Myocardial Tomography Using Technetium-99m-Tetrofosmin to Evaluate Coronary Artery Disease

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To assess the clinical value of the ^{99m}Tc-labeled myocardial perfusion agent, ^{99m}Tc-tetrofosmin, the findings of stress and rest myocardial tomography were compared with those of stress and 3-hr delayed ^{201}Tl tomography and coronary arteriography. **Methods:** Twenty-five patients who had coronary arteriography were studied with both stress tetrofosmin and ^{201}Tl tomography. **Results:** The image quality of tetrofosmin was superior to that of ^{201}Tl despite a shorter acquisition time. Both the tetrofosmin and ^{201}Tl studies were quite sensitive to detect coronary artery disease (100% and 95%, respectively) (p = ns). The two studies showed similar sensitivity (75% and 73%) and specificity (80% and 77%, respectively) for the detection of significant (≥75% diameter) coronary artery stenosis. Stress distribution of tetrofosmin tended to be slightly higher than that of ^{201}Tl (% uptake: 63.3% ± 13.5% versus 60.4% ± 12.2%, p = 0.0006; uptake score: 2.33 ± 1.03 versus 2.22 ± 1.07, p = 0.007), indicating less defect contrast in the former. A high concordant rate (89%) of the stress perfusion score was observed between the two radiopharmaceuticals. Reversible perfusion abnormalities were observed to be similar between stress-rest tetrofosmin and stress-delayed ^{201}Tl studies. **Conclusions:** Stress tetrofosmin perfusion tomography is a valuable method to detect coronary artery disease and to assess tissue viability with accuracy similar to that of stress ^{201}Tl tomography.

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

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Stress and redistribution ^{201}Tl imaging has been widely applied to the detection of coronary artery disease (CAD) and the assessment of tissue viability (*1–3*). However, the long physical half-life of the tracer limits the injected dose, resulting in relatively low counts in the myocardium. In addition, the low-energy photons emitted from ^{201}Tl degrade the image quality with a relatively large photon attenuation. Furthermore, the need for off-site cyclotron production may limit rapid availability of ^{201}Tl.

To overcome the physical limitations of ^{201}Tl, several ^{99m}Tc-labeled compounds have been developed. Among them, ^{99m}Tc-methoxyisobutylisonitrile (sestamibi) presently provides the best biological properties for clinical application (*4–6*). Heating of this agent is required for ^{99m}Tc labeling; imaging cannot begin until the liver activity is cleared at about 1 hr.

Recently, a number of ^{99m}Tc-labeled phosphine compounds have been introduced. Among them, ^{99m}Tc-1,2-bis(bis(2-ethoxyethyl)phosphino)ethane (tetrofosmin or P53) is a perfusion agent with high uptake and retention in the myocardium and rapid clearance from the liver. In addition, this freeze-dry kit is labeled with ^{99m}Tc at room temperature and hence does not require a heating process (*7–10*). Thus, this new agent is easy to prepare and permits early imaging. A Phase I clinical study has confirmed the safety of this radiopharmaceutical and has shown an excellent myocardial image with rapid clearance from the blood (*9,10*).

In order to assess the clinical value of this agent, the findings of stress and rest myocardial perfusion images after the administration of this agent were compared to those of stress and redistribution ^{201}Tl tomography, as well as those of the coronary arteriography, with respect to the detection of CAD and the assessment of reversibility of perfusion defects.

METHODS

Patient Population

Twenty-five patients suspected with CAD who had undergone coronary arteriography were recruited as part of the Phase II and III clinical trials in Japan. Those who could not perform exercise were excluded from this study. The group consisted of 20 males and 5 females, with the mean age of 62.2 ± 6.7 yr, ranging from 45 to 76 yr. The coronary arteriogram in two projections showed significant (≥75% diameter) stenosis in at least one major coronary artery in 22 patients, 12 of whom with a prior myocardial infarction more than 1 mo after the onset. The remaining three patients had a normal coronary artery or insignificant stenosis

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(<50%) on the coronary arteriogram and one received percutaneous coronary angioplasty 3 mo prior to the radionuclide studies.

