Reverse Redistribution of Technetium-99m-Sestamibi Following Direct PTCA in Acute Myocardial Infarction

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A pattern of reverse redistribution (RR) has not been documented in myocardial ^{99m}Tc-sestamibi imaging. The purpose of the study was to clarify the time-related changes in myocardial distribution of ^{99m}Tc-sestamibi in patients with acute myocardial infarction. **Methods:** Myocardial SPECT with ^{99m}Tc-sestamibi was performed in 27 patients with acute myocardial infarction within 1 wk after the onset. Twenty-three patients received direct percutaneous transluminal coronary angioplasty (PTCA) and 4 patients did not. Myocardial images were obtained 1 hr (early) and 3 hr (delayed) after the injection of ^{99m}Tc-sestamibi. Regional myocardial uptake of ^{99m}Tc-sestamibi was scored from 4 (normal) to 0 (no activity), and the RR pattern was defined as a decrease of more than 1 in the regional score at the 3-hr delayed images. Regional myocardial uptake and clearance of ^{99m}Tc-sestamibi was also assessed quantitatively. Coronary arteriography and left ventriculography were performed 1 mo later. **Results:** Out of 22 patients with successful PTCA, RR of ^{99m}Tc-sestamibi was observed in 15 patients (68%). Persistent defects (PD) were seen in 12 patients (7 patients with successful PTCA, 1 patient with unsuccessful PTCA, and 4 patients who did not receive angioplasty). In patients with RR, regional uptake of ^{99m}Tc-sestamibi in the area of myocardial infarction decreased from 54% ± 10% in the early images to 43% ± 8% in the delayed images ($p < 0.01$). Technetium-99m-sestamibi clearance from the myocardium was faster in the infarct area than in the normal area (26% ± 7% versus 9% ± 6%, $p < 0.01$). Coronary arteriography performed 1 mo later revealed that the patency of the infarct related artery was 100% (15/15) in patients with RR and 50% (6/12) in those with PD ($p < 0.01$). The extent and severity of a wall motion abnormality were less in patients with RR than in those with PD (extent: 24 ± 10 versus 36 ± 9 chord, $p < 0.01$; severity: −2.7 ± 0.4 versus −3.4 ± 0.6 s.d./chord, $p < 0.01$). **Conclusion:** The RR of ^{99m}Tc-sestamibi was observed in 68% of patients after successful direct PTCA and was associated with the accelerated clearance of ^{99m}Tc-sestamibi from the myocardium. The presence of RR in ^{99m}Tc-sestamibi imaging indicates the patency of the infarct-related artery and predicts the preserved left ventricular function.

Key Words: technetium-99m-sestamibi; acute myocardial infarction; percutaneous transluminal coronary angioplasty

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A pattern of reverse redistribution is defined as the worsening of a perfusion defect during the redistribution phase of ^{201}Tl scintigraphy (*1,2*). This phenomenon includes either the worsening of a perfusion defect apparent on the initial images or the appearance of a new perfusion defect on the redistribution images. Reverse redistribution of ^{201}Tl on the redistribution images has been shown after exercise (*1,2*), pharmacologic vasodilation with dipyridamole (*3*), and resting ^{201}Tl scintigraphy (*4*). Reverse redistribution has been found to be associated with acute myocardial infarction following thrombolytic therapy (*5,6*) and chronic coronary artery disease of varying severity (*1–4,7*). It has also been reported in patients after bypass surgery with a patent graft (*8*). Although the reverse redistribution phenomenon on ^{201}Tl images has been extensively investigated, its pathophysiological meanings, including etiology, mechanism and clinical significance, have not been completely settled (*9*).

Technetium-99m-methoxyisobutyl isonitrile (^{99m}Tc-sestamibi) has been used as a myocardial perfusion tracer (*10,11*). Unlike ^{201}Tl, an apparent lack of redistribution of ^{99m}Tc-sestamibi has been shown in experimental and clinical studies (*12,13*). Therefore, ^{99m}Tc-sestamibi permits the delayed imaging after the injection, because the late images still represent the myocardial perfusion at the time of injection (*14*). However, it has recently been reported that redistribution of ^{99m}Tc-sestamibi is detectable in patients with chronic coronary artery disease (*15,16*). Although reverse redistribution of ^{201}Tl has been most commonly observed following coronary thrombolysis in patients with acute myocardial infarction (*5*), time-related changes in myocardial ^{99m}Tc-sestamibi distribution have not been examined in these patients.

