

Usefulness of resting thallium-201 delayed imaging for detecting myocardial viability in patients with previous myocardial infarction

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To test the feasibility of resting thallium-201 (^{201}Tl) initial and delayed scintigraphy for detecting the area of viable myocardium, we performed single photon emission computed tomography (SPECT) in 57 patients with previous myocardial infarction (MI). All had received coronary arteriography (CAG) and left ventriculography (LVG). Initial and delayed myocardial imagings were carried out 10 min and 2 hours, respectively, after the injection of ^{201}Tl at rest. Redistribution was judged by visual interpretation and/or the circumferential profile curve, and found in the infarcted or its adjacent area in 40 of the 57 cases (70.2%). A negative washout (net increase of ^{201}Tl uptake in delayed image) was detected in 17 of these 40 cases. In 10 of the 57 patients, both exercise and rest-injected ^{201}Tl myocardial images were obtained at exercise and rest, and compared visually. The areas of abnormal perfusion were smaller in the resting delayed images than those seen after exercise in 9 of the 10 cases, and were equal in one case. Thus, resting ^{201}Tl delayed myocardial scintigraphy appears to reduce the underestimation of the size of the viable myocardium by the usual ^{201}Tl images obtained after exercise or by single initial images obtained at rest in patients with previous MI.

Key words: redistribution, negative washout, myocardial viability, thallium-201, rest injection

INTRODUCTION

THALLIUM-201 (^{201}Tl) single photon emission computed tomography (SPECT) is widely used to detect myocardial ischemia and identify myocardial viability.¹ The area showing a persistent defect on the initial and delayed images after exercise is generally considered to be "infarcted", while the area with a redistribution of ^{201}Tl on the delayed scan is considered to be consistent with viable myocardium. Since revascularization therapy, such as a coronary artery bypass graft (CABG) surgery or percutaneous transluminal coronary angioplasty (PTCA), are increasingly used, it becomes essential to detect the

surviving myocardium accurately even in patients with previous myocardial infarction (MI).²⁻⁴ Our objective was to determine whether resting ^{201}Tl delayed myocardial SPECT images would be useful in evaluating the viability of the myocardium in the "infarcted" and the adjacent area. Accordingly, we compared the size of perfusion abnormalities in the resting ^{201}Tl images with those obtained after exercise. The correlation between the redistribution in resting scans and the wall motion on the left ventriculogram (LVG), or collaterals on the coronary arteriogram (CAG) and number of diseased coronary arteries, was also evaluated.

MATERIALS AND METHODS

Patients

We evaluated 57 patients, 46 men and 11 women aged 26 to 76 years (average 56.2 years), who had experienced myocardial infarction at least 2 weeks before the performance of ^{201}Tl scintigraphy. The

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diagnosis was confirmed by the increase in serum enzymes, ECG changes and clinical symptoms. None of these patients had received revascularization therapy during the acute phase.

Resting ^{201}Tl myocardial scintigraphy

The patients were injected intravenously with 148 MBq (4 mCi) of ^{201}Tl while seated. They were then placed supine on a scintigraphic imaging table. Single photon emission computed tomography (SPECT) imaging was carried out with a 180° imaging arc (45° RAO to 45° LPO) and 19 acquisitions of 50 sec each. Data were acquired with a large field-of-view rotating gamma camera (ZLC-7500, Siemens Co. Ltd) equipped with a high resolution collimator, and stored in an on-line computer (Scintipac 2400, Shimadzu, Japan). Initial and delayed images were acquired at 10 min and 2 hours after the administration of ^{201}Tl , respectively. None of the patients experienced chest pain or discomfort during these studies.

