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Prognostic values of perfusion-metabolic mismatch in Tl-201 and BMIPP scintigraphic imaging in patients with chronic coronary artery disease and left ventricular dysfunction undergoing revascularization

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Objectives: The aim of this study was to assess the prognostic value of the amount of perfusion-metabolic mismatch in revascularized patients with left ventricular (LV) dysfunction by means of Thallium (Tl)-201 and BMIPP imaging. ***Methods:*** Seventy-six patients with LV dysfunction and coronary artery disease underwent Tl-201 and BMIPP imaging. They were revascularized with either coronary artery bypass graft or balloon angioplasty and were entered into this study. To quantify the amount of perfusion-metabolic mismatch, SPECT images were displayed as polar maps and analyzed semiquantitatively. The patients were followed up for a mean period of 32 months for cardiac mortality and non-fatal cardiac events. Standard follow-up left ventriculography was performed 6 to 12 months after revascularization. ***Results:*** Thirty-two patients exhibited a large amount of perfusion-metabolic mismatch (≥ 7 segments, group A), 28 patients had a small amount of perfusion-metabolic mismatch (2 to 6 segments, group B), and 16 patients were found to have no perfusion-metabolic mismatch (group C). Similar pre-revascularization LVEF of 35 ± 5%, 34 ± 8% and 36 ± 6% increased to 45 ± 8% ($p < 0.0001$), to 38 ± 8% ($p < 0.05$), and to 36 ± 3% (n.s.), respectively, after revascularization. The functional improvement after revascularization in group A was accompanied by a low rate of cardiac events during follow-up and better cardiac event free survival as judged by the Kaplan-Meier method ($p < 0.05$, vs. group B and C). ***Conclusion:*** In revascularized patients with severe LV dysfunction, the presence of a large amount of perfusion-metabolic mismatch evaluated by Tl-201 and BMIPP imaging identifies patients with the best prognosis.

Key words: fatty acid metabolism, left ventricular dysfunction, viability, revascularization, long-term prognosis

INTRODUCTION

THE EXTENT of myocardial viability in patients with chronic coronary artery disease (CAD), previous myocardial infarction (MI), and reduced left ventricular systolic function has both prognostic and therapeutic significance. Its assessment is therefore important in the clinical treatment of such patients, especially when a revascularization procedure is being considered. Nevertheless, such viable metabolically active but dysfunctional myocardium represents an unstable substrate that is likely to lead to ischemic events. Recent studies have repeatedly suggested that Thallium (Tl)-201 imaging may be useful in the prediction of functional recovery after revascularization.[1–5] It has also been demonstrated that the presence of hypoperfused but viable myocardium at Tl-201 scintigraphy is a powerful predictor of subsequent cardiac events and gives incremental prognostic information in patients with chronic CAD. In addition, previous data acquired with rest Tl-201 scintigraphy or myocardial fatty acid metabolism imaging by iodine-123-labeled 15-*p*-iodephenyl-3 (*R,S*)-methylpentadecanoic acid (BMIPP) indicate that improvement in global LV systolic function

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is related to the anatomical extent of myocardial viability, as assessed preoperatively.[6–12] But, to date, there are no reports on the influence of the amount of perfusion-metabolic mismatch between Tl-201 and BMIPP uptake on long-term prognosis of revascularized patients with CAD and left ventricular dysfunction. Because left ventricular systolic function is known to be an important predictor of survival in patients with CAD, one can await the prognostic impact of the quantification of the amount of perfusion-metabolic mismatch by using both myocardial perfusion and fatty acid metabolism imaging. This study was therefore designed to assess the prognostic value of the amount of dysfunctional myocardium as indicated by Tl-201 and BMIPP single photon emission tomography (SPECT) in revascularized patients with CAD and left ventricular dysfunction.

