Assessment of Improvement of Myocardial Fatty Acid Uptake and Function after Revascularization Using Iodine-123-BMIPP

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We used beta-methyl iodophenyl pentadecanoic acid (BMIPP) to evaluate changes in myocardial fatty acid utilization before and after revascularization and the ability of BMIPP to predict functional recovery in patients with chronic coronary artery disease. **Methods:** Thirty-four patients with chronic coronary artery disease (60 ± 10 yr) underwent BMIPP and ^{201}Tl SPECT (stress-reinjection ^{201}Tl in 29 patients and resting ^{201}Tl in 5 patients) before and 2–5 wk after percutaneous transluminal angioplasty (n = 23) or coronary artery bypass surgery (n = 11). Cardiac function was evaluated by gated blood-pool scintigraphy (n = 26) or two-dimensional echocardiography (n = 8) before and after revascularization. **Results:** In 32 patients with reduced BMIPP uptake before revascularization, scintigraphic findings with ^{201}Tl improved in 28 patients after revascularization. In these 28 patients, BMIPP uptake improved in 20 patients (71%). Wall motion abnormality was observed in 16 of these 20 patients before revascularization, with 15 showing wall motion improvement after revascularization. In eight patients without improvement of BMIPP uptake, despite ^{201}Tl uptake improvement, wall motion abnormality was observed in four patients before revascularization; after revascularization, one showed wall motion recovery, and three did not. Ejection fraction (EF) improvement after revascularization correlated best with the area of improved BMIPP uptake ($r = 0.84$, $p < 0.0005$). EF improvement also correlated with the area of improved reinjection ^{201}Tl uptake ($r = 0.54$, $p < 0.05$) and improved ^{201}Tl uptake at stress after revascularization ($r = 0.48$, $p < 0.05$). The area of discordant uptake of BMIPP less than reinjection ^{201}Tl uptake before revascularization was a good predictor of EF improvement after revascularization ($r = 0.58$, $p < 0.01$); however, the area of reversible ^{201}Tl defect was not ($r = 0.34$, $p = 0.15$). **Conclusion:** In patients with chronic coronary artery disease, functional improvement after revascularization is closely related to the recovery of BMIPP uptake. Discordant BMIPP uptake less than reinjection ^{201}Tl uptake is a potential predictor of functional recovery.

Key Words: fatty acid; thallium-201; coronary artery disease; revascularization

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Free fatty acids, carried by serum albumin from adipose tissue, are the predominant source of myocardial energy under normal aerobic conditions (*1–3*). In ischemic but viable myocardium, fatty acid metabolism is suppressed and the energy supply from glucose increases (*4,5*). Restoration of blood flow by percutaneous transluminal angioplasty or coronary artery bypass grafting has become an established therapeutic intervention for patients with coronary artery disease. Metabolic conditions in ischemic myocardium can recover after resolution of ischemia. PET with [^{18}F]fluorodeoxyglucose ([^{18}F]FDG) showed that the FDG uptake decreased after revascularization in patients with coronary artery disease (*6*). In canine myocardium, fatty acid metabolism, evaluated by [^{11}C]palmitic acid can recover gradually after transient ischemia (*7*). However, little is known about the changes in fatty acid metabolism before and after revascularization in patients with coronary artery disease.

Recently, the structurally modified fatty acid, [^{123}I]15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid ([^{123}I]BMIPP), has been proposed as a fatty acid probe for myocardial fatty acid utilization (*8–11*). Recent studies reported that decreased BMIPP uptake, compared with ^{201}Tl or ^{99m}Tc-sestamibi uptake, was observed, and these areas with discordant uptake showed ischemia on stress ^{201}Tl scintigraphy (*12–17*). In addition, wall motion abnormality was more severe in these discordant uptake regions in acute myocardial infarction and chronic coronary artery disease (*12,16*).

We hypothesized that fatty acid uptake in these ischemic segments would recover after resolution of ischemia by revascularization with improvement in regional and global function. This study was conducted to investigate the changes in fatty acid myocardial uptake using [^{123}I]BMIPP and the functional recovery in patients with chronic coronary artery disease before and after revascularization.

MATERIALS AND METHODS

Patients

Thirty-four consecutive patients who underwent BMIPP and ^{201}Tl myocardial SPECT before and after percutaneous transluminal angioplasty (n = 23) or coronary artery bypass surgery (n = 11) were evaluated. The study group was composed of 30 men and four women with chronic coronary artery disease, based on the following criterion: at least one major coronary artery stenosis (more than 75% luminal narrowing) without acute myocardial infarction (within 1 mo from the onset). Average age was 60 ± 10 yr, ranging from 32 to 77 yr. All patients underwent coronary angiography during the same hospital stay. Coronary arteriograms were read by at least two experienced angiographers, and the maximal luminal narrowing for each major coronary artery was estimated visually and classified by consensus. Nineteen patients had one-vessel disease, 11 had two-vessel disease and four had three-vessel disease. Fourteen patients had a history of old myocardial infarction. None of the patients had valvular heart disease or cardiomyopathy.

Radiopharmaceuticals

The [^{123}I]BMIPP used in this study was a commercially available product. Its radiochemical purity was more than 98%, and 111 MBq of [^{123}I]BMIPP (1.5 ml) contained 0.6 mg of carrier BMIPP (*16*).

