Myocardial Viability Assessment with Technetium-99m-Tetrofosmin and Thallium-201 Reinjection in Coronary Artery Disease

Ichiro Matsunari, Susumu Fujino, Junichi Taki, Junji Senma, Takahiko Aoyama, Takanobu Wakasugi, Jun-ichi Hirai, Takashi Saga, Kenji Ichiyanagi and Kinichi Hisada

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

Exercise-rest ^{99m}Tc-tetrofosmin myocardial perfusion images with a 2-day protocol was compared to exercise-redistribution-reinjection ^{201}Tl images to assess the ability of ^{99m}Tc-tetrofosmin to detect viable myocardium. **Methods:** We studied 25 patients with coronary artery disease and regional or global left ventricular dysfunction. Myocardial SPECT images with ^{99m}Tc-tetrofosmin were obtained 10 min after injection during exercise and 1 and 3 hr after rest injection. Within 1 wk of the ^{99m}Tc-tetrofosmin study, exercise-redistribution-reinjection ^{201}Tl SPECT imaging was performed. **Results:** Visual analysis demonstrated concordance between ^{201}Tl and ^{99m}Tc-tetrofosmin imaging for defect reversibility in 126 of 209 segments (60%), with initial defects on both exercise ^{201}Tl and ^{99m}Tc-tetrofosmin images. In the remaining discordant 83 segments (40%), 73 (88%) appeared nonreversible on ^{99m}Tc-tetrofosmin imaging but were reversible on ^{201}Tl imaging. **Conclusion:** On the basis of defect reversibility by visual analysis, exercise-rest ^{99m}Tc-tetrofosmin imaging underestimates myocardial viability compared to ^{201}Tl reinjection imaging. The identification of viable myocardium with both ^{99m}Tc-tetrofosmin and ^{201}Tl can be greatly enhanced to a similar degree if the severity of reduction in activity within nonreversible defects is considered. These two agents may provide comparable information about myocardial viability by quantitative analysis of defect severity.

Key Words: technetium-99m-tetrofosmin; thallium-201; myocardial viability; coronary artery disease

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In patients with coronary artery disease (CAD), the extent of myocardial viability is an important issue in deciding to proceed with revascularization. Exercise-redistribution ^{201}Tl imaging has been used to assess myocardial viability for over a decade (*1,2*). It also has been shown, however, that exercise-redistribution ^{201}Tl imaging frequently underestimates myocardial viability because of the lack of ^{201}Tl redistribution in severely ischemic but viable myocardium, as assessed by improved function or perfusion after revascularization (*1,2*) or by metabolic imaging with PET (*3*) as the gold standard. To overcome this limitation, efforts have been made using late redistribution (*4*) or the reinjection imaging technique (*5,6*). Recent studies have shown that ^{201}Tl reinjection after exercise-redistribution imaging may provide relevant information about myocardial viability, which is similar to that obtained by PET imaging (*7–9*).

Technetium-99m-tetrofosmin is a new myocardial perfusion imaging agent that is used as an alternative to conventional ^{201}Tl imaging (*10–13*). Tetrofosmin has a high diagnostic accuracy comparable to thallium for detecting CAD (*14–16*). Because of the higher physical energy of ^{99m}Tc compared to ^{201}Tl, it is likely that ^{99m}Tc-tetrofosmin could provide myocardial images of better quality with less soft-tissue attenuation than ^{201}Tl (*17*). Previous studies of exercise-rest ^{99m}Tc-tetrofosmin imaging have shown defect reversibility similar to that demonstrated by exercise-redistribution ^{201}Tl imaging (*14–16*). The ability of ^{99m}Tc-tetrofosmin to identify viable myocardium, however, has not yet been established. Furthermore, recent studies on myocardial viability assessment with ^{99m}Tc-sestamibi, which is considered to have similar characteristics to ^{99m}Tc-tetrofosmin, have demonstrated that ^{99m}Tc-sestamibi underestimates reversibility compared to thallium with reinjection (*18,19*).

This study directly compares ^{99m}Tc-tetrofosmin imaging results with those of ^{201}Tl reinjection in identifying viable myocardium. We also evaluated delayed imaging after rest injected ^{99m}Tc-tetrofosmin and quantitative analysis of regional activity of ^{99m}Tc-tetrofosmin to assess myocardial viability, since such approaches are reportedly beneficial for viability assessment in ^{99m}Tc-sestamibi studies (*19*).