Each patient gave written informed constant approved by the Kyoto University Human Study Committee.

Stress ^{201}Tl Scan

Treadmill exercise was performed following the standard Bruce protocol with 12-lead ECG monitoring during each minute of exercise. Exercise end points were physical exhaustion, development of severe angina pain, greater than 0.2 MeV of ST-segment depression or dangerous arrhythmia on ECG, or exertional hypotension.

At peak exercise, 100 MBq (2.7 mCi) of ^{201}Tl was intravenously injected and exercise continued for an additional minute. Imaging started approximately 10 min after the end of exercise. SPECT was performed with a rotational gamma camera equipped with a low-energy, general-purpose collimator (Starcam 3,000; General Electric Co., Milwaukee, WI), collecting 32 views of 30 sec each over 180° from 45° left posterior oblique to 45° right anterior oblique projections. The total acquisition time was approximately 18 min. Redistribution tomographic images were collected 3 hr later in a similar fashion (*11–13*). Each patient refrained from eating carbohydrates until the end of the redistribution imaging. A reinjection scan was not performed in this study.

Preparation of ^{99m}Tc-Tetrofosmin

Technetium-99m-tetrofosmin was prepared from a freeze-dry kit (Myoview, Amersham International, England) (*9*) by reconstitution with approximately 5 ml of a sterile sodium pertechnetate solution containing 555–740 MBq (15–20 mCi).

Tetrofosmin Imaging Protocol

The stress tetrofosmin perfusion study was performed within 2 wk of the thallium study. Following an overnight fast, injections were performed both at rest and during exercise.

For the stress tetrofosmin study, the patients were stressed to the same duration as in the ^{201}Tl study. At peak exercise, 370–592 MBq (10–16 mCi) of ^{99m}Tc-tetrofosmin was intravenously injected, and exercise was continued for an additional minute. After 10–15 min of recovery, each patient was asked to have a light meal or a glass of milk to accelerate hepatobiliary clearance. Imaging started approximately 30–40 min after the radiopharmaceutical administration. Tomography was obtained with a rotational gamma camera collecting 32 20-sec views over 180°. The total acquisition time was approximately 12 min.

The resting tetrofosmin study was performed 24–72 hr after the stress imaging. Following administration with 370–592 MBq (10–16 mCi) of ^{99m}Tc-tetrofosmin at rest in a fasting state, a light meal or a glass of milk was given. About 40 min after the tracer administration, resting tomography was performed in a similar fashion.

Image Analysis

After tomographic acquisition, projection data were stored on a hard disk. The projection data were smoothed using a Hanning filter with a cutoff frequency of 0.5 cycles per pixel, and a series of 6-mm thick transverse slices were reconstructed using a filtered backprojection with a Ramp filter. Data were reoriented to obtain the oblique angle tomograms parallel to the long-axis and short-axis of the left ventricle. No attenuation- or scatter-correction was performed (*11–13*).

In the interpretation of tomographic images, all short-axis and long-axis tomograms were displayed on transparent films. Separate films were obtained displaying aligned slices of the stress and

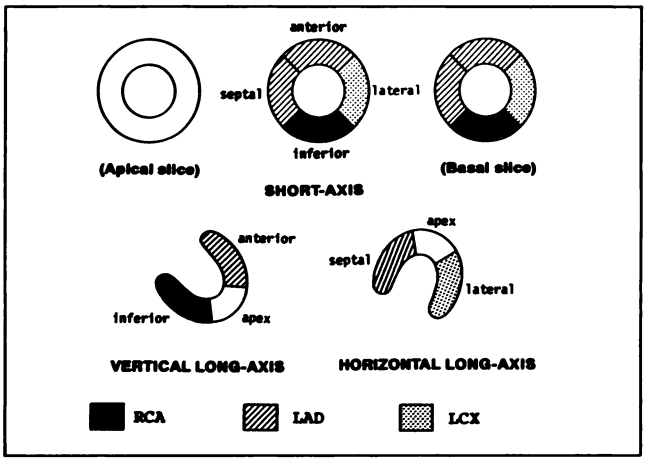

FIGURE 1. Schematic presentation of three short-axis slices and mid-ventricular vertical and horizontal long-axis slices displays five myocardial segments. The distribution of three major coronary arteries were also described.

