- Galt JR, Garcia EV, Robbins WL. Effects of myocardial wall thickness on SPECT quantification. IEEE Trans Med Imag 1990;9:144-150.
- Kahn JK, Henderson EB, Akers AS, et al. Prediction of reversibility of perfusion defects with a single postexercise technetium-99m RP-30A gated tomographic image: the role of residual systolic thickening [Abstract]. J Am Coll Cardiol 1988;11:31A.
- Kumita S, Kumazaki T. Assessment of left ventricular function with ^{99m}Tc-MIBI gated myocardial SPECT using 3 head rotating gamma camera. *Jpn J Nucl Med* 1994;31:43-52.
- Takeda T, Toyama H, Ishikawa N, et al. Quantitative phase analysis of myocardial wall thickening by technetium-99m 2-methoxy-isobutyl-isonitrile SPECT. Ann Nucl Med 1992;6:69-78.
- Kouris K, Clarke GA, Jarritt PH, Townsend CE, Thomas AN. Physical performance evaluation of the Toshiba GCA-9300A triple-headed system. J Nucl Med 1993;34: 1778-1789.
- Ichihara T, Ogawa K, Motomura N, Kubo A, Hashimoto S. Compton scatter compensation using the triple-energy window method for single- and dual-isotope SPECT. J Nucl Med 1993;34:2216-2221.
- National Electrical Manufacturers Association. NEMA standards publication for performance measurements of scintillation cameras (No. NU1-1980), Washington, DC: NEMA: 1980.
- Garcia EV, Train KV, Maddahi J, et al. Quantification of rotational thallium-201 myocardial tomography. J Nucl Med 1985;26:17-26.
- Klein JL, Garcia EV, DePuey EG, et al. Reversibility bull's-eye: a new polar bull's-eye
 map to quantify reversibility of stress-induced SPECT thallium-201 myocardial
 perfusion defects. J Nucl Med 1990;31:1240-1246.
- Akaike H. A new look at the statistical model identification. IEEE Trans Autom Control 1974;AC19:716-723.
- Lieberman AN, Weiss JL, Jugdutt BI, et al. Two-dimensional echocardiography and infarct size: relationship of regional wall motion and thickening to the extent of myocardial infarction in the dog. Circulation 1981;63:739-746.
- Matsuzaki M, Tanaka N, Toma Y, et al. Effect of changing afterload and inotropic states on inner and outer ventricular wall thickening. Am J Physiol 1992;263:H109– H116.
- Mochizuki T, Murase K, Fujiwara Y, Tanada S, Hamamoto K, Tauxe WN. Assessment of systolic thickening with thallium-201 ECG-gated single-photon emission computed

- tomography: a parameter for local left ventricular function. J Nucl Med 1991;32:1496-1500.
- Weyman AE. Cross-sectional echocardiography Philadelphia: Lea & Febiger; 1982: 493-496.
- Clarke LP, Leong LL, Serafini AN, Tyson IB, Silbiger ML. Quantitative SPECT imaging: influence of object size. Nucl Med Commun 1986;7:363-372.
- Smart SC, Sawada S, Ryan T, et al. Low-dose dobutamine echocardiography detects reversible dysfunction after thrombolytic therapy of acute myocardial infarction. Circulation 1993;88:405-415.
- Kisslo J, von Ramm OT, Thurstone FL. Cardiac imaging using a phased array ultrasound system: II. Clinical technique and application. Circulation 1976;53:262– 267.
- Yamashita K, Tamaki N, Yonekura Y, et al. Quantitative analysis of regional wall motion by gated myocardial positron emission tomography: validation and comparison with left ventriculography. J Nucl Med 1989;30:1775-1786.
- Williams KA, Sheridan CM. Regional thickening on gated tomographic polar map Fourier amplitude images as an index of reversible ischemia in severe stress Tc-99m-sestamibi perfusion defects: comparison with resting thallium images [Abstract]. J Nucl Med 1996;37:105P.
- Gradel C, Staib LH, Heller EN, et al. Limitations of ECG-gated SPECT for assessment of regional thickening: experimental comparison with ECG-gated MRI [Abstract].
 J Am Coll Cardiol 1996:27:241A.
- Bartlett ML, Buvat I, Vaquero JJ, Mok D, Dilsizian V, Bacharach SL. Measurement of myocardial wall thickening from PET/SPECT images: comparison of two methods. J Comput Assist Tomogr 1996;20:473-481.
- Bacharach SL, Bartlett M, Vaquero JJ, Mok DY, Dilsizian V. Myocardial thickness by gated PET and SPECT: variability and bias [Abstract]. J Nucl Med 1993;34(suppl):
- Cooke CD, Garcia EV, Folks RD, Ziffer JA. Myocardial thickening and phase analysis from ^{99m}Tc-sestamibi multiple-gated SPECT: development of normal limits [Abstract]. J Nucl Med 1992;33:926.
- Cooke CD, Garcia EV, Cullom SJ, Faber TL, Pettigrew RI. Determining the accuracy
 of calculating systolic wall thickening using a fast Fourier transform approximation: a
 simulation study based on canine and patient data. J Nucl Med 1994;35:1185-1192.