METHODS

Patients

The study population consisted of 25 patients (21 men, 4 women; aged 40–77 yr, mean age 62 yr) with CAD, which was documented by coronary angiography and impaired regional or global left ventricular function. Nineteen patients had previous myocardial infarction (10 anterior wall infarctions, 8 inferior wall infarc-

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For correspondence or reprints contact: Ichiro Matsunari, MD, Nuklearmedizinische Klinik und Poliklinik, Der Technischen Universität München, Klinikum Rechts der Isar, Ismaninger Strasse 22, 81675 München, Germany.

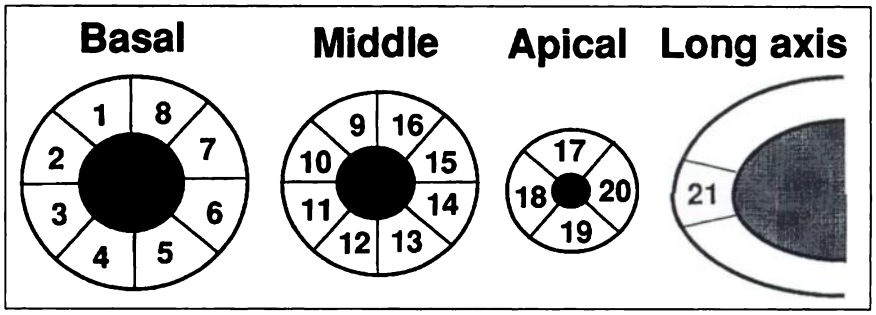

FIGURE 1. On the basis of three short-axis and one sagittal long-axis tomograms, the left ventricular myocardium was divided into 21 segments. For quantitative analysis, a square ROI of 5 × 5 pixels was placed on each segment.

tions and 1 lateral wall infarction). Mean left ventricular ejection fraction by radionuclide angiography was 44% ± 9%, ranging from 24% to 57%. Prior to the imaging studies, all patients underwent physical examination, chest radiography, electrocardiography (EKG) and coronary arteriography. The scintigraphic studies were comprised of exercise-rest ^{99m}Tc-tetrofosmin myocardial SPECT with a two-day protocol and exercise thallium SPECT with reinjection.

Coronary artery disease was defined as ≥ 50% reduction in the luminal diameter of at least one major epicardial coronary artery as determined by coronary angiography which was performed during the same stay period of the radionuclide studies. Seventeen patients had significant stenosis of one vessel, four of two vessels and four of three vessels (mean 1.5 vessels per patient). We studied only patients with stable CAD; patients with unstable angina or recent myocardial infarction (< 4 wk prior to investigation) were excluded. Two patients underwent previous percutaneous transluminal coronary angioplasty and another two patients had had coronary artery bypass surgery. All patients gave informed consent in accordance with the guidelines of the hospital's Human Clinical Study Committee prior to participation in the study.

Exercise-Redistribution-Reinjection Thallium SPECT

Exercise stress ^{201}Tl SPECT was performed on a supine bicycle ergometer. Exercise was started with a workload of 25 W and increased by 25-W intervals for every 2 min of stress. Exercise was terminated when either severe chest pain, serious arrhythmia, ST depression of more than 0.2 mV and/or fatigue occurred. One minute before cessation of exercise, 74 MBq ^{201}Tl were injected intravenously, and the patient continued exercising for 1 min. At 5 min and 3 hr postinjection, exercise and redistribution SPECT images were obtained. Immediately after completion of redistribution ^{201}Tl imaging, an additional dose of ^{201}Tl (55 MBq) was injected at rest, and reinjection imaging was started within 10 min of the second injection.

Preparation of Technetium-99m-Tetrofosmin

Technetium-99m-tetrofosmin was prepared from a freeze-dried kit (Myoview, Amersham International) by reconstitution with approximately 5 ml of sterile pertechnetate solution containing 740–1110 MBq.