Technetium-99m-sestamibi distribution could be serialy changed in the reperfused myocardium, where there is a mixture of scarring with stunned or hibernating myocardium. The purpose of the present study was to: (a) assess the prevalence of ^{99m}Tc-sestamibi reverse redistribution pattern after direct percutaneous transluminal coronary angioplasty (PTCA) in patients with acute myocardial infarction and (b) evaluate the clinical implications of this phenomenon.

METHODS

Subjects and Study Protocol

We examined 27 consecutive patients with acute myocardial infarction. Acute myocardial infarction was defined as nitroglycerin-resistant chest pain persisting for more than 30 min accompanied by an ECG with more than 0.1-mV ST-segment elevation in two or more contiguous leads (*17*). Twenty-three patients admitted within 6 hr after the onset of symptoms received direct PTCA. The remaining 4 patients did not receive PTCA or thrombolytic therapy because they were admitted late after the onset of pain. Intravenous heparin and lidocaine were given to all patients. Patients receiving PTCA were immediately transported to the catheterization laboratory and underwent coronary arteriography followed by direct PTCA if indicated. The angioplasty was considered to be technically successful when there was a residual stenosis of less than 50% and an angiographic TIMI grade was 2 or 3 at the end of angioplasty procedure.

Myocardial perfusion imaging with ^{99m}Tc-sestamibi was performed within 1 wk (average 3 days after the onset). Coronary arteriography and left ventriculography were performed after 1 mo

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to evaluate patency of the infarct-related artery and left ventricular wall motion. Informed written consent was obtained from all patients.

Myocardial Perfusion Imaging with Technetium-99m-Sestamibi

Data Acquisition and Processing. Myocardial SPECT was performed in all patients as previously described (*18–20*). Briefly, after an overnight fast, a 740-MBq dose of ^{99m}Tc-sestamibi was injected intravenously in the resting supine position. The patients ate a meal after the ^{99m}Tc-sestamibi injection to hasten the excretion of the isotope through the gallbladder into the bowel. Data acquisition was carried out 1 hr and 3 hr after the ^{99m}Tc-sestamibi administration. All images were obtained on a large field of view rotating gamma camera equipped with a parallel-hole, high-resolution collimator. Energy discrimination was provided by a 20% window centered at 140 keV. An anterior projection planar image was accumulated for 5 min. Then 32 images were obtained over a 180° arc from the 30° right anterior oblique to the 60° left posterior oblique positions. Each image was accumulated for 30 sec. The data were stored on a 64 × 64 matrix. Data processing was performed on a nuclear medicine computer system. A series of 6-mm thick contiguous transaxial images was reconstructed with a filtered back-projection algorithm without attenuation correction. These transaxial images were then reoriented in the short-axis, vertical long-axis and horizontal long-axis of the left ventricle.

Image Interpretation. The myocardial distribution of ^{99m}Tc-sestamibi was analyzed in the three standard orthogonal tomographic imaging planes as follows: the anterior, septal, inferior and lateral regions in the short-axis view; the anterior, apical and inferior regions in the vertical long-axis view; and the septal, apical and lateral regions in the horizontal long-axis view. The left ventricle was divided into 9 segments by splitting the anterior, septal, inferior and lateral wall into basal and apical segments, including an extra segment for the apex (*21*). The image was interpreted by two independent observers (Y.T. and S.F.) who were unaware of the clinical histories and angiographic findings of the patients. A five-point scoring system was used for evaluating the regional myocardial uptake of the tracer as described previously (*21*): 4 = normal, 3 = slightly reduced, 2 = moderately reduced, 1 = severely reduced and 0 = no activity. Reverse redistribution was defined as a decrease of more than 1 in the segmental score at the 3-hr delayed images. The grading was settled by consensus between the two observers. When they disagreed on the results, the third observer reviewed the images and made the final judgment.

Quantification of Myocardial Images. Myocardial accumulation of the tracer was assessed quantitatively by previously described methods (*22*). Six regions of interest (ROIs), 4 × 4 pixels in size (6 × 6 mm), were determined over the myocardium on the short-axis images. The mean counts in each ROI was measured and normalized to the maximal value in the myocardium. The clearance of ^{99m}Tc-sestamibi from the myocardium was calculated from the absolute counts in early (Ce) and delayed (Cd) images as follows:

$$\text{Clearance} = (Ce - Cd \times Cf) \times 100/Ce$$

$$Cf = 1/(1/2)^x,\ x = (Td - Te)/6$$

where Td = time for delayed image and Te = time for early image.