Significance of Late Redistribution Thallium-201 Imaging after Rest Injection for Detection of Viable Myocardium

Ichiro Matsunari, Susumu Fujino, Junichi Taki, Junji Senma, Takahiko Aoyama, Takanobu Wakasugi, Jun-ichi Hirai, Takashi Saga, Shinichiro Yamamoto and Norihisa Tonami

Departments of Radiology, Cardiology and Cardiovascular Surgery, Fukui Prefectural Hospital, Fukui, Japan; and Department of Nuclear Medicine, Kanazawa University School of Medicine, Kanazawa, Japan

The aim of this study was to determine whether late redistribution imaging after rest injection of ²⁰¹Tl would provide further information on myocardial viability over conventional rest-early redistribution ²⁰¹Tl imaging. **Methods:** Twenty-nine patients with coronary artery disease and left ventricular dysfunction underwent rest, early (3-4 hr) and late (20-24 hr) redistribution 201Tl and gated blood pool studies. In 14 patients with successful revascularization, gated blood pool study was repeated after the coronary intervention. Results: Nine of 29 patients showed early redistribution, and six additional patients showed further redistribution on the late images. Of 136 segments with initial 201Tl defects, 18 showed early redistribution, and 10 showed late redistribution. When a threshold of 60% of peak activity was used as an index of myocardial viability, only a small fraction (3%) of the initial 201TI defects were additionally considered viable by the late images. In 14 patients who underwent revascularization, the positive (69%) and negative (87%) predictive values of the early redistribution images for functional recovery were similar to those obtained by the late images (68% and 86%, respectively). Conclusion: Although late redistribution after rest

For correspondence or reprints contact: Ichiro Matsunari, MD, Department of Nuclear Medicine, Kanazawa University School of Medicine, 13-1 Takara-machi, Kanazawa, 920 Japan.

injection of ²⁰¹Tl occasionally occurs, most of the clinically relevant information on myocardial viability may be obtained by conventional rest-early redistribution ²⁰¹Tl imaging when the defect severity is considered an index of tissue viability.

Key Words: thallium-201; late redistribution; myocardial viability

J Nucl Med 1997; 38:1073-1078

Detection of viable myocardium is an important issue in patients with coronary artery disease (CAD) and left ventricular (LV) dysfunction, in whom coronary revascularization is under consideration (1,2). Viable myocardial areas are most likely to benefit from revascularization, whereas revascularization of scarred myocardium will not lead to improvement of LV contractile function. It has been shown that 3- to 4-hr delayed imaging after stress injection of 201 Tl frequently underestimates the presence of viable myocardium within persistent defects, as evidenced by improved myocardial perfusion after revascularization (3) or by metabolic imaging with [18 F]fluorodeoxyglucose and PET (4,5). Modified 201 Tl protocols, such as late redistribution imaging after stress injection (6-8) and reinjection (9-12), have been shown to enhance the detection of viable myocardium.

Received Jul. 8, 1996; revision accepted Nov. 23, 1996.

Rest/redistribution ²⁰¹Tl imaging is another established non-invasive diagnostic protocol for the detection of such viable, but compromised, myocardium (13,14). Initial distribution of ²⁰¹Tl is considered to reflect myocardial blood flow at rest, whereas redistribution ²⁰¹Tl imaging is considered to reflect myocardial viability rather than mere perfusion. Although preliminary results suggest that late (18- to 72-hr) redistribution after rest injection of ²⁰¹Tl may occur (15), the potential benefit of the resting late redistribution protocol, as compared to conventional rest-early (3- to 4-hr) redistribution protocol, has not yet been fully elucidated.

This study was therefore conducted to determine whether late redistribution imaging after rest injection of ²⁰¹Tl would provide further information on myocardial viability over conventional rest-early redistribution ²⁰¹Tl imaging.

MATERIALS AND METHODS

Patients

This study consisted of 29 patients with CAD and global or regional LV dysfunction. Only patients who had ²⁰¹Tl defects in at least one myocardial segment on initial resting ²⁰¹Tl images were considered eligible for the study. The patients ranged in age from 47 to 82 yr (mean, 67 yr); there were 20 men and 9 women. Twenty-four (83%) patients had a history of previous myocardial infarction (10 anterior wall infarctions, 13 inferior wall infarctions and 1 anterior and inferior infarction). The mean LV ejection fraction (LVEF) by radionuclide angiography was 39 \pm 10%. We studied only patients with stable CAD; patients with unstable angina or recent myocardial infarction (<4 wk before investigation) were excluded. Four patients had undergone previous percutaneous transluminal coronary angioplasty (PTCA), and another patient had a history of coronary artery bypass grafting surgery (CABG). All cardiac medications were continued during the study without interruption. All subjects signed an informed consent form based on the guidelines of the hospital's human clinical study committee before participating in the study.