Technetium-99m-Tetrofosmin SPECT

Within 1 wk of the ^{201}Tl study, exercise-stress ^{99m}Tc-tetrofosmin SPECT imaging was also performed on the supine bicycle ergometer. When the patient exercised to the same workload level as that in the stress ^{201}Tl study, approximately 400 MBq ^{99m}Tc-tetrofosmin were injected intravenously, and the patient continued exercising for 1 min. SPECT imaging was started 10 min after injection (*11,12*). Within 5 days of the exercise study, during rest, each patient was injected with 500–600 MBq ^{99m}Tc-tetrofosmin intravenously, and SPECT imaging was started 1 and 3 hr postinjection using the same acquisition conditions in the exercise study.

Myocardial SPECT Image Acquisition

Myocardial SPECT imaging was performed using a three-headed 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/view for exercise ^{201}Tl and exercise-rest ^{99m}Tc-tetrofosmin SPECT, and 40 sec/view for redistribution and reinjection ^{201}Tl SPECT. The energy discriminator was centered on 70 keV for ^{201}Tl and 140 keV for ^{99m}Tc with a 20% window. The data were recorded in 128 × 128 matrices on a magnetic disk. To reconstruct transaxial tomographic images from each acquisition, Butterworth and ramp filters were used. The parameter of the Butterworth filter was order 8, and the cutoff frequency was 0.15–0.17 cycle/pixel. Short- and long-axis slices, 3.2 mm thick, were also generated. Then, three serial slices (9.6 mm thick) of the SPECT images were added.

Data Analysis

Qualitative analysis of myocardial imaging. SPECT data analysis was based on one vertical long-axis slice and three short-axis slices. In each patient, corresponding vertical long- and short-axis tomograms from exercise-redistribution-reinjection thallium and exercise-rest ^{99m}Tc-tetrofosmin SPECT sets were aligned. Additionally, one vertical long-axis slice and three short-axis slices from the apical, middle and basal ventricular levels were chosen for comparison. The vertical long-axis slice was used to evaluate the apical region, whereas the basal and midventricular short slice was divided into eight segments and the apical ventricular short-axis slice into four segments (Fig. 1). A total of 525 myocardial segments from 25 patients were analyzed. The exercise-redistribution-reinjection thallium and exercise-rest ^{99m}Tc-tetrofosmin images were displayed and analyzed by three experienced observers who were unaware of the patient's clinical history. Semiquantitative visual analysis was performed by assigning regional tracer activities on a four-point scoring system, ranging from 0 to 3, with 0 representing severe reduction in activity and 3 normal activity. Disagreements in interpretation were resolved by consensus. On the basis of exercise-redistribution thallium images, myocardial segments were classified as follows:

1 Normal ^{201}Tl uptake, a segment with a score of 3 on the exercise ^{201}Tl image.
2 Thallium redistribution, a segment with a score of ≤ 2 on the exercise ^{201}Tl image which improved or normalized on the redistribution image.
3 No ^{201}Tl redistribution, a segment with a score of ≤ 2 on the exercise ^{201}Tl image which persisted on the redistribution image.

The segments with no ^{201}Tl redistribution were then further subgrouped according to the presence or absence of improvement in score on the ^{201}Tl reinjection images following the redistribution images. A ^{201}Tl defect that improved in score on the subsequent redistribution or reinjection images was considered to represent viable myocardium.

For the ^{99m}Tc-tetrofosmin study, the segmental analysis was performed on the basis of both exercise-early (1 hr) rest images and exercise-delayed (3 hr) rest images. A segment was nonreversible if the assigned score was abnormal on the exercise image which persisted on the rest image. Similarly, a segment was reversible if the assigned abnormal score on the exercise image increased or normalized on the rest image.

Quantitative analysis. Quantitative analysis was performed in a similar manner to previously reported procedures (*20*). Briefly, a square region of interest (ROI) of 5 × 5 pixels (3.2 mm per pixel) was placed on the center of each segment used in the qualitative analysis. For SPECT data, the maximum value (average counts per pixel) of all 21 myocardial segments per patient was taken as 100%; other values were calculated as a percentage of this maximum (relative regional uptake). Nonreversible defects on redistribution ^{201}Tl imaging and early (1 hr) rest ^{99m}Tc-tetrofosmin imaging defined by visual analysis were further subgrouped on the basis of the severity of reduction in activity: mild-to-moderate (51% or more of peak activity) and severe (≤ 50% of peak activity) defects. For individual patient analysis, myocardial regions were grouped for each patient as viable or nonviable on the basis of the severity of reduction in tracer activity and the presence or absence of reversibility. In addition, a severe nonreversible defect on redistribution ^{201}Tl imaging was considered nonviable regardless of the presence or absence of fill-in after reinjection if the activity in that region after reinjection remained ≤ 50% of peak activity (*7*). The use of 50% of peak activity as the threshold for viability determination is based on the value derived for ^{201}Tl from studies in which independent assessment of viability was made (*7–9*).