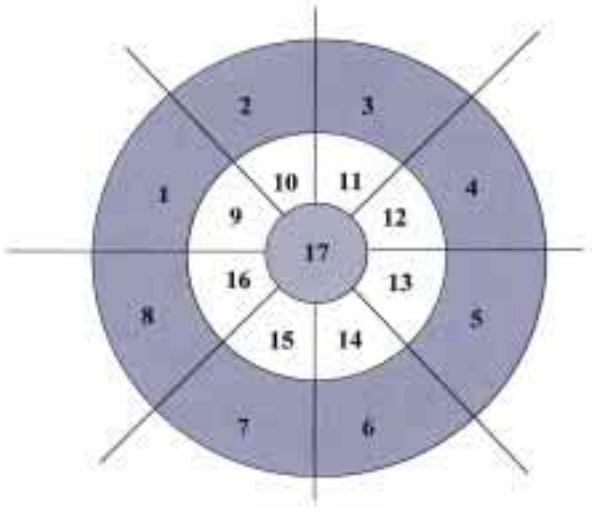

Fig. 1 Polar maps were divided into 17 segments.

MATERIALS AND METHODS

Patients. From among the patients with chronic CAD and left ventricular dysfunction referred to our laboratory for the evaluation of myocardial viability, 93 consecutive patients for whom coronary revascularization had been planned were included in the study. Exclusion criteria were: recent (<3 months) myocardial infarction or unstable angina, heart disease other than coronary artery disease, or a history of prior revascularization procedures.

The study protocol included the performance of Tl-201 and BMIPP SPECT before revascularization. All major epicardial branches with significant stenosis underwent revascularization, by coronary artery bypass grafting (CABG) in 43 cases and by percutaneous transluminal coronary angioplasty (PTCA) in the remaining 50 patients. One patient with perioperative myocardial infarction was excluded by using the usual clinical, enzymatic and electrocardiographic criteria. At least 6 to 12 months later, follow-up left ventriculography was performed to evaluate the evolution of regional and global left ventricular function. In patients treated with PTCA, 16 patients with restenosis were excluded on the basis of follow-up angiography. Informed consent for participation in the study was obtained from all patients. The Ethics Committee of our institution had previously approved the study. Finally, 76 patients were enrolled in the present study.

Coronary angiography. Coronary angiography was performed with the transfemoral or transbrachial technique. Percent diameter stenosis was evaluated with automated edge detection. Vessels showing >50% lumen reduction were considered diseased.

Image protocol. Before revascularization, all patients underwent Tl-201 and BMIPP SPECT in random order within 1 week. For all acquisitions, SPECT data were obtained at 6° increments for 30 sec per increment during a 180° rotation from the 45° left anterior oblique to the 45° right anterior oblique view with a large-field-of-view rotating gamma camera, a high-resolution, parallel-hole collimator and a minicomputer (Shimadzu SNC5100R/Scintipac 24000, Tokyo, Japan). The data were in a 64- × 64-word matrix nuclear medicine computer system. After transaxial reconstruction with a filtered backprojection algorism, short-axis, vertical long-axis and horizontal long-axis tomograms were obtained without attenuation correction, and circumferential profile analysis was performed. In each patient, scintigraphic studies were analyzed by the same methods by observers who were unaware of the angiographic findings.

Myocardial perfusion imaging: To delineate regional myocardial perfusion, a Tl-201 SPECT was performed under resting conditions. The imaging was started 10 min after intravenous injection of 111 MBq of Tl-201.

BMIPP imaging: BMIPP was prepared and supplied by Nihon Medi-Physics Co., Ltd. It contained 111 MBq of I-123 labeled 15-*p*-iodophenyl-3-*R,S*-methyl pentadecanoic acid (0.6 mg) dissolved in 10.5 mg of ursodeoxycholic acid. SPECT was performed 20–30 min after administration of 111 MBq of BMIPP at rest with the patient in a fasting state for more than 3 hrs.

Image analysis. Semiquantitative analysis of the SPECT data was performed. Circumferential count profiles (60 radii, highest pixel activity/radius) were generated from the Tl-201 and BMIPP short axis slices, discarding the slices containing the outflow tract. Apical activity was measured from a vertical long axis tomogram. The available slices were presented in a polar map. The polar maps were divided into 17 segments (Fig. 1). Each polar map was normalized for peak activity (100%). If the activity of Tl-201 was less than 50%, the uptake was considered severely reduced. We evaluated the number of segments

in severely reduced Tl-201 uptake. In addition, when BMIPP uptake exceeded Tl uptake by 8.5% in the septal region and by 7% in the remaining left ventricular region, the myocardial segment was classified as a perfusion-metabolic mismatch. The threshold was documented by Tamaki et al.[16] in the previous report.