Coronary Arteriography

Coronary arteriography was performed using standard percutaneous techniques and was performed during the same hospital stay period of the radionuclide studies. Coronary stenosis was visually assessed from multiple projections by at least three experienced observers and scored using the following system: 0, 0%–25%; 1, 25%–50%; 2, 50%–75%; 3, 75%–90%; 4, 90%–99%; and 5, 100%. A computer-aided quantitative analysis was performed in case of disagreements in interpretation. When a significant coronary artery stenosis was defined as >50% reduction in the luminal diameter, 15 patients had significant stenosis of all three vessels, 6 had stenosis of two vessels and 8 had stenosis of one vessel (mean, 2.2 vessels per patient).

Rest-Redistribution Thallium-201 Imaging

All patients underwent initial rest and early and late redistribution ²⁰¹Tl SPECT imaging. After an overnight fast, patients were injected with 111 MBq (3 mCi) of ²⁰¹Tl at rest, and SPECT images were obtained 5-10 min (initial), 3-4 hr (early redistribution) and 20-24 hr (late redistribution) after injection.

Imaging was performed using a three-head SPECT system with low-energy, high-resolution parallel hole collimators. The detector system was interfaced to a dedicated nuclear medicine computer. A total of 60 projection images were obtained over 360° in 6° increments, with 30 sec per view for rest ²⁰¹Tl SPECT and 40 sec per view for early and late redistribution ²⁰¹Tl SPECT. The energy discriminator was centered on 70 keV with a 20% window. The

data were recorded in 128×128 matrices on the magnetic disk. To reconstruct transaxial tomographic images from each of the acquisition data, Butterworth and Ramp filters were used. The parameter of the Butterworth filter was order 8, and the cutoff frequency was 0.15 cycles/pixel. Short-axis slices, 3.2-mm-thick, were also generated. Then, four serial short-axis slices were added, resulting in a thickness of 12.8 mm. For further analysis, all the image data were transferred to a Macintosh-based image analysis system via ethernet (16).

Data Analysis

SPECT data analysis was performed on the basis of three short-axis tomograms representing an apical, distal and basal left ventricle chosen for each patient. After confirmation of image registration, circumferential analysis was performed on an operator-defined region of interest drawn around the LV activity of each tomogram. The center of each tomogram was determined, and the region of interest was automatically subdivided into 128 sectors. The maximum pixel activities within each sector for the rest and early and late redistribution ²⁰¹Tl images were normalized to the peak activity, which was assigned as 100%. The activity in all other myocardial regions was expressed as a percent of this maximum. The sectors from distal and basal slices were then grouped into four myocardial segments, corresponding to the septal, anterior, inferior and lateral walls, and segmental activity was defined as the average of the individual sector activities within that segment. The apical myocardial activity was determined from the first apical tomogram; the distal septal, anterior, inferior and lateral myocardial activities were determined from the distal LV tomogram, and the basal anterior, inferior and lateral myocardial activities were determined from the basal LV tomogram. Thus, a total of 261 segments from 29 patients (9 segments per patient) were analyzed. For comparison with coronary angiography, apical, anterior and septal regions were considered to be supplied by the left anterior descending artery, the lateral regions by the left circumflex artery and the inferior regions by the right coronary artery (17).

On the basis of this nine-segment model, each segment on the initial resting image was visually determined to be normal or abnormal by two experienced observers. An abnormal segment required to have a regional activity of less than 75% of peak activity. Disagreement in interpretation was resolved by consensus. Abnormal segments by visual analysis were further subgrouped on the basis of changes in regional activity on the subsequent early redistribution images. An abnormal segment was considered to be reversible if the regional activity increased by $\geq 10\%$ from initial to early redistribution image, whereas a segment was considered to be irreversible if the change in regional activity was <10%. The segments with irreversible 201 Tl defects on the early redistribution images were further subgrouped according to the presence or absence of late redistribution, which was defined as a $\geq 10\%$ increase in activity from the initial to the late redistribution image.

On the basis of reduction in regional 201 Tl activity on the early or late redistribution images, a segment was considered viable if the assigned regional activity was more than 60% of peak activity. Conversely, a segment with severe reduction in regional activity ($\leq 60\%$ of peak) was considered nonviable. The use of 60% of peak activity as the threshold for viability determination was based on the value derived for rest-redistribution 201 Tl SPECT reported by Udelson et al. (18). In this study, viable myocardium within dysfunctional area was defined as that which is potentially reversible in contractile function after revascularization. Therefore, such chronically dysfunctional but viable myocardium may represent hibernation (1), intermittent stunning (19) or both.