Statistical Analysis

Data are presented as mean ± s.d. Differences in hemodynamic parameters between ^{201}Tl and ^{99m}Tc-tetrofosmin studies were compared using Student's paired t-test. Comparisons of regional tracer activities of corresponding myocardial segments also used a paired two-tailed t-test. Linear regression was performed by least squares analysis. Statistical significance was defined as $p < 0.05$.

RESULTS

Exercise Results

The hemodynamic parameters recorded under control conditions and during exercise are presented in Table 1. Exercise duration and workload were identical for both tracer studies. Peak heart rate, peak systolic blood pressure and pressure rate products were also similar between the two studies (ns).

Qualitative Analysis

All patients had abnormal scans on both exercise ^{201}Tl and ^{99m}Tc-tetrofosmin imaging. Excellent ^{99m}Tc-tetrofosmin exercise and rest SPECT images were obtained in all patients.

Of 525 myocardial segments, 258 (49%) were classified as normal, 91 (17%) as redistribution and 176 (34%) as no redistribution by qualitative analysis of standard exercise-redistribution thallium SPECT. Of 176 segments with no redistribution on exercise-redistribution ^{201}Tl imaging, 71 segments (40%) showed new fill-in after ^{201}Tl reinjection, while 105 segments remained nonreversible even after ^{201}Tl reinjection. Exercise-early (1 hr) rest ^{99m}Tc-tetrofosmin myocardial SPECT identified 302 of 525 (58%) segments as normal, 58 (11%) as reversible, and 165 (31%) as nonreversible. Of the 267 segments showing abnormal activities on exercise ^{201}Tl images, 209 segments were also identified as abnormal on exercise ^{99m}Tc-tetrofosmin images.

TABLE 1
Hemodynamic Parameters during Baseline and Exercise

	Thallium	^{99m}Tc-tetrofosmin
Duration of exercise (min)	7.0 ± 2.1	7.0 ± 2.1
Exercise workload (watts)	84 ± 29	84 ± 29
Heart rate (bpm)		
Baseline	71 ± 15	72 ± 15
Peak exercise	119 ± 23	122 ± 22
Systolic blood pressure (mmHg)		
Baseline	135 ± 19	133 ± 19
Peak exercise	182 ± 31	180 ± 22
Diastolic blood pressure (mmHg)		
Baseline	79 ± 10	77 ± 10
Peak exercise	85 ± 11	91 ± 20
Double product (bpm × mmHg × 10^3)	21.8 ± 6	21.8 ± 6

The concordance and discordance for myocardial defect reversibility in the segments with initial defects on both ^{201}Tl and ^{99m}Tc-tetrofosmin imaging is shown in Figure 2. When the 209 myocardial segments with initial defects for both ^{201}Tl and ^{99m}Tc-tetrofosmin studies were classified as reversible or nonreversible, exercise-rest ^{99m}Tc-tetrofosmin and exercise-redistribution-reinjection ^{201}Tl imaging provided concordant information regarding defect reversibility in 126 (60%) segments, with 42 (20%) identified as reversible and 84 (40%) as nonreversible. Of the 115 segments with reversible defects identified by ^{201}Tl imaging, however, 73 (63%) were identified as nonreversible by ^{99m}Tc-tetrofosmin imaging. In contrast, of the 94 segments with nonreversible defects identified by ^{201}Tl imaging, only 10 (11%) were identified as reversible by ^{99m}Tc-tetrofosmin. Thus, on the basis of defect reversibility, ^{99m}Tc-tetrofosmin misidentified ischemic myocardium as nonviable in 73 of 209 abnormal segments (35%) compared with ^{201}Tl.

When delayed (3 hr) rest ^{99m}Tc-tetrofosmin images are used for analysis instead of early (1 hr) rest images, concordance for defect reversibility was obtained in 119 of 209 segments (57%). In the remaining discordant 90 segments, 78 (87%) were nonreversible on ^{99m}Tc-tetrofosmin images but were reversible on ^{201}Tl images. Thus, 3-hr delayed imaging after rest ^{99m}Tc-tetrofosmin provided no additional data on myocardial viability between ^{201}Tl and ^{99m}Tc-tetrofosmin studies. A representative case of discordant defect reversibility between ^{99m}Tc-tetrofosmin and ^{201}Tl is shown in Figure 3.

