Prediction of Functional Outcome after Myocardial Infarction Using BMIPP and Sestamibi Scintigraphy

Philippe R. Franken, Paul Dendale, Frank De Geeter, Doris Demoor, Axel Bossuyt and Pierre Block
Departments of Nuclear Medicine and Cardiology, University Hospital, Free University of Brussels, Brussels, Belgium

We determined the predictive value of combined beta-methyl iodophenyl pentadecanoic acid (BMIPP) and sestamibi scintigraphy for the functional outcome after myocardial infarction and compared the value of this approach with dobutamine echocardiography. **Methods:** Rest BMIPP, rest sestamibi and low-dose dobutamine echocardiographic studies were obtained in 18 patients 4 to 10 days after infarction (mean 6.7 ± 2.0 days). Six months later, a rest echocardiographic study was performed to assess functional outcome. **Results:** Wall motion improved in 27/33 segments (82%) which showed mismatching but not in 19/21 segments (90%) with matched defects ($p < 0.001$). The accuracy of combined BMIPP and sestamibi SPECT in predicting segmental functional outcome was higher (85%) than that of sestamibi uptake alone (77%). Wall motion improved in 16/20 segments (80%) showing contractile reserve and not in 21/34 segments (63%) with the negative dobutamine test, giving an accuracy of 69% for dobutamine echocardiography. Combination of the two techniques resulted in higher positive (94%) and negative predictive values (94%). **Conclusion:** Mismatching of BMIPP and sestamibi uptake is predictive for long-term functional recovery after acute myocardial infarction. In contrast, segments with matched defects contain only scar tissue. Combined BMIPP and sestamibi scintigraphy offers increased accuracy compared to dobutamine echocardiography.

Key Words: myocardial viability; fatty acids; technetium-99m-sestamibi

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Early after acute myocardial infarction, it may be difficult to differentiate reversible from fixed left ventricular dysfunction because the return of contractility in tissue salvaged by reperfusion may be delayed for several weeks. The same myocardial region may contain an admixture of variable amounts of subendocardial scar and subepicardial viable myocardium in which stunning and hibernation can occur simultaneously (*1*). Since prognosis correlates with ventricular function, early and accurate identification of reversible dysfunction that can benefit from revascularization is critical for optimal patient management. Low-dose dobutamine echocardiography (*2*) and assessment of myocardial perfusion, cell membrane integrity and metabolic activity using cardiac nuclear imaging techniques have been proposed to identify reversible dysfunctional myocardium (*3*).

Radiolabeled fatty acids have potential interest as cardiac imaging agents for the identification of reversible dysfunction in subacute myocardial infarction. Beta-methyl iodophenyl pentadecanoic acid (BMIPP) is a structurally modified fatty acid that has prolonged retention time in the myocardium. It allows noninvasive metabolic studies with SPECT systems (*4*). Discrepancies between BMIPP uptake and perfusion have been reported after myocardial infarction. Regions showing more reduced BMIPP uptake than ^{201}Tl or sestamibi uptake at rest were associated with successful reperfusion (*5–7*), redistribution on stress ^{201}Tl studies (*8*), increased glucose uptake (*9*) and with low-dose dobutamine responsive wall motion (*10*).

The aims of this work were to determine the predictive value of combined BMIPP and sestamibi imaging for the long-term functional outcome after acute myocardial infarction and to compare the value of this approach with that of low-dose dobutamine echocardiography.

MATERIALS AND METHODS

Patients

The patient population consisted of 16 men and 2 women aged 37–73 yr (mean 53 yr). All 18 patients presented with persistent regional wall motion abnormalities 4–10 days after acute myocardial infarction. The diagnosis of infarction was established on the basis of clinical, enzymatic and electrocardiographic criteria. Wall motion abnormalities involved the anterior wall in nine patients and the infero-lateral wall in the nine other patients. ECG showed Q-waves in all but one patient. No patient had previous myocardial infarction, coronary bypass surgery, valvular or congenital heart disease, arterial hypertension or nonischemic cardiomyopathy.