Radionuclide Angiography

Analysis of the regional wall motion was performed within 1 mo (mean, 3 wk) of revascularization in all patients and repeated at a mean of 8 wk (range, 4-19 wk) after revascularization in patients with successful revascularization. Each patient underwent electrocardiographic gated blood pool scintigraphy to assess global and regional LV wall motion at rest using red blood cells labeled in vivo with 740 MBq of ^{99m}Tc. Images were acquired in anterior, left anterior oblique and lateral views. LVEF was calculated by computer analysis of the scintigraphic data, and regional wall motion was assessed visually by two experienced observers who were unaware of clinical and myocardial SPECT data from the images displayed in cine format. The apical and anterior walls were assessed from the anterior view; septal and lateral were assessed from the left anterior oblique view; and inferior and posterior walls were assessed from the left lateral view. The regional wall motion was graded on a semiquantitative five-point scoring system as follows: grade 4, normal; grade 3, mild hypokinesis; grade 2, severe hypokinesis; grade 1, akinesis; and grade 0, dyskinesis. Disagreements in interpretation were resolved by consensus. A region was considered to have improved wall motion if the assigned abnormal wall motion (defined by a score ≤3) normalized or increased by ≥1 in wall motion score after revascularization. In the patients who underwent CABG, the septal segment was excluded from the final calculation of predictive accuracies for functional recovery because of frequent paradoxical motion after surgery (20,21).

Statistical Analysis

Data are reported as mean \pm s.d. Comparisons of mean values were performed using one-way ANOVA, followed by a Bonferroni Student's t-test when the ANOVA demonstrated a statistically significant result. Comparison of proportions or predictive accuracies was performed with chi-square test or Fisher's exact test where appropriate. Statistical significance was defined as p < 0.05.

RESULTS

Thallium-201 Findings

All patients showed late redistribution ²⁰¹Tl images of acceptable quality, and no patients were excluded from analysis because of poor image quality. On a patient-by-patient basis, nine of 29 patients (31%) showed reversible defects on the early redistribution images, and six additional patients (21%) showed further redistribution on the late redistribution images. A representative case with late redistribution is shown in Figure 1.

Of a total of 261 myocardial segments in 29 patients, 125 segments were considered normal on the initial images by visual analysis. The remaining 136 segments were considered to have perfusion defects on the initial resting images. Of these, 18 were considered to be reversible on the early redistribution images, and 10 additional segments were considered to be reversible on the late redistribution images.

Relation to Stenosis Severity and Regional Wall Motion

As shown in Table 1, there were no significant differences in the mean stenosis severity scores between the segments with early and late redistribution. The coronary occlusion rates (with collaterals) for the normal, early redistribution, late redistribution and fixed defect groups were 12 (10)%, 0%, 10 (10)% and 17 (11)%, respectively (ns). The mean regional wall motion score in the segments with late redistribution was lower than that of normal segments, but it was not significantly different from that in the segments with early redistribution or in the segments with fixed defects.

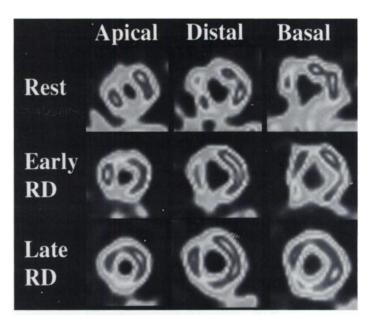


FIGURE 1. Short-axis tomograms from a patient with three-vessel CAD. Rest ²⁰¹Tl images show partially reversible anterior and minimally reversible inferior defects that further redistribute on late (20- to 24-hr) images.

Comparison between Early and Late Redistribution Images by Quantitative Analysis

When the segments with regional activity >60% of peak were considered viable, 14 of the 18 segments (78%) with early redistribution were considered viable by the early redistribution images, whereas the remaining 4 segments had regional activity $\le 60\%$ of peak activity and hence considered nonviable. None of these 4 segments had further redistribution on the late redistribution images and were thus, again, considered nonviable by the late redistribution images. Of 10 segments with late redistribution, 5 were considered viable by the early redistribution images, and 3 had regional activity $\le 60\%$ on the both early and late redistribution images and hence were considered nonviable. The remaining two segments were considered viable only on the late redistribution images.

When the 136 segments with initial 201 Tl defects were analyzed, the majority (n = 80, 59%) were considered viable on the basis of defect severity on the early redistribution images, whereas the remaining 56 segments were considered nonviable. Of the 56 nonviable segments on the early redistribution images, 52 segments were again considered nonviable by the late redistribution images; only 4 segments (3%) were additionally considered viable by the late images. These four segments consisted of two segments with late redistribution and two other

TABLE 1
Stenosis Severity and Wall Motion Scores in Relation to Thallium-201 Findings

	Stenosis severity score	Wall motion score
Normal (n = 125)	2.29 ± 1.69	3.28 ± 0.89
Early RD (n = 18)	2.94 ± 1.26	2.67 ± 1.14
Late RD (n = 10)	2.70 ± 1.06	2.00 ± 1.33
Fixed (n = 108)	2.83 ± 1.50	2.28 ± 1.12*
p value (ANOVA)	0.091	< 0.01

Values are expressed as mean \pm s.d. Normal = normal 201 Tl uptake; Early RD = reversible 201 Tl defect on early redistribution image; Late RD = reversible 201 Tl defect on late redistribution image; Fixed = fixed 201 Tl defect on early and late redistribution image; n = number of segments.