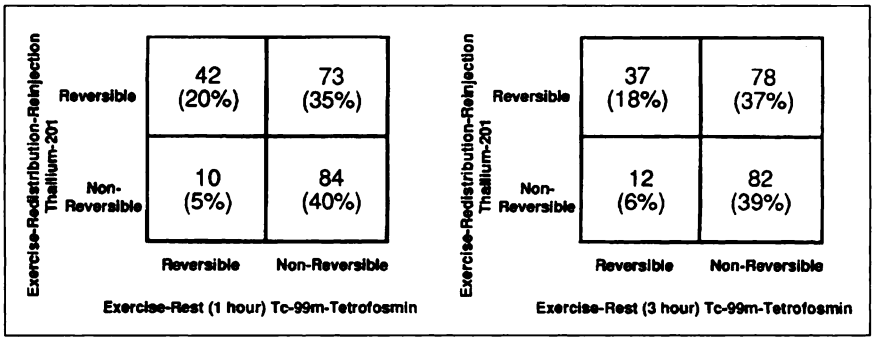

FIGURE 2. Diagrams show concordance and discordance defect reversibility data between exercise-redistribution-reinjection ^{201}Tl imaging and exercise-rest ^{99m}Tc-tetrofosmin imaging. (Left) Exercise-rest (1 hr) ^{99m}Tc-tetrofosmin data, and (right) exercise-rest (3 hr) ^{99m}Tc-tetrofosmin data.

Quantitative Analysis of Thallium and Tetrofosmin

Relative regional uptake of ^{201}Tl and ^{99m}Tc-tetrofosmin in the segments with initial defects is shown in Table 2. The relative regional uptake on exercise ^{99m}Tc-tetrofosmin imaging was higher than that on exercise ^{201}Tl imaging. In addition, the difference in tracer activity between reinjection and exercise ^{201}Tl images was significantly higher than that between rest and exercise ^{99m}Tc-tetrofosmin images.

Quantitative regional activities for both ^{201}Tl and ^{99m}Tc-tetrofosmin images are shown for individual segments in Figure 4. There were highly significant correlations both between quantitative regional redistribution ^{201}Tl activity and early (1 hr) resting ^{99m}Tc-tetrofosmin activity and between reinjection thallium activity and early resting ^{99m}Tc-tetrofosmin activity ($r = 0.90$, $p < 0.001$, and $r = 0.92$, $p < 0.001$, respectively).

Figure 5 shows the concordance and discordance regarding myocardial viability between ^{201}Tl and ^{99m}Tc-tetrofosmin imaging after quantitative analysis. Of the 94 segments with nonreversible ^{201}Tl defects based on visual analysis, 56 had mild-to-moderate reduction in ^{201}Tl activity (> 51% of peak activity) and were therefore viable; 38 had severe reduction in ^{201}Tl activity (≤ 50% of peak activity) and were nonviable. On the other hand, visual analysis revealed six segments with new fill-in after ^{201}Tl reinjection that were classified as nonviable because these segments still had severe reduction in ^{201}Tl activity after reinjection.

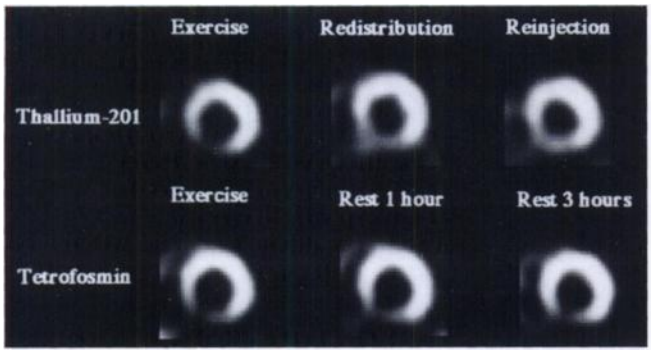

FIGURE 3. Short-axis tomograms from a patient with reversible ^{201}Tl and nonreversible ^{99m}Tc-tetrofosmin defects. Thallium images reveal a partially reversible inferior defect that improved after reinjection. Exercise-rest (1 hr) ^{99m}Tc-tetrofosmin images demonstrate a nonreversible inferior defect. Delayed (3 hr) rest ^{99m}Tc-tetrofosmin image also shows no reversibility in the region.