Fourteen patients who were admitted to the CCU within 6 hr after the onset of chest pain received thrombolytic therapy consisting of streptokinase 1.5×10^6 U in 30 min followed by heparin 3×10^4 U/day. In addition, PTCA was performed in three patients immediately after thrombolysis because of recurrence of symptoms. All patients were clinically and hemodynamically stable at the time of the study.

Study Design

Patients were investigated 4–10 days after the acute event. BMIPP and sestamibi studies were obtained on two separate days. Both tracers were injected at rest. Baseline and low-dose dobutamine echocardiograms were obtained within 24 hr of the scintigraphic studies. Patients were investigated after giving informed consent. The study protocol was approved by the Commission of Medical Ethics of the Free University Brussels (VUB).

All patients underwent coronary arteriography before hospital discharge. They received the appropriate treatment according to standard indications, but the results of the BMIPP study were not taken into account in the decision for revascularization. Four patients underwent PTCA and six patients had coronary artery bypass surgery 2–6 wk after the acute event.

Six months after infarction, all patients underwent a second echocardiographic study at rest to assess functional outcome.

Metabolic and Perfusion Imaging

BMIPP was prepared as previously described (*10*) using 15-(4-iodo-phenyl)-3-pentadecanoic acid and the Cu(I) assisted isotopic-exchange reaction developed by Mertens et al. (*11*). Iodine-123-BMIPP (111–148 MBq) was injected intravenously during resting conditions after at least 6 hr fasting. Lugol's solution was given to the patients before injection to block thyroidal uptake of free iodine. Tomographic imaging was started 20 min after injection using a three-head gamma camera equipped with medium-energy collimators. Ninety-six projections (3 × 32 projections, 128 × 128

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For correspondence or reprints contact: Philippe R. Franken, MD, PhD, Department of Nuclear Medicine, University Hospital, Laarbeeklaan 101, B-1090, Brussels, Belgium.

pixels matrix, 60 sec/projection) were obtained over 360° in the 159-keV photopeak with a 15% window.

The sestamibi study was obtained with 925 MBq ^{99m}Tc-2-methoxy isobutyl isonitrile (sestamibi) injected intravenously at rest the day after the BMIPP study. Tomographic imaging was started 60 min after injection, exactly as for the BMIPP study but in the 140-keV photopeak and with a 30-sec acquisition time per projection to obtain approximately the same count density as in the BMIPP study.

The left ventricular myocardium was divided into nine segments: apex, midventricular septal, anterior, lateral and inferior segments, and basal septal, anterior, lateral and inferior segments. For each segment, BMIPP and sestamibi uptake were graded semiquantitatively using a color-coded scale by two experienced observers who had no knowledge of the clinical and echocardiographic data. Scores were attributed on a four-point basis system by taking into account both the extent and the severity of the defects: normal uptake (score 0: activity 65% or more of the maximal activity); mildly reduced uptake (score 1: activity between 50 and 65% of the maximum); moderately reduced uptake (score 2: activity between 35 and 50%) or severely reduced uptake (score 3: less than 35%). When the BMIPP and sestamibi scores were different, the segment was considered to show mismatching. When the scores were the same, the segment was considered to show matched BMIPP and sestamibi uptake. A 10% difference between sestamibi and BMIPP uptake values was required to consider mismatching.

Echocardiography and Dobutamine Stimulation

Standard two-dimensional echocardiograms were obtained with a commercially available system equipped with a 2.5-MHz transducer. Patients were studied in a left lateral decubitus. The long-axis and the short-axis left parasternal views, as well as the apical four- and two-chamber views were obtained in all patients. ECG and blood pressure were continuously monitored during dobutamine stimulation. Dobutamine was given intravenously at rate of 5 and 10 μg/kg per min for 5 min each. Beta-blockers were stopped at least 24 hr before the test. All studies were recorded on videotape and digitized on a personal computer for subsequent analysis. All patients were in sinus rhythm. No patient had major arrhythmia or bundle branch block at the time of the study.