(1) Visual interpretation of perfusion abnormalities and redistribution

With a 64×64 matrix, the pixel size was adjusted so that the actual thickness of the slice was 6 mm/pixel. Six tomographic projection images (i.e. transverse, coronal, sagittal, vertical long axial, horizontal long axial and short axial) in each initial and delayed acquisition were reconstructed for visual interpretation. Thallium-201 SPECT images were interpreted jointly by three experienced physicians without knowledge of the patient's identity or catheterization findings. Redistribution was considered to have occurred when there was "filling in" of the defects or an improvement in the hypoperfusion in delayed SPECT images. The perfusion abnormalities were located with reference to the seven angiographic ventricular segments recommended by the American Heart Association (AHA).⁵

(2) Analysis of redistribution with circumferential profile curves

Redistribution was also evaluated from the circumferential profile curves generated from the resting initial and delayed SPECT images in the 57 patients. A vertical long axial image in the largest left ventricular (LV) lumen and a short axial image at the midway portion between the apex and the base was chosen, and a computer-generated circumference was constructed around the outer edge of the left ventricle. Radii were then constructed by the computer from the center to each point of the circumference with 10° separation of each radius (36 radii).^{6,7} Peak activity per pixel along the radius was calculated, and a curve representing the ^{201}Tl activity against the angular location was described. The highest count in each initial and delayed curve was adjusted to

represent 100% and the counts on all other radii were normalized to the highest count in each initial and delayed curve. Redistribution was judged to be positive when the fraction was improved by more than 10% on more than three consecutive radii, excluding the following areas: LV outflow tract ($0-30^\circ$, $340-360^\circ$ in the vertical long axial image) and the defect area with less than 30% of the maximal counts on the initial image. No background was subtracted from the images.

(3) Calculation of washout rate

The washout rate along each radius was calculated from the original counts as follows:⁷

Washout rate (%)

$$= (\text{Initial counts} - \text{Delayed counts}) / (\text{Initial counts}) \times 100$$

The negative washout area was defined as the area in which the calculated washout rate was negative (net increase of ^{201}Tl uptake in delayed image) in more than three consecutive radii.

^{201}Tl myocardial scintigraphy after exercise

In 10 of the 57 patients, ^{201}Tl myocardial imaging was performed after graded exercise on a bicycle ergometer by means of standard protocols⁸ within one month before or after imaging at rest. Exercise was terminated when the patient developed chest symptoms (6/10) or lower limb fatigue (4/10). The same dose of ^{201}Tl as used in the resting study (148 MBq) was injected intravenously 1 min before the end of the exercise. The patients were imaged at 10 min and again at 3 hours post exercise as described above. The initial and delayed SPECT images were analyzed visually, and the area showing redistribution was compared with those of the rest images.

Cardiac catheterization

All patients received contrast LVG in the right and left oblique projections and CAG within two weeks of the performance of resting ^{201}Tl imaging. A separate group of three experienced physicians scored regional wall motion by consensus in the seven myocardial segments of AHA⁵ with a four-point scale as normal, hypokinesis, akinesis or dyskinesis without knowledge of the scintigraphic data. Organic stenosis of more than 75% was considered to be significant. Patients were divided into three groups according to the number of diseased coronary arteries. The three observers scored the development of collaterals to the infarcted area on a three-point scale as good, poor or none.