3-hr delayed ^{201}Tl studies as well as the stress and rest tetrofosmin studies. At first, two experienced observers judged which image sets from the composite ^{201}Tl and tetrofosmin were superior in image quality on the basis of statistical noise, target-to-background count ratio and sharpness without knowledge of the radiopharmaceutical or patient identity. For each study, the left ventricular myocardium was divided into five large segments: anterior, septal, inferior, lateral and apical (Fig. 1) (*11*). The ^{201}Tl and tetrofosmin images were separately interpreted and the uptake of the tracer in each segment was scored by the consensus of the two experienced observers using a four-point grading system (3 = normal; 2 = mildly reduced; 1 = moderately reduced; and 0 = defect) without knowing the clinical histories, results of coronary arteriography or other radionuclide findings.

A segment was considered abnormal when the stress score was ≤2. A reversible defect was defined as an abnormal segment showing an improved score on the delayed ^{201}Tl or resting tetrofosmin scans.

For quantitative analysis of tracer distributions, a circumferential profile curve was generated from apical to basal short-axis slices to a bull's eye polar map of 100% as a maximum count in each tetrofosmin and ^{201}Tl image (*14*). The mean counts (% count) of the tracer distribution in the five myocardial segments were calculated.

The assignment of vascular territories was based upon our previous study on ^{201}Tl tomographic imaging (*11–13*). In brief, anterior and septal segments include the left anterior descending artery territory, lateral segments include the left circumflex artery territories, and inferior segments include the right coronary artery territories (Fig. 1).

Statistical Analysis

Data were expressed as means ± s.d. The differences in perfusion and reversibility scores were compared using a paired t-test. Comparison of proportions was made with chi-square analysis with Yate's correction when appropriate. Probability values of <5% were considered significant.

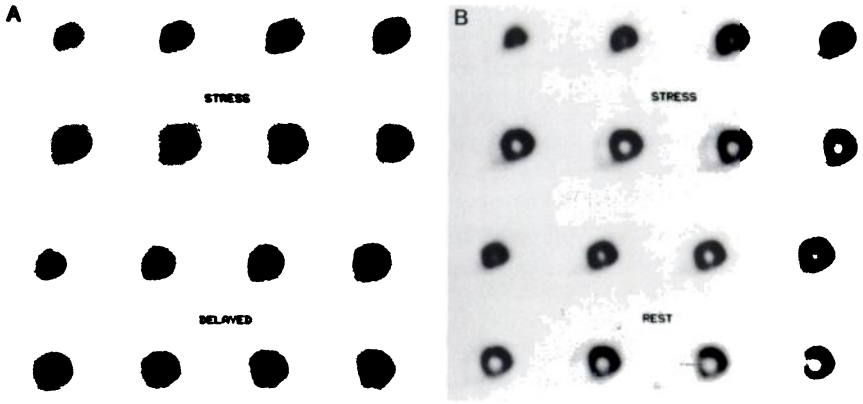

FIGURE 2. A series of short-axis slices of stress (top) and 3-hr delayed (bottom) thallium images (A) and stress (top) and resting (bottom) tetrofosmin images (B) of a patient with inferior wall myocardial infarction. Thallium images show perfusion defect without redistribution in inferior regions. Tetrofosmin images showed similar findings. However, the image quality is better on the resting tetrofosmin imaging than the delayed thallium imaging.