Systolic wall thickening and inward wall motion were evaluated qualitatively by two experienced observers who had no knowledge of the scintigraphic results. The left ventricle was divided into nine segments corresponding to those described for the scintigraphic studies. Each segment was graded on a four-point scoring system as normal (score 0), hypokinetic (score 1), akinetic (score 2) or dyskinetic (score 3). Improved segmental wall motion during dobutamine infusion or at follow-up was defined as a systolic wall thickening and inward wall motion in areas of akinesis or dyskinesis at baseline, or a normalization of thickening and wall motion in areas of hypokinesis at baseline. The agreement rate between the two observers was 91%. Consensus was achieved after reviewing the recordings.

Coronary Arteriography

The degree of coronary artery stenosis was determined quantitatively by using calipers on selective coronary arteriograms in multiple views by two observers not involved in the study. The anterior and septal segments were considered to be in the left anterior descending coronary artery distribution (LAD), the lateral segments in the left circumflex coronary artery distribution (LCx) and the inferior segments in the right coronary artery distribution (RCA). The right coronary territory was reassigned to the left circumflex when the latter was dominant. The attribution of apical abnormalities depended on coexistent abnormalities in adjacent regions.

Statistical Analysis

Values are expressed as mean ± standard deviation. Groups were compared by the Mann-Whitney U-test. Fisher's exact test was used to test the association between segmental recovery, and BMIPP and sestamibi uptake. Probability values less than 0.05 were considered significant.

RESULTS

Wall Motion, Sestamibi and BMIPP Uptake Early after Myocardial Infarction

Early after myocardial infarction, wall motion was abnormal in 54 segments, of which 18 were hypokinetic and 36 akinetic. The number of abnormal segments averaged 3.0 ± 1.1 per patient (range 1 to 5).

Of the 54 segments showing wall motion abnormalities, sestamibi uptake was normal in 9 segments, mildly reduced in 16 segments (score 1), moderately reduced in 18 segments (score 2) and severely reduced in 11 segments (score 3). BMIPP uptake was similar to that of sestamibi in 21 segments (matched defects) and more reduced than sestamibi uptake in 33 segments (mismatched defects). A relative excess of BMIPP was not observed.

Mismatching was observed in at least one myocardial segment in 12 patients. Six patients showed only matched defects. In all patients, sestamibi and BMIPP abnormalities were observed in the vascular territory of the culprit coronary artery.

A typical example illustrating BMIPP and sestamibi distribution is given in Figure 1.

Functional Outcome at Six Months

Six months after myocardial infarction, regional wall motion improved in 29 of the 54 segments with early dysfunction.

Left ventricular function improved in nine patients (Group 1) and was unchanged in the nine other patients (Group 2). Regional wall motion did not deteriorate in any patient. Table 1 summarizes the baseline clinical data and the findings on coronary arteriography before hospital discharge in the two groups of patients. No significant differences were found with respect to clinical presentation, culprit coronary artery and the occurrence of early or late revascularization procedures.

Predictive Value of BMIPP and Sestamibi Defects

A significant association ($p < 0.001$) was found between the relative uptake of BMIPP and sestamibi and the functional outcome 6 mo later (Table 2). Wall motion improved in 27 of the 33 segments showing mismatching (positive predictive value = 82%) but in only 2 of the 21 segments with matched defects (negative predictive value = 90%), resulting in a sensitivity of 93% and a specificity of 76%. The overall accuracy of the combination of BMIPP and sestamibi uptake to predict segmental functional outcome was 85%.

Figure 2 compares the specific degree of functional impairment as a function of the BMIPP and sestamibi relationship for each of the involved segments at baseline and after 6 mo.

Table 3 gives the relationship between BMIPP and sestamibi uptake scores in the 54 segments with abnormal wall motion early after infarction and their functional outcome 6 mo later. The probability of wall motion improvement was higher when sestamibi uptake was better. In each sestamibi uptake category, however, the segments that improved had, on average, a relatively lower BMIPP score than segments with no improvement.