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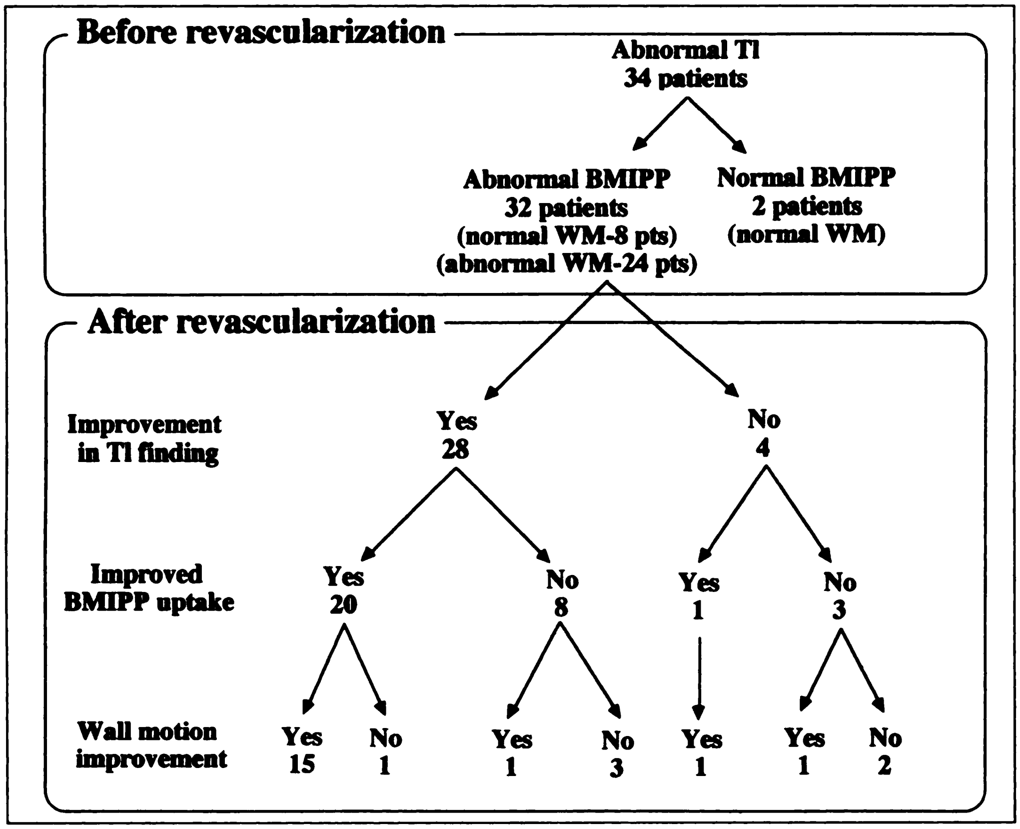

FIGURE 1. Changes in the BMIPP and thallium SPECT findings before and after revascularization are described in relation to the regional wall motion recovery. WM = wall motion.

SPECT

Intravenous bolus injection of 111 MBq [^{123}I]BMIPP was performed at rest. Each patient was instructed to fast overnight on the day of the BMIPP study. Data acquisition was started 20 min after radionuclide injection using a three-headed SPECT system, equipped with low-energy, high-resolution parallel-hole collimators, which covered up to 169 KeV with less than 5% septal penetration, and a dedicated nuclear medicine computer. The energy discrimination was centered on 159 KeV with a 20% window. A total of 60 projection images was obtained in a 128 × 128 matrix over 360°, with 30 sec per view. After reduction of the matrix size of the projection data to 64 × 64, a series of transaxial slices was reconstructed using a ramp filter with a Butterworth filter (order 8; cutoff frequency, 0.43 cycles/cm). Attenuation correction was not performed. Vertical long-axial and short-axial images were generated. BMIPP SPECT was repeated 2–3 wk after percutaneous transluminal angioplasty and 4–5 wk after bypass surgery (22 ± 9.9 days after revascularization).

Exercise-Reinjection Thallium-201 SPECT

Exercise stress ^{201}Tl SPECT was performed within 1 wk of BMIPP SPECT in 29 patients, and resting ^{201}Tl tomography was performed in five patients before and 17 ± 11 days after revascularization. No cardiac events occurred during the study period. Using a supine bicycle ergometer, exercise was started at 25 W and increased by 25 W every 2 min. Exercise was terminated when either severe chest pain, serious arrhythmia, electrocardiographic ST segment depression with more than 0.2 mV, and/or fatigue occurred. At peak exercise, 74 MBq ^{201}Tl was injected intravenously, and the patient was encouraged to continue exercising for an additional 1 min. Within 10 min of ^{201}Tl injection, SPECT data acquisition was started. In 21 patients, the same SPECT system used in BMIPP imaging was used for data acquisition and reconstruction except for the energy discrimination centered at 70 KeV with a 25% window. In the remaining patients, a dual-headed SPECT system with low-energy, high-resolution parallel-hole collimators was used for ^{201}Tl imaging. The energy discrimination was centered on 70 KeV with a 25% window. Data acquisition used 64 × 64 matrices with 60 projection images over 360° for 30 sec per image. Projection data were transferred to the system used for the BMIPP imaging, and transaxial, vertical long-axial and short-axial images were reconstructed using the same filter used in [^{123}I]BMIPP SPECT (ramp filter after Butterworth filtering (order 8; cutoff frequency, 0.43 cycles/cm)). Three hr after the initial injection, 37 MBq ^{201}Tl was reinjected at rest, and 10 min later, SPECT was performed with the same protocol used in exercise ^{201}Tl imaging. Attenuation correction was not performed.

Image Analysis

For the semiquantitative SPECT data analysis, two short-axial slices and a vertical long axial slice were selected for both BMIPP and ^{201}Tl images. Two short-axial slices from near the cardiac base and mid-to-apical portion were divided into eight segments each. The apex was divided into two segments (anterior and inferior) using the vertical long-axial image. Thus, there were 18 segments for each patient (*16*). Using a color-coded scale, BMIPP and ^{201}Tl uptake in each segment were scored semiquantitatively using a five-point grading system [0, normal (activity 70% or more of the maximal activity); 1, mildly reduced (activity between 70 and 55% of the maximal activity); 2, moderately reduced (activity between 55 and 45% of maximum); 3, severely reduced (activity between 45 and 30% of maximum); and 4, absent uptake (less than 30% of maximum)]. When the score in each segment was different for the two tracers and score improvement from stress to reinjection of ^{201}Tl was present, the segment was considered to show discordant uptake and fill-in, respectively. A difference of more than 10% between BMIPP and ^{201}Tl uptake and between stress and reinjection ^{201}Tl uptake values was required to consider discordant uptake and ^{201}Tl fill-in, respectively (*12,16,18*).