Statistical analysis

Statistical analysis was performed by the chi-square

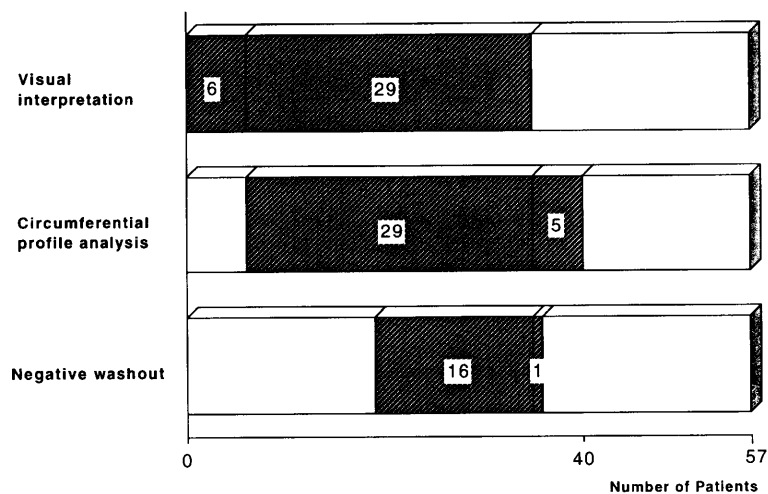


Fig. 1 Incidence of ^{201}Tl redistribution in resting myocardial delayed SPECT images by visual interpretation and by circumferential profile analysis. Cross-hatched area corresponds to the redistribution-positive patients, and light area to the redistribution-negative patients. Numbers on columns indicate the number