplane left ventriculography was performed in the 30° right anterior oblique and 60° left anterior oblique views. Regional contraction was graded qualitatively by a consensus of two readers. Contractility was classed as normal, hypokinetic, akinetic, or dyskinetic when more than 25% of the circumference of either view was involved, as previously described from this laboratory (*12*). Prior myocardial infarction was defined as the presence of 0.04-sec electrocardiographic Q waves and either a) a compatible clinical history or b) diagnostic enzyme elevations.

Myocardial imaging. Imaging was performed three times in each patient as follows:

1. Immediately following exercise as previously described in this laboratory (*4,13*). In brief, patients had multistage treadmill exercise testing according to the Bruce protocol and were stopped at their own symptomatic maximum (*13*). Thallium-201 (2.0 mCi) was injected 30–60 sec before the termination of exercise and imaging was begun within 10 min. Five views were obtained in the following order: anterior, 30° left anterior oblique, 45° left anterior oblique, 60° left anterior oblique, and left lateral.

2. Four to five hours after the exercise injection, three views were repeated using an identical imaging technique. The three late images always included an anterior and one of the left anterior oblique views, and were selected from the initial five views on the basis of which views best demonstrated the exercise defect. Only three, rather than five, delayed views were obtained because of the prolonged imaging times.

3. For resting images, the patient subsequently returned to the laboratory 5–10 days later. Imaging was started 20 min after injection, and the same five views were obtained as for the exercise study. In two patients, rest images were obtained first and exercise/redistribution images 1 wk later. In these two patients, an additional set of images was obtained at 15–16 hr following exercise.

For all studies, 300,000-count images were obtained using a scintillation camera with a medium-resolution, low-energy, parallel-hole collimator. The time from injection and the imaging duration were recorded on each scintiphoto. All images were recorded and subsequently interpreted directly from the original, unprocessed tri-lens Polaroid scintiphotos.

Image interpretation. This was done by two observers who had no knowledge of clinical or catheterization data. A *subjective* estimate of overall image quality between the rest and redistribution studies was made in each case and the images were judged either equal, or one better than the other. This subjective assessment of quality probably depends mainly on contrast between myocardium and background and amount of activity in contiguous structures such as the gastrointestinal tract and liver, but no attempt was made to determine this. The two observers agreed in this judgment in 30/41 cases (71%) and reached a consensus when disagreement was present. Subsequently, the rest/exercise pair of images was interpreted qualitatively as previously described in this laboratory (*4,13,14*). In brief, a defect was defined as a discrete region of absent or decreased activity seen in at least two views. The rest/exercise pair of images fell into four classes: a) normal (at rest)/normal (under exercise), b) normal/defect, c) defect/no change, and d) defect/increased size of defect or new defect. The redis-

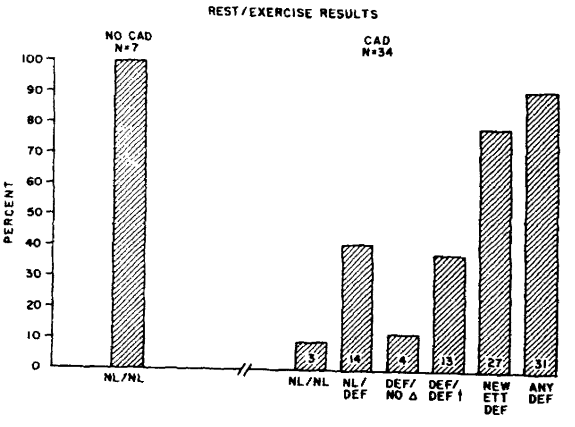

FIG. 1. Results of rest exercise pairs of Tl-201 myocardial images. At left are patients without coronary artery disease (CAD) and at right those with significant disease. Below, initial notation refers to rest image, second notation to exercise image. NL = normal; DEF = defect; NO Δ = no change between rest and exercise; DEF ↑ = defect enlarges or an additional defect appears; ETT = exercise tolerance test; ANY DEF = defect with either rest and/or exercise.