Follow-up. After coronary revascularization, all patients were followed up by contact with the treating physician in 1- to 3-month intervals. The patients were followed up for cardiac mortality and nonfatal cardiac events including MI, unstable angina pectoris (AP) requiring hospitalization, and hospitalization for heart failure. MI was defined as a hospital admission for prolonged chest pain, electrocardiographic changes and an increase in plasma cardiac enzyme activity. Unstable AP was defined by resting anginal symptoms requiring hospitalization with parental nitrates and/or heparin therapy. Heart failure requiring hospitalization was identified by dyspnea, need for intravenous inotropic and/or diuretic therapy. The mean follow-up period was 32 ± 18 months.

Table 1 Baseline patient characteristics

	Group A (n = 32)	Group B (n = 28)	Group C (n = 16)
Men	30	26	15
Age (yr)	58 ± 8	60 ± 8	59 ± 7
Previous history			
Myocardial infarction	26	20	15
Stable angina	22	22	12
Hypertension	12	14	7
Diabetes	16	17	10
Hyperlipidemia	9	8	4
Smoking	12	9	3
Extent of vessels			
Single vessel disease	4	3	3
Multiple vessel disease	26	23	12
Left main disease	2	2	1
Revascularization method			
CABG	18	14	10
PTCA	14	14	6
No. of segments in severely reduced Tl-201 activity	7.4 ± 2.2	6.9 ± 3.3	8.8 ± 4.2

Values are expressed as number of patients or mean ± S.D.
CABG: coronary artery bypass grafting surgery
PTCA: percutaneous transluminal coronary angioplasty

Statistical analysis. To define the cutoff for differentiating between groups with large and small amounts of perfusion-metabolic mismatch, five criteria were tested to best discriminate these two groups according to the risk of developing cardiac events. By means of the Fisher exact test, the cutoff value of seven perfusion-metabolic mismatching segments was found to have the greatest statistical power for stratification. The lower cutoff values five and six were not able to discriminate the group with increased risk of developing cardiac events. Furthermore, we actually defined three groups based on this cutoff value. Group A consisted of patients with a large amount of perfusion-metabolic mismatch (≥ 7 segments); group B included patients with a small amount of perfusion-metabolic mismatch (2 to 6 segments); and group C comprised patients with no mismatch segments. Clinical data are given as the mean ± SD for continuous variables or as a number (percent) for categorical variables. Comparisons were performed for group A, B and C, for systolic functional parameters before and after revascularization. Differences in continuous variables were tested

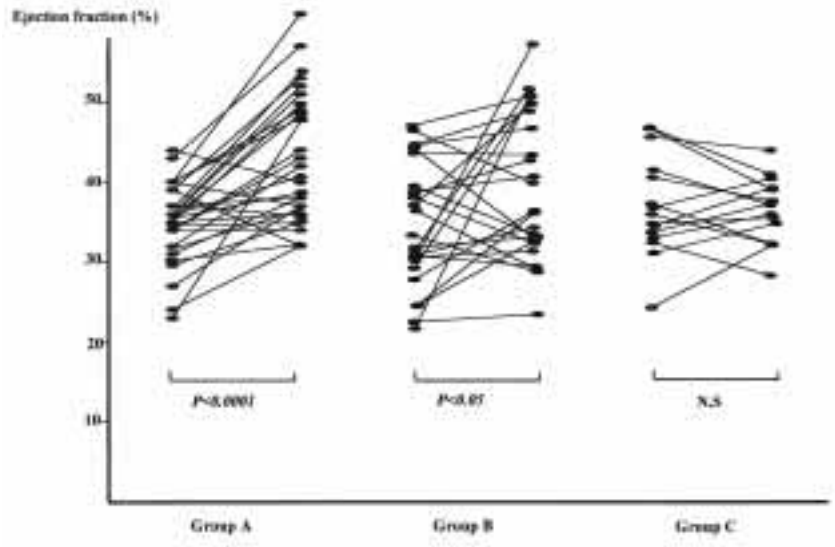

Fig. 2 Left ventriculography results of groups A, B and C. In patients with a large amount of perfusion-metabolic mismatch (group A), the ejection fraction was the greatest improvement in postrevascularization LV systolic function.

by Mann-Whitney or Wilcoxon tests; differences in categoric variables were evaluated using the chi-square test with Yates correction or Fisher exact test. The Cox proportional hazard model was utilized to analyze the relationship between cardiac event-free survival and the following variables potentially relating to the patients' prognosis: the presence of a large amount of perfusion-metabolic mismatch, age, the type of revascularization, pre-revascularization LVEF, and the number of segments in severely reduced Tl-201 activity. The hazard ratio and the corresponding 95% confidence intervals (CI) of these risk factors were also calculated. In addition, Kaplan-Meier time to event curves were used to estimate the absolute risk of cardiac event in group A, B and C. A p-value < 0.05 was considered significant.