RESULTS

Exercise Results

The exercise duration was identical to the tetrofosmin and ^{201}Tl studies (8.4 ± 2.0 min and 8.4 ± 2.0 min, respectively). The peak heart rate and pressure rate products were also similar between the two studies (128 ± 14 versus 130 ± 17 bpm, and 21,200 ± 400 versus 22,100 ± 400, respectively) (p = ns).

Image Quality

In the stress perfusion imaging, tetrofosmin tomograms were superior in quality to ^{201}Tl tomograms in 17 of the 25 patient studies. In the remaining eight patients, the tomograms were judged to be of equal quality. In the resting perfusion imaging, tetrofosmin images were superior in all the patient studies (Figs. 2 and 3). In general, the tetrofosmin images had more counts with less statistical noise, despite shorter acquisition time required for tomographic imaging (12 and 18 min for tetrofosmin and ^{201}Tl, respectively). A liver uptake was higher in the tetrofosmin images but this did not interfere with the interpretation of the regional myocardial uptake in any patient study.

Overall Sensitivity

Overall sensitivities for detecting CAD were 95% (21/22) for ^{201}Tl imaging and 100% (22/22) for tetrofosmin imaging (Table 1). In a study of three patients with no significant coronary stenosis, stress ^{201}Tl imaging revealed normal perfusion in one patient and stress tetrofosmin imaging was normal in two patients. The remaining patient who received percutaneous coronary angioplasty 3 mo prior to the study showed a transient perfusion defect both on ^{201}Tl and tetrofosmin imaging (Table 1).

Sensitivity and Specificity for Identifying Stenosed Vessels

The sensitivity for detecting stenosed (≥75% in diameter) vessels was 73% by ^{201}Tl imaging and 75% by tetrofosmin imaging with 77% and 80% specificity, respectively (Table 2). The overall accuracies were similar between the two studies (75% and 77%, respectively) (p = ns). The accuracy was similar when patients without prior myocardial infarction were studied (Table 2). The sensitivities were 78% and 83% for ^{201}Tl and tetrofosmin imaging, respectively, while the specificities were 90% and 95%, respectively.

The sensitivity and specificity values in individual coronary arteries are shown in Table 3. The sensitivity and specificity values of ^{201}Tl and tetrofosmin for detecting left anterior descending artery stenosis (83% versus 89% sensitivity and 71% versus 86% specificity, respectively), left circumflex (50% sensitivity and 100% specificity, respectively), and right coronary stenosis (80% sensitivity and

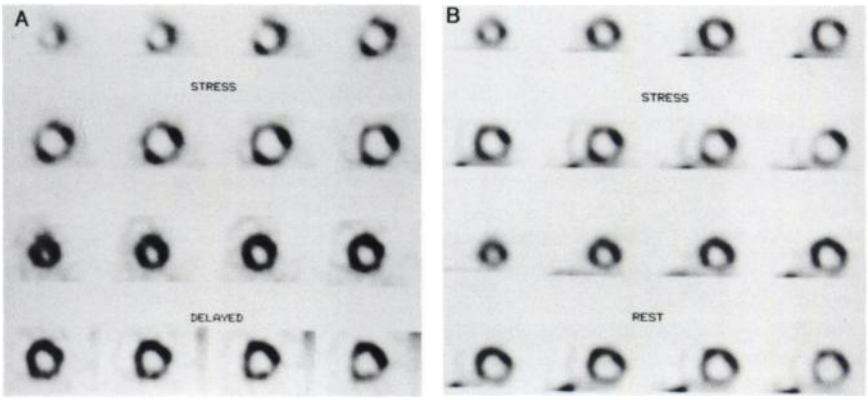

FIGURE 3. A series of short-axis slices of stress (top) and 3-hr delayed (bottom) thallium images (A) and stress (top) and resting (bottom) tetrofosmin images (B) of a patient with CAD. Thallium images show perfusion defect with significant redistribution in the apical, anterior and septal regions. Tetrofosmin images showed mild hypoperfusion at stress with normal perfusion at rest in the same areas. Although the lesion contrast is better on the thallium images, image quality is much better with higher contrast on the tetrofosmin images. This coronary angiogram showed 90% stenosis of proximal portion of the left anterior descending artery.