Circumferential profile analysis was applied to each of the short-axis slices from apex to base as previously described (*23*). These circumferential profiles were plotted in polar coordinates and arranged into a bull's eye map. Male and female normal files had been separately constructed from 17 men and 15 women normal subjects. In the present study, each pixel was compared with the corresponding pixel in the gender-matched profile. Pixels that were more than 2 s.d.s below the normal mean value were defined as abnormal and displayed on a color-coded standard deviation map. The ratio of the numbers of abnormal pixels to those of total pixels was defined as an extent score.

Heart-to-Background Count Ratio. On the anterior planar image, square ROIs were defined for areas of the left upper lung field (6 × 6 pixels in size), the left ventricular myocardium (4 × 4 pixels), and the liver (6 × 6 pixels) (*24*). The myocardial ROI was placed over the myocardium with the peak count density. The lung ROI and liver ROI were placed over the most intense activity in the lung and liver areas, respectively. Heart-to-lung and heart-to-liver count ratios were calculated as a fraction of the mean counts per pixel in the myocardium divided by those in the lung and liver, respectively.

Coronary Arteriography and Left Ventriculography

Coronary arteriography was performed after 1 mo in multiple projections with the standard Judkins' technique for assessing patency of the infarct-related artery. The biplane left ventriculograms were obtained for the assessment of left ventricular function. Regional wall motion was analyzed by the centerline method using 100 chords (*25*). Each shortening fraction was normalized to the end-diastolic perimeter of the left ventricle. This normalized motion was converted into units of normal standard deviations from the normal mean at each chord, previously determined in 13 normal subjects (*26*). The circumferential extent of a wall motion abnormality was assessed as the number of contiguous chords with motion of less than 2 s.d.s below the normal mean value. The degree of a wall motion abnormality was expressed as the sum of the standard deviations for all abnormal chords divided by the number of abnormal chords.

Statistical Analysis

Data were reported in mean ± 1 s.d. Continuous variables were compared by a Student's t-test, and the differences in proportion (categorical variables) were examined by a chi square test. A p value of <0.05 was considered significant.

RESULTS

Of the 23 patients who received direct PTCA, successful coronary reflow was achieved in 22 patients (Table 1). In one patient, the infarct-related artery could not be opened.

Interpretation of Technetium-99m-Sestamibi Images

Myocardial perfusion images with ^{99m}Tc-sestamibi of a patient with acute anterior myocardial infarction are shown in Figure 1. In this case, a direct PTCA was successfully performed to the left anterior descending artery. In the early images, there are perfusion defects in the anterior and septal regions of the left ventricle. The worsening of these defects is seen on the delayed images (reverse redistribution).

Figure 2 shows myocardial short-axis images with ^{99m}Tc-sestamibi of a patient with acute inferior myocardial infarction. Successful coronary reperfusion was obtained by a direct PTCA to the right coronary artery. The reverse redistribution of ^{99m}Tc-sestamibi is also observed in the inferior region of the left ventricle.

Such reverse redistribution of ^{99m}Tc-sestamibi was observed in 15 of 22 patients (68%) with successful direct PTCA. The remaining 7 of 22 patients showed persistent defects of ^{99m}Tc-sestamibi. Persistent defects were also observed in a patient who failed to achieve coronary reflow and in 4 patients who did not receive PTCA. There were no differences between the patients with reverse redistribution and persistent defects regarding the age, sex, the site of myocardial infarction and the location of the infarct-related artery (Table 1). Out of 5 patients