^{*}p < 0.01 vs. normal.

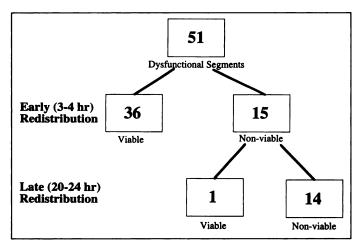


FIGURE 2. Flow diagram showing concordance and discordance between early (3- to 4-hr) redistribution and late (20- to 24-hr) redistribution images in the segments with impaired baseline contractile function in 14 patients who underwent revascularization. A segment was considered viable if the assigned regional activity was >60% of peak.

segments with <10% increase in activity but with regional activity >60% of peak on the final images.

Impact of Late Redistribution Imaging on Clinical Decision-Making

When the presence of at least one dysfunctional but viable segment was considered an indication of revascularization for that vascular territory, three of the four segments that were considered viable by only the late images were accompanied by such viable segments in the same vascular territory on the early redistribution image and hence would be considered indicative for revascularization. Thus, only one of 29 patients (3%) would be additionally considered indicative for revascularization by the late redistribution images.

Effect of Revascularization on Regional Wall Motion

Coronary revascularization was performed in 17 of the 29 patients. During coronary intervention, an attempt was made to revascularize all stenosed arteries, depending on coronary anatomy. Three patients were excluded from further analysis (1 restenosis after PTCA, and 2 did not return for the follow-up study), and 14 were considered to have successful coronary revascularization (12 had CABG and 2 PTCA), which was confirmed by the follow-up coronary arteriography performed 1–3 mo after the intervention. There were nine men and five women, with a mean age of 67 ± 8 yr. Ten (71%) patients had a history of previous myocardial infarction. Significant coronary artery stenosis was present in a mean of 2.4 ± 0.7 vessels per patient. The mean LVEF for this patient group was $41 \pm 8\%$.

Of a total of 63 asynergic segments in these patients, 51 were considered to be successfully revascularized by the follow-up coronary angiography. Of these, 27 segments (53%) showed an improvement in function after revascularization, whereas the remaining 24 segments did not improve.

Prediction of Functional Recovery by Thallium-201 Imaging

When 51 segments with regional dysfunction at baseline from 14 patients who underwent revascularization were analyzed, there were highly concordant results on viability between the early and late redistribution images, with only one segment considered viable by the late image alone (Fig. 2). Of 36 segments that were considered viable by the early redistribution images, 25 had functional recovery after revascularization

(positive predictive value, 69%). Of 15 segments that were considered nonviable by the early redistribution images, 13 did not recover in function (negative predictive value, 87%).

Of the 51 revascularized segments, there were 4 segments with early redistribution and 3 with late redistribution. All 4 segments with early redistribution had regional activity of >60% on the early images and showed functional recovery after revascularization. Of three segments with late redistribution, one with regional activity of >60% on the early redistribution image showed functional recovery; one with regional activity of >60% even on the late image had no functional improvement; and the remaining segment had regional activity of >60% on the late image, but functional recovery did not occur. Finally, positive and negative predictive values for functional recovery on the late redistribution images were 68% and 86%, respectively (both were not significant versus the early redistribution images).

There were 19 dysfunctional septal segments in patients who underwent CABG. Based on the early redistribution ²⁰¹Tl images, 13 of the 19 segments were considered viable by the early redistribution images, and the remaining 6 were considered nonviable. Of the 13 scintigraphically viable segments, only 5 (36%) showed regional functional recovery after revascularization, whereas five of six scintigraphically nonviable segments showed no functional improvement. Thus, as expected, these septal segments had a low positive predictive accuracy for functional recovery.

DISCUSSION

The major findings of this study were that late redistribution of ²⁰¹Tl after rest injection was occasionally noted in patients with CAD and LV dysfunction; when a threshold cutoff of 60% of peak was used as an index of tissue viability, only a small fraction of the segments (3%) with initial ²⁰¹Tl defect were additionally considered viable by the late redistribution images; and the use of late redistribution ²⁰¹Tl images did not significantly improve the prediction of functional recovery after revascularization.

Late Redistribution of Rest-Injected Thallium-201

Late redistribution imaging has been used primarily after stress scintigraphy to identify redistribution that was not evident 3-4 hr after injection (6-8,22,23). Several studies have demonstrated the use of late redistribution ²⁰¹Tl imaging after stress injection in assessing myocardial viability (7,8,22). Late imaging, however, is inconvenient for patients as well as for busy laboratories because of next-day imaging. Furthermore, it may potentially yield poor image quality (24), although the image quality appeared acceptable in the current study, as presented in Figure 1, partially because of the use of a multidetector camera system and longer imaging time, which is consistent with the previous results (8).