of patients. A total of 29 patients were positive for redistribution by both methods, while 6 patients were positive only by visual interpretation, and 5 were positive only by circumferential profile analysis. By either assessment, 70.2% (40 of 57 patients) were judged to be positive for ^{201}Tl redistribution.

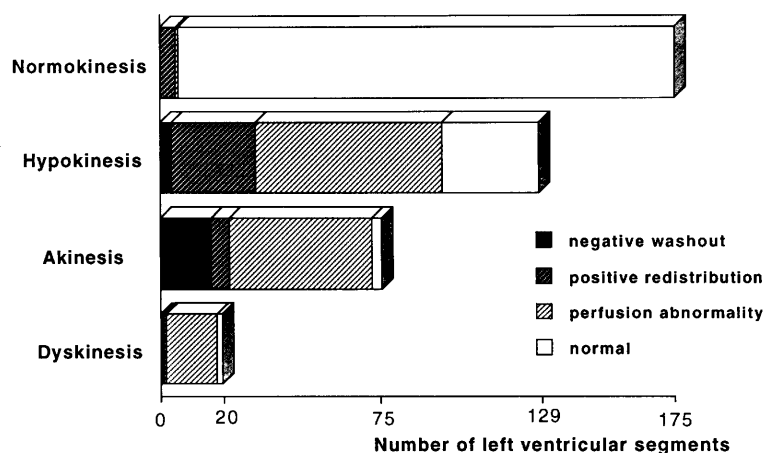
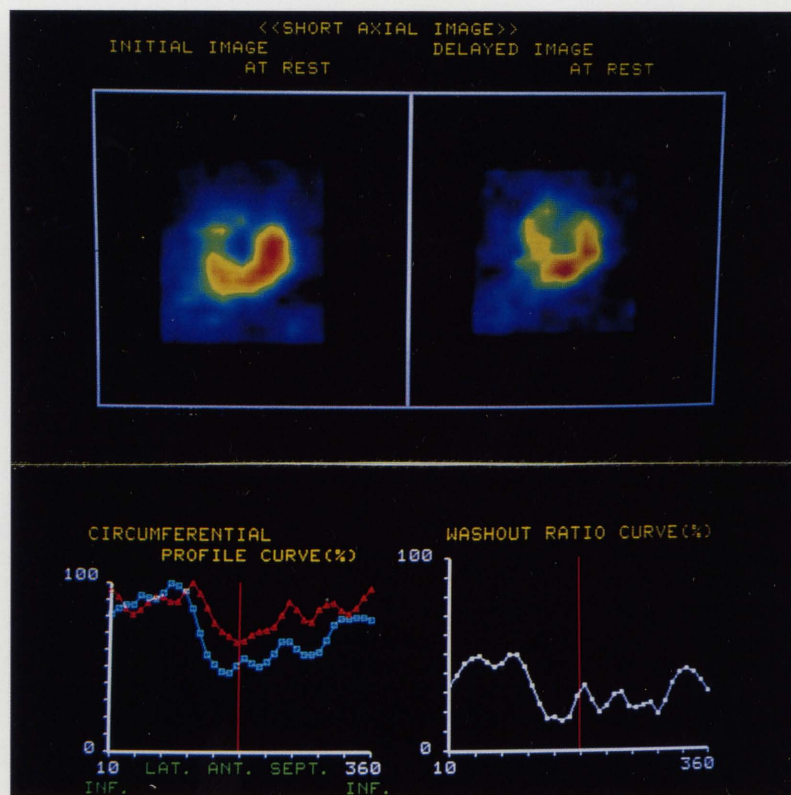
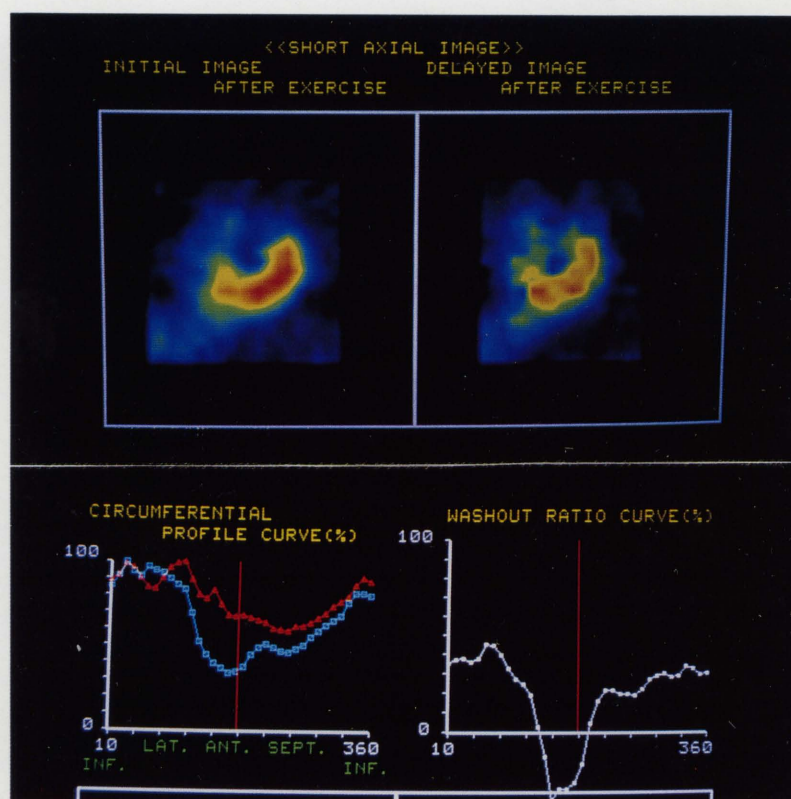