Table 2 Cardiac events in group A, B and C patients

	group A	group B	group C
Cardiac events within 30 days after revascularization			
Death	0	1	1
non-fatal MI	0	0	0
Late cardiac events			
Death	0	1	2
non-fatal MI	1	1	0
unstable angina	1	2	1
hospitalization for CHF	0	2	4
Sum of cardiac events	2	7	8
Non-cardiac death	1	0	0

Values are expressed as number of patients.
MI: myocardial infarction, CHF: congestive heart failure

Table 3 Ranked independent predictors of cardiac events by Cox multivariate analysis

Variables	χ^2	RR	95% CI	p-Value
No. of perfusion-metabolic mismatch segments	8.28	0.740	0.603–0.909	0.004
Age	0.019	1.005	0.936–1.079	0.891
CABG	1.983	0.465	0.161–1.349	0.465
LVEF	2.983	1.085	0.989–1.191	0.084
No. of segments in severely reduced Tl-201 activity	0.409	1.057	0.891–1.254	0.523

RR: relative risk, CI: confidence interval

RESULTS

Baseline characteristics. Based on the number of perfusion-metabolic mismatches assessed with Tl-201 and BMIPP SPECT, the patients were divided into three groups. Group A consisted of 32 patients with a large amount of perfusion-metabolic mismatch. The mean number of perfusion-metabolic mismatches was 7.8 ± 1.6 (range, 7 to 13). Group B contained 28 patients with a small amount of perfusion-metabolic mismatch. The mean number was 3.2 ± 1.6. Group C was composed of 16 patients with no perfusion-metabolic mismatch. The baseline and post-revascularization characteristics of the three groups are shown in Table 1. There were no significant differences in age, gender distribution, occurrence of risk factors for CAD, extent of diseased coronary arteries, type of revascularization method, post revascularization medication, the number of segments in severely reduced Tl-201 activity or any other variables potentially related to patient prognosis.

Clinical and functional postrevascularized outcome. Figure 2 represents a comparison of left ventriculographic variables before and 6 to 12 months after revascularization.

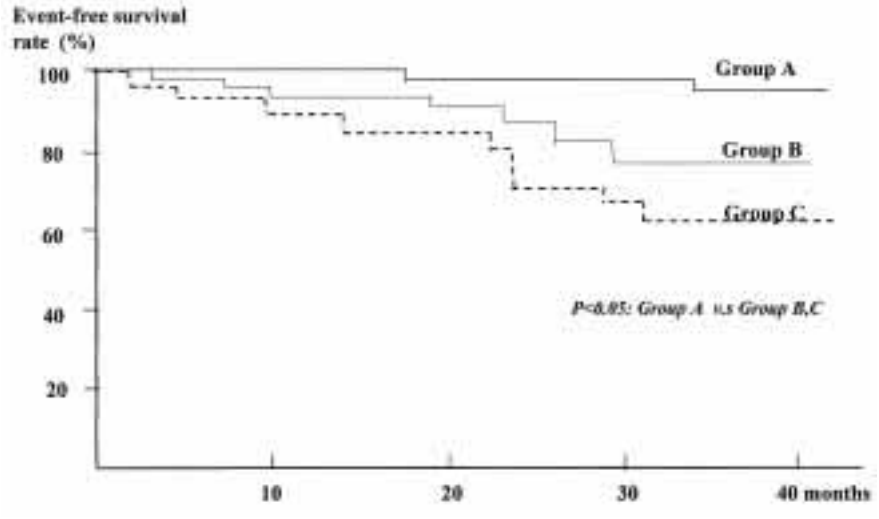

Fig. 3 Kaplan-Meier curve showing survival free of cardiac events (including death, nonfatal MI, unstable AP and hospitalization for heart failure) in groups A, B and C. Event free survival was significantly better in group A than in groups B or C, both being $p < 0.05$.