TABLE 1. TI-201 EXERCISE REDISTRIBUTION SUSPECT CAD (N = 41)

N	Rest image	ETT image	Redistribution			
			Complete	Incomplete	Absent	Not possible
10*	NL	NL				10**
14	NL	Defect	10**	4		
4	Defect	No change				4
13	Defect	Defect ↑	5	6	2	

* Includes all 7 patients with normal coronary arteries
** Information finalized after redistribution study
CAD = Coronary artery disease; ETT = exercise tolerance test; NL = normal; ↑ = defect enlarged or a new defect appeared

tribution images were then compared with the rest and exercise images as follows.

1. Redistribution was considered complete when the redistribution and the rest images were identical in the face of an exercise-induced defect ("identical" meaning that the presence and extent of image defects were not judged to differ).
2. Redistribution was considered incomplete when the presence or the extent of the defect on the redistribution study exceeded that of the rest study. A difference in extent was judged qualitatively in the same manner that rest images showing defects were compared with the exercise images.
3. Redistribution was absent if the exercise and redistribution images were identical in the face of an exercise-induced defect.
4. Redistribution was not possible if no new, exercise-induced defect was present.

Two observers independently agreed on image interpretation in 34/41 (83%) cases, and in the remainder a consensus was agreed upon.

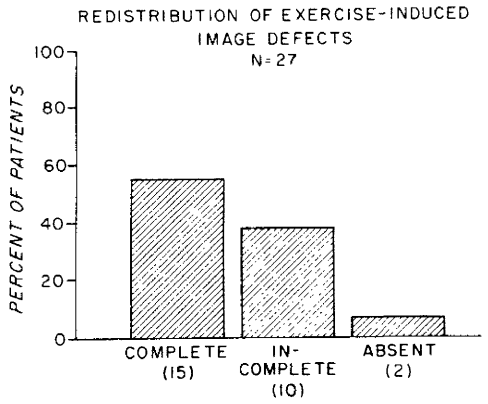

FIG. 2. Among patients with exercise-induced image defects, redistribution was complete in 56%, incomplete in 37%, and absent in 7%.

RESULTS

Of the 41 patients with chest-pain syndromes, seven had normal coronary arteries and were otherwise normal at cardiac catheterization. These seven patients all had normal images at rest, exercise, and redistribution. Results of the rest, exercise, and redistribution image studies for all patients are shown in Fig. 1 and Table 1. Of the 34 patients with significant coronary artery disease 31/34 (91%) had a defect on either the rest or exercise image, and 27/34 (79%) had new, exercise-induced defects (Fig. 1). Among patients with coronary artery disease, redistribution was complete in 15/34 (44%), incomplete in 10/34 (29%), absent in 2/34 (6%), and not possible (i.e., no new defect developed with exercise) in 7/34 (21%) (Table 1). If these last seven patients are excluded, 15/27 (56%) patients with exercise-induced defects showed complete redistribution, 10/27 (37%) had incomplete redistribution, and 2/27 (7%) had absent redistribution, as illustrated in Fig. 2. Figure 3 illustrates the image findings in a patient with an exercise-induced inferoposterior defect. There is minimal or incomplete redistribution in the image performed at 4 hr, and a substantial defect persists (right-hand column). The rest image (left-hand column), however, was entirely normal. Images from another patient are shown in Fig. 4. In this patient with a prior inferior myocardial infarction, there was a small inferior defect on the rest image (left column). Following exercise, the defect was enlarged considerably and showed minimal or incomplete redistribution at 4 hr. Additionally, images at 15 hr following exercise showed no further redistribution (right-hand column).