Regional Wall-Motion Analysis

To assess regional wall motion, gated blood-pool scintigraphy or two-dimensional echocardiography was performed within 1 wk of BMIPP SPECT before and 18 ± 10 days after revascularization. Twenty-six patients underwent gated blood-pool scintigraphy in the left anterior oblique projection and/or anterior projection after intravenous injection of 740 MBq ^{99m}Tc in vivo-labeled red blood cells. Cardiac cycle was divided into 24 frames. Eight patients underwent two-dimensional echocardiography before and after revascularization. The left ventricle was divided into nine segments in echocardiography (basal and distal anterior, septum, lateral, inferior and apex) and into nine segments in gated blood-pool scintigraphy (anterobasal, anterior, apex and inferior in anterior image, basal and distal septum, basal and distal lateral and inferoapical in the left anterior oblique image). Gated blood-pool scintigraphy and echocardiography were reviewed by two experienced observers, and the wall motion was visually graded into normal (score 0), mild hypokinesis (score 1), severe hypokinesis (score 2), akinesis (score 3) and dyskinesis (score 4) by consensus. When wall motion abnormality improved by at least one grade after revascularization, functional recovery was considered to be present. Left ventricular ejection fraction (EF) was calculated by gated blood-pool scintigraphy. After spatial and temporal smoothing, the left ventricular edge was detected by 65% threshold of maximal ventricular count in each frame before background subtraction. Left ventricular EF was obtained by dividing stroke counts by background corrected end-diastolic counts.

Relationship Between Thallium-201 and BMIPP Uptake and Wall Motion Recovery

All but four patients underwent revascularization to one coronary artery. The four exceptions underwent bypass surgery to two coronary arteries, which covered the areas with abnormal scintigraphic findings. Twenty-six left anterior descending coronary arteries, seven right coronary arteries and five circumflex coronary arteries were revascularized. BMIPP and ^{201}Tl uptake of the myocardium in each patient was defined as improved when at least two segments covered by the revascularized coronary artery showed recovery of uptake, and the improvement of the tracer uptake and wall motion was compared. In the four patients who underwent revascularization to two coronary arteries, tracer uptake and functional recovery were defined as positive when recovery was observed in at least one coronary artery territory in each patient. The septal segment was excluded from the regional wall motion analysis because of frequent postoperative paradoxical septal motion (*19,20*).

Statistical Analysis

The data are expressed as mean ± 1 s.d. For the analysis of EF change before and after revascularization, paired Student's t-test was used. Chi-square analysis was used to determine differences in the proportions of segments with improved BMIPP uptake after revascularization in relation to the presence or absence of discordant BMIPP and reinjection ^{201}Tl uptake before revascularization. Simple regression equations were calculated by the least-squares fitting; p values of less than 0.05 were considered to be significant.

TABLE 1
Relationship of Iodine-123-BMIPP and Reinjection Thallium-201 Defect Scores Before Revascularization

Reinjection Tl defect score	BMIPP defect score 0	1	2	3	4	Total
0	46	23	13	1	—	83
1	22	21	31	6	—	80
2	1	8	24	22	3	58
3	—	—	2	17	10	29
4	—	—	—	—	17	17
Total	69	52	70	46	30	267

Defect scores: 0 = normal; 1 = mildly reduced; 2 = moderately reduced; 3 = severely reduced; 4 = absent uptake.

TABLE 2
Relationship of Iodine-123-BMIPP and Reinjection Thallium-201 Defect Scores After Revascularization

Reinjection Tl defect score	BMIPP defect score 0	1	2	3	4	Total
0	116	28	7	4	—	155
1	5	20	17	8	—	50
2	—	2	9	23	1	35
3	—	—	—	7	7	14
4	—	—	—	—	13	13
Total	121	50	33	42	21	267

See Table 1 for defect scores.

RESULTS

All 34 patients showed abnormal stress or resting ^{201}Tl scintigraphy before revascularization, and abnormal BMIPP uptake was observed in 32 patients (Fig. 1). In 32 patients with reduced BMIPP uptake before revascularization, scintigraphic findings with ^{201}Tl improved in 28 patients (in 24 patients, stress-induced ischemia improved, and in four patients, resting ^{201}Tl scintigraphy improved) after revascularization. Of these 28 patients with improved ^{201}Tl uptake after revascularization, BMIPP uptake improved in 20 patients (71%). Wall motion abnormality was observed in 16 of these 20 patients before revascularization and 15 showed wall motion improvement after revascularization. In eight patients with improvement of ^{201}Tl findings and without improvement of BMIPP uptake, wall motion abnormality was observed in four patients before revascularization and one showed wall motion recovery, whereas three did not show recovery after revascularization. In four patients whose stress ^{201}Tl findings (n = 3) and resting ^{201}Tl (n = 1) did not improve, BMIPP uptake did not improve in three patients with improvement of wall motion in one patient and without improvement of wall motion in two patients after revascularization. In one patient without ^{201}Tl improvement, BMIPP uptake and wall motion abnormality improved (Fig. 1). The change of BMIPP findings after revascularization was 88% (21 of 24 patients) accurate in predicting postrevascularization improvement in regional wall motion [positive and negative predictive values are 94% (16 of 17) and 71% (5 of 7),

TABLE 3
Improvement of Iodine-123-BMIPP Uptake After Revascularization

Prerevascularization BMIPP defect score	Postrevascularization BMIPP defect score 0	1	2	3	4	Total
1	31 (15)	2 (8)	—	–	—	52 (23)
2	22 (17)	22 (12)	23 (14)	3 (1)	—	70 (44)
3	3 (3)	3 (3)	9 (5)	31 (18)	—	46 (29)
4	—	—	1 (1)	8 (7)	21 (5)	30 (13)
Total	56 (35)	46 (23)	33 (20)	42 (26)	21 (5)	198 (109)

Numbers in parentheses are the numbers of segments with discordant BMIPP uptake less than reinjection Tl before revascularization.