Similar prerevascularization left ventricular ejection fraction of 35 ± 5%, 34 ± 8%, 36 ± 6% increased to 45 ± 8% ($p < 0.0001$), to 38 ± 8% ($p < 0.05$) and to 36 ± 3% (n.s), respectively, after revascularization. Improvement in left ventricular systolic function was significantly greater in patients with a large amount of perfusion-metabolic mismatch.

Early and late postrevascularized outcome. There were 2 (in groups B and C) in-hospital deaths, resulting in an early postoperative mortality rate of 2.6%. In one case in group C, death was due to refractory congestive heart failure and the inability to wean from inotropic support. In the case of group B, sudden death occurred on postoperative day 8 after an otherwise uneventful postoperative course. Among hospital survivors, the mean period of follow-up was 32 ± 14 months. Four additional deaths occurred during follow-up. One death in group A was due to a noncardiac cause (lung cancer). Of the 3 remaining deaths, 2 (in group B and C) resulted from refractory congestive heart failure and one in group C was sudden cardiac death 13 months after PTCA. In addition, of the 70 remaining survivors, 12 patients suffered major cardiac events except death. They consisted of 2 events in group A, and 5 events each in groups B and C. The detailed characteristics of these major cardiac events are shown in Table 2.

Results of Cox multivariate analysis are reported in Table 3. In this Cox model stepwise elimination with the presence of a large amount of perfusion-metabolic mismatch forced in the first step was performed.

The major cardiac event rate was significantly lower in patients with a large amount of perfusion-metabolic mismatch (group A) than in the other patients (group B and C). This observation is in accord with the Kaplan-Meier event-free survival analysis in group A rather than in groups B and C (both $p < 0.05$). There were no differences between groups B and C in event-free survival (Fig. 3).

DISCUSSION

The findings of the present study demonstrate that application of discriminate analysis that combines the information provided by Tl-201 and BMIPP scintigraphic imaging was valuable as the predictor of prognosis in patients with chronic coronary artery disease, and in selecting those patients in whom substantial improvement in global left ventricular function may be obtained. In patients with a large amount of perfusion-metabolic mismatch, it is believed that there is more pronounced functional improvement after revascularization and probably better prognosis than in those having only a small amount or no such mismatch.

Detection of viable myocardium by radionuclide imaging. Recent studies have demonstrated that Tl-201 imaging is useful in the identification of viable myocardium in patients with chronic ischemic LV dysfunction.[1–5] But, Tl-201 imaging has shown to have very high sensitivity but suboptimal specificity.[4] It is also to be noted that the common use of Tl-201 data in a binary fashion is a practical but restrictive interpretation of the continuous pathophysiological relationship that exists between Tl-201 uptake and improvement of systolic function after revascularization. In the present study, a clear relationship was not found between the number of segments in severely reduced Tl-201 activity and systolic function after revascularization. These findings indicate that the dyssynergic regions with severely reduced uptake of Tl-201 contain a considerable amount of jeopadized myocardium.

On the other hand, it is conceivable that better identification of viability may be derived from a combined evaluation of metabolic and functional information. In addition to the assessment of perfusion and sarcolemmal function by thallium activity, myocardial fatty acid metabolism was evaluated with BMIPP imaging. Myocardial BMIPP activity is proportional to the intracellular ATP level,[14] and reduced myocardial activity of BMIPP is a sensitive indicator of ischemic stage. BMIPP imaging can detect metabolic injury in viable myocardium, and the perfusion-metabolism mismatch contributes to determining the extent of metabolic dysfunctional but viable myocardium in an ischemic zone.