The sequence in which studies were performed is shown in Fig. 5, a branching diagram. Covering all 41 patients, the figure shows that when the exercise/redistribution study was performed first, the redistribution image was normal in 49% (20/41) of all patients and in 29% (10/34) of patients with cor-

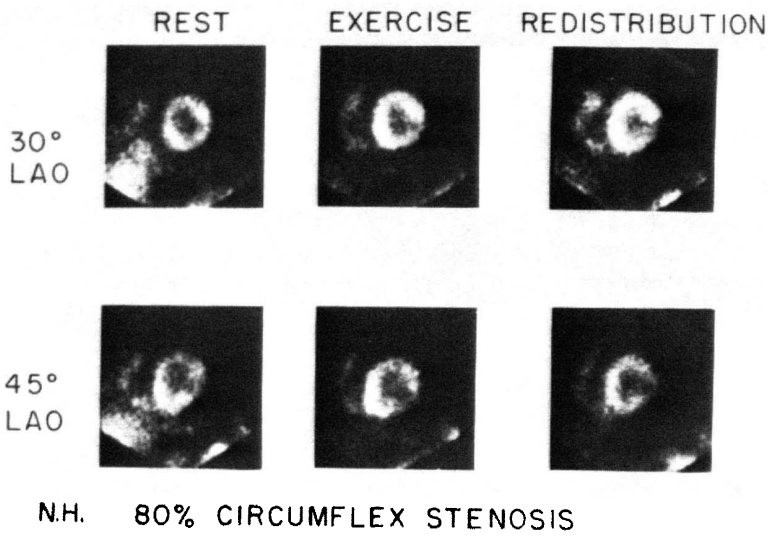

FIG. 3. Rest images (left) were normal in this patient with an isolated 80% circumflex stenosis and inferior hypokinesis but without prior myocardial infarction. Exercise-induced posteroinferior defect (center) shows incomplete redistribution at four hours (right).

onary artery disease. Hence, in a study of a group of patients with suspected coronary artery disease, all diagnostic information is completed in about half of the patients as soon as the redistribution study is done (top entry, middle and right-hand columns of Fig. 5). In the remaining 21 patients (39% of the entire study group, 71% of the group with coronary artery disease), an image defect was present on the redistribution image. This precluded, a priori, any knowledge of the possibility and/or completeness of redistribution without direct comparison with the rest image (bottom four entries, right-hand column of Fig. 5). In 57% of these patients (12/21) with a defect on the redistribution image, defect size was smaller (incomplete) (10/12) or absent (2/12) in the rest study (Fig. 5, right-hand column). The 24% of patients (5/21) with complete redistribution (with a defect present on redistribution image) and the 19% (4/21) with no possible redistribution (i.e., no additional defect with exercise) could not be distinguished from the others in this group unless a comparison with the rest image was available (Fig. 5, right-hand column).

Among 17 patients with prior myocardial infarction documented by electrocardiographic Q wave, redistribution was complete in 44% (6/13) with an exercise-induced defect against 64% (9/14, P = NS) in those without prior infarction and exercise-induced defects. Among those patients without prior myocardial infarction, the proportion with 100% coronary occlusions in the region of the defect was not significantly different from those with complete (2/9, 22%) or incomplete redistribution (2/5, 40%, P = NS, Fischer's Exact Chi-Square Test). There were similarly no significant differences in the presence of abnormal regional wall motion in the area

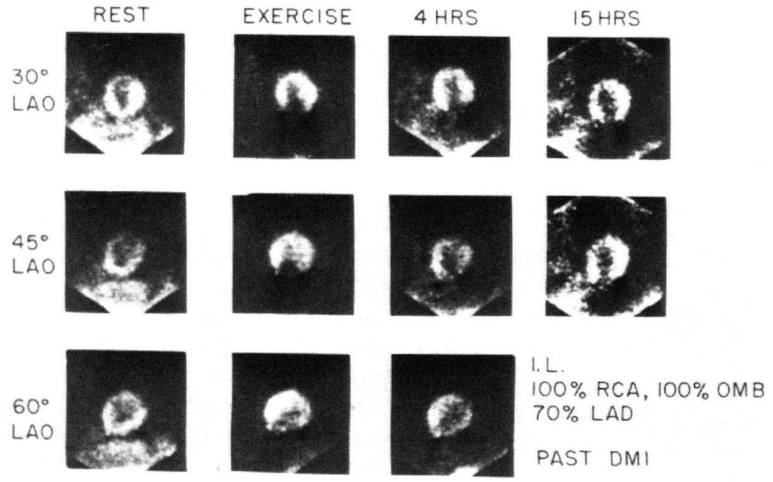

FIG. 4. This patient with a prior diaphragmatic myocardial infarction (DMI) had small inferior defect on rest image (left). With exercise, this enlarged considerably and showed incomplete redistribution at 4 hr and little further change at 15 hr.