TABLE 4
Prerevascularization BMIPP and Reinjection Thallium Findings in Relation to Improvement of BMIPP Uptake After Revascularization

Defect score	Improvement of BMIPP uptake: Yes	No	Total
BMIPP > Tl	63 (64%)	46 (46%)	109
BMIPP ≤ Tl	36 (36%)	53 (54%)	89
Total	99 (100%)	99 (100%)	198

$p < 0.05$.

TABLE 6
BMIPP and Thallium Defect Scores in Relation to Wall Motion Scores After Revascularization

BMIPP and Tl defect score	Wall motion score: 0	1	2	3 or 4	Total
0	408/420	1/21	1/2	—	410/443
1	21/14	23/20	3/11	—/2	47/47
2	10/6	14/10	5/14	3/5	32/35
3	2/1	15/4	21/9	4/—	42/14
4	—	4/2	7/1	4/4	15/7
Total	441	57	37	11	546

Numbers of segments were expressed as BMIPP/Tl. See Table 5 for details. Septal segments were excluded from the analysis in patients with bypass surgery.

respectively]. On the other hand, the change of ^{201}Tl findings after revascularization was 75% (18/24) accurate in predicting postrevascularization improvement in regional wall motion [positive and negative predictive values are 80% (16 of 20) and 50% (2 of 4), respectively].

Before revascularization, in the myocardial segments that were successfully revascularized, a total of 267 segments were abnormal by exercise ^{201}Tl or reinjection ^{201}Tl or BMIPP images (Table 1). Discordant BMIPP uptake less than reinjection ^{201}Tl, observed in 109 segments, equally decreased uptake of both tracers in 89 and decreased reinjection ^{201}Tl uptake more than BMIPP uptake in 33. After revascularization, each pattern was observed in 95, 49 and 7 segments, respectively (Table 2). Table 3 shows the number of the segments with improvement in BMIPP uptake after revascularization. Abnormal BMIPP uptake improved more frequently in the segments with discordant BMIPP uptake less than reinjection ^{201}Tl (63 of 99 segments, 64%) than in the segments without discordant BMIPP uptake less than reinjection ^{201}Tl (46 of 99 segments; 46%) ($p < 0.05$) (Table 4).

Before revascularization, good correlation between the BMIPP and ^{201}Tl uptake and the regional wall-motion abnormality was observed ($r = 0.87$, $p < 0.001$ and $r = 0.84$, $p < 0.001$, respectively) (Table 5). After revascularization, BMIPP and ^{201}Tl uptake also correlated well with the regional wall motion ($r = 0.84$, $p < 0.001$ and $r = 0.74$, $p < 0.001$, respectively) (Table 6).

When only the patients with wall motion abnormality before revascularization were analyzed, EF increased from 48.7 ± 9.3% before revascularization to 53.6 ± 10.5% after revascularization($p < 0.001$). The area of discordant uptake of BMIPP less than ^{201}Tl before revascularization had a significant correlation with EF improvement after revascularization ($r = 0.58$, $p < 0.01$) (Fig. 2). The area of ischemic but viable myocardium demonstrated by ^{201}Tl fill-in with stress-reinjection scintigraphy before revascularization did not correlate with EF improvement ($r = 0.34$, $p = 0.15$). The area of concordantly decreased uptake of BMIPP and reinjection ^{201}Tl uptake did not correlate either with EF improvement ($r = 0.10$, $p = 0.69$). EF improvement after revascularization correlated best with the area of improved BMIPP uptake ($r = 0.84$, $p < 0.0005$) (Fig. 3). EF improvement after revascularization also correlated with the area of improved reinjection ^{201}Tl uptake ($r = 0.54$, $p < 0.05$) (Fig. 4) and improved ^{201}Tl uptake at stress after revascularization ($r = 0.48$, $p < 0.05$).

When myocardial viability was considered present, if ^{201}Tl showed reversible defects or more than 50% of maximal uptake in reinjection or resting images, positive and negative predictive values of ^{201}Tl scintigraphy for the improvement of the regional wall motion abnormality were 76% (13 of 17 patients) and 29% (2/7), respectively (Table 7). When discordant BMIPP uptake less than reinjection or resting ^{201}Tl was considered to be a sign of myocardial viability, positive and negative predictive values of combined BMIPP and ^{201}Tl scintigraphy for the wall motion

TABLE 5
BMIPP and Thallium Defect Scores in Relation to Wall Motion Scores Before Revascularization

BMIPP and Tl defect score	Wall motion score: 0	1	2	3 or 4	Total
0	400/399	13/25	1/4	—	414/428
1	17/31	28/29	6/20	1/—	52/80
2	18/6	18/6	29/31	5/15	70/58
3	1/—	6/5	25/13	14/11	46/29
4	—	—	10/3	20/14	30/17
Total	436	65	71	40	612

Numbers of segments were expressed as BMIPP/Tl. See Table 1 for defect scores. Wall motion scores: 0 = normal; 1 = mild hypokinesis; 2 = severe hypokinesis; 3 = akinesis; 4 = dyskinesis.