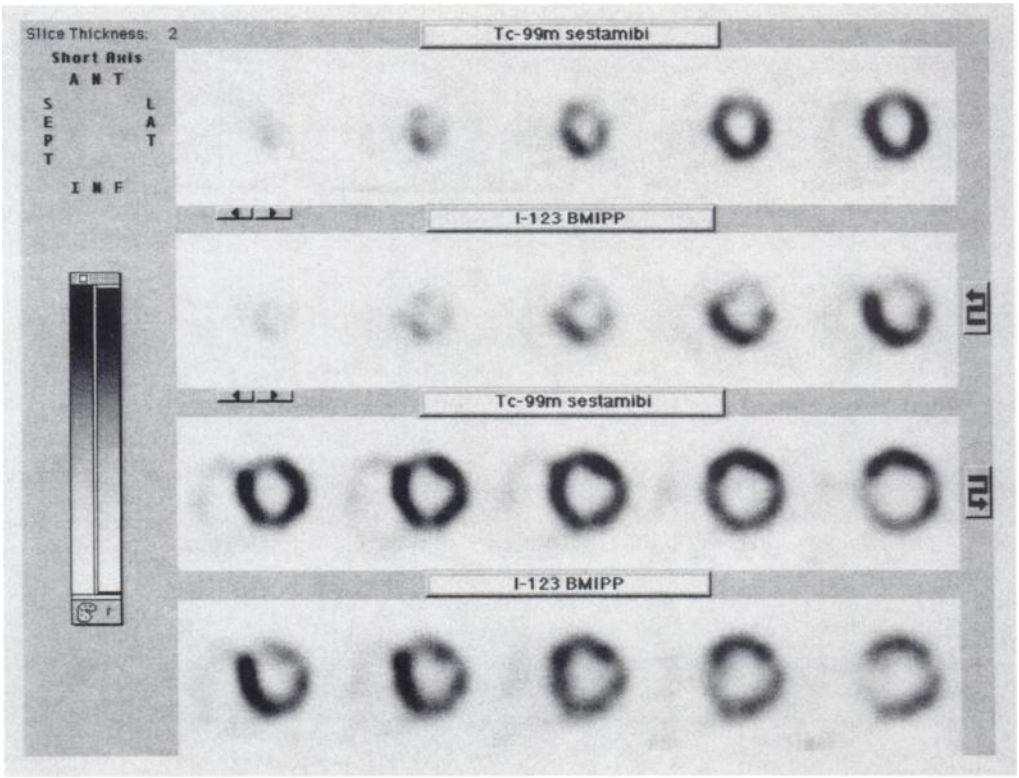

FIGURE 1. Sestamibi (first and third rows) and BMIPP (second and fourth rows) left ventricular short-axis slices obtained 7–8 days after anterior myocardial infarction. There is mild-to-moderate reduction of sestamibi uptake in the apical and mid-ventricular anterior segments. BMIPP study demonstrates similar defect intensity in the apex (matching) but more severe defects in the anterior and lateral walls (mismatching).

Predictive Value of Dobutamine Echocardiography

Sixteen of the 20 segments (80%) showing contractile reserve early after myocardial infarction improved at 6 mo. Wall motion also improved in 13 of the 34 segments (38%) with a negative response to low-dose dobutamine. There was no relationship between dobutamine response and the severity of residual coronary artery stenosis. The sensitivity, specificity and accuracy of dobutamine echocardiography for segmental recovery were 55%, 84% and 69%, respectively.

Predictive Value of Combining Scintigraphy with Dobutamine Echocardiography

Figure 3 gives the positive and negative predictive values for segmental functional outcome of dobutamine-responsive wall motion, rest sestamibi uptake alone (uptake ≥50%, i.e., scores 0 or 1 versus uptake <50%, i.e., scores 2 or 3) and relative BMIPP uptake (mismatched versus matched defects). The three tests had similar positive predictive values: 80%, 84% and 82%, respectively. On the other hand, the negative predictive value of combined BMIPP and sestamibi scintigraphy was substantially higher than that of the other tests: a matched BMIPP and sestamibi defect had a 90% predictive value for the absence of functional improvement at 6 mo. Values for sestamibi uptake alone and for dobutamine echocardiography were 72% and 62%, respectively.

The combination of a positive dobutamine response and sestamibi uptake ≥50% (13 segments, 24%) had a 85% positive predictive value, while the absence of dobutamine response associated with sestamibi uptake <50% (23 segments, 43%) had a 83% negative predictive value.

Sixteen segments (30%) showed both a mismatched sestamibi and BMIPP pattern, as well as contractile reserve. Wall motion improved in 15 of these 16 segments (positive predictive value = 94%). Sixteen other segments (30%) showed both a matched defect and no contractile reserve. Wall motion did not change at follow-up in 15 of these 16 segments (negative predictive value = 94%).