Fig. 2 Relationship between the grade of wall motion on LVG and perfusion abnormality and redistribution on resting delayed images. A total of 399 segments were examined in 57 patients with previous MI. Perfusion abnormalities were detected in the resting initial images in 6 segments (3.4%) of normokinesis, 96 (74.4%) of hypokinesis, 72 (96.0%) of akinesis and 19 (95.0%) of dyskinesis. The incidence of redistribution in these abnormally perfused segments was 83.3% (5 of 6 abnormal segments) in normokinesis, 33.3% (32 of 96 abnormal segments) in hypokinesis, 31.9% (23 of 73 abnormal segments), and 10.5% (2 of 19 abnormal segments) in dyskinesis, respectively. Negative washout (net increase of the counts) was seen at the rate of 0% (0/5) of normokinetic segments with redistribution, 12.5% (4/32) of hypokinetic, 73.9% (17/23) of akinetic, and 50.0% (1/2) of dyskinetic segments with redistribution.



3A



3B

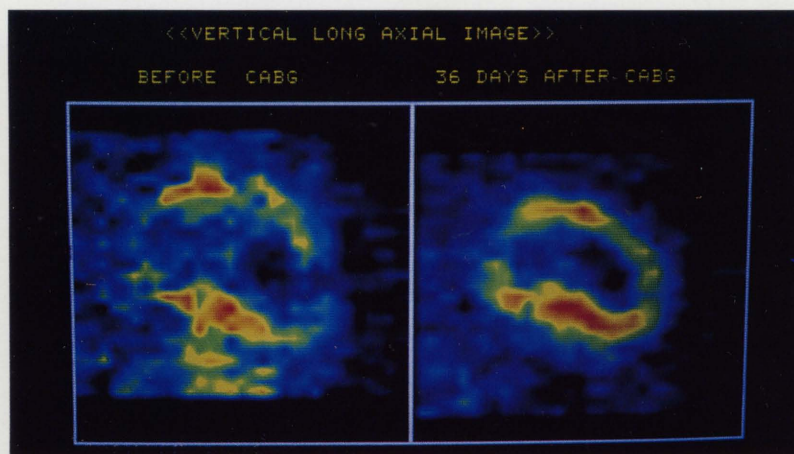


Fig. 4 Case 2, 45-year-old man with previous anterior MI. Vertical long axial delayed images obtained following injection of ^{201}Tl at rest, before and 36 days after revascularization. Coronary arteriogram had revealed triple vessel disease, and CABG surgery was performed on the three major coronary arteries. The myocardial SPECT image then demonstrated a reduction in the size of the left ventricular lumen and an improvement of ^{201}Tl uptake in the inferior and anterior wall and apex. In retrospect, this improvement was greater than would be expected from the first resting delayed image.

test. A probability (p) value less than 0.05 was considered to be statistically significant.

RESULTS

Incidence of redistribution in resting ^{201}Tl scintigraphy

All 57 patients exhibited abnormalities on the resting initial ^{201}Tl myocardial images based on the analysis of both their visual and circumferential profiles. In the delayed images, redistribution was found in 35 of 57 cases (61.4%) by visual interpretation, and in 34 of 57 cases (59.6%) by circumferential profile analysis, as shown in Fig. 1. A total of 29 patients were judged to be redistribution-positive on both assessments, while 6 patients were positive only

by visual interpretation, and 5 were positive only by circumferential profile analysis. The last 5 patients had relatively slight redistribution. Visual interpretation was useful in 6 patients since, in some cases, redistribution was small (less than 3 consecutive radii) but prominent. The other cases could be evaluated only from the projections other than the vertical long axial and short axial views. By either analysis, redistribution in resting ^{201}Tl delayed images was observed in 40 of 57 patients (70.2%). A region with negative washout, showing a net increase in counts in the delayed vs. the initial image, was found in 17 of the 40 redistribution-positive patients.

◀ **Fig. 3** Case 1, 69-year-old man with anteroseptal MI. Short axial initial and delayed images are shown at rest (Fig. 3-A) and after exercise (Fig. 3-B). He had developed an acute MI 5 months before these imagings. Both imagings were taken 28 days apart, and clinical findings were stable during this interval. Electrocardiogram recorded just before the imaging revealed abnormal Q wave and inverted T wave in right precordial leads. Visually, defect and hypoperfusion of ^{201}Tl were seen in the anteroseptal area in all four images. However, the defect and hypoperfused area were smaller in the resting images than in those obtained after exercise, even though at almost same LV slices were presented. The resting delayed image demonstrates the smallest defect and hypoperfusive area in septum, which indicates its ability to detect the largest viable myocardium. The circumferential profile curve was generated from the short axial image. The blue line indicates the initial, and the red line demonstrates the delayed curves. The maximal count on each curve was normalized as 100%. The washout rate was independently calculated from the original counts on the radii on the short axial images (see text). The washout rate curve shows low washout at rest and negative washout in anterior wall after exercise.

Correlation of resting ^{201}Tl redistribution with LV wall motion and CAG findings

The wall motion observed on contrast LVG and the redistribution on the resting ^{201}Tl SPECT images in 399 left ventricular segments were compared in 57 patients (Fig. 2). Perfusion abnormalities (defect or hypoperfusion) in the resting initial images were detected visually in each grade of wall motion at the following rates: 6/175 (3.4%) in normokinesis, 96/129 (74.4%) in hypokinesis, 72/75 (96.0%) in akinesis, and 19/20 (95.0%) in dyskinesis. Redistribution as judged by visual interpretation and/or circumferential profile analysis of the abnormally perfused segments on the initial image was detected in each grade of wall motion as follows: 32/96 (33.3%) in hypokinesis, 23/72 (31.9%) in akinesis, and 2/19 (10.5%) in dyskinesis. In these redistributed segments, negative washout was seen in 4/32 (12.5%) of hypokinesis, 17/23 (73.9%) of akinesis, and 1/2 (50.0%) of dyskinesis. Thus, the incidence of redistribution was very close in the hypokinetic (33.3%) and akinetic segments (31.9%).