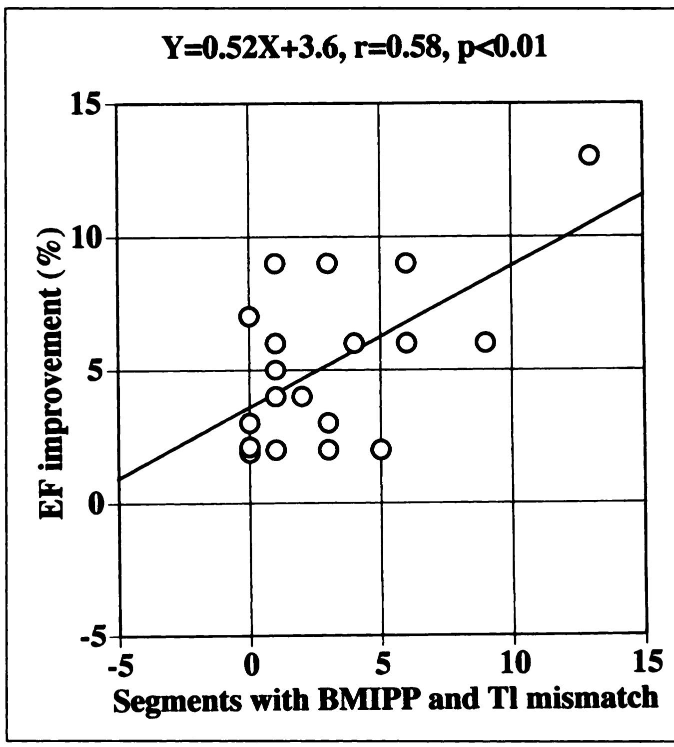

FIGURE 2. Relationship between the number of the segments with BMIPP and ^{201}Tl uptake mismatch (BMIPP uptake less than reinjection ^{201}Tl) before revascularization and EF improvement after revascularization is described.

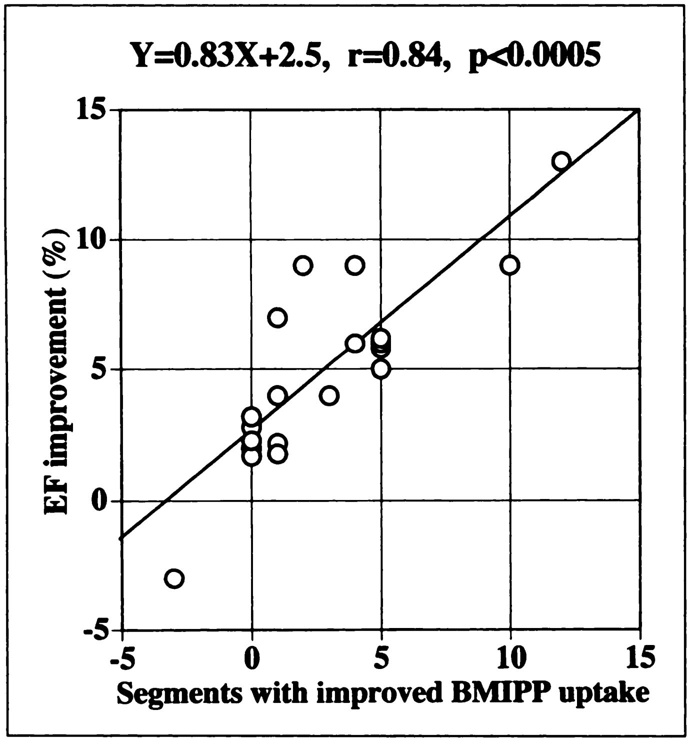

FIGURE 3. Relationship between the number of the segments with improved BMIPP uptake after revascularization and EF improvement after revascularization is described. There is an excellent positive correlation (r = 0.84).

recovery after revascularization were 85% (17 of 20 patients) and 75% (3/4), respectively (Table 8).

A representative case is shown in Figure 5. A 59-yr-old man with angina pectoris shows reversible ^{201}Tl defect in inferolateral wall. BMIPP uptake is more severely decreased in inferolateral wall than reinjection ^{201}Tl (Fig. 5A). Gated blood- pool

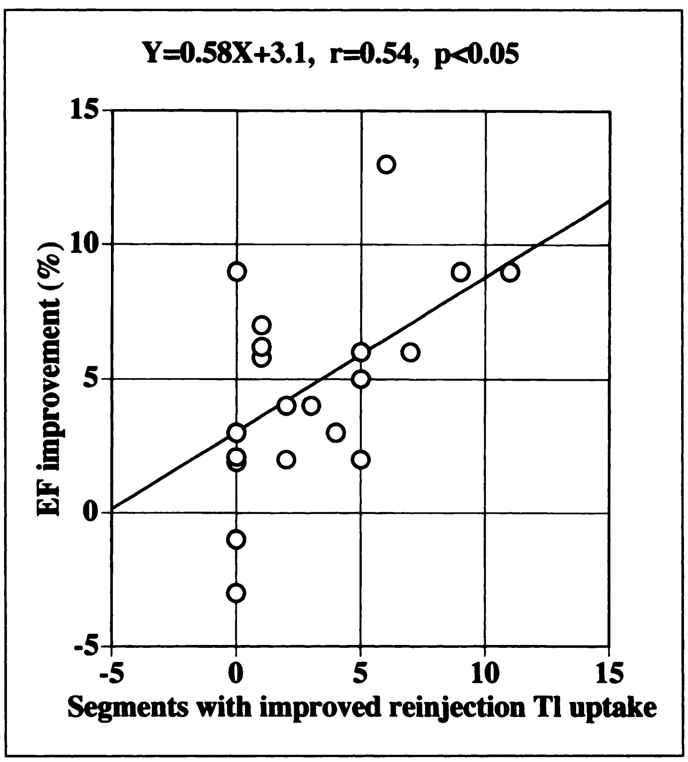

FIGURE 4. Relationship between the number of the segments with improved reinjection ^{201}Tl uptake after revascularization and EF improvement is described.