In this study, where ²⁰¹Tl was injected during resting conditions, we observed that 31% of the patients and 13% of the segments with initial ²⁰¹Tl defects showed redistribution on the early (3–4 hr) redistribution images. In addition, 21% of the patients and 8% of the segments with fixed ²⁰¹Tl defects on the early redistribution images showed further redistribution on the late (20- to 24-hr) redistribution images, suggesting that late redistribution after rest injection of ²⁰¹Tl occasionally occurs. This is consistent with a previous report published in an abstract form that assessed the frequency of late (18- to 72-hr) redistribution after rest injection of ²⁰¹Tl (15), although the prevalence of redistribution in our study appears to be slightly lower, possibly because of differences in patient population and methodology.

In the study of Dilsizian et al. (25), on the other hand, where 24-hr delayed imaging was performed after reinjection of ²⁰¹Tl, only 1 of 30 segments (3%) with irreversible defects immediately after reinjection showed further redistribution on the late imaging. Because the reinjection ²⁰¹Tl image is a composite of resting perfusion on a redistribution image and therefore differs from resting ²⁰¹Tl image, it is difficult to directly compare their data to our findings. The mechanisms of late redistribution of ²⁰¹Tl after rest injection may be explained by a similar manner as proposed for stress study, i.e., ²⁰¹Tl may be unavailable for additional uptake at 3-4 hr because of low blood ²⁰¹Tl concentration in the area of hypoperfusion, and a very slow process of redistribution may result in late redistribution.

In this study, neither the severity of coronary artery stenosis nor rate of coronary occlusion in the segments with late redistribution was significantly different from that in the area of early redistribution. Gutman et al. (6) and Kiat et al. (7), on the other hand, reported that stenosis in the areas of late redistribution after stress injection was more severe than in the areas with early redistribution. Although the exact mechanisms accounting for the discordant results are uncertain, there are several potential mechanisms that could have contributed to our results. First, the stenosis severity is not necessarily a good determinant of resting myocardial blood flow as demonstrated by PET (26), and thus, myocardial blood flow at rest may be regulated by more complex factors than mere stenosis severity of epicardial coronary arteries. Second, because the majority of our patient population had multivessel CAD and redistribution is defined as differential washout of the tracer relative to remote regions, the occurrence of late redistribution could have been influenced by remote areas supplied by stenosed arteries, as suggested by Gutman et al. (6). Finally, they performed serial ²⁰¹Tl imaging after stress injection, whereas ²⁰¹Tl was injected at rest in the current study; this methodological difference in hemodynamic conditions also could have contributed to the discordant results.

Value of Quantification for Assessment of Myocardial Viability

It has been demonstrated that a fixed defect on rest-redistribution ²⁰¹Tl imaging does not necessarily indicate nonviable myocardium and that a major part of mild-to-moderate ²⁰¹Tl defects are considered viable, as evidenced by functional recovery after revascularization (14,18,27) or the preserved metabolic activity with PET and [¹⁸F]fluorodeoxyglucose (28). This is especially true in rest-redistribution ²⁰¹Tl imaging as compared with stress ²⁰¹Tl imaging because irreversible mild-to-moderate defects are a more common finding than reversible resting defects. The concept that tracer content represents myocardial viability has been well documented by several studies (14,18,27).

Chronically dysfunctional but viable myocardium may represent hibernation (1), intermittent stunning (19) or both. Hibernating myocardium represents impaired contractile function coupled with hypoperfusion that would recover after revascularization. Stunning, on the other hand, represents impaired contractile function that persists after an ischemic episode despite restoration of blood flow. The differentiation of these situations is complicated because they may often coexist in the clinical setting. The advantage of quantitative analysis is that the amount of ²⁰¹Tl uptake on the redistribution image may represent the extent and amount of viable myocardium regardless of underlying pathophysiology.

The use of 60% of peak as a threshold cutoff for viability in this study is based on the value proposed for rest-redistribution

²⁰¹Tl SPECT to predict functional recovery after revascularization (18). Our data confirms their findings, resulting in reasonable predictive accuracies for functional recovery observed in this study. Using this quantitative approach, the majority of irreversible ²⁰¹Tl defects were identified as viable in this study, which is in agreement with the published data (28). Furthermore, by this quantitative approach, only a small fraction of the segments were additionally considered viable by the late redistribution images. Finally, only one of 29 patients (3%) would have been additionally indicated for revascularization by the late redistribution images, suggesting that most of the clinically relevant information on myocardial viability may be obtained by conventional rest-early redistribution protocol when defect severity is considered as an index of viability. This is supported by the functional outcome data that the early and late redistribution images had quite similar predictive accuracies for functional recovery after revascularization.

There are several potential explanations to our results that, unlike the published stress studies (6-8,22), the late imaging after 201 Tl injection at rest did not significantly improve the detection of viable myocardium. First, the prevalence of late redistribution is apparently lower than those reported for stress 201 Tl imaging (6-8,22). Second, a considerable number of the segments with late redistribution are considered viable by the early redistribution imaging based on defect severity. Finally, a reversible but still severe resting 201 Tl defect ($\leq 60\%$ of peak) may not improve in function if the amount of viable myocardium is not sufficient to show functional recovery of that region.