DISCUSSION

Early after myocardial infarction, two patterns of distribution of BMIPP and sestamibi were identified in myocardial segments showing persistent wall motion abnormalities: more reduced BMIPP uptake than sestamibi uptake (mismatching) and matched BMIPP and sestamibi defects. Only one dysfunctional segment showed normal BMIPP uptake. Wall motion in most segments with mismatched defects normalized or improved at 6 mo follow-up. In contrast, wall motion usually did not recover in segments showing matched defects.

BMIPP Uptake and Retention Mechanisms

BMIPP is a branched fatty acid analog which follows the initial biochemical pathways of uptake and transport of the native fatty acids within the myocardial cells (*4,12*). BMIPP follows the initial activation of fatty acids to acyl-CoA. BMIPP accumulation is positively correlated with the intracellular concentration of adenosine triphosphate, which is required in this activation process (*13*). BMIPP cannot be catabolized through beta-oxidation because of the methyl group but is esterified to triglycerides and stored into the cytosolic lipid pool (*4*). Therefore, BMIPP accumulation reflects mostly the initial, energy-dependent metabolic sequestration and retention of fatty acid. Excellent images are obtained because of long tracer retention, as compared to the straight chain fatty acids which are rapidly metabolized and washed out from the myocardium.

Discrepancies between BMIPP and Flow Tracer Uptake

Although BMIPP is primarily distributed in the myocardium according to blood flow, discrepancies between BMIPP uptake and flow tracers have been observed in hypertrophic cardiomyopathy (*14,15*) and in patients with coronary artery disease (*5*). In patients with recent myocardial infarction, less BMIPP uptake than ^{201}Tl uptake (*6*) or sestamibi uptake (*7*) were found more frequently in areas subtended by recanalized, as opposed to occluded, coronary arteries following thrombolysis. In a comparative study with ^{18}F-labeled fluorodeoxyglucose (FDG) uptake as a marker of exogenous glucose utilization, Tamaki et

TABLE 1
Clinical and Angiographic Data in Patients with (Group 1) and without (Group 2) Functional Improvement Six Months after Infarction

	Group 1 (n = 9)	Group 2 (n = 9)
Age (yr)	53.6 ± 10.1	52.8 ± 17.3
Gender (M/F)	8/1	8/1
AMI localization (Anterior/Inferolateral)	5/4	4/5
Left ventricular ejection fraction (Day 1)	42.4 ± 15.6	42.1 ± 14.3
Culprit coronary artery		
LAD	4	4
LCx	3	1
RCA	2	4
%Diameter stenosis		
<70%	3	4
70–95	4	3
>95%	2	2
Other diseased vessels (≥70% stenosis)	5	5
Early thrombolysis/PTCA	8	6
Late revascularization (PTCA, CABG)	6	4

AMI = acute myocardial infarction; LAD = left anterior descending coronary artery; LCx = left circumflex artery; RCA = right coronary artery.

al. (*9*) found that the reduced uptake of BMIPP correlated with an increase in FDG uptake, indicating that BMIPP could be used to identify ischemic but viable myocardium on the basis of alterations of myocardial energy metabolism. In a study correlating BMIPP uptake with wall motion and contractile reserve in patients with subacute myocardial infarction (*10*), most segments with more reduced BMIPP uptake than sestamibi uptake showed evidence of residual viability, i.e., wall motion was either normal at rest or demonstrated inotropic reserve during low-dose dobutamine stimulation. In contrast, segments with matched defects showed abnormal wall motion and did not demonstrate inotropic reserve.

Predictive Value of BMIPP and Sestamibi Uptake

A recent study by Udelson et al. (*16*) found 1-hr sestamibi scintigraphy to be equivalently predictive of viability as 4-hr redistribution thallium scintigraphy. From present study, however, as well as from the work of Altehoefer et al. (*17*), it became evident that prediction of viability is most certain in segments with either very high (>80% of peak activity) or very low (<40% of peak) flow tracer activity. Activities between these limits have intermediate probabilities for viability, and in these, additional information from metabolic studies could be helpful to establish viability with more certainty.