TABLE 7
Relationship Between Prerevascularization Thallium Findings and Regional Wall-Motion Improvement After Revascularization

Prerevascularization viability in Tl study	Wall motion after revascularization: Improved	Wall motion after revascularization: Not improved	Total
Positive	13 (76%)	4 (24%)	17
Negative	5 (71%)	2 (29%)	7
Total	18	6	24

Positive viability in Tl study was defined as when Tl defect was reversible or percent uptake was more than 50% of maximal uptake.

scintigraphy showed inferolateral hypokinesis (Fig. 5B). After bypass surgery to the right coronary artery and the left anterior descending coronary artery, stress-induced ischemia improved, and BMIPP uptake recovered (Fig. 5A). Wall motion abnormality in inferolateral wall also improved after revascularization (Fig. 5B).

DISCUSSION

Our results showed that BMIPP uptake was reversible after resolution of ischemia by revascularization, indicating that impaired fatty acid utilization is reversible. In addition, discordant uptake of BMIPP less than reinjection ^{201}Tl was a predictor of EF and regional wall motion improvement after revascularization, and ventricular functional recovery, expressed as EF improvement, correlated more closely with the area with improved BMIPP uptake than the area with improved ^{201}Tl uptake at stress and reinjection, suggesting that ventricular function was more closely related to metabolic status than perfusion.

Metabolic Abnormality Due to Ischemic Injury and BMIPP Uptake

Fatty acid metabolism is very sensitive to ischemia. In ischemic myocardium, oxidation of fatty acid is significantly suppressed, and glucose metabolism is augmented (*21–23*). BMIPP, a methyl-branched fatty acid analog, is hardly metabolized by beta-oxidation and therefore is suitable for tomographic imaging because of its prolonged myocardial retention. Myocardial BMIPP uptake is initially dependent on regional perfusion and is rapidly incorporated into triglycerides through the enzymatic conversion to BMIPP-CoA (*9*). The concentration of adenosine-5′-triphosphate, which is required in the first step of the common pathway of fatty acid metabolism, correlates closely with BMIPP accumulation (*24*). Our previous study with dynamic SPECT demonstrated that the BMIPP washout was observed early after BMIPP injection (2–6 min after injection) in the segments with reversible ^{201}Tl defects but not in the segments with normal ^{201}Tl uptake and fixed ^{201}Tl defects (*15*). In addition, early dynamic SPECT images in

TABLE 8
Relationship Between Prerevascularization Thallium and BMIPP Findings and Regional Wall-Motion Recovery After Revascularization

Prerevascularization score	Wall motion after revascularization: Improved	Wall motion after revascularization: Not improved	Total
BMIPP > Tl	17 (85%)	3 (15%)	20
BMIPP ≤ Tl	1 (25%)	3 (75%)	4
Total	18	6	24

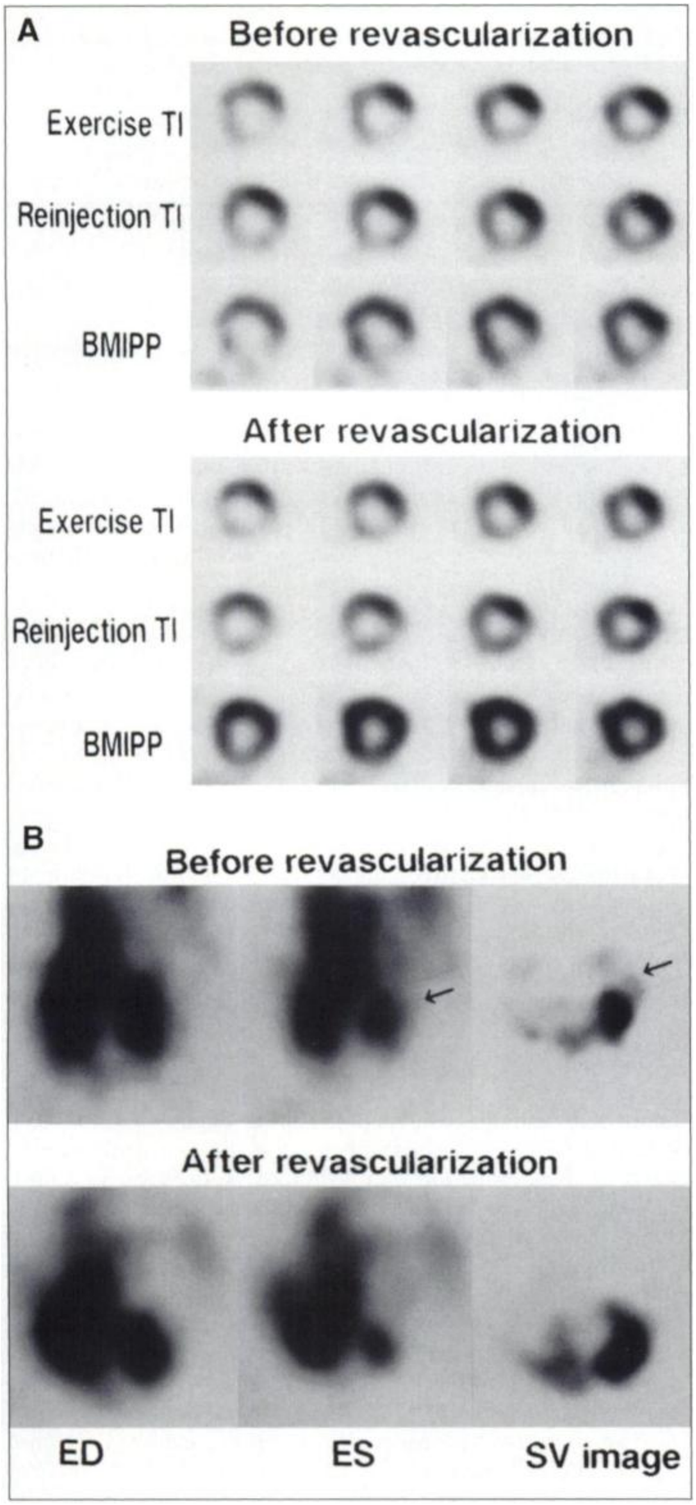

FIGURE 5. Exercise-reinjection ^{201}Tl and [^{123}I]BMIPP scans (A) and gated blood-pool scintigraphy with stroke volume (SV) image (B) before and after revascularization are shown. Inferolateral wall shows reversible ^{201}Tl defect with discordantly decreased BMIPP uptake less than reinjection ^{201}Tl (A). Hypokinesis is observed in this area (arrows) (B). After bypass surgery to the right coronary artery and the left anterior descending coronary artery stress-induced ischemia improved, and BMIPP uptake recovered (A). Wall motion abnormality in inferolateral wall also improved after revascularization (B).