TABLE 1
Clinical Data and Radionuclide Results on Thallium and Tetrofosmin Perfusion Imaging in 25 Patients Suspected with CAD

Patient no.	Age/Sex	History of MI	ST change on ECG	Stenosis on CAD			Thallium findings	Tetrofosmin findings
				RCA	LAD	LCX		
1	55/F	—	—		25%		Normal	Normal
2	64/M	—	—	25%			SE-RD	Normal
3	69/M	—	II,III,aVf,V5,6		25% (postPTCA)		AP-RD	AP-RD
4	76/M	—	V5,V6	75%	90%		SE-RD,AN-RD,AP-RD	SE-RD,AN-RD
5	57/F	—	—		99%		Normal	AN-RD
6	73/M	—	II,III,aVf	100%	90%	75%	AN-FD,IN-RD,AP-RD	AN-FD,IN-RD
7	67/M	—	—	90%	75%		IN-RD,AP-RD	IN-RD,AP-RD
8	54/M	—	II,III,aVf		75%	99%	AN-FD	AN-FD
9	65/M	—	V5,6		75%		SE-RD,AP-RD	SE-RD
10	60/F	—	—		75%	50%	IN-FD	IN-RD
11	70/M	—	—	100%	75%		SE-RD,IN-RD,AP-RD	SE-RD,IN-RD,AP-RD
12	54/M	—	II,III,aVf		75%	50%	AN-FD	AN-FD
13	60/F	—	II,III,aVf	99%	75%	75%	IN-RD,LA-RD,AP-RD	IN-RD,LA-RD,AP-RD
14	58/M	ant MI	—		100%	99%	SE-RD,AN-RD,AP-RD	SE-RD,AN-FD,AP-RD
15	65/M	ant MI	II,III,aVf		90%		AN-FD,IN-FD,AP-FD	AN-FD
16	57/M	ant MI	V5,6	90%	90%		AN-FD,IN-FD	AN-FD,IN-FD
17	65/M	ant MI	—		100%		SE-RD,AN-RD,AP-FD	SE-RD,AN-RD,AP-FD
18	59/M	ant MI	—	100%	100%	100%	SE-RD,AP-FD	SE-RD,AP-FD
19	62/M	ant MI	II,III,aVf,V5,6	50%	75%	100%	IN-FD,AN-FD,LA-RD	IN-FD,AN-FD,LA-RD
20	64/M	ant MI	—		75%	99%	SE-FD,AN-FD,AP-FD	SE-FD,AN-FD,AP-FD
21	69/M	inf MI	—	75%		100%	IN-FD,LA-FD	IN-FD,LA-FD
22	45/M	inf MI	—			75%	IN-FD,LA-FD	IN-FD,LA-FD
23	58/M	inf MI	II,III,aVf	100%			IN-FD	IN-FD
24	68/M	inf MI	II,III,aVf		75%	99%	IN-FD,LA-FD	SE-RD,IN-FD,LA-FD
25	62/F	ant and inf MI	—	100%	75%	90%	IN-FD,LA-FD	IN-FD,LA-FD

MI = myocardial infarction; ECG = electrocardiogram; RCA = right coronary artery; LAD = left anterior descendence; LCX = left circumflex artery; SE = septal; AN = anterior; IN = inferior; AP = apical; LA = lateral; RD = redistribution; and FD = fixed defect.

60% specificity, respectively). There were no statistically significant differences among these values between the two studies. Similar sensitivity and specificity values were also obtained when patients without prior myocardial infarction were analyzed (Table 3).