TABLE 1
Patient Characteristics and Angiographic and Scintigraphic Results

Patient No.	Sex	Age (yr)	Site of infarction	IRA	CAG	PTCA	RR	Uptake (%)		Clearance (%)
								Early	Delay	
1	M	68	POST	RCA	100	Successful	+	53	44	22
2	F	68	INF	RCA	99	Successful	−	47	43	−1
3	F	78	LAT	LCX	100	Successful	+	51	42	17
4	M	67	ANT, SEP	LAD	100	Unsuccessful	−	35	31	14
5	M	60	LAT	LMT	100 *	Successful	+	63	50	30
6	F	77	POST, LAT	RCA	100	Successful	−	51	50	15
7	M	56	ANT	LAD	99	Successful	+	51	38	37
8	M	86	INF	RCA	100	Successful	−	46	43	21
9	M	66	ANT, SEP	LAD	100	Not performed	−	39	42	−3
10	M	56	INF	RCA	100	Successful	+	50	41	15
11	M	57	ANT	LAD	100	Successful	−	55	51	15
12	M	52	ANT	LAD	100 *	Successful	+	52	37	32
13	F	59	INF	RCA	99	Successful	−	58	55	14
14	M	56	LAT	LCX	99	Successful	+	51	43	30
15	M	48	ANT, SEP	LAD	100	Successful	+	52	41	25
16	M	70	ANT	LAD	100	Successful	−	59	57	16
17	M	49	ANT, SEP	LAD	99 *	Successful	+	84	67	33
18	M	52	INF	RCA	100	Successful	+	48	40	21
19	M	69	INF, POST	LCX	100	Not performed	−	53	50	20
20	M	73	ANT, SEP	LAD	100 *	Not performed	−	40	42	5
21	F	77	POST, LAT	LCX	99	Successful	+	44	36	20
22	M	75	INF	RCA	90	Not performed	−	61	57	17
23	F	63	ANT, SEP	LAD	100	Successful	+	56	43	32
24	M	67	ANT, SEP	LAD	100	Successful	+	49	39	28
25	M	62	INF	RCA	99	Successful	−	48	49	−4
26	F	69	INF	RCA	100 *	Successful	+	59	48	30
27	M	71	ANT, SEP	LAD	99	Successful	+	47	39	20

*Patients with collateral vessels filling of epicardial coronary artery.

ANT = anterior; SEP = septal; INF = inferior; POST = posterior; LAT = lateral; IRA = infarct-related artery; LAD = left anterior descending artery; RCA = right coronary artery; LCX = left circumflex artery; CAG = coronary arteriography; PTCA = percutaneous transluminal coronary angioplasty; RR = reverse redistribution. + = positive; − = negative.

with collateral vessels before PTCA, 4 patients showed reverse redistribution of ^{99m}Tc-sestamibi.

Quantitative Analysis of Technetium-99m-Sestamibi Images

In patients with reverse redistribution, regional uptake of ^{99m}Tc-sestamibi in the area of myocardial infarction decreased significantly from 54% ± 10% in the early images to 43% ± 8% in the delayed images ($p < 0.01$, Fig. 3). In patients with persistent defects, ^{99m}Tc-sestamibi uptake in the infarct area was unchanged between the early and delayed images (49% ± 8% versus 48% ± 8%). Technetium-99m-sestamibi uptake in the normal area was not different between the early and delayed images in patients with reverse redistribution (82% ± 9% versus 80% ± 10%) and persistent defects (83% ± 8% versus 84% ± 11%). In patients with reverse redistribution, extent scores of ^{99m}Tc-sestamibi defects were larger in the delayed images than in the early images (0.46 ± 0.15 versus 0.38 ± 0.13, $p < 0.01$). In patients with persistent defects, the extent scores were unchanged between the early and delayed images (0.40 ± 0.15 versus 0.42 ± 0.13).

In patients with reverse redistribution, ^{99m}Tc-sestamibi clearance from the myocardium was higher in the infarct area than in

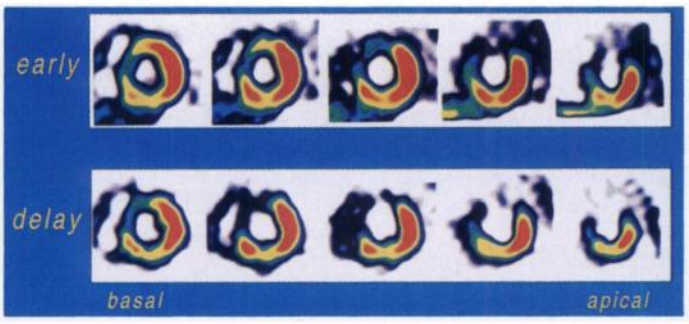

FIGURE 1. Short-axis images of myocardial ^{99m}Tc-sestamibi imaging in a patient (No. 24 in Table 1) with acute anterior myocardial infarction. Upper panels are early images and the lower panels are delayed images. Left anterior descending artery was occluded, and successful coronary reflow was achieved by direct PTCA. Perfusion defects are seen in the anterior and septal regions of the left ventricle, and these defects are more extensive in the delayed images (reverse redistribution).