ischemic heart disease showed similar BMIPP uptake with ^{201}Tl in spite of the discordant BMIPP uptake less than ^{201}Tl in 30-min BMIPP images (*25*). These data suggest that, in ischemic myocardium, just after the distribution of BMIPP to myocardium dependent on blood flow, back-diffusion of free BMIPP, which was not incorporated into the triglyceride pool, may occur and may show discordant BMIPP uptake less than ^{201}Tl in the usual images obtained at 20–30 min after BMIPP injection. A PET study demonstrated that the myocardium with discordant BMIPP uptake less than ^{201}Tl showed a higher clearance rate constant of [^{11}C]acetate and FDG-to-perfusion ratio than the myocardium with concordantly reduced BMIPP and ^{201}Tl uptake, indicating that BMIPP uptake provided metabolic information independent of ^{201}Tl uptake (*26*). In acute myocardial infarction, BMIPP uptake and myocardial perfusion agents at rest showed discordant uptake, with BMIPP uptake usually more depressed than ^{201}Tl or ^{99m}Tc-sestamibi (*12–14*). We previously reported that, in ischemic myocardium demonstrated by a reversible defect on exercise-reinjection ^{201}Tl imaging, BMIPP uptake frequently decreased more discordantly than reinjection ^{201}Tl (*16*). In addition, in ischemic myocardium, wall motion abnormality was more severe in the myocardium with discordant BMIPP uptake less than reinjection ^{201}Tl than in myocardium without discordant uptake less than ^{201}Tl, suggesting that fatty acid utilization was more impaired in severe wall-motion abnormality, even if ^{201}Tl uptake was not severely depressed.

Reversibility of Metabolic Alteration and Function after Resolution of Ischemia

Impaired myocardial metabolism induced by ischemia should be reversible (*6,27,28*). Schwaiger et al. (*27*) showed that, after transient ischemia in a dog model that is considered representative of stunned myocardium, metabolic abnormality demonstrated by PET imaging with [^{11}C]palmitic acid recovered slowly paralleled by slow functional recovery for 4 wk. Metabolic indices recovered most markedly between 24 hr and 1 wk after reperfusion, in parallel with the time course of functional recovery. However, in chronic dysfunctional myocardium due to chronic ischemia, which is referred to as hibernating myocardium, the time course of the metabolic and functional recovery after restoration of ischemia is not fully known. In an animal experiment in which 5-hr nontransmural ischemia was induced by partial coronary artery stenosis, regional dysfunction persisted for at least 3 days after resolution of ischemia (*29*). Regional dysfunction in patients with chronic ischemia has been shown to recover immediately or several days after bypass surgery or angioplasty (*30–33*). However, hibernating myocardium, once revascularized, may go through a phase of stunning before full functional recovery, or hibernation itself may be partially caused by repetitive episodes of stunning rather than chronic hypoperfusion. In one study, patients with noninfarcted collateral-dependent myocardium with chronically depressed wall motion abnormality meeting the criteria for hibernation showed markedly blunted flow reserve and marked ultrastructural alterations in spite of nearly normal resting flow and oxygen consumption, suggesting that repeated episodes of ischemia may account for impaired function (*34*). Little is known about metabolic recovery after revascularization for chronic ischemia. Clinically, increased FDG uptake in ischemic myocardium decreased 5–7 wk after restoration of blood flow by bypass surgery, associated with improvement of wall motion abnormality (*6*). In this study, 2–5 wk after revascularization, in patients with improvement of ischemia, wall motion abnormality improved in most of the patients with fatty acid uptake improvement (15 of 16 patients); however, asynergy did not improve in five of the seven patients without improvement of fatty acid uptake. Furthermore, EF improvement after revascularization correlated more closely with the number of segments with improved fatty acid uptake ($r = 0.84$) than the area of improved reinjection ^{201}Tl uptake ($r = 0.54$) and the area of

^{201}Tl uptake at stress (r = 0.48), suggesting that wall motion recovery correlated more closely with metabolic recovery than perfusion recovery.

Prediction of Functional Recovery

Treatment of coronary artery disease is directed toward the elimination of ischemia and functional recovery. Positron emission CT, with the combination of [^{13}N]ammonia and FDG, is directed toward the evaluation of perfusion and of metabolism-predicted functional recovery after bypass surgery, respectively (*35*). Most of the myocardial segments with wall motion abnormality with normal or decreased perfusion and normal or increased FDG uptake showed functional recovery after bypass surgery. FDG-PET and BMIPP SPECT studies demonstrated that the myocardial areas with BMIPP uptake less than ^{201}Tl correlated with an increase in FDG uptake, whereas most of the segments with concordant decrease of BMIPP and ^{201}Tl uptake did not show increased FDG uptake (*36*). Then, discordant BMIPP uptake less than ^{201}Tl (perfusion) may indicate substrate change from fatty acid to glucose and may offer similar information obtained by PET as relatively increased FDG uptake than perfusion. If so, areas with discordant BMIPP uptake less than ^{201}Tl may indicate potentially reversible ischemic myocardium and functional abnormality. In patients with acute myocardial infarction, BMIPP and perfusion mismatch was a predictor of wall motion recovery (*37,38*). In this study, in patients with chronic coronary artery disease, the area of the discordant BMIPP uptake less than reinjection ^{201}Tl was able to predict EF improvement after revascularization, whereas the area with reversible ^{201}Tl defect did not. These data are not surprising because the viable myocardium, demonstrated by reversible ^{201}Tl defect, showed a variety of functional statuses at rest, and resting function is supposed to correlate with resting perfusion (^{201}Tl uptake at rest) and metabolic condition (BMIPP uptake), rather than ^{201}Tl defect at exercise and reversibility.