Our results confirm the ability of BMIPP scintigraphy to provide such information. In segments with mild sestamibi defects (score 1), matched BMIPP activity could identify the necrotic segments. In segments with moderate sestamibi defects (score 2), necrosis was more probable with matched BMIPP activity.

TABLE 2
Relationship between BMIPP and Sestamibi Scores and Functional Outcome Six Months after Myocardial Infarction

	BMIPP and sestamibi uptake		
	Mismatched defects	Matched defects	No. of defects
Improved wall motion	27	2	29
No change	6	19	25
Total	33	21	54

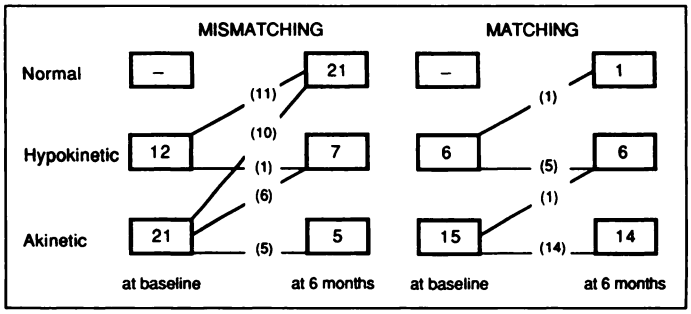

FIGURE 2. Comparison of specific degree of functional impairment as a function of BMIPP and sestamibi relationship for each of the involved segments at baseline and after 6 mo.

Overall, we found a significant association between the relative uptake of BMIPP and sestamibi early after acute myocardial infarction and the functional outcome 6 mo later. Most segments (82%) with more reduced BMIPP uptake than sestamibi uptake showed improved wall motion. In contrast, 90% of the segments with matched defects did not recover. The overall accuracy of combined BMIPP and sestamibi tomoscintigraphy in predicting segmental functional outcome was 85%. These results are similar to those obtained with metabolic studies using FDG-PET to differentiate viable from nonviable myocardium. In a recent review article (*18*), a pattern of preserved accumulation of FDG (a blood flow to metabolism mismatch) was associated with recovery of contractile function in 72%–95% of segments. In segments with concordantly diminished flow and FDG accumulation, 75%–100% did not improve after revascularization.

Low-Dose Dobutamine Echocardiography

Low-dose dobutamine stimulation to enhance regional systolic wall thickening during two-dimensional echocardiography is being used increasingly in the clinical setting to detect the presence of residual viable myocardium (*2,19,20*). In the present series, 80% of the segments with inotropic reserve had improved wall motion 6 mo later. Wall motion also improved in 38% of the segments with a negative response to dobutamine, resulting in a high positive but low negative predictive value.

The low predictive value observed in this and other studies (*3*) could be explained by difficulties related to the dobutamine dose. Although the study of Smart et al. (*2*) showed an optimal dose of 4 μg/kg per min, recent animal studies have indicated that the dose needed to determine the amount of viable myocardium depends on the transmural extent of infarction; maximal wall thickening was noted at a dobutamine dose of 15 μg/kg per min (*21*). The low dose of dobutamine used currently

TABLE 3
Relationship between Functional Improvement and BMIPP and Sestamibi Scores in Segments with Abnormal Wall Motion

		Sestamibi uptake score				
		0	1	2	3	No.
BMIPP uptake score	0	**0/1**	—		—	**0/1**
	1	**6/6**	**0/2**	—	—	**6/8**
	2	**1/2**	**14/14**	**2/7**	—	**17/23**
	3	—	—	**6/11**	**0/11**	**6/22**
	Total	**7/9**	**14/16**	**8/18**	**0/11**	**29/54**

Numbers in bold are those segments that improved after 6 mo.