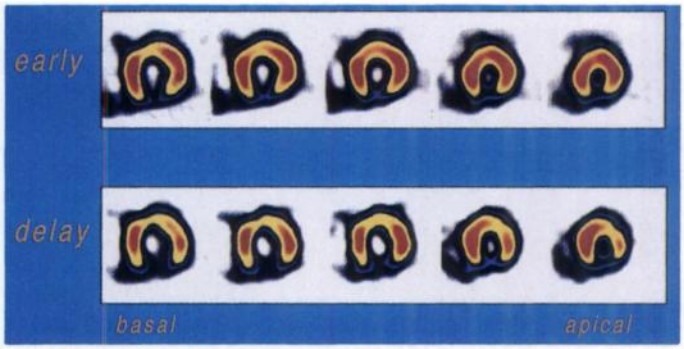

FIGURE 2. Short-axis images of ^{99m}Tc-sestamibi in a patient (No. 10 in Table 1) with acute inferior myocardial infarction. Right coronary artery was successfully reperfused by direct PTCA. Reverse redistribution of ^{99m}Tc-sestamibi is evident in the inferior region of the left ventricle.

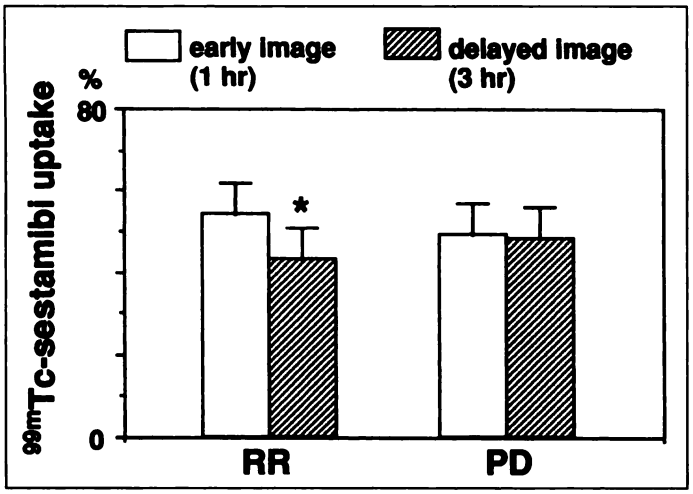

FIGURE 3. Changes in regional ^{99m}Tc-sestamibi uptake in the area of myocardial infarction from the early to the delayed images. RR = reverse redistribution; PD = persistent defects. *p < 0.01.

the normal area (26% ± 7% versus 9% ± 6%, p < 0.01, Fig. 4). Technetium-99m-sestamibi clearance from the infarct area was higher in patients with reverse redistribution than in those with persistent defects (26% ± 7% versus 11% ± 9%, p < 0.01).

Heart-to-background count ratios were obtained from the anterior planar images. A heart-to-lung ratio in the early (2.6 ± 0.6 versus 2.5 ± 0.5) and delayed (2.9 ± 1.1 versus 3.1 ± 1.3) images was not different between the patients with reverse redistribution and persistent defects. A heart-to-liver ratio was also comparable between the patients with reverse redistribution and persistent defects (early: 0.8 ± 0.3 versus 0.6 ± 0.3, delayed: 1.8 ± 0.5 versus 1.7 ± 0.6).

Relation of Reverse Redistribution of Technetium-99m-Sestamibi with the Patency of the Infarct-Related Artery and Left Ventricular Function

Coronary arteriography performed 1 mo later revealed that the infarct-related artery was patent in all patients with reverse redistribution (15/15, 100%). However, in patients with persistent defects the patency of the infarct-related artery was confirmed in 6 of 12 patients (50%, p < 0.01). In 2 of 7 patients with persistent defects after successful PTCA, the infarct-related coronary artery was occluded.

Left ventriculography was also performed after 1 mo to evaluate a left ventricular wall motion abnormality. As shown in Figure 5, the circumferential extent of segments with decreased wall motion was less in patients with reverse redistribution than in those with persistent defects (24 ± 10 versus 35 ± 9 chord, p < 0.01). The degree of regional wall motion abnormality was also less in patients with reverse redistribution than in those with persistent defects (−2.6 ± 0.4 versus −3.4 ± 0.6 SD/chord, p < 0.01).