Defect Severity

To assess the differences in the severity of the perfusion abnormality between the two studies, the perfusion scores in hypoperfused segments were compared (Table 4). The perfusion score in stress tetrofosmin imaging was greater (2.33 ± 1.01) than that in stress ^{201}Tl imaging (2.23 ± 1.05; p = 0.007), indicating lower defect contrast in the former. When segments showing redistribution on stress ^{201}Tl imaging were analyzed, the differences in the stress perfusion scores were more striking (1.58 ± 0.91 versus 1.17 ± 0.62; p = 0.004). Similar results were obtained when the tracer distribution was studied using a bull's eye polar map. The stress distribution of tetrofosmin in hypoperfused segments was slightly higher (63.3% ± 13.5%) than that of ^{201}Tl (60.4% ± 12.2%; p = 0.0006). When the segments showing redistribution on the stress ^{201}Tl images were analyzed, the differences in the stress distribution were striking (63.9% ± 11.5% versus 59.8% ± 8.7%; p = 0.004). The resting distribution of tetrofosmin in hypoperfused segments was also slightly higher (67.6% ± 14.0%) than that of delayed ^{201}Tl (65.4% ± 12.5%; p = 0.002).

The scores were identical in 111 of the total 125 segments (89%). Among 52 abnormal perfusion segments by stress perfusion imaging, 38 segments (73%) had identical scores. On the other hand, stress tetrofosmin imaging showed a lower perfusion score in 12 segments (23%) (Fig. 3), but a higher score in only two segments (4%) (Table 4).

TABLE 2
Sensitivity and Specificity for Detecting Stenosed Vessels

	Thallium	Tetrofosmin
Overall		
Sensitivity	29/40 (73%)	30/40 (75%)
Specificity	27/35 (77%)	28/35 (80%)
Accuracy	56/75 (75%)	58/75 (77%)
Patients without prior myocardial infarction		
Sensitivity	14/18 (78%)	15/18 (83%)
Specificity	19/21 (90%)	20/21 (95%)
Accuracy	33/39 (85%)	35/39 (90%)

TABLE 3
Sensitivity and Specificity for Detecting Individual Stenosed Vessels

	LAD		LCX		RCA	
	Thallium	Tetrofosmin	Thallium	Tetrofosmin	Thallium	Tetrofosmin
Overall						
Sensitivity	15/18 (83%)	16/18 (89%)	6/12 (50%)	6/12 (50%)	8/10 (80%)	8/10 (80%)
Specificity	5/7 (71%)	6/7 (86%)	13/13 (100%)	13/13 (100%)	9/15 (60%)	9/15 (60%)
Accuracy	20/25 (80%)	22/25 (88%)	19/25 (76%)	19/25 (76%)	17/25 (68%)	17/25 (68%)
Patients without prior myocardial infarction						
Sensitivity	8/10 (80%)	9/10 (90%)	2/3 (67%)	2/3 (67%)	4/5 (80%)	4/5 (80%)
Specificity	2/3 (67%)	3/3 (100%)	10/10 (100%)	10/10 (100%)	7/8 (88%)	7/8 (88%)
Accuracy	10/13 (77%)	12/13 (92%)	12/13 (92%)	12/13 (92%)	11/13 (85%)	11/13 (85%)

There were 24 segments that showed redistribution on stress ^{201}Tl imaging. This was more often observed in the segments with a lower perfusion score (8/12; 75%) on tetrofosmin imaging than those with identical scores (13/38; 34%) ($\chi^2 = 4.92$; $p = 0.03$).

Defect Reversibility

Of the 24 patients with regional hypoperfusion on stress ^{201}Tl imaging, 12 (50%) had redistribution. Stress tetrofosmin showed reversible hypoperfusion in 14 patients (58%) (Table 1) (p = ns).