Value of Initial Resting Thallium-201 Imaging

Based on the results of this study and others (14,18,27), one might argue that initial resting ²⁰¹Tl imaging may not be necessary for clinical decision-making regarding revascularization. If the question being asked is whether or not a dysfunctional region would recover after revascularization, either early or late redistribution ²⁰¹Tl imaging without initial resting imaging may be used. A recent study, however, has demonstrated that the medically treated CAD patients with ²⁰¹Tl redistribution at rest have a higher death rate than those without redistribution (29), suggesting that the presence or absence of redistribution at rest may have an important prognostic value. This information would be lost if the initial imaging is skipped. Therefore, both the initial and redistribution ²⁰¹Tl images may be important for the patient management and for the clinical decision-making.

Study Limitations

There are several limitations of the study. First, we assessed regional wall motion by planar gated blood pool imaging to correlate with SPECT data. Because planar imaging provides only two-dimensional information, correlation with three-dimensional data such as SPECT is not ideal. Therefore, some misalignments may not be completely excluded, although care was taken for image registration between the two techniques.

Second, quantitative coronary angiographic data was not available in every patient, and visual interpretation of the coronary angiograms was mainly used to assess the severity of stenosis, as in other recent studies (17,30). Although quantitative angiography may result in more reproducible measurements, accurate assessment of the angiographic severity of coronary artery stenosis is still difficult in terms of the functional severity of CAD. The visual assessment of coronary angiograms by experienced observers is currently widely used in most laboratories.

Third, because the number of patients with functional out-

come data was limited, as is common in such viability studies, and only one segment was additionally considered viable by the late image in our patient subpopulation, the conclusive statements with respect to the outcome of such myocardium is not possible from the current data. Further clarification may be needed of this particular situation. Nevertheless, this reflects the high agreement on viability between the early and late redistribution images, and therefore, it is unlikely that our conclusion could have been significantly affected by this limitation.

Finally, we arbitrarily assumed that a vascular territory would be eligible for revascularization if there is at least one dysfunctional but viable segment in that vascular territory in the current study. We are aware that the mere presence of a small amount of viable myocardium is not clinically relevant. At this time, however, it is difficult to determine how many segments are required to justify the subsequent revascularization. Further prospective studies are required to address this issue.

Clinical Implications

Rest-redistribution ²⁰¹Tl imaging is a well-established diagnostic protocol for assessing myocardial viability. Although many laboratories currently use early (3- to 4-hr) redistribution imaging to determine the extent and amount of viable myocardium, the optimal timing for redistribution imaging has not yet been determined. Having provided that early (3- to 4-hr) redistribution ²⁰¹Tl imaging after rest injection provides comparable information on myocardial viability to late (20- to 24-hr) redistribution imaging, the early redistribution imaging protocol is time-saving for both the patients and the laboratory and may reduce the cost for the next-day imaging. The results of this study indicate that most of the clinically relevant information may be obtained by conventional rest-early redistribution imaging when defect severity is considered as an index of tissue viability, providing the confirmatory data to the use of the early redistribution ²⁰¹Tl imaging for assessing viability.

REFERENCES

- 1. Rahimtoola SH. The hibernating myocardium. Am Heart J 1989;117:211-221.
- Dilsizian V, Bonow RO. Current diagnostic techniques of assessing myocardial viability in patients with hibernating and stunned myocardium. Circulation 1993;87: 1-20
- Liu P, Kiess MC, Okada RD, et al. The persistent defect on exercise thallium imaging and its fate after myocardial revascularization: does it represent scar or ischemia? Am Heart J 1985;110:996-1001.
- Brunken R, Schwaiger M, Grover-McKay M, Phelps ME, Tillisch J, Schelbert HR. Positron emission tomography detects tissue metabolic activity in myocardial segments with persistent thallium perfusion defects. J Am Coll Cardiol 1987;10:557-567.
- Tamaki N, Yonekura Y, Yamashita K, et al. Relation of left ventricular perfusion and wall motion with metabolic activity in persistent defects on thallium-201 tomography in healed myocardial infarction. Am J Cardiol 1988;62:202-208.
- Gutman J, Berman DS, Freeman M, et al. Time to completed redistribution of thallium-201 in exercise myocardial scintigraphy: relationship to the degree of coronary artery stenosis. Am Heart J 1983;106:989-995.
- Kiat H, Berman DS, Maddahi J, et al. Late reversibility of tomographic myocardial thallium-201 defects: an accurate marker of myocardial viability. J Am Coll Cardiol 1988;12:1456-1463.