Possible Limitations

In this study, we used reinjection ^{201}Tl images after exercise as perfusion images under resting conditions instead of a resting ^{201}Tl image. It is considered that the ^{201}Tl reinjection image represents the summation of the resting perfusion image and 3-hr redistribution images after exercise. However, previous reports demonstrated that the reinjection images were quite similar to resting images (*39,40*), and reinjection ^{201}Tl images and resting ^{201}Tl images were identical in the same 28 patients (*41*).

Data acquisition of ^{201}Tl scintigraphy was performed with triple-headed and dual-headed SPECT systems. However, phantom studies that compared both SPECT systems showed no significant difference in defects (1 and 2 cm in diameter) detectability or severity (data not presented) when 64×64 matrix data were used for reconstruction.

The distribution of the ^{201}Tl in inferior, posterior and lower septum is substantially more underestimated than that of ^{123}I by photon attenuation because the photon energy of ^{201}Tl is lower than that of ^{123}I. Thus, careful comparison should be done in evaluating the uptakes of the two tracers in these areas. In this study, most of the discordant reinjection ^{201}Tl uptakes less than BMIPP were observed in inferior, posterior and lower septum, which might be due to the differences in attenuation between the tracers rather than any difference in the true distribution of the tracers in some cases.

We compared wall motion, evaluated by two-dimensional ECG-gated blood-pool scintigraphy, and BMIPP and ^{201}Tl uptake, obtained by SPECT, in most of the patients. There might be intrinsic limitations in comparing two-dimensional wall motion data and three-dimensional scintigraphic data.

CONCLUSION

In patients with chronic coronary artery disease, BMIPP uptake was reversible after restoration of ischemia, and functional improvement after revascularization was more closely related to the recovery of BMIPP uptake than to the improvement of stress ^{201}Tl uptake and reinjection ^{201}Tl uptake. Discordant BMIPP uptake, less than reinjection ^{201}Tl, was a predictor of global and regional functional recovery.

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Technetium-99m-MIBI Myocardial SPECT: Supine Versus Right Lateral Imaging and Comparison with Coronary Arteriography

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Myocardial perfusion SPECT using the prone position improves inferior wall counts and decreases motion problems as compared with the usual supine position. Nonetheless, it is not suitable for women. In addition, it is associated with artifactual anteroseptal defects and hot spots. **Methods:** The right lateral (RL) position was evaluated instead of the prone position in 72 patients (26 women). RL imaging was performed immediately after the supine imaging during a routine 2-day ^{99m}Tc-sestamibi exercise protocol. The SPECT images were scored semiquantitatively by three physicians. Moreover, regional myocardial counts, as well as extent and severity of defects, were assessed by quantitative polar map analysis. **Results:** All patients tolerated the RL position well and there was no significant patient movement in either position. Higher inferior myocardial counts per pixel were observed in the RL than in supine images. Inferior wall defects (especially mild ones) were more common in the supine than the RL images, whereas defects in other regions were not different. Quantitative analysis confirmed these findings. Analysis of 34 patients with recent coronary arteriography revealed an overall coronary artery disease (CAD) supine- and RL-imaging specificity of 50% and 75%, respectively, and the sensitivities of both were 93%. Right CAD sensitivity, specificity and normalcy rates for the supine position were 100%, 44% and 55%, whereas those of the RL position were 94%, 75% and 90%, respectively. **Conclusion:** The RL position improves CAD diagnostic accuracy, particularly right CAD, without significant artifacts in other myocardial regions. Unlike the prone position, the RL position is well tolerated by both women and men.

Key Words: technetium-99m-sestamibi; SPECT; myocardial perfusion; right lateral

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SPECT perfusion myocardial imaging is an accurate technique not only for the diagnosis of coronary artery disease (CAD) but also for the evaluation of the site and extent of jeopardized myocardium (*1–3*). Inferior wall attenuation by the left hemidiaphragm is a considerable problem that seriously contributes to imaging artifacts and the potential decrease of diagnostic accuracy (*4–10*). Image acquisition with patients in the prone position was promoted by some investigators to improve inferior wall counts (*11–14*), in addition to reducing motion problems when patients are unable to tolerate the supine position (*15*). The drawbacks of this method are contrasting septal artifacts as well as photon attenuation by the imaging table, unless a specially designed table is used. Furthermore, this technique is not suitable for women. Another method using the semidecubital position also requires a specially constructed imaging table and has yet to be proven (*16,17*).

The increased interest in attenuation correction and gated SPECT techniques to routinely eliminate attenuation artifacts reflects the importance of this common problem. Nonetheless, these new sophisticated methods are technically demanding and not widely accessible. A simple solution requiring no costly modifications or sophisticated new equipment is not yet available.

This study evaluated the ability of right lateral (RL) SPECT imaging to resolve inferior wall-count attenuation, explored whether this method could create any new artifacts and assess whether CAD diagnostic accuracy improves with this technique.

MATERIALS AND METHODS

Patient Population

We evaluated 72 patients (46 men, 26 women; mean age 50.0 ± 11.5 yr) who were scheduled for routine exercise ^{99m}Tc-sestamibi myocardial perfusion studies. Twenty patients had a low likelihood

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