Myocardial viability and LV functional outcome. Considering the entire study population, the amount of perfusion-metabolism mismatch was predictive of EF improvement at follow-up. It is noteworthy that the extent of perfusion-metabolism mismatch was the best predictor of functional improvement after revascularization. The threshold of seven segments of perfusion-metabolism mismatch was associated with the best improvement in EF. This finding suggests that not only the presence but also the extent of viable myocardium is critical in determining LV functional outcome after successful revascularization in patients with severe LV function and CAD. In addition, these results are in agreement with the observations suggesting that the improvement in LV function after revascularization correlates with the extent of the area of flow-metabolism mismatch.[7,8,15–18]

Quantification of the amount perfusion-metabolism mismatch and survival. Recent studies have repeatedly suggested that patients with CAD and LV dysfunction with nonrevascularized viable myocardium have a propensity to suffer later cardiac events and that revascularization improves their survival.[19–23] The main result of the present study was that patients with a large amount of perfusion-metabolism mismatch exhibited significantly fewer cardiac events and better cardiac-event survival than those with a small amount or no

perfusion-metabolism mismatch. To the best of our knowledge, there are no reports about long prognosis on the effect of the amount of perfusion-metabolism mismatch assessed by Tl-201 and BMIPP SPECT. Marinho et al.[24] and Vanoverschelde et al.[25] found that in most cases chronic impairment of LV function is not associated with a reduced baseline myocardial blood flow, suggesting that LV dysfunction may be caused by repeated episodes of ischemia. Moreover, the close correlation of the extent of perfusion-metabolism mismatch with subsequent functional improvement suggests that viable, but metabolically impaired, myocardium is hibernated. The metabolic impairment in viable myocardium may be elucidated by the initial manifestation of reduced aerobic beta-oxidation of fatty acid and high-energy phosphate depletion due to ischemia. Therefore, these scintigraphic approaches may be particularly useful in the prognostic classification of revascularized patients with CAD and severely depressed LV function.

Study limitations. The limitations of the present study cannot be ignored when interpreting its results. First, the number of patients in our study was relatively small. In addition, our study is biased in that it is not representative of the entire pool of patients with low LVEF referred for PTCA and CABG because of those with poor LV function and poor run-off if the coronary artery might not have been referred for revascularization. In addition, our study included a significant number of patients with congestive heart failure, who may be at increased risk for both short- and long-term complications after revascularization. Although it may be difficult to apply from our findings to all patients with poor ventricular function undergoing the revascularization procedure, the present study does apply to a significant proportion of such patients.

CONCLUSION

Our data suggest that in patients with CAD and severe LV dysfunction referred for coronary revascularization, the identification, and especially the quantification of perfusion-metabolism mismatch is of great clinical importance. The presence of a large amount of perfusion-metabolism mismatch as evaluated by Tl-201 and BMIPP SPECT identifies patients with the best prognosis.

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REFERENCES

1. Kiat H, Berman DS, Maddahi J, et al. Late reversibility of tomographic myocardial thallium-201 defects: an accurate marker of myocardial viability. *J Am Coll Cardiol* 1989; 12: 1456–1463.
2. Dilsizian V, Rocco TP, Freedman NM, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. *N Engl J Med* 1990; 323: 141–146.
3. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution Tl-201 imaging in the detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. *Circulation* 1993; 87: 1630–1641.
4. Charney R, Schwinger ME, Chun J, et al. Dobutamine echocardiography and rest-redistribution thallium-201 scintigraphy predicts recovery of hibernating myocardium after coronary revascularization. *Am Heart J* 1994; 128: 864–869.
5. Pace L, Perrone-Filardi P, Mainenti PP, et al. Effects of myocardial revascularization on regional thallium-201 uptake and systolic function in regions with reverse redistribution on tomographic thallium-201 at rest patients with chronic coronary artery disease. *J Nucl Cardiol* 1998; 5: 153–160.
6. Knapp FF Jr, Franken PR, Kropp J. Cardiac SPECT with iodine-123-labeled fatty acids: evaluation of myocardial viability with BMIPP. *J Nucl Med* 1995; 36: 1022–1030.
7. Nohara R, Otsuka K, Ogino M, et al. Evaluation of myocardial viability with iodine-123-BMIPP in a canine model. *J Nucl Med* 1996; 37: 1403–1407.
8. Tamaki N, Tadamura E, Kawamoto M, et al. Decreased uptake of iodinated branched fatty acid analog indicates metabolic alterations in ischemic myocardium. *J Nucl Med* 1995; 36: 1974–1980.
9. Fukuzawa S, Inagaki M, Morooka S, Inoue T, Sugioka J, Ozawa S. An effective tool to detect lesions causing unstable angina with multivessel disease: iodine-123 beta-methyl-p-iodophenyl pentadecanoic acid single photon emission computed tomography. *J Cardiol* 1996; 28: 191–198.
10. Dilsizian V, Perrone-Filardi P, Arrighi JA, et al. Concordance and disconcordance between stress-redistribution-reinjection and rest-redistribution thallium imaging for assessing viable myocardium: comparison with metabolic activity by positron emission tomography. *Circulation* 1993; 88: 941–952.
11. Tamaki N, Tadamura E, Kudoh T, et al. Prognostic value of iodine-123 labelled BMIPP fatty acid analogue imaging in patients with myocardial infarction. *Eur J Nucl Med* 1996; 23: 272–279.
12. Taki J, Nakajima K, Matsunari I, et al. Assessment of improvement of myocardial fatty acid uptake and function after revascularization using iodine-123-BMIPP. *J Nucl Med* 1998; 39: 1492–1499.
13. Hammbye AS, Dobbeleir AA, Vervaet AM, Van den Heuvel PA, Franken PR. BMIPP imaging to improve the value of sestamibi scintigraphy for predicting functional outcome in severe chronic ischemic left ventricular dysfunction. *J Nucl Med* 1999; 40: 1468–1476.
14. Fujibayashi Y, Yonekura Y, Takemura Y, et al. Myocardial accumulation of iodinated beta-methyl branched fatty acid