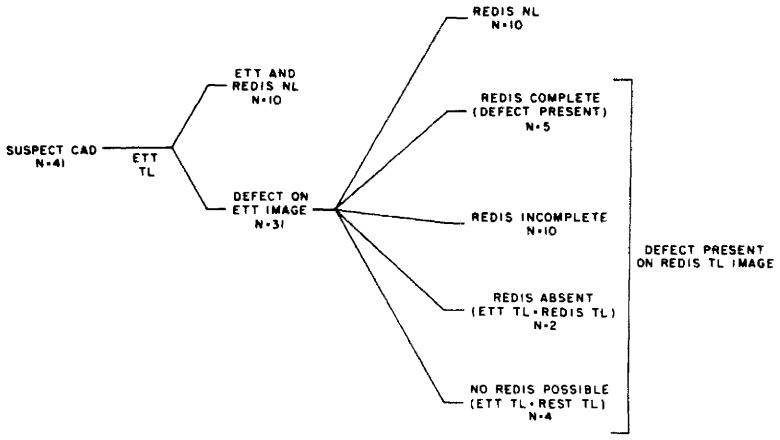

FIG. 5. Branching diagram to illustrate steps one would take in studying patients with suspected coronary artery disease shown in left-hand column. Normal exercise images (ETT) are found in about one quarter of patients (top, middle column) and redistribution or rest studies are not needed. Of those patients with exercise defects (bottom, middle column), redistribution images become normal in an additional one quarter of patients (top, right hand column). All information in these patients is finalized. In the remaining half of patients (lower four categories, right), with defect present on redistribution image, it is not possible to distinguish between complete, incomplete, absent, or no possible redistribution unless a rest image is obtained. CAD = coronary artery disease; REDIS = redistribution.

of the defect in the two groups; 40% (2/5) had hypokinesis in the incomplete-redistribution group and 33% (3/9) had hypokinesis in the complete-redistribution group (P = NS, Fischer's Exact Chi-Square). Mean percentage of diameter stenosis of the coronary artery supplying the zone of the defect also did not differ between the patients with incomplete redistribution [(90 ± 5)% (s.e.m.)] against those with complete redistribution [(81.7 ± 5.6)%, P = NS, unpaired t-test]. In the group with coronary artery disease, 13 patients showed defects on the rest image and developed new, exercise-induced defects. Only 38% of these (5/13) had complete redistribution, against 78% (10/14) in the group with exercise-induced defects and normal rest images (P < 0.07, Fischer's Exact Chi-Square). Both patients with entirely absent redistribution showed defects on the rest image; one of these also had electrocardiographic evidence of prior myocardial infarction.

Overall image quality was judged equal in 56% of the studies (23/41); in 27% (11/41) the rest image was of higher quality, and in 17% (7/41) the redistribution image was of higher quality. These differences were not statistically significant. Five-view imaging times for the rest studies were 39.3 ± 8.0 (s.d.) min, three-view times for the rest study were 23.1 ± 5.1 min. Three-view times for the exercise study were 32.6 ± 8.4 min, and three-view imaging times for the redistribution study were 40.3 ± 10.5 min. The three-view redistribution imaging times were not significantly different from the five-view rest image times, but were longer than the three-view times for either the rest or exercise images (P < 0.001, paired t-test).