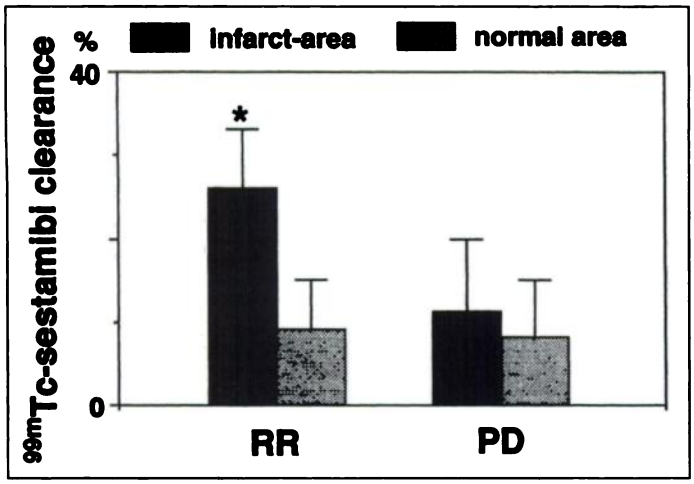

FIGURE 4. Comparison of ^{99m}Tc-sestamibi clearance from the myocardium. RR = reverse redistribution; PD = persistent defects. *p < 0.01.

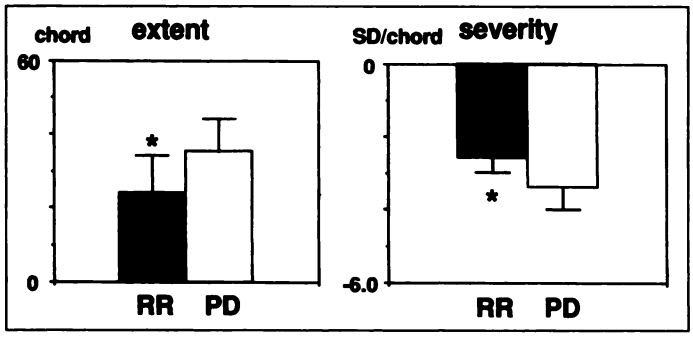

FIGURE 5. Comparison of the extent and severity of a wall motion abnormality between patients with reverse redistribution (RR) and those with persistent defects (PD). *p < 0.01.

DISCUSSION

We demonstrated that reverse redistribution of ^{99m}Tc-sestamibi was evident after direct PTCA in patients with acute myocardial infarction. The presence of reverse redistribution of ^{99m}Tc-sestamibi was associated with the patent infarct-related artery and the preserved left ventricular function.

Redistribution of Technetium-99m-Sestamibi

Technetium-99m-sestamibi has a very slow washout from the myocardium with minimal redistribution. Okada et al. (*12*) found that clearance of ^{99m}Tc-sestamibi was similar from the normal and ischemic myocardial regions in dogs, and that redistribution was not evident. Therefore, ^{99m}Tc-sestamibi imaging can be delayed after the injection, because myocardial perfusion at the time of injection can be frozen by ^{99m}Tc-sestamibi. Thus, ^{99m}Tc-sestamibi has been used for assessing the amount of myocardium at risk in acute myocardial infarction without any delay in initiating the revascularization therapy (*14*).

Li et al. (*27*) examined time-related changes in myocardial distribution of ^{99m}Tc-sestamibi in reperfused dog hearts. They reported that following transient ischemia and reperfusion, ^{99m}Tc-sestamibi underwent myocardial redistribution, although the process was slower and less complete than ^{201}Tl. Sinusas et al. (*28*) reported that there was detectable redistribution of ^{99m}Tc-sestamibi in the presence of a severe coronary stenosis in open-chest dogs. It has been recently reported that redistribution of ^{99m}Tc-sestamibi is detectable in patients with chronic coronary artery disease (*15,16*). In the present study, 2 patients showed slight redistribution on the delayed images by visual inspection. They were categorized in a persistent defects group, because the increase of ^{99m}Tc-sestamibi uptake on the delayed images was not evident by quantitative analysis. It may require further examination to clarify the clinical significance of redistribution of ^{99m}Tc-sestamibi in patients with acute myocardial infarction.