Table 1 shows the number of patients with or without ^{201}Tl redistribution in each group classified by the number of diseased coronary arteries or by the degree of collateral circulation. There was no significant correlation between the appearance of redistribution on the resting delayed image and the number of diseased arteries or the development of collaterals ($p > 0.2$, $p > 0.2$, respectively, by chi-square analysis). The incidences of redistribution were also compared with the degree of stenosis in the infarct-related arteries. Of the 26 regions supplied by a totally occluded coronary artery, 19 regions were associated with the redistribution of ^{201}Tl . However, the incidence of redistribution did not correlate significantly with the degree of stenosis statistically.

Comparison of ^{201}Tl myocardial scintigraphy at rest and exercise

To evaluate the extent of viable myocardium, the size of the perfusion abnormality was compared visually in each initial and delayed image obtained

at rest and after exercise in 10 patients with previous MI. As shown in Table 2, the size of the hypoperfused area was the largest in the initial image obtained immediately after exercise, and the smallest in the resting delayed image. Comparison of the two delayed SPECT images showed that the abnormally perfused area was smaller in the resting delayed images in 9 of 10 patients, even though the interval between the injection of ^{201}Tl and the delayed imaging was longer in the resting scans. In addition, in 7 of these 10 patients, the abnormally perfused area on the delayed image after exercise was larger than that on the resting initial image, whereas these two images were equivalent in the remaining 3 patients. These observations indicate that the delayed image obtained after exercise as well as the resting initial image tend to underestimate the viable myocardium.

Case presentation

Case 1: Figure 3 represents the initial and delayed SPECT images obtained at rest and following exercise in a patient with antero-septal MI. Of the four images, the resting delayed image showed the smallest area of abnormal perfusion. This case demonstrates that the resting ^{201}Tl delayed image is more likely to detect the largest amount of viable myocardium.

Case 2: A patient with previous anterior MI and triple vessel disease is presented in Fig. 4. After CABG, the hypoperfused area became smaller than would be expected from the pre-CABG image. This case illustrates the underestimation of viable myocardium even on the resting delayed image.

DISCUSSION

The ability to differentiate the viable myocardium accurately from the irreversibly infarcted myocardium is essential in establishing the indications for revascularization therapy in patients with previous MI. Stress ^{201}Tl myocardial scintigraphy with exercise or with the administration of dipyridamole⁹ has generally been performed to detect ischemia. Although these stress imagings are feasible for the

Table 1 Relationship between number of diseased coronary arteries, degree of collateral circulation and redistribution in resting ^{201}Tl delayed images

	Number of diseased coronary arteries			Degree of collateral circulation		
	1-VD	2-VD	3-VD	none	poor	good
Redistribution (+)	18	8	14	14	13	13
Redistribution (−)	6	7	4	4	8	5

1-VD: one vessel disease, 2-VD: two vessel disease, 3-VD: triple vessel disease. Numbers represent the number of patients in each category. There was no significant correlation between redistribution and the number of diseased coronary arteries ($p > 0.2$) or degree of collateral circulation ($p > 0.2$).

detection of latent ischemic myocardium, one may underestimate the viable myocardium according to the studies on the ^{201}Tl scintigraphy performed following revascularization by means of CABG¹⁰ or PTCA.^{2,3,11} Detecting the viable myocardium may be more essential than enhancing the ischemia in patients with an obvious MI history. In the present study, we carried out resting ^{201}Tl myocardial scintigraphy to determine whether this procedure would be useful in reducing the underestimation of viable myocardium. Although resting redistribution has been reported in patients with acute MI¹² or unstable angina,^{13,14} a study of resting delayed imaging is uncommon during the chronic phase of the patients with previous MI. In this study, we observed redistribution in 70.2% of the patients with previous MI and no new episode of chest pain. It is suggested that a careful reading of the resting ^{201}Tl images in combination with the circumferential profile analysis would be useful for detecting the viable myocardium of patients with previous MI.