Of the total of 125 segments, stress ^{201}Tl imaging identified 24 segments with reversible hypoperfusion (19%), whereas stress tetrofosmin imaging revealed 22 segments with reversible hypoperfusion (18%) (p = ns) (Table 5). Nine segments showed greater reversibility on ^{201}Tl imaging, whereas seven segments did so on tetrofosmin imaging (p = ns). A study of the segments with perfusion abnormalities, the reversibility of the perfusion score did not differ between ^{201}Tl (0.50 ± 0.58) and tetrofosmin imaging (0.57 ± 0.65) (p = ns).

Among the 12 patients with myocardial infarction, stress ^{201}Tl imaging showed reversibility in six segments, whereas stress tetrofosmin imaging did so in seven segments (p = ns).

DISCUSSION

These preliminary results indicate that stress myocardial tomographic imaging with tetrofosmin provide a sensitive means for detecting CAD and identifying stenosed coronary arteries. The diagnostic accuracy and reversibility were similar to that of stress ^{201}Tl tomography. Although the defect contrast tended to be lower in the tetrofosmin imaging, a high concordance rate of the perfusion score was achieved between the two studies. Since tetrofosmin tomography provided better image quality with a shorter acquisition time, it is considered a feasible means for assessing CAD with a more confident interpretation.

Advantages of Tetrofosmin

The favorable patient dosimetry allows a dose of tetrofosmin ten times higher than ^{201}Tl to be administered, providing higher quality perfusion images. The favorable emitting energy of ^{99m}Tc lowers the photon attenuation from that of ^{201}Tl. The high proton flux and energy are suitable for SPECT. In this study, the image quality of tetrofosmin tomography was superior to that of ^{201}Tl in most of the patients, despite the shorter acquisition time in the former.

Among various ^{99m}Tc perfusion agents, tetrofosmin can be labeled with ^{99m}Tc at room temperature (*7–10*), as compared to sestamibi which requires heating for approximately 20 min. Its high uptake and retention in the myocardium makes myocardial perfusion imaging feasible (*7–10*). In addition, a significantly faster clearance from both lung and liver may offer the possibility of earlier imaging or higher quality images at a comparable imaging time (*9,10*). To facilitate hepatobiliary excretion, each patient was asked to have a light meal or a glass of milk after tetrofosmin administration. In this study, myocardial imaging was achieved approximately 30–40 min after tetrofosmin ad-

TABLE 4
Number of Segments Showing the Perfusion Score on Stress Tetrofosmin Imaging in Relation to Stress Thallium Imaging

		Tetrofosmin			
		3	2	1	0
Thallium	3	73 (0)*	2 (0)	0 (0)	0 (0)
	2	4 (3)	12 (4)	0 (0)	0 (0)
	1	2 (1)	6 (5)	14 (8)	0 (0)
	0	0 (0)	0 (0)	0 (0)	12 (3)

*Parenthesis denotes the number of segments showing redistribution on thallium scan.

TABLE 5
Number of Segments Showing the Reversibility on Stress Tetrofosmin Imaging in Relation to Stress Thallium Imaging

		Tetrofosmin			
		+2	+1	0	Normal
Thallium	+2	0	2	0	0
	+1	4	13	1	4
	0	0	1	23	2
	Normal	0	2	0	73

ministration, and excellent myocardial images with high contrast were obtained. Similar results have also been reported in the international Phase III clinical trials using the planar technique (*15*) and in the Phase I and II clinical trials in Japan using tomography (*16,17*).

Because the radiopharmaceutical was not redistributed, two separate injections at both rest and stress may be required to differentiate the ischemic from the necrotic myocardium, just as in the sestamibi studies. In this study, rest and stress injections were performed upon two separate days to identify reversibility and to avoid any cross-talk between the two sets of images.

Clinical Value of Tetrofosmin

This clinical trial assesses the diagnostic value of this agent to detect CAD and identify ischemic myocardium by comparison with stress ^{201}Tl imaging and coronary arteriography. In a comparative study with coronary arteriographic findings, stress tetrofosmin imaging provided high sensitivity to detect coronary disease patients and stenosed vessels. Since this study only included patients who received coronary arteriography, only three with normal coronary arteriographs were included. Therefore, the specificity for detecting CAD may not be accurate. On the other hand, the sensitivity to identify stenosed vessels was high.