Reverse Redistribution of Thallium-201

Reverse redistribution of ^{201}Tl was commonly observed following thrombolytic therapy in acute myocardial infarction (*5,6*). Weiss et al. (*5*) reported that this phenomenon was a sign of nontransmural myocardial infarction with a patent infarct-related coronary artery. Reverse redistribution of ^{201}Tl has also

been noted soon after coronary artery bypass surgery in the presence of a patent graft (*8*). It has been described after exercise (*1,2,7*), pharmacologic vasodilation with dipyridamole (*3*) and resting ^{201}Tl scintigraphy (*4*) in patients with chronic coronary artery disease of varying severity. Although the reverse redistribution phenomenon on ^{201}Tl images has been extensively investigated, its pathophysiological meaning has not been completely settled (*9*).

A pattern of reverse redistribution includes either the worsening of a perfusion defect apparent on the initial images or the appearance of a new perfusion defect on the delayed images. Pace et al. (*4*) reported that, out of the total 375 segments analyzed, the former pattern was noted in 6 segments and the latter pattern of ^{201}Tl reverse redistribution was in 26 segments. They showed that myocardial segments with the latter pattern of ^{201}Tl reverse redistribution were supplied by severely stenosed coronary arteries, although ^{201}Tl uptake was normal on the early images. In the present study, 1 of 15 patients with reverse redistribution of ^{99m}Tc-sestamibi showed the latter pattern. This patient had a 99% stenosis at the proximal left anterior descending artery along with the presence of well-developed collateral vessels from the right coronary artery. In this patient, left ventriculography performed 1 mo later showed near-normal wall motion in myocardial segments with reverse redistribution.

Technical Considerations

In the present study, patients ate after the ^{99m}Tc-sestamibi injection to decrease gallbladder activity. However, activity excreted from the biliary tract into the bowel might interfere with the image interpretation in the inferior wall of the heart in some patients. Taking a meal would influence ^{99m}Tc-sestamibi clearance and redistribution as noted in ^{201}Tl. However, there was no difference in the location of myocardial infarction between the patients with reverse redistribution and persistent defects.

An increase of background activity might possibly impair precise assessment of myocardial distribution and clearance of ^{99m}Tc-sestamibi. In the present study, heart-to-lung and heart-to-liver count ratios were not different between the patients with reverse redistribution and persistent defects. Thus, the background activity did not modify the present results.

Possible Mechanism of Reverse Redistribution of Technetium-99m-Sestamibi

A pattern of reverse redistribution of ^{99m}Tc-sestamibi has not been previously documented in either experimental or clinical studies. Because reverse redistribution of ^{201}Tl has been most commonly observed in patients with acute myocardial infarction following thrombolytic therapy (*5*), such a phenomenon could be detected in the case of administering ^{99m}Tc-sestamibi after direct PTCA.

The following possible mechanism for reverse redistribution of ^{99m}Tc-sestamibi might be suggested. The infarct-myocardium can receive the initially delivered ^{99m}Tc-sestamibi after the revascularization procedure, but cannot hold ^{99m}Tc-sestamibi in the myocardium with time. A mixture of viable but stunned myocardium with nonviable myocardium exists in the reperfused myocardium following direct PTCA. The ability of myocytes to retain the tracer may be impaired in this stunned myocardium (*9*). In the present study, four of five patients with collateral opacification before coronary angioplasty showed reverse redistribution of ^{99m}Tc-sestamibi. All myocardial regions with reverse redistribution of ^{99m}Tc-sestamibi were subtended by a patent infarct-related artery. Left ventriculography performed 1 mo later showed that reverse redistribution of ^{99m}Tc-sestamibi was associated with the preserved left ventricular wall motion. The viable but stunned myocardium might recover their function after 1 mo (*29*).

Beller et al. (*30*) have recently reported that in the reperfused dog hearts, sestamibi uptake and retention are dependent on myocardial viability as well as regional flow. They show that necrotic cells can neither extract nor retain sestamibi, and sestamibi may be a valid viability agent in the setting of reperfusion. Udelson et al. (*29*) have recently showed that ^{99m}Tc-sestamibi uptake is higher in the viable myocardium than in the nonviable myocardium. In the present study, ^{99m}Tc-sestamibi uptake on the early images tended to be higher in patients with reverse redistribution than in those with persistent defects (54% ± 10% versus 49% ± 8%, p = ns).