- Taki J, Nakajima K, Bunko H, Kawasuji M, Tonami N, Hisada K. Twenty-four-hour quantitative thallium imaging for predicting beneficial revascularization. Eur J Nucl Med 1994;21:1212-1217.
- Dilsizian V, Rocco TP, Freedman NMT, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stressredistribution imaging. N Engl J Med 1990;323:141-146.
- Ohtani H, Tamaki N, Yonekura Y, et al. Value of thallium-201 reinjection after delayed SPECT imaging for predicting reversible ischemia after coronary artery bypass grafting. Am J Cardiol 1990;66:394-399.
- Tamaki N, Ohtani H, Yonekura Y, et al. Significance of fill-in after thallium-201 reinjection following delayed imaging: comparison with regional wall motion and angiographic findings. J Nucl Med 1990;31:1617-1623.
- Rocco TP, Dilsizian V, McKusick KA, Fischman AJ, Boucher CA, Strauss HW. Comparison of thallium redistribution with rest "reinjection" imaging for the detection of viable myocardium. Am J Cardiol 1990;66:158-163.
- Mori T, Minamiji K, Kurogane H, Ogawa K, Yoshida Y. Rest-injected thallium-201 imaging for assessing viability of severe asynergic regions. J Nucl Med 1991;32:1718– 1724
- 14. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution 201Tl imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. Circulation 1993;87:1630-1641.
- Takemoto KA, Kiat H, Friedman J, et al. The frequency of late redistribution in rest thallium-201 scintigraphic studies [Abstract]. Circulation 1991;84(suppl):II-88.
- Matsunari I, Tanishima Y, Taki J, et al. Early and delayed technetium-99m-tetrofosmin myocardial SPECT compared in normal volunteers. J Nucl Med 1996;37:1622-1626.
- Matsunari I, Fujino S, Taki J, et al. Impaired fatty acid uptake in ischemic but viable myocardium identified by thallium-201 reinjection. Am Heart J 1996;131:458-465.
- Udelson JE, Coleman PS, Metherall J, et al. Predicting recovery of severe regional ventricular dysfunction. Comparison of resting scintigraphy with ²⁰¹Tl and ^{99m}Tcsestamibi Circulation 1994;89:2552-2561.
- Vanoverschelde JLJ, Wijns W, Depre C, et al. Mechanisms of chronic regional postischemic dysfunction in humans. New insights from the study of noninfarcted collateral-dependent myocardium. Circulation 1993;87:1513–1523.
- vom-Dahl J, Eitzman DT, Al-Aouar ZR, et al. Relation of regional function, perfusion
 and metabolism in patients with advanced coronary artery disease undergoing surgical
 revascularization. Circulation 1994;90:2356-2366.
- Tamaki N, Kawamoto M, Tadamura E, et al. Prediction of reversible ischemia after revascularization. Perfusion and metabolic studies with positron emission tomography. Circulation 1995;91:1697-1705.
- Cloninger KG, DePuey EG, Garcia EV, et al. Incomplete redistribution in delayed thallium-201 single photon emission computed tomographic images: an overestimation of myocardial scarring. J Am Coll Cardiol 1988;12:955-963.
- Yang LD, Berman DS, Kiat H, et al. The frequency of late reversibility in SPECT thallium-201 stress-redistribution studies. J Am Coll Cardiol 1990;15:334-340.
- Kayden DS, Sigal S, Soufer R, Mattera J, Zaret BL, Wackers FJT. Thallium-201 for assessment of myocardial viability: quantitative comparison of 24-hr redistribution imaging with imaging after reinjection at rest. J Am Coll Cardiol 1991;18:1480-1486.
- Dilsizian V, Smeltzer WR, Freedman NMT, Dextras R, Bonow RO. Thallium reinjection after stress-redistribution imaging. Does 24-hr delayed imaging after reinjection enhance detection of viable myocardium? Circulation 1991;83:1247-1255.
- Severi S, Underwood R, Mohiaddin RH, Boyd H, Paterni M, Camici PG. Dobutamine stress: effects on regional blood flow and wall motion. J Am Coll Cardiol 1995;26: 1187–1195.
- Marzullo P, Parodi O, Reisenhofer B, et al. Value of rest thallium-201/technetium-99m sestamibi scans and dobutamine echocardiography for detecting myocardial viability. Am J Cardiol 1993;71:166-172.
- Dilsizian V, Perrone-Filardi P, Arrighi JA, et al. Concordance and discordance between stress-redistribution-reinjection and rest-redistribution thallium imaging for assessing viable myocardium. Comparison with metabolic activity by positron emission tomography. Circulation 1993;88:941-952.
- Gioia G, Milan E, Giubbini R, DePace N, Heo J, Iskandrian AS. Prognostic value of tomographic rest-redistribution thallium-201 imaging in medically treated patients with coronary artery disease and left ventricular dysfunction. J Nucl Cardiol 1996;3: 150-156.
- Nicolai E, Cuocolo A, Pace L, et al. Adenosine coronary vasodilation quantitative technetium-99m-methoxy isobutyl isonitrile myocardial tomography in the detection and localization of coronary artery disease. J Nucl Cardiol 1996;3:9-17.