Similar diagnostic values were obtained in the comparative study with stress ^{201}Tl imaging. The agreement between tetrofosmin and ^{201}Tl imaging regarding the presence of stress defects was high. The diagnostic accuracies in the present study were similar to those in the study of stress sestamibi imaging (*18–27*), and those previously reported by our group using stress ^{201}Tl tomography (*11–13,28*). The higher energy photon of ^{99m}Tc may provide a better quality image which increases confidence in the interpretation (*29*), and gives a better true-negative rate. In particular, myocardial tomographic imaging requires higher counts, which may be more easily achieved by ^{99m}Tc perfusion imaging than by ^{201}Tl imaging. This study showed that the quality of stress tetrofosmin tomographic images were superior to those of stress ^{201}Tl tomographic images despite shorter acquisition time. Another SPECT study using the same acquisition time as that in ^{201}Tl SPECT may provide better image quality using a high-resolution collimator or sharper filter for reconstruction. Previous clinical studies using sestamibi showed a better image quality (*19*), and thus, a high diagnostic accuracy: specificity value was higher than that achieved with stress ^{201}Tl imaging (*19–23*). The advantages of ^{99m}Tc perfusion agents over ^{201}Tl have been enhanced using tomographic analysis (*19,20,24–27*).

Reversibility Assessment

Stress and rest perfusion imaging with two separate injections of tetrofosmin showed similar reversibility to those by stress and 3-hr delayed ^{201}Tl imaging. Similar results have also been reported in a study of stress and rest perfusion imaging using ^{99m}Tc-sestamibi (*19*). Recent reports have indicated that reinjection or 24-hr delayed ^{201}Tl imaging may show reversibility more often than the conventional 3–4-hr delayed imaging (*11,30–33*). In this respect, tetrofosmin imaging may not provide additional value for assessing tissue viability over the conventional stress and 3-hr delayed ^{201}Tl imaging.

This study showed that the stress distribution of tetrofosmin tended to be slightly higher, indicating a lower defect contrast, particularly in the areas where redistribution was observed on the stress ^{201}Tl images. This may be the result of a lower extraction fraction with slower blood clearance of tetrofosmin than of ^{201}Tl (*34*). Thus, even though resting tetrofosmin imaging may show normal or greater perfusion scores compared with the 3-hr delayed ^{201}Tl imaging, a similar defect reversibility may be seen between the two studies. A lower extraction fraction in sestamibi has also been found in experimental studies (*35,36*). This may cause a mild degree of ischemia to be missed by ^{99m}Tc perfusion agents. However, a more precise analysis of wide clinical studies using a greater number of normal individuals and patients with CAD is warranted to clarify this issue.

Limitations

In our clinical trials of tetrofosmin, we could not include an adequate number of patients with normal coronary arteries or a low likelihood of CAD. To assess the diagnostic value of this new radiopharmaceutical, a greater number of normal individuals should be studied to provide more accurate value of specificity and the normalcy rate of this study.

In the reversibility study, the tetrofosmin scans were compared with only those of stress-delayed ^{201}Tl scans. A new comparison with newly developed stress-reinjection ^{201}Tl scan may provide slightly different results.

Clinical Implications

These preliminary results suggest that stress and rest tetrofosmin tomography provided similar diagnostic accuracy for the detection of CAD and for the identification of the reversibility as those of stress and delayed ^{201}Tl tomography. The greater photon flux available with ^{99m}Tc may also allow the simultaneous assessment of myocardial perfusion and function by either first-pass radionuclide ventriculography or multigated tomography (*37–42*). More importantly, this may provide myocardial perfusion images of higher quality, and thus, a more confident interpretation is expected. In conclusion, stress tetrofosmin perfusion tomography is a feasible and valuable means for detection of CAD and for assessing tissue viability.

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