Clinical Implications

The development of noninvasive methods to assess the patency status of the infarct-related artery is urgent, because silent reocclusion of the infarct-related artery is occasionally documented following successful reperfusion (*17,31*). From our observation, the presence of reverse redistribution of ^{99m}Tc-sestamibi indicates that the patency of the infarct-related artery has been maintained and predicts the reversibility of regional wall motion abnormality after reperfusion. Reverse redistribution of ^{99m}Tc-sestamibi after direct PTCA will provide a clue for successful revascularization and, thus, myocardial viability.

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Regional Myocardial Perfusion Assessed with Generator-Produced Copper-62-PTSM and PET

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We have previously demonstrated that myocardial perfusion can be estimated accurately in experimental animals with the generator-produced positron-emitting tracer, ^{62}Cu-pyruvaldehyde bis (N^4-methylthio-semicarbazone)(^{62}Cu-PTSM) and PET. This study evaluated the feasibility of quantifying regional myocardial blood flow using ^{62}Cu-PTSM and PET in human subjects. **Methods:** Regional perfusion was estimated using a previously described and validated two-compartment model from dynamic PET scans obtained after an intravenous bolus of ^{62}Cu-PTSM in 10 healthy volunteers and in 6 patients with coronary artery disease at rest; and in 9 of the volunteers and 4 of the patients after administration of dipyridamole intravenously. Flow estimates were compared with those obtained using $H_2{}^{15}O$. **Results:** Contrast was high between myocardium and blood or lung with ^{62}Cu-PTSM, resulting in high-quality myocardial images. Liver uptake was also high. At flows of up to 1.5 ml/g/min, flow estimated with ^{62}Cu-PTSM correlated closely with estimates obtained with $H_2{}^{15}O$ ($y = 0.71x + 0.21$, $n = 169$ regional comparisons, $r = 0.66$, $p < 0.05$), but this relationship was not maintained at higher flows. **Conclusion:** The results demonstrate that quantification of myocardial perfusion with ^{62}Cu-PTSM is feasible in human subjects but cannot be used to estimate hyperemic flows due most likely to the strong binding of the tracer to human serum albumin. Copper-62-PTSM congeners with less avidity for human albumin may prove more suitable for evaluation of hyperemic flows.

Key Words: PET; myocardial blood flow; copper-62-PTSM

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Delineation of myocardial perfusion and perfusion reserve is paramount for the diagnosis of coronary artery disease and for the evaluation of therapies designed to enhance nutritive myocardial perfusion. PET has been shown to be excellent for quantification of regional myocardial blood flow because of its ability to accurately delineate the distribution of positron emitting radionuclides within the myocardium. PET has been shown to be highly sensitive and specific for the delineation of coronary artery disease with the cyclotron-produced flow tracers ^{13}N-ammonia (*1,2*) or ^{15}O-water (*3–8*) as well as with generator-produced ^{82}Rb-chloride (*9–13*). Generator-produced PET radiopharmaceuticals free operations from the necessity of a hospital-based cyclotron and add flexibility and convenience to patient studies.

Our group has shown, in experimental studies, that accurate quantitative flow measurements can be obtained with ^{82}Rb-chloride over a wide range of physiological flows with a two-compartment kinetic model (*14*). Nonetheless, the short physical half-life of this tracer (1.3 min) makes ^{82}Rb-chloride less than ideal for the quantification of myocardial perfusion and there has been interest in the development of alternative generator-produced PET flow tracers. The lipophilic compound copper(II) pyruvaldehyde bis (N^4-methylthiosemicarbazone) (Cu-PTSM), is one candidate. Copper-PTSM can be labeled with several single-photon radionuclides as well as with generator-produced, positron-emitting ^{62}Cu ($t_{1/2}$ = 9.7 min). Although the parent, ^{62}Zn, only possesses a 9.3-hr half-life, it and ^{62}Cu-PTSM are easily produced in the quantities that would be required for regional or nationwide delivery (*15,16*). Copper-62-PTSM is highly extracted and retained in organs for prolonged periods of time due to intracellular reductive decomposition of the lipophilic Cu-PTSM complex to liberate the ^{62}Cu ion which cannot rapidly escape the cell (*17,18*) facilitating imaging of heart, kidney and brain, and making this tracer an attractive one for multi-organ flow imaging (*19–21*).

In studies on intact dogs, myocardial extraction of Cu-PTSM

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