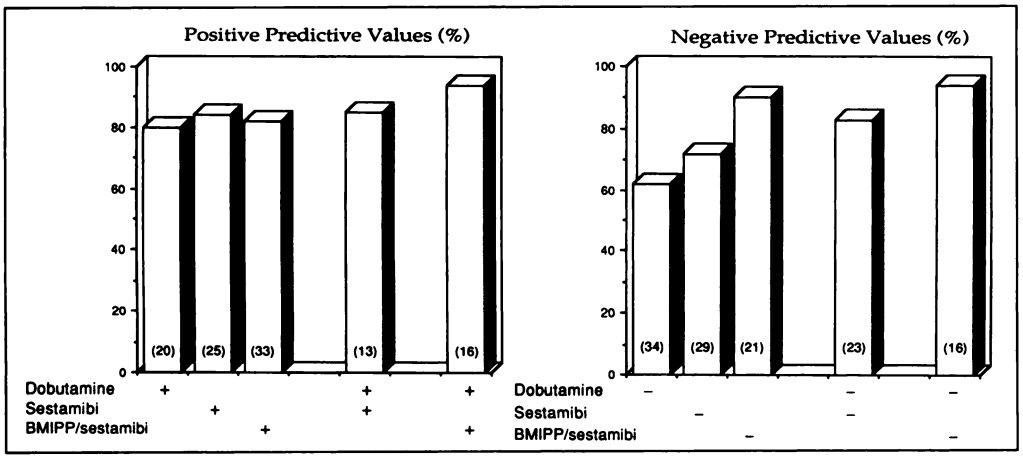

FIGURE 3. Predictive values of low-dose dobutamine echocardiography, sestamibi uptake (≥50% of peak activity) and BMIPP mismatching to predict functional improvement after myocardial infarction. Number of segments in each group is shown at the bottom of each bar.

in clinical practice may therefore significantly underestimate the extent of viable myocardium. On the other hand, in patients with critically stenosed coronary arteries, higher doses of dobutamine may produce myocardial ischemia and persistent regional dysfunction because of the increased demand in the setting of exhausted coronary flow reserve (*22*). An a priori knowledge of the residual coronary artery stenosis might therefore be necessary to determine the optimal regimen of dobutamine stimulation.

Study Limitations

In this study, images were analyzed semiquantitatively. There are inherent limitations in comparing two-dimensional echocardiography with three-dimensional tomoscintigraphic data. To minimize these errors, the left ventricular myocardium was divided into nine large segments. In large segments, a semiquantitative visual score may more accurately reflect the real situation than a quantitative score based on average pixel content. The method has been proven to be sufficiently reliable and reproducible (*10*) to classify the segments into three clinically useful categories: normal BMIPP and sestamibi uptake, mismatched defects and matched defects.

CONCLUSION

Mismatching of BMIPP and sestamibi uptake at rest is indicative of residual viability and is predictive for long-term functional recovery in dysfunctional segments after acute myocardial infarction. In contrast, segments with matched defects contain only scar tissue. The additional information provided by BMIPP and sestamibi uptake substantially increases the accuracy of low-dose dobutamine echocardiography and sestamibi uptake alone to predict functional outcome after acute myocardial infarction.