DISCUSSION

The redistribution thallium-201 myocardial image, to the extent that it is comparable with the resting myocardial image, offers significant savings in tracer cost, radiation exposure, and patient time. This study has shown that image quality of the two studies is essentially the same, and that in most cases with exercise-induced defects, some redistribution (complete or incomplete) occurred in most patients with coronary artery disease (25/27 = 93%). Thus, in most patients undergoing exercise stress thallium-201 imaging, the redistribution image appears satisfactory for the detection, per se, of "any" reversible ischemia. The extent or magnitude of image defects on the redistribution study, however, exceeded that in the rest images in 44% of patients (12/27), thus presumably underestimating the extent of reversible ischemia and overestimating the extent of irreversible scar. Earlier clinical studies have shown a good correlation between the magnitude of defects obtained in the rest image and prior myocardial infarction as assessed by the extent of abnormally contracting myocardial segments on contrast angiography (*14–16*).

The time course of thallium-201 redistribution in experimental animals has been studied by Pohost et al. (*7*), Beller et al. (*9*), and Schwartz et al. (*10*). In these studies, one normal coronary artery was temporarily occluded, and both thallium-201 and labeled microspheres were injected, both during the period of occlusion and then later, following release of the occlusion. These studies have shown that initial thallium-201 activity paralleled initial blood flow measured by microspheres in the area of oc-

clusion, and that following release of the occlusion, thallium-201 activity in this zone increased. Schwartz et al. (*10*) demonstrated that redistribution was detectable as soon as 5 min following occlusion release, and that thallium-201 activity in the occluded zone increased from 5.5% to 69% of that of the normal zone at 105 min. They also showed that, compared with controls, a prolonged positive myocardial arteriovenous extraction ratio (net uptake) occurred during the period of redistribution, and they postulated that prolonged uptake from low systemic blood levels was the major mechanism of redistribution. They noted that all experimental studies have employed a model of occlusion release in which redistribution occurs in an entirely normal coronary artery. They speculated that redistribution might not occur as readily in a clinical situation in which the underlying coronary arteries are highly stenotic, and the involved heart segment variably supplied through collateral vessels and possibly not subject to the reactive hyperemia that occurred in the experimental model (*10*). The data herein support that reservation in that redistribution was incomplete or absent in 44% of patients (12/27) with exercise-induced defects. In this series, there were no clinical parameters—such as the extent of coronary stenosis or prior myocardial infarction—that correlated with incomplete redistribution. The presence of a defect in the rest image, possibly an indirect reflection of hypoperfusion not otherwise detectable, did correlate with incomplete redistribution (*17*). It seems likely that in patients with incomplete or absent redistribution, a combination of low levels of tracer in the blood, together with persistent and pronounced coronary artery stenosis, prevented complete redistribution. Inadequate delay between the redistribution and exercise study does not appear to explain the phenomenon, as shown in the two cases in which imaging at 15–18 hr showed no further redistribution. Blood et al. (*18*) have recently reported findings similar to those of the present study. In their report, the rest and redistribution studies were not comparable in 21% of patients. They found that in all but one of these cases, the presence or extent of a redistribution defect exceeded that of the rest image and was often associated with prior myocardial infarction.

The clinical implications of this study are several. First, reversible or exercise-induced defects will be correctly identified, qualitatively, in most patients by a redistribution study. That is, the presence or absence of reversible ischemia per se will be identified. Second, since the magnitude of the redistribution defect exceeds that on the rest image in one-third to one-half of cases, decisions about the extent of reversible scar should be made with caution. The extent or presence of prior myocardial infarction is often overestimated by the redistribution technique. Specifically, if the thallium image is being used to assess the probability of viable myocardium for surgical graft placement, a rest image should probably be performed. Third, image quality of the two studies was similar, and the longer imaging times for the redistribution study routinely allowed collection of only three views. However, this longer imaging time was not found to be a disadvantage provided that a physician interpreted the exercise study and selected the best three views before the redistribution study was run.

In summary, the late or redistribution thallium image is of similar overall quality to that of the rest study, and can usually supplant it in the diagnosis, per se, of reversible myocardial ischemia. The redistribution image, however, often overestimates the extent of irreversible myocardial fibrosis. If the redistribution study is of poor technical quality or if the magnitude of irreversible scar is uniquely important, the rest image may provide additional information.

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