Since all of our patients were clinically stable and free of chest pain, it is hard to believe their ischemia could have deteriorated during these studies. Most of their redistributions were incomplete and occurred in the peri-infarcted area where blood flow is considered to be low, but adequate for survival. Therefore, this redistributed myocardium may be consistent with the "hibernating myocardium" proposed by Braunwald et al.¹⁵ In fact, following revascularization, some of our patients exhibited an improved ^{201}Tl uptake in these areas as shown in Fig. 4. Rigo et al.¹⁶ stated that the presence of non-jeopardized collaterals contributed to the alleviation of ischemia during exercise. Imamura et al.¹⁷ and Nakatsuka et al.¹⁸ also found that the presence of viable myocardium in peri-infarcted areas, such as those detected by redistribution after exercise, was related to the degree of collaterals. However, the patients were evaluated after exercise in all of these studies. The initial perfusion abnormalities in those areas were caused by the enhanced myocardial ischemia. In our series, resting redistribution was not significantly correlated with either the number of diseased coronary arteries or the development of collaterals or the degree of stenosis in the infarct-related arteries. A different mechanism may contribute to the resting redistribution such as damage to the microcirculation which can not be detected by CAG or a disorder of the thallium extraction,¹⁹ since myocardial blood flow was considered to be stable during resting studies.

A negative washout was observed in 17 of the 40 redistribution-positive patients. This phenomenon was considered to be due to slow wash-in rather than to slow washout, because slow washout cannot ac-

count for this net increase in ^{201}Tl accumulation on delayed images. The negative washout was observed in 73.9% of akinetic segments. It may be therefore related to an extremely slow uptake into the surviving myocytes in the severely damaged myocardium.

We also compared the redistribution of ^{201}Tl on resting images with that observed on the images obtained after exercise. It was demonstrated that resting ^{201}Tl delayed images could detect a larger area of viable myocardium than the images after exercise in 9 of the 10 patients so tested. No patient showed smaller redistribution in resting images than those obtained after exercise. From these observations, we conclude that 3 hours is still insufficient for redistribution after exercise, and that the images obtained after exercise are not suitable for accurately detecting the size of the viable myocardium, even if they are useful in detecting the ischemic myocardium. Comparing the resting initial and the resting delayed images, we found that the area of abnormal perfusion became smaller in the resting delayed image in 7 of the 10 patients. The re-injection method²⁰ has recently been developed. However, the image obtained by this method may perhaps underestimate the viable myocardium, since this image is basically similar to the resting initial images represented as I_R in Table 2.

Recent studies on myocardial perfusion with ^{13}N -ammonia and metabolism with ^{18}F -fluorodeoxyglucose by positron emission tomography (PET) have revealed that metabolic viability was observed in the segments with persistent defect on the ^{201}Tl SPECT images after exercise.^{8,21,22} However, PET is not practical for studying every ischemic patient. Thus, it becomes important to accurately detect the viable myocardium by the commonly used ^{201}Tl

Table 2 Size of abnormally perfused area determined from thallium-201 SPECT images at exercise and rest

Patient	Size of abnormally perfused area	Redistribution at rest
1	$D_R < I_R < D_E < I_E$	+
2	$D_R < I_R < D_E < I_E$	+
3	$D_R < I_R < D_E < I_E$	+
4	$D_R < I_R = D_E < I_E$	+
5	$D_R = I_R < D_E < I_E$	—
6	$D_R < I_R < D_E < I_E$	+
7	$D_R = I_R < D_E < I_E$	—
8	$D_R < I_R = D_E < I_E$	+
9	$D_R < I_R < D_E < I_E$	+
10	$D_R = I_R = D_E < I_E$	—

D_R , I_R , D_E , I_E : Size of perfusion abnormalities (defect, hypoperfusion) in the delayed image at rest, in the initial image at rest, in the delayed image after exercise and in the initial image after exercise, respectively.

scintigraphy. As we have shown, the resting ^{201}Tl initial and delayed myocardial imaging enables one to detect a larger amount of viable myocardium than that obtained after exercise. We conclude that resting initial and delayed ^{201}Tl scintigraphy with both visual and circumferential profile analysis should be performed in patients with previous MI to evaluate myocardial viability.

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