Of the 157 segments with nonreversible ^{99m}Tc-tetrofosmin defects by visual analysis, 118 had mild-to-moderate reduction in ^{99m}Tc-tetrofosmin activity and were considered viable and 39 had severe reduction in activity and were considered nonviable. Thus, when quantitative analysis of regional activities of both ^{201}Tl and ^{99m}Tc-tetrofosmin with a threshold cutoff point of 50% was performed, the overall concordance for myocardial viability increased to 90% (Fig. 5). A representative case demonstrating concordant defect severity between ^{201}Tl and ^{99m}Tc-tetrofosmin is shown in Figure 6.

DISCUSSION

Thallium-201 myocardial imaging has become an indispensable diagnostic tool for evaluating myocardial perfusion and viability. It is well known that reversibility of a stress-induced ^{201}Tl defect represents viable myocardium (*1,2*). Despite the excellent physiological characteristics of ^{201}Tl for imaging and viability assessment, its low photon energy (68–80 keV) and relatively long half-life are suboptimal. Recently, ^{99m}Tc-tetrofosmin was introduced as an alternative to ^{201}Tl (*10–12*). The favorable emission energy of ^{99m}Tc (140 keV) eliminates photon attenuation compared to ^{201}Tl. The greater photon flux with ^{99m}Tc may also

TABLE 2
Degree of Defect Severity and Reversibility with Thallium and Technetium-99m-Tetrofosmin in 209 Myocardial Segments with Initial Defects

Thallium exercise	52.8 ± 14.3
Thallium redistribution	56.6 ± 14.8
Thallium reinjection	61.7 ± 14.6
Tetrofosmin exercise	56.1 ± 13.6*
Tetrofosmin rest	58.9 ± 14.0
Diff. thallium reinjection-exercise	8.8 ± 8.8
Diff. tetrofosmin rest-exercise	2.8 ± 7.5†

*$p < 0.001$ thallium exercise.
†$p < 0.001$ Diff. thallium reinjection-exercise.
Diff. thallium reinjection-exercise is the difference in tracer activity between reinjection and exercise thallium images. Diff. tetrofosmin rest-exercise is the difference in tracer activity between rest and exercise ^{99m}Tc-tetrofosmin images. Values are expressed as mean ± s.d. (% of peak activity).

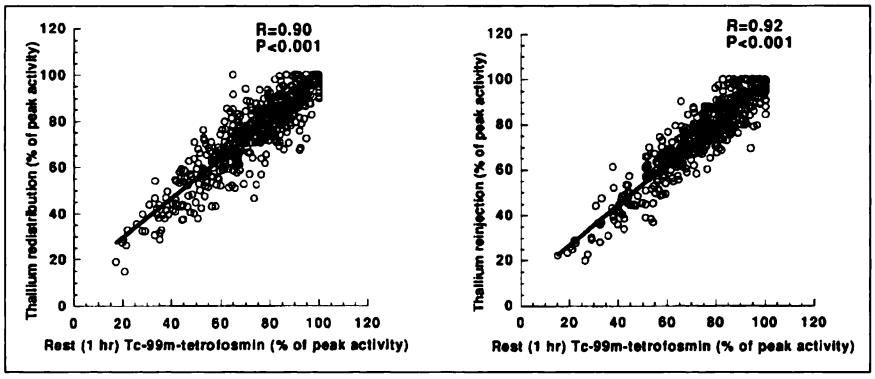

FIGURE 4. Scatter plots show correlation of quantitative regional tracer activities between redistribution ^{201}Tl and early (1 hr) rest ^{99m}Tc-tetrofosmin imaging (left) and between reinjection ^{201}Tl and early (1 hr) rest ^{99m}Tc-tetrofosmin imaging (right).

allow simultaneous assessment of myocardial perfusion and function by first-pass radionuclide ventriculography (*21*).