analog, iodine-125-15-(p-iodophenyl)-3-(R,S) methylpentadecanoic acid (BMIPP), in relation to ATP concentration. *J Nucl Med* 1990; 31: 1818–1822.
15. Nishimura T, Uehara T, Strauss HW, et al. Radionuclide assessment of stunned myocardium by alterations in perfusion, metabolic and wall motion. *Jpn Circ J* 1991; 55: 913–918.
16. Tamaki N, Kawamoto M, Yonekura Y, et al. Regional metabolic abnormality in relation to perfusion and wall motion in patients with myocardial infarction: assessment with emission tomography using an iodinated branched fatty acid analog. *J Nucl Med* 1992; 33: 649–657.
17. Matsunari I, Sago M, Taki J, et al. Kinetics of iodine-123-BMIPP in patients with prior myocardial infarction: assessment with dynamic rest and stress images compared with stress thallium-201 SPECT. *J Nucl Med* 1994; 35: 1758–1765.
18. Kawamoto M, Tamaki N, Yonekura Y, Tadamura E, Fujibayashi Y, Magata Y, et al. Combined study with I-123 fatty acid and thallium-201 to assess ischemic myocardium: comparison with thallium redistribution and glucose metabolism. *Ann Nucl Med* 1994; 8: 47–54.
19. Lee KS, Marwick TH, Cook SA, et al. Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction. Relative efficacy of medical therapy and revascularization. *Circulation* 1994; 90: 2687–2694.
20. Williams MJ, Odabashian J, Lauer MS, Thomas JD, Marwick TH. Prognostic value of dobutamine echocardiography in patients with left ventricular dysfunction. *J Am Coll Cardiol* 1996; 27: 132–139.
21. Eitzman D, Al-Aouar Z, Kanter HL, et al. Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. *J Am Coll Cardiol* 1992; 20: 559–565.
22. Di Carli MF, Davidson M, Little R, et al. Value of metabolic imaging with positron emission tomography for evaluating prognosis in patients with coronary artery disease and left ventricular dysfunction. *Am J Cardiol* 1994; 73: 527–533.
23. Gioia G, Powers J, Heo J, Iskandrian AS, Russell J, Cassel D. Prognostic value of rest-redistribution tomographic thallium-201 imaging in ischemic cardiomyopathy. *Am J Cardiol* 1995; 75: 759–762.
24. Marinho NVS, Keogh BE, Costa DC, Lammerstma AA, Ell PJ, Camici PG. Pathophysiology of chronic left ventricular dysfunction. New insights from the measurement of absolute myocardial blood flow and glucose utilization. *Circulation* 1996; 93: 737–744.
25. Vanoverschelde J-LJ, Wijns W, Depre C, et al. Mechanisms of chronic regional postischemic dysfunction in humans: new insights from the study of noninfarcted collateral-dependent myocardium. *Circulation* 1993; 87: 1513–1523.