REFERENCES

1. Bolli R. Myocardial stunning in man. *Circulation* 1992;86:1671–1691.
2. Smart SC, Sawada S, Ryan T, et al. Low-dose dobutamine echocardiography detects reversible dysfunction after thrombolytic therapy of acute myocardial infarction. *Circulation* 1993;88:405–415.
3. Dilsizian V, Bonow RO. Current diagnostic techniques of assessing myocardial viability in patients with hibernating and stunned myocardium. *Circulation* 1993;87: 1–20.
4. Knapp FF Jr, Ambrose KR, Goodman MM. New radioiodinated methyl-branched fatty acid for cardiac studies. *Eur J Nucl Med* 1986;12:S39–S44.
5. Saito S, Yasuda T, Gold HK, et al. Differentiation of regional perfusion and fatty acid uptake in zones of myocardial injury. *Nucl Med Commun* 1991;12:663–675.
6. 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;33:659–667.
7. De Geeter F, Franken PR, Knapp FF Jr, Bossuyt A. Relationship between blood flow and fatty acid metabolism in subacute myocardial infarction: a study by means of ^{99m}Tc-MIBI and ^{123}I-beta-methyl iodophenyl pentadecanoic acid. *Eur J Nucl Med* 1994;21:283–291.
8. Kawamoto M, Tamaki N, Yonekura Y, et al. Combined studies with ^{123}I fatty acid and ^{201}Tl to assess ischemic myocardium: comparison with thallium redistribution and glucose metabolism. *Ann Nucl Med* 1994;8:47–54.
9. Tamaki N, Kawamoto M, Yonekura Y, et al. Assessment of fatty acid metabolism using ^{123}I-branched fatty acid: comparison with positron emission tomography. *Ann Nucl Med* 1993;7(suppl 2):41–47.
10. Franken PR, De Geeter F, Dendale P, Demoor D, Block P, Bossuyt A. Abnormal free fatty acid uptake in subacute myocardial infarction after coronary thrombolysis: correlation with wall motion and inotropic reserve. *J Nucl Med* 1994;35:1758–1765.
11. Mertens J, Eersels J, Vanryckeghem W. New high yield Cu(I) assisted ^{123}I radioiodination of 15(p-I-phenyl)-9-methyl pentadecanoic acid, a potential myocardial tracer. *Eur J Nucl Med* 1987;13:159–160.
12. Ambrose KR, Owen BA, Goodman MM, Knapp FF Jr. Evaluation of the metabolism in rat hearts of two new radioiodinated 3-methyl-branched fatty acid myocardial imaging agents. *Eur J Nucl Med* 1987;12:486–491.
13. Fujibayashi Y, Yonekura Y, Takemura Y, et al. Myocardial accumulation of iodinated beta-methyl-branched fatty acid analog, iodine-125-15-(p-iodo-phenyl)-3-(R,S) methylpentadecanoic acid (BMIPP), in relation to ATP concentration. *J Nucl Med* 1990;31:1818–1822.
14. Takeishi Y, Chiba J, Abe S, Tonooka I, Komatani A, Tomoike H. Heterogeneous myocardial distribution of iodine-123-15-(p-iodophenyl)-3-R,S-methyl-pentadecanoic acid (BMIPP) in patients with hypertrophic cardiomyopathy. *Eur J Nucl Med* 1992;19:775–782.
15. Kurata C, Tawarahara K, Taguchi T, et al. Myocardial emission computed tomography with iodine-123-labeled beta methyl branched fatty acid in patients with hypertrophic cardiomyopathy. *J Nucl Med* 1992;33:6–13.
16. Udelson JE, Coleman PS, Metherall J, et al. Predicting recovery of severe regional ventricular dysfunction: comparison of resting scintigraphy with ^{201}Tl and ^{99m}Tc-sestamibi. *Circulation* 1994;89:2552–2561.
17. Altehoefer C, vom Dahl J, Biedermann M, et al. Significance of defect severity in technetium-99m-MIBI SPECT at rest to assess myocardial viability: comparison with fluorine-18-FDG PET. *J Nucl Med* 1994;35:569–574.
18. Maddahi J, Schelbert H, Brunken R, Di Carli M. Role of thallium-201 and PET imaging in evaluation of myocardial viability and management of patients with coronary artery disease and left ventricular dysfunction. *J Nucl Med* 1994;35:707–715.
19. Pierard LA, De Landsheere CM, Berthe C, Rigo P, Kulbertus HE. Identification of viable myocardium by echocardiography during dobutamine infusion in patients with myocardial infarction after thrombolytic therapy: comparison with positron emission tomography. *J Am Coll Cardiol* 1990;15:1021–1031.
20. Barilla F, Gheorghiade M, Alam M, Khaja F, Goldstein S. Low-dose dobutamine in patients with acute myocardial infarction identifies viable but not contractile myocardium and predicts the magnitude of improvement in wall motion abnormalities in response to coronary revascularization. *Am Heart J* 1991;122:1522–1531.
21. Sklenar J, Ismail S, Villaneuva FS, Goodman NC, Glasheen WP, Kaul S. Dobutamine echocardiography for determining the extent of myocardial salvage after reperfusion: an experimental evaluation. *Circulation* 1994;90:1502–1512.
22. McGillem MJ, DeBoer SF, Friedman HZ, Mancini GBJ. The effects of dobutamine on regional function in the presence of rigid coronary stenoses and subcritical impairments of reactive hyperemia. *Am Heart J* 1988;115:970–977.