Previous studies have demonstrated excellent agreement between standard exercise-redistribution ^{201}Tl and exercise-rest ^{99m}Tc-tetrofosmin imaging for assessing myocardial viability (*14–16*). These comparisons, however, have been performed only with standard exercise-redistribution ^{201}Tl imaging protocols. A large population of persistent ^{201}Tl defects on redistribution imaging exhibit improved perfusion or function after revascularization (*1,2*), indicating that conventional exercise-redistribution thallium imaging underestimates myocardial viability. Furthermore, PET can demonstrate metabolic activity and, hence, viable myocardium in the majority of patients with persistent defects on redistribution images (*3*). This limitation has been overcome by a modified ^{201}Tl imaging protocol incorporating reinjection of a second dose of ^{201}Tl after redistribution imaging (*5–9,22,23*), resulting in remarkably improved detection of viable myocardium.

Comparison of Tetrofosmin and Thallium Reinjection

In this study, we used a two-day protocol to identify several myocardial segments classified as reversible on exercise-redistribution-reinjection ^{201}Tl images but were nonreversible on exercise-rest ^{99m}Tc-tetrofosmin images. We noted significantly higher differences in regional tracer activity between reinjection and exercise thallium images than on rest and exercise ^{99m}Tc-tetrofosmin images. This result agreed with visual analysis of the images. Interestingly, our data are similar to the published results for myocardial viability assessment with ^{99m}Tc-sestamibi (*18,19*), another technetium-based myocardial perfusion imaging agent with no significant redistribution. Cuocolo et al. found additional stress defect reversibility using an exercise-redistribution-reinjection thallium protocol compared with an exercise-rest sestamibi protocol (*18*). Their results were confirmed by Dilsizian et al. using PET as the gold standard (*19*).

Two possible factors may partly account for the underestimation of defect reversibility with ^{99m}Tc-tetrofosmin in the present study. First, the presence of stress-induced ischemia may be underestimated because of tetrofosmin's relatively low extraction fraction (*24*). Nakajima et al. have shown lower detectability of stress-induced ischemia associated with infarction with an exercise-rest ^{99m}Tc-tetrofosmin protocol (*14*). Tamaki et al. also reported that stress distribution of ^{99m}Tc-tetrofosmin was slightly higher than that of ^{201}Tl, which indicates a lower defect contrast, especially in the areas of ^{201}Tl redistribution after exercise (*16*). Technetium-99m-tetrofosmin has been reported to underestimate myocardial blood flow at high flows induced

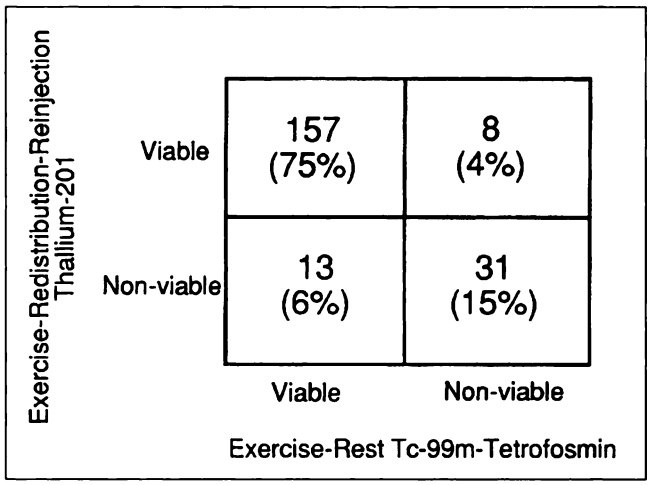

FIGURE 5. Concordance and discordance between exercise-redistribution-reinjection thallium and exercise-rest (1 hr) ^{99m}Tc-tetrofosmin imaging for myocardial viability by quantitative analysis of regional activities with a threshold cutoff of 50%.

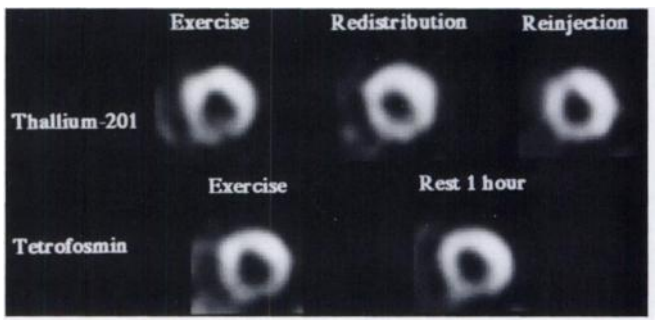

FIGURE 6. Short-axis tomograms show concordant reduction in tracer activity for ^{201}Tl and ^{99m}Tc-tetrofosmin. The ^{201}Tl and ^{99m}Tc-tetrofosmin images show mild-to-moderate defects in the inferior region.

by pharmacological coronary vasodilatation (*25*), which may also contribute to the lower defect contrast with this agent.

Second, ^{99m}Tc-tetrofosmin is considered to be a radiopharmaceutical with no redistribution (*13,14*), whereas ^{201}Tl can redistribute over time. Based on the lack of ^{99m}Tc-tetrofosmin redistribution compared with ^{201}Tl, this agent may underestimate defect reversibility and myocardial viability, especially in regions with reduced regional myocardial perfusion at rest where the initial delivery of the tracer will be reduced.

It has been shown that ^{99m}Tc-sestamibi may redistribute over time to some degree (*26*) and that the presence of redistribution enhances the detection of viable myocardium when an additional delayed image is obtained (*19*). Unlike the published results with ^{99m}Tc-sestamibi (*19*), 3-hr delayed imaging with rest injected ^{99m}Tc-tetrofosmin did not enhance defect reversibility, possibly because of the complete lack of ^{99m}Tc-tetrofosmin redistribution, as evidenced by Sridhara et al. (*13*) and the results in this report.

An indirect result of our study meriting further attention is that 58 segments with initial thallium defects were missed by ^{99m}Tc-tetrofosmin. This may be explained by lower defect contrast with tetrofosmin. Further studies are warranted to determine similarities in defect size with tetrofosmin and thallium.

Quantitative Analysis

Exercise-redistribution-reinjection ^{201}Tl imaging may still underestimate myocardial viability compared to PET imaging (*27*). Quantitation of myocardial ^{201}Tl activity, however, appears to enhance the detection of viable myocardium within apparently nonreversible ^{201}Tl defects (*7,8*). Most nonreversible defects with only mild-to-moderate reduction in ^{201}Tl activity represent viable myocardium as confirmed by [^{18}F]fluorodeoxyglucose PET (*7–9*). In ^{99m}Tc-sestamibi studies, such quantitative methods are reportedly useful for identifying viable myocardium (*19,28*). Correspondingly, quantitative analysis of ^{99m}Tc-tetrofosmin activity within apparently nonreversible defects may also contain such information. In this regard, highly significant correlation of regional tracer activities between ^{201}Tl and ^{99m}Tc-tetrofosmin observed in the present study is encouraging for quantitative assessment of myocardial viability.

Potential Limitations

In this study, we directly compared the results of exercise-rest ^{99m}Tc-tetrofosmin imaging to those of exercise-redistribution-reinjection ^{201}Tl imaging; there are no data on reversibility in wall motion after revascularization. Therefore, although numerous studies have shown the usefulness of ^{201}Tl imaging with reinjection to identify viable myocardium (*5–9,22,23*), definitive statements regarding the use of ^{99m}Tc-tetrofosmin imaging in the management of patients with left ventricular dysfunction are not possible from the current data. Furthermore, we arbitrarily used 50% of peak activity as the viability threshold determination with ^{99m}Tc-tetrofosmin. Therefore, the threshold cut-off value may in fact not be 50%, and thus requires further study. We think that our observation, however, could be of interest for future trials aimed at detecting viable myocardium in patients undergoing revascularization. Another possible limitation of this study is that the fundamental characteristics and mechanism of tetrofosmin myocardial uptake have not been fully clarified. Therefore, further studies are needed, in particular, to determine whether transmembrane uptake and tetrofosmin retention within myocardial cells correlate with cellular viability.

CONCLUSION

On the basis of visual analysis of defect reversibility, exercise-rest ^{99m}Tc-tetrofosmin imaging with a two-day protocol underestimates the presence of viable myocardium compared to exercise-redistribution-reinjection ^{201}Tl imaging. Unlike ^{99m}Tc-sestamibi, 3-hr delayed imaging after rest injection of ^{99m}Tc-tetrofosmin provides no additional data on myocardial viability, due to the complete lack of tetrofosmin redistribution. Detection of viable myocardium with both ^{201}Tl and ^{99m}Tc-tetrofosmin can be greatly enhanced to a similar degree if the severity of reduction in tracer activity within nonreversible